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Official Transactions

Edited by

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Secretary-General

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Biomed

FOURTH DAY, THURSDAY, SEPTEMBER 12TH

AFTERNOON SESSION—3 P.M.

PROF. ROBERT CAMPANA, of Rome, DR. JAMES NEVINS HYDE, of Chicago, and DR. SAMUEL SHERWELL, of Brooklyn, Vice-Presidents, in the Chair.

THEME II.—TROPICAL DISEASES OF THE SKIN

PRESENTED BY SURGEON-GENERAL P. M. RIXEY, DR. H. RADCLIFFE-CROCKER, DR. WILLIAM DUBREUILH, AND DR. CH. WARDELL STILES

THE RELATION OF THE NAVY TO THE STUDY OF TROPICAL DISEASES

BY SURGEON-GENERAL P. M. RIXEY, U. S. NAVY

When I first received the highly appreciated invitation of the Organization Committee of the Sixth International Dermatological Congress to make a short address upon the relation of the Navy to the study of tropical diseases, it naturally appeared fitting that I should first take up the consideration of that branch of tropical medicine dealing with affections of the skin. The importance of this section of the diseases of the tropics is, however, so paramount in the Navy that I shall only be able to briefly refer to the lines of investigation which have been and are being pursued by the officers of the Medical Corps of the Navy in relation to cutaneous medicine.

That this statement is based upon fact and not expressed merely for the purpose of harmonizing with the object of this Congress is best shown by the statement that, taking a period of ten years, I find diseases of the skin caused practically twice as great damage to the health of the Navy as was caused by all other diseases of a quarantinable nature. When it is

considered that I include such diseases as diphtheria, measles, small-pox, scarlet fever, rōtheln, etc., in this latter category, the full import of my statement can be appreciated. The actual proportion was as 1 to 1.8. Were I to include syphilitic affections of the skin, this disproportion would be greatly increased.

This is an age of research and of exact diagnosis, consequently the practice which prevailed in years past of designating every internal disorder of the tropics malaria and every cutaneous manifestation as syphilis, yaws, oriental sore, or lupus, according to the trend of local medical opinion, no longer holds good.

With the fevers it must now be determined by the aid of the microscope that the malarial parasite is present—otherwise, our attention is directed to the possibilities of affections not formerly recognized. The oft-repeated story that every tropical febrile case is deluged with quinine prior to death or diagnosis is familiar to all of you who have considered the matter of tropical diseases.

With skin affections I feel sure it must be the same, and with this idea in mind, my first aim when appointed Surgeon-General of the Navy, in 1902, was to establish a school where the young officers of the Medical Corps of the Navy could be grounded in the essentials of medical research.

It was unreasonable to expect our medical schools to curtail the periods devoted to the essentials of practice of medicine and surgery in order that a more extended course in laboratory work as applied to tropical medicine should be given. Consequently, in the fall of 1902, the first detail of recently appointed medical officers of the Navy was made to the Naval Medical School.

For a proper appreciation of the many tropical skin diseases due to animal parasites, and of the many which may hereafter be found to be of such etiology, it is my belief that a sound working foundation in medical zoölogy is not only desirable but essential. The Naval Medical School is fortunate in this respect inasmuch as the instruction in this branch is given by a zoölogist who is not only eminently practical in his teaching, but who possesses in rare degree the faculty of

imparting enthusiasm to those who study under him. I refer to Dr. Charles Wardell Stiles—the American authority in medical zoölogy.

For honest and capable work in any branch of tropical medicine, it is necessary that the worker be grounded not only in clinical observation, but he must possess a fair degree of proficiency in bacteriology, a good working knowledge of animal parasitology and, besides, have enthusiasm for his work. Scientific curiosity to be of value to the profession must be bred of knowledge, animated by enthusiasm, and controlled by judgment.

The medical officers of the Navy are, while in tropical waters, constantly required to study or treat such affections as ringworm and the peculiarly virulent cutaneous manifestations of syphilis. As regards syphilis, I have been struck by the favorable reports which have reached me from our naval hospital in the Philippines, in which attention is called to the infrequency of the intractable skin lesions, so common previously, after the routine employment of hypodermatic mercurial medication. Mercury by the mouth, or, preferably, by inunction, may control the ravages of the disease in temperate climates, but some factor in the tropics tends to lessen the power of such forms of treatment to control the disease in hot climates.

While serving on shore stations in the tropics, or when cruising in such waters, the naval medical officer is constantly in contact with such diseases as yaws, leprosy, ground itch, elephantiasis, tropical ulcer, and the like, and, in consequence, these diseases are of great interest as well as of importance to him in the performance of his duties. These affections, however, are of such common interest and of such general knowledge that I shall pass them over to present to your attention three or four diseases, our knowledge of which I am very desirous that some of our medical officers may advance by throwing some light upon their etiology and pathology. Of these I shall first call your attention to gangosa or rhinopharyngitis mutilans. This disease, which was studied by Daniels in the Fiji Islands, is unfortunately very prevalent in our island possession of Guam. The clinical manifestations

of the disease as observed in Guam were first brought out by Surgeons Arnold and Leys of the Navy, later by Assistant Surgeons McLean and Mink, and recently by Surgeon McCullough and P. A. Surgeon Geiger, the latter of whom is giving particular attention to the etiology and pathology. During the summer of 1906 I detailed Surgeon Stitt of the Navy to investigate the cause of this disease. The result of his investigation, which was published in my report for the year 1906, was of a negative character. From the work which had been done in connection with the etiology of syphilis and yaws he entertained the hope that a spirochæte might be found to belong to *gangosa*, but as to this he was unable to establish any evidence. It is possible that with some of the more recent methods of staining better success may be had.

Dr. Fordyce, the Secretary-General of this Congress, has also investigated the lesions of this peculiar disease, but, so far as I have been able to learn, without success as to determining its etiology. Here is a disease which starts as a small membranous patch of the throat, which in a few days proceeds to perforation of the hard palate and thence to the most frightful ulcerations of the nasal cavities. Those who have studied it most carefully are positive it is not syphilis and absolutely sure it is not leprosy—what is it?

Sir Patrick Manson recently, in conversation with one of the members of our corps, remarked that in Samoa there should be a splendid field for renewal of the work in connection with filariasis, especially from a pathological standpoint. The determination of the exact method by which lymphatic obstruction is brought about in this disease would be of the greatest importance. One of the medical officers, who served for an extended period of time in Samoa, informed me that although the sailors of our Navy were constantly exposed to infection by mosquitoes while ashore, yet there had never developed among them a case of any filarial disease. The only striking point of difference in habits was in the fact of our sailors drinking distilled water—is it possible that there are other methods of transmission of this disease than by the mosquito?

Another puzzling affection is what is generally termed "climatic bubo." Here we have a pathological condition which presents the picture of a prolonged continued fever following more or less the increase or decrease of the glandular swellings. It is not related to any venereal affection and the question comes up—has it any relation to Dhobie itch or other mould affection of the skin, as some think?

Speaking of Dhobie itch and the various affections of the skin so common in the tropics, including prickly heat, I am forced to believe that some of the so-called tropical neurasthenia may be connected with these affections.

The constant irritation induced by such conditions, with the attendant loss of sleep, must result in a mental state which, in a person not leading a life adapted to the tropics, will bring on a deterioration of the mental as well as the physical side.

While alcoholic excess and undue exposure to the rays of the mid-day sun may not account for all the phenomena of mental deterioration in the tropics, yet it cannot be gainsaid that such factors will produce marked aggravation of skin lesions and incidentally lead to conditions surely conducive to nervous prostration.

While in temperate climates one may not suffer seriously from neglect of treatment of simple skin affections, yet in the tropics it is a different matter, and in consideration of the fact that the greater part of the time of our force afloat is spent in tropical waters, the importance of this question for the Navy cannot be overestimated.

TROPICAL DISEASES OF THE SKIN

BY DR. H. RADCLIFFE-CROCKER, OF LONDON

In accepting the task of opening a discussion on Tropical Diseases of the Skin, I assumed a responsibility of more difficulty than I at first anticipated. The size and complexity of the subject are so great that it is difficult to compress into the twenty minutes at my disposal anything more than a skeleton of the subject, and I could scarcely hope that out of such dry bones as I could set before you that a fruitful and practical discussion could arise even from such an audience of experts from all parts of the globe as those whom I have the honor of addressing. Yet there are only too many moot points in most of the subjects, while the important and well-known lepra, though by no means exclusively tropical, embraces enough for a congress all to itself, which, indeed, it has already had without settling any of the points in dispute. Great Britain, however, from its numerous colonies and world-wide commerce, is frequently receiving its own wanderers and those from other lands, bringing with them various diseases from the tropics, and as a fair share of them has come my way, I thought a little of my personal experience might put a little flesh on some of the *bones* of my skeleton, and might aid in suggesting points for discussion.

Unfortunately, the isolated character of the cases, and the fact that they are nearly all private cases, and that in many instances the patients have left the tropics for some time, are great and often insuperable obstacles to studying the pathology of these affections, and my observations are therefore chiefly clinical. One of the great obstacles to our obtaining correct opinions of the nature and relationships of tropical diseases to those of temperate climates, is that very few who have lived and worked in tropical climates have had a dermatological training, and good observers and recorders though they may be, yet they lack the advantage of being

able to compare with first-hand knowledge the two classes of diseases. We, on our part, are in a similar position as regards many tropical diseases.

TROPICAL DISEASES OF THE SKIN

DISEASES DUE TO VEGETABLE PARASITES

Scaly	{ Tinea Tropica { Tinea Imbricata	{ Various species of large-spored trichophyton, rarely microsporon. { A large-spored trichophyton, very like European trichophytons.		
Pigmentary Diseases	{ Pinta { Mal del Pinto { Cute { Carate { Cative { Quirica	{ Mexico { Colombia { Venezuela { Granada { Guatemala { Honduras { Panama	{ Identical or analogous diseases.	
Deep-seated Suppurating Lesions	{ Actinomycosis { Mycetoma { Protozoic Dermatitis	{ Pale { Black { Red	{ Buenos Ayres and California. { Fungus like Blastomycosis, but with visceral implications.	

ANIMAL PARASITES

Nematoda	{ Dracontiasis { Craw-Craw { Elephantiasis Arabum		
Trypanosoma	{ Trypanosomiasis or Sleeping Sickness. { Furunculus Orientalis { Pemphigus Contagiosus	{ Immature Trypanosoma or Leishman bodies.	
Insecta	{ Chigoe { Myaces { Ixodes		

FUNGATING GRANULOMA LESIONS

Framboesia	{ Yaws { Paranghi { Krocma { Dana Bai { Khunscarata { Khi Kai Chine { Khi Mo { Coko { Tona { Tonga { Verruga { Bombas	{ West Indies { Ceylon { Upper Burmah { Cambodia { Siam { South Lastea { North Lastea { Fiji { Polynesia { NortChelaaniod { Peru { Brazil	{ General spirochaetic diseases.	
Local	Granuloma Inguinale Tropicum	West Indies, India, and Fiji.		

TROPICAL ULCERS, ETC.

Furunculus Orientalis	{	Aleppo Boil Delhi " Biskra Bouton Gafsa " Kandahar Sore Pendjeh " Endemic " of Bahia Annamite Ulcer Puru of Malay	}	Leishman bodies— Early forms of Trypanosoma.
Phagedena Tropica, Aden, Malabar, and Madagascar Ulcers	{	Same as Hospital Gangrene due to an aërobic bacillus. (Boinet), an anaërobic bacillus (Matzenauer).	}	
Veld or Natal Sore Barkoo Rot	{	South Africa Queensland	}	Staphylococcus aureus.

A glance at the above tables shows that practically all exclusively tropical diseases of the skin are due to parasites of various kinds, and although there is still much room for further investigation, they also show that much of our knowledge of their pathology has been worked out quite recently, and now that so many of those who are going to practise in the tropics are undergoing a course of training in modern pathological methods, we may well expect that in the near future still greater additions to our exact knowledge will be made, and it is only exact knowledge which will enable us, not perhaps to treat the diseases themselves better than we do now, but still better to adopt the most efficient means for the prevention and spread of affections in which the disabling effects and mortality are so great. How much can be done in this direction the results of the discovery of the relation of the mosquito to filaria, malaria, and yellow fever are known to all.

The tables do not pretend to give a scientific classification of tropical skin diseases, but I trust that they may be helpful in grouping the principal pathological and clinical features. I have not put lepra down, as it is a disease which extends from pole to pole and at all events stands by itself.

TROPICAL RINGWORM:

I have met with numerous cases of tropical ringworm from China, Burmah, India, Ceylon, Northeast and Southwest Africa, the West Indies, and various parts of South America

—it is probably universal in all tropical countries. While its special site is in the crutch and axillæ, it may attack other parts where its characters are less marked than in the usual positions, and so its nature may be overlooked, and I have seen several instances where the neck, legs, feet, and nails have been the seat of lesions. On the legs, the lesions are more or less circinate and well defined, but on the soles, the circle is often fragmentary, and only here and there a segment may be found which, with the history of residence in a tropical country, may afford a clue. The nails present nothing characteristic, but they will probably be thickened, crumbling, discolored, dull, and with an uneven surface. One fact must be borne in mind, of which I have seen several instances, *viz.*, that in temperate climates, the eruption may die away altogether for months in the cold season, and reappear with renewed vigor when the climatic temperature is raised.

While the clinical characters of the eruption do not sensibly vary in cases from different parts of the world, it is otherwise with their cultural characters. I have handed to my colleague, Mr. Pernet, many specimens, *i.e.*, scrapings of skin and nails from ringworm from various parts of the globe, amongst which may be mentioned Manila, China, the Cape, Japan, and India, and under the microscope they were all large-spored trichophytions; but they differed considerably in their cultures. Pernet writes to me as follows: "Microscopically, they varied in appearance, but it was more common to find long, sometimes very long, slender dichotomously branching mycelial filaments, often plain or only showing short segmentation here and there. In other cases, the sporulation was extremely well marked, the individual segments varying in shape and size, being either squarish or shortly rectangular, barrel-shaped, oval or distinctly round—in the latter case with a central dot. In some instances, the nails were also affected and fungus was found in those structures. As to cultivations chiefly on maltose agar, they also varied. In one instance, the growth was of a distinctly pale pink hue at first. In another, a case of Dhobie itch, the second sub-culture was more like trichophyton megalosporon ectothrix, opaque, white, and powdery. It is probable that the

fungi belong to the trichophyton megalosporon group, but of different varieties. This would agree with Sir Patrick Manson's view that eastern ringworms are attributable to a large variety of fungi, and probably many of them are derived from the lower animals. I have not found the microsporon minutissimum of erythrasma which Manson thinks produces many cases of Dhobie itch.

At University College Hospital, there have been several instances of packers undoing Japanese goods, which often arrive packed in straw or a kind of reed, contracting an agminated pustular folliculitis with circular lesions made up of closely aggregated pin's-head pustules on an erythematous base, but not raised up with the kerion-like appearance of Leloir's "Conglomerative pustular perifolliculitis." On microscopical examination, fungus elements with large-spored ectothrix characters were readily found on cultivation. A pure culture from the first was produced with the typical characters of trichophyton megalosporon ectothrix, proving also the pyogenic properties of the fungus.

Jeanselme describes cases of negroes of Senegal with tinea tonsurans due to microsporon Audouini, but admits that most come from trichophytons, different both from each other and from French specimens. Courmon isolated two varieties. Sabouraud, in a young African from the Soudan, obtained a faviform culture from what was clinically a tinea tonsurans.

It is evident, therefore, that while the great majority of cases of tropical ringworm are due to trichophytons—of various species—the other forms of fungi play some part in their production.

Manson goes farther and asserts that the microsporon minutissimum of erythrasma will in a tropical summer excite a dermatitis of a bright red color which resembles the inflammation produced by a trichophyton, and that many cases of so-called Dhobie itch are really inflamed erythrasma which has extended beyond its usual limits, and, secondly, pus inoculation may be produced by the violent scratching.

In cold weather it dies down with the usual reddish-brown discoloration.

The microsporon furfur of pityriasis versicolor produces,

as is well known, on the skins of the dark races, patches paler than the normal pigmented skin, the yellowish fungi flourishing exceedingly in hot climates and forming a yellow layer concealing the pigment beneath. Inflammation of the skin may also be excited by this fungus in hot weather, and again Manson says some cases of Dhobie itch are due to this fungus.

Tokelau ringworm, on the other hand, appears to be confined to the southeastern portion of the globe, Polynesia, the Indo-Chinese peninsula, and the south coast of China, Siam, Assam, and Tonquin, but I have no personal observations on the subject, and as I can, therefore, only quote from the well-known authorities on the subject, I will leave it to others to discuss this contagious disease, merely remarking that Nieuwenhuis, of Java, and Sabouraud regard the fungus as a large-spored trichophyton like the animal forms of Europe.

The same might be said of Pinta and its congeners, and as it is a disease of this continent, I shall hope to hear personal experience and research from some members of this Congress.

I should like to hear whether the diseases comprised under these names are one pathological entity or several closely allied affections due to different organisms.

I have never had a mycetoma under my care, but have had an actinomycosis from the west coast of Africa, in a colonial surgeon in whom it had commenced two years before, as an abscess over the left hip, which had resulted in a brawny hardness with numerous sinuses from which yellowish-gray granules, from a pin's-point to a No. 4 shot, could be squeezed; these presented the usual microscopic characters. Incidentally he owned to being a morphia and cocaine consumer, and had taken ninety grains of the first, and fifty of the second, per diem.

Sabouraud says that there is in the extreme East an undescribed dermatomycosis, of which he has seen three examples which the patients said were due to frequent and prolonged immersion in stagnant water (Karaaté is also said to be due to this). One of Jeanselme's patients also attributed it to having his feet in marshes, and said that the lesions began on the lower extremities below his drawers.

Original lesions consist of erythematous plaques, more

scaly than red, which become circinate when over two or three centimeters in diameter—but circination is incomplete or segmentary. The lesions may be extremely numerous and predominate on the lower half of the body. In independent positions, there may be large polycyclic patches, but only one-third or one-half circles; the rest is badly defined. The base is bistre brown or even black. The border is scored by excoriation from scratching, sometimes with bloody crusts, as the itching is sometimes ferocious; hence may follow thickening of the skin, with lichenification principally at the circinate border. This border may then present polymorphic lesions, scaly, finely vesicular, lichenified, and excoriated lesions, but the aspect as a whole is quite characteristic.

The microscope easily shows mycelium, separate, not double-contoured, and of diverse forms, but with banana-like curves predominating, while the mycelial spores are round, of variable diameter, and are shed without forming a filament by their union. Jeanselme was unable to obtain cultivations. In one case there was a double-contoured mycelium, and altogether he considers it a very distinctive dermatomycosis. He considers the patches on the inside of the thighs and buttocks particularly constant and characteristic. Cases came from Japan, Tonkin, and Indo-China. One patient acquired it twice, but the disease disappeared gradually and spontaneously in Europe.

Mercury, sulphur, pyrogallic acid, salicylic acid, and resorcin in large proportions failed, while chrysarobin, one per cent. to three per cent., cured it rapidly.

Erythrasma, due to *microsporon minutissimum*, is very frequent in the tropics (so Manson also says), and forms dull red patches in the groins and axillæ in cold, while in hot weather it becomes bright red and itching, and then extends beyond its usual limits to neighboring parts. The patient scratches, inoculates pus germs, and small abscesses and boils may ensue.

Jeanselme has also observed on the coast of Annam and other parts of Indo-China a vitiliginous squamous dermatosis which the people of Laos at Bangkok called *Khi*. He suspects it to be parasitic, but had not examined it.

It begins in infancy or adult age, and progresses very

slowly. The palms and soles are double their usual thickness by a horny layer which forms deep sulci at the natural folds. At the base of this keratosis diffusa, numerous horny discs, more or less adherent, which are situated at the dilated orifices of the sweat glands, become detached. The keratoderma spreads to the back of the hands or feet and reaches above the wrists and ankles.

At the level of the invaded area the skin loses its elasticity and cracks. It is sown with little horny masses, chiefly grouped on the back of the metacarpo-phalangeal and inter-phalangeal articulations.

The affected skin presents achromic portions punched out like a puzzle and with a remarkable sharpness of contours which alternate with islets of hyperpigmentation of a sepia tint.

At the upper margin of the lesion at the level of the wrist or ankle, the vitiligo is gradually transformed into an erythemato-squamous condition. This zone of activity and extension, of which the design is very capricious, is bordered by a fringe of psoriasiform scales, or rather is covered with papules low and obtuse, of a brownish-lilac shade resembling lichen obtusus. Beyond this lichenoid or psoriasiform fringe are irregularly scattered islets in ectasic glands. The nails of the fingers and toes are often thickened and stratified. They split and crumble without offering any resistance. It is somewhat itchy in the recent parts, but is not painful in the rainy season, the moisture restoring some of the elasticity to the skin, but in the dry season the keratosis hardens and cracks into bleeding fissures which cripple the victims of the malady.

The malady is incurable, it is not in any way related to leprosy, and may be associated with chronic rheumatism.

The most striking feature is its family prevalence, which was marked in three out of five cases there.

He gives a table and as in this husband and wife were affected, he infers contagion more than heredity.

Jeanselme states that since he published this he has found that Nieuwenhuis, on *tinea imbricata* (*Archiv f. Derm. u. Syph.*, vol. xlv., 1898, p. 164), has described a similar disease

in Java. He says that parasiticides such as sublimate, iodine, and chrysarobin can cure the disease, and thinks its parasitic nature is certain.

FURUNCULUS ORIENTALIS

The sores, which have various local names, as in the list given in the tables, have all similar characters, and probably are all of the same pathogenic origin. It is best known in the East, but de Souza's observations on the endemic sore of Bahia show that it occurs in the West also, and probably it will be recognized in other districts as more accurate studies are prosecuted. Diplococci have been described by several observers as the pathogenic organism, but Wright's (of Boston) more recent observations suggest that the Leishman bodies are the real agents. These are minute spherical or oval bodies with two chromatic masses, one very minute and deeply staining, the other large and less deeply staining. Leonard Rogers (confirmed by Leishman himself) and Christopher have shown that in a suitable culture medium they develop into flagellated organisms of the trypanosoma type, but differ from the ordinary form.

Manson suggests, "that the 'Leishman body' leaves the human organism in the discharges from ulcerated surfaces; that it is ingested by some foul-feeding fly, in which it undergoes evolutionary changes and probably of multiplication perhaps sexually. The fly then implants it in the human organism by bite or broken skin surface, and then in the human host it multiplies asexually by division."

Morphologically the "Leishman body" of Oriental sore is identical with that of Kala-azar, and Manson suggests that its virulence may have been removed by transmission through the camel, but this is only a suggestion.

According to Manson, the affection he has described as pemphigus contagiosus is also due to "Leishman bodies."

As far as our present knowledge goes, therefore, we have to regard these affections as localized forms of trypanosomiasis which is somewhat startling and must widen our conception considerably of trypanosomiasis.

Clinically, I have met with one case in which a sarcoma developed on the site of the sore, and afterwards generalized with fatal results. In another case, a young lady who had had a Delhi boil as a child, when she grew up, in the scar a tuft of dark hair developed, which I removed by electrolysis.

As the first of these cases occurred in an army surgeon, on the left cheek, his description of its mode of development is probably accurate and therefore of value. His age was 31; I first saw him on May 15, 1894. The sore began in July, 1893, like a blind pimple or acne spot, visible and palpable, but painless; it enlarged subcutaneously to the size of a pea; then the skin exfoliated and it looked like an abrasion. It continued to enlarge with a succession of thin scabby exfoliations, and when the scab was removed an ulcer was exposed the size of half an inch, shallow and punched out with a foul but even surface. Then at the end of October it began to fungate and had gradually increased in diameter to the size of one inch across and one-fourth to one-third of an inch high, forming a strawberry-like plateau. In January, an attempt at cicatrization occurred in the centre and it became regularly cupped and occasionally a hair formed. This is interesting in relation to the other case where hair subsequently developed in the scar, and shows that the ulceration is not very deep. The cicatrization lasted three or four weeks, and then broke down and there was a longitudinal furrow in the centre of the fungating sore. About thirty minims of dirty-looking pus were removed every morning. Up to a month before removal there was scarcely any infiltration round the fungation. My colleague, Mr. Arthur Barker, shaved it off level with the skin and then tried erosion, but the tissue was too tough and so he dissected the whole lesion out. The patient had complained of abdominal pain just before the operation, but the true cause of this was not suspected, but soon tumors could be felt, and he died, between five and six weeks after the operation, of generalized sarcomatosis.

GENERAL TRYPANOSOMIASIS

I have met with one instance of the erythema of general

trypanosomiasis. The lesions when fully developed consist of rings or segments of rings from about a couple of inches to as much as a foot in diameter. The very large ones occur on the trunk, but on the face a single ring may embrace the whole cheek. Some describe these rings as well defined, but in one, two inches across, one week old, only a segment was well defined, the other portion shading off.

An early one that I saw began as a red spot about one inch in diameter, like an ill-defined pink blush, but they are by some said to be well-defined in some instances. In a case of Manson's he especially remarked that they were ill-defined. These patches increase peripherally, and clear in the centre until a ring is produced, or it may die down at one portion, and then a crescent is produced. Each lesion lasts from one to three weeks, but a week is the rule.

Besides these characteristic rings there may also be large ill-defined blotches of erythema scattered about, and Manson also mentions rubeoloid spots. My patient was the wife of a missionary on the Congo, who stated that the symptoms began soon after an insect bite on the leg. This was followed by frequently repeated attacks of fever, supposed to be malarial, and she was given quinine in huge doses for a long period, and the erythema was at first ascribed to the drug. She ultimately died of sleeping sickness. Patrick Manson reported this case as the first recognized in England. Habershon has had an exact replica of this case from the Congo also. Mott, who has examined the nervous system, shows that "there is a universal meningo-encephalitis in the form of a small cell perivascular infiltration" (Manson), and it is this neurovascular paresis thus produced which explains the ringed and other forms of erythema. Although the trypanosoma Gambiense is found in all these cases, it is not yet conclusively proved to be the sole pathogenetic organism. Thus Mott and the Portuguese observers have found a diplococcus pervading the tissues of the body, especially numerous in the lymphatic glands. The species of tsetse fly known as *glossina palpalis*, is the transmitter of the trypanosoma Gambiense to man. As is now well known, *filaria perstans* has been found in a large proportion of cases, and was supposed to be the *materies*

morbi until it was shown that sixty per cent. of the Indians of Demerara had filaria perstans, but sleeping sickness was unknown there. Moreover, in Africa, numerous cases of sleeping sickness were found with no filaria perstans present.

The "Veld," the "Natal sore," and the "Barkoo rot" of Queensland are probably identical, and Harland claims that the staphylococcus pyogenes aureus is the *materies morbi* of the Veld sore. If this is correct it will in all probability be the same for the Natal sore and Barkoo rot—though it is maintained by the same writer that the Natal sore and the Veld sore are not the same.

The phagedenic ulceration of the tropics, Aden and Malabar ulcer, and the Madagascar sore are probably identical. Phagedena tropica is met with in tropical latitudes all over the world, both east and west, and even in more northern latitudes, such as Algiers, Egypt, the shores of the Red Sea, while it is at its worst in Cochin China and Tonkin. It may be mild and chronic, or acute and severe; it starts often from a trifling lesion, and is almost entirely propagated by inoculation. It is by the majority of observers thought to be identical with hospital gangrene, for which Matzenauer found an anaërobic bacillus, while Boinet in phagedena tropica found an aërobic bacillus, so that the true organism is not yet decided.

YAWS

Yaws is one of the most serious of tropical diseases, on account of the severity of its lesions, and of the enormous number of its victims in the countries in which it is endemic, which comprises practically the whole tropical zone, very few natives escaping, partly because mothers often deliberately inoculate their children to get it over, though some authors assert that it is not protective, while others say that it generally is, but that second and third attacks may occur (Nicholls). This is an important point on which I hope that some members of this Congress with practical experience may enlighten us. The main question is whether yaws and syphilis are identical or only analogous diseases. We all know that Mr. Hutchinson

has written a large volume setting forth that they are identical, but only the evidence of trained, practical observers of yaws, supplemented by experiments, clinical and pathological, are of value in settling such an important point. One difficulty has arisen in the past, viz., that it is probable that some observers have in their descriptions of yaws in some instances mixed up the lesions of syphilis with those of yaws.

Quite recently a spirochæte resembling the spirochæta pallida of syphilis has been described by Castellani. This and the clinical fact that the manifestations of yaws yield to mercury and iodide of potassium, judiciously given, no doubt lends more color to the theory of identity, but it by no means proves it. Similarity of form and staining reactions are a long way from proof of identity, of which the bacilli of tubercle and leprosy are a striking example; while if yaws is due to a spirochæte analogous but not identical with that of syphilis, an explanation would be afforded of the good effects of mercury and iodide of potassium. Probably inoculation experiments on anthropoid apes would assist in clearing up the point. Meanwhile we must still rely on carefully observed and recorded clinical facts, and these are difficult to obtain in an indisputable form. Thus, as above stated, some say that yaws is not protective against itself, while others say that it usually is, while syphilis we know is protective in a very high degree against itself. Then some say that yaws cannot protect against syphilis, nor syphilis against yaws, while others hold the contrary opinions. This, it seems to me, is the crux of the whole matter. Powell and Charlouis, both good and reliable observers, have each observed two cases in which persons with yaws have contracted syphilis with the usual symptoms co-existing with the yaws lesions. If the truth of these observations be admitted, it appears to me that the controversy is at an end and that yaws and syphilis are absolutely distinct diseases. Still, it would be more satisfactory to have further corroboration on the clinical side on the one hand, and further investigation on the differentiation, or otherwise, of the respective spirochætic organisms. A few other differences may be mentioned: it is said that auto-inoculation of yaws can be carried on indefinitely, while

in syphilis this is not possible. The initial lesion of yaws is like the subsequent ones and does not start especially on the genital organs, and the mucous membranes escape except in the later stage of maltreated cases. Moreover, while it is contagious, it is never hereditary, and the lesions are neither polymorphic nor symmetrical in the early stage, and do not leave scars unless irritated or injured.

The resemblances are: the tendency to form circinate eruptions and for the lesions to group round the anus and other mucous orifices; nocturnal osteo-arthritic pains may be present, and mercury and iodide of potassium are important remedial drugs, though they must be given cautiously, mercury being said to be injurious in the primary and early part of the secondary stage, while iodide of potassium is not so efficacious against yaws as it is against syphilitic tertiary lesions.

Yaws, boubas of Brazil, and verrugas of Peru are evidently closely allied affections, and if a spirochæte is the pathogenic organism of yaws, it is a fair guess that spirochætes will be found also in verrugas and boubas.

GRANULOMA INGUINALE TROPICUM

I have met with a case of this disease in a full-blooded negro. A point of interest in his case was that he had left the West Indies five years before it began as a flat sore on the penis behind the corona, attributed to impure intercourse nine days previously. He told Pringle, into whose hands he subsequently fell, that it began as a pea-sized boil in the right groin, which was scratched into a sore and spread down the scrotum at the side and up along the groin. Probably each of these statements was true for each situation, but that the penis was the primary point of infection. This case occurred before the publication of Conger's and Daniel's monograph, which showed that it was fairly common in British Guiana and the West Indies. Since then it has been noted in India, Fiji, the New Hebrides, and New Guinea, and it probably occurs in all tropical countries. Goldsmith records a case in a white man who had had intercourse with a black woman.

An apparently identical but less extensive condition may occur in white persons in temperate climates, and it seems therefore probable that the excessive development is racial rather than climatic, corroborated by my case having left the tropics for five years before it began, and having contracted it from a white woman. I am inclined, therefore, to regard it as an instance of staphylococcic infection which takes a virulent form in black races, but this is only conjecture, and it ought not to be long before the real pathogenic agent is discovered. Removal has to be radical or the disease recurs.

CRAW-CRAW

I should much like to hear any first-hand information about *Craw-craw*. I have had two cases from the west coast of Africa in which the patients were told they had *Craw-craw*, but one was a case of common scabies and the other of *tinea tropica*. Brault, after analyzing the descriptions of other authors, came to the conclusion that it was a sort of limbo into which African skin diseases which were not diagnosed were cast, and that it was not a distinct morbid entity—but Geber came to the same conclusion with regard to *furunculus orientalis*, which is now universally accepted as a separate disease. Emily, a French colonial surgeon, gives a very succinct account of it, as a severely itching disease, producing deep ulcers, some as large as a five-franc piece, but these may easily be the result, in a hot country, of violent scratching. Janselme apparently regarded it as a virulent boil. Nicholls saw it in St. Lucia, and coolie itch resembled Emily's description of *Craw-craw*.

The finding of filaria in connection with *Craw-craw* goes for very little, as Manson has pointed out that the central African population are almost universally affected by filaria perstans.

I am conscious of the fragmentary character of the above observations, but they will, I trust, yield sufficient material for fruitful discussion.

REPORT ON TROPICAL DISEASES OF THE SKIN

BY DR. WILLIAM DUBREUILH, OF BORDEAUX

The object of the reports read before a congress is to start the discussion and to induce the members present to give their opinions on the question which is proposed. As I cannot bring forward the result of any personal experience in tropical dermatoses, I think I can better fulfil my object by going over the whole field of tropical dermatoses, not to repeat what is known and tolerably certain, but to point out what is uncertain or unknown.

It may happen that some of these points are well known by those who have abundant experience of tropical diseases, but—perhaps because they are considered as commonplace—they are not clearly explained in text-books. My point of view is that of the student trying to get an idea of tropical dermatoses by reading.

Parasitic diseases, especially those which are due to large parasites, seem likely to be better known, but even there a great uncertainty prevails on many points.

A great many dipterous larvæ can prey on man in different ways. The bluebottle fly lays its eggs, or rather larvæ, in foul-smelling ulcers, and the maggots live in the matter, but not on the living tissues; they are not true parasites.

The *Sarcophila wohlfarti* of Northern Europe and the *Lucilia macellaria* of South America lay their eggs in foul ulcers, in the nostrils or the ears of man, especially if ozena or otorrhea are present, and the maggots, always very numerous, eat their way through the living tissues and live there until the pupæ develop—that is, during eight or ten days. Their enormous voracity, and most likely the irritant saliva they excrete, cause abundant suppuration, hemorrhages, gangrene,

and often death after very few days, through suppurative meningitis. The larvæ of *Lucilia macellaria*, or screw-worm, are well known in Central America, but are hardly mentioned elsewhere. However, Depied has quite recently observed in Tonkin a screw-worm quite similar in appearance and habits to that of America. What is then the geographical distribution of the screw-worm, and is it the same larva in all tropical countries?

The larvæ of the European botfly (*Hypoderma bovis* and *H. diana*) who live nearly a year in the body of their host and travel therein in the most extraordinary way, have no analogue in tropical climates.

Cutaneous larvæ were observed in Central America more than two centuries ago by La Coudamine and by many others since, among whom I may quote Justin Goudot, who first reared the fly. The larvæ found in the skin vary considerably as to their size and shape, but it appears, from the papers published by Magalhaes and R. Blanchard who have most carefully studied the question, that the worms known in different countries under various names are but the successive stages of development of the larva of *Dermatobia cyaniventris* which seems to be common all over tropical America.

The way the larvæ enter the body of their host is still unknown. Some authors mention a sharp sting in the spot where the worm is to appear later; most have noticed nothing of the sort, but in countries where mosquitoes are common, a sting can easily be overlooked amidst many others. It is most unlikely that the egg is inoculated in the skin by the mother fly, therefore the egg must be deposited on the skin or on the neighboring objects and the larva bores its way through the skin. It is most likely that it goes through its whole development in the same spot, as all those who have observed the larva on themselves have seen the lesion increase from a mere pimple to a large boil in the same place, and have seen none of the disappearances or changes of place so striking in the European botfly. The whole development takes place in about two months, whereas the larva of the hypoderma lives in its host nearly a year.

The points to be studied are, therefore, the exact duration of the disease and the way the larva enters the body.

Dipterous larvæ living under or in the skin have been observed almost all over Africa, but their zoölogical position has not been clearly established.

The best known of all is the "Ver du Cayor," found in Senegal where it has been particularly studied, formerly by Coquerel and later by Bérenger-Féraud. It is the larva of *Ochromya anthropophaga*, and reaches its full development in a week. In this case also we ignore the way the larva gets under the skin.

The other larvæ observed in other parts of Africa seem to be different, and Gedoelst distinguishes the *Bengalia depressa* of South Africa, especially Natal, whose larva lives a fortnight, and the *Cordylobia anthropophaga* of East Africa, whose larval life lasts five or six weeks. He admits that these three species are not the only ones and that there may be others, still unknown. As it does not appear that the flies have been reared out of the maggots taken from man, the whole history of these larvæ is still rather obscure and deserves further study.

Quite recently a new parasitic larva has been discovered in Africa, the Congo floor-maggot, the larva of the *Auchmeromya luteola*. It lives in the crevices of the huts and comes out at night to prey on the inhabitants, sucking their blood exactly like bugs. Very little is known about it.

The chigger or sand-flea has been spreading wonderfully of late. Fifty years ago it was confined to the northern part of South America, especially Guiana and Brazil, but like Phylloxera and other American parasites it thrives most deplorably in the Old World. In 1872 the chigger was brought over to the West Coast of Africa and in the space of twenty years it spread over the whole continent from one ocean to the other. In 1899 it was carried to Madagascar where it has become a real pest. Quite lately it has been found in India and in China. In a very few years all tropical countries will most likely be provided with it.

Two points are still obscure in the life history of the chigger: the way the eggs are laid, and the influence they seem to

have in the grievous complications brought on by that parasite.

Most authors say nothing of the way the chigger lays its eggs, but it has been observed that when a mature chigger is expelled artificially or by suppuration, it lays all its eggs at once. Wellman, in a recent paper, reports that the chigger drops its eggs one by one without leaving its host, and comes out when all the eggs have been expelled. The eggs ripen successively, so that when the chigger is prematurely separated from its host and lays, all in a lump, its whole stock of eggs, they are unripe and cannot hatch. It is therefore quite useless to destroy the chiggers which have been extracted from the skin. That point could easily be ascertained by experiment.

It is generally admitted that the presence of the chigger's eggs in the wound is an unfortunate circumstance. However, nobody thinks that the eggs can hatch in the skin. Toussaint believes that the eggs contain some toxin which irritates the skin, and that they are the real cause of the many serious complications which befall the patients affected with chiggers.

The same question arises about the *Filaria medinensis*, as the presence of embryos in the host's tissues appears to be a powerful cause of inflammation.

The treatment of guinea-worm has remained until now very much what it was in the days of Galen, rolling up the worm upon a bit of stick and drawing it out little by little, day after day. Some years ago, a surgeon of the French navy, Emily, proposed injecting a solution of corrosive sublimate, 1 to 1000, in or around the worm, thus killing it. If the skin is open, the worm can be drawn out at one sitting; if it is not, the dead worm is absorbed without any inflammation, just as a bit of aseptic catgut. Considering the gravity and duration of the guinea-worm disease and the apparent advantages of Emily's treatment, it should be interesting to know, of those who have had the opportunity of trying it, what results they have obtained and what improvements they may have added to the original method.

Elephantiasis is common in hot climates and is generally ascribed to filariasis of the blood. But elephantiasis can be found in temperate climates with the same appearance; in

tropical countries many people have elephantiasis without filariasis, filariasis without elephantiasis. European elephantiasis appears to be caused by a chronic infection with streptococci which occasionally take on an increased virulence and provoke acute attacks of lymphangitis. The same process is observed in hot countries. Therefore the part of filaria in elephantiasis is obscure and even doubtful.

Tinea imbricata or Tokelau is a disease whose clinical characteristics are well marked and easily recognized. The presence of a fungus has been observed long ago, but whereas most authors describe it as a trichophyton and Nieuwenhuis reports having cultivated and successfully inoculated a fungus closely allied to the trichophyta, Tribondeau has found an aspergillus with characteristic fructification. I, myself, and also Wehmer, have found the same reproductive organ in scabs supplied by Tribondeau. Since then Tribondeau tells me that he has found the same fungus in other cases and has cultivated an aspergillus. It is most desirable that researches should be made on a large number of patients to ascertain if that aspergillus is constant, and also inoculations made with the cultures, but such are only likely to succeed in hot countries.

In several tropical countries are found diseases whose principal feature is the discoloration of the skin, and which are generally ascribed to fungi. They may be joined under the heading of dyschromic dermatomycoses. We may mention the following which seem to be distinct, but their list is perhaps not complete.

1st—The caraté of Columbia with its numerous varieties of color—white, black, blue, red, violet, etc. Montoya has described in them fungi of the genus aspergillus belonging to different species, according to the color of the caraté. He has cultivated them from the skin of his patients and even found some of these fungi in the waters of the country whence the patients came.

2d—The Pinto or Mal del Pinto of Mexico.

3d—The "achromie parasitaire à recrudescence estivale," observed in Indo-China by Jeanselme, who found in it a fungus very like that of pityriasis versicolor.

4th—*Tinea albigena* observed in Java by Nieuwenhuis

who found in it a fungus, and which appears to be the same disease found in Annam by Jeanselme under the name of Khi-Huen.

5th—The case described by Legrain in North Africa, "Pinta d'Afrique."

It is very difficult to have a clear idea of these diseases, especially of the American ones. Those who have written on them have made general descriptions, from a number of cases, descriptions which are more or less biassed by the personal opinions of the author upon the nature of the disease. The result is most confusing for the reader who has not seen the disease. It would be a great deal better to publish a certain number of cases, carefully described, followed up during as long a time as possible, with photographs and a report of microscopical examinations. Fifty cases, well taken, would give a better idea of the caraté than as many general—and conflicting—descriptions.

The history of yaws was very confusing some years ago, because the vernacular names of yaws, pian, parangi, boubas, etc., were used for various diseases, among which was often itch or syphilis. Some authors still maintain that yaws is but a form of syphilis, but it is now generally admitted that the two diseases are quite distinct. There are, however, many analogies, and recently Castellani has found in yaws a spirochæta which, in shape and size, is not to be distinguished from that of syphilis.

Breda has described a disease occurring in Brazil where it is called boubas, the same name as is used for yaws in Brazil, but the disease is, however, quite another one. The similarity of names must not create a confusion as to the nature of the diseases.

Verruga peruana is an infectious disease—special to certain parts of Peru. The most characteristic lesion of the disease and that which has given it its name, is an eruption of vascular warts of the size of a pin head, or a hazel-nut. These bright red, soft nodules often ulcerate and bleed most abundantly; their ordinary seat is the skin of the limbs, but they may be found everywhere else, and also in deep parts, in the muscles, the intestines, the liver, etc. The course of the

disease is generally a slow one, beginning with fever, pains in the limbs, and anæmia, which subside when the eruption comes out, but which may recur; the eruption may also recur several times, and the disease may last many months. At any time, either before or after the eruption, the general symptoms may acquire a great intensity, with high fever, excessive pains in the limbs, incessant vomiting, diarrhœa, and rapid anæmia, terminating in death after a few weeks. This form is called Oroya fever because it was observed especially among the men working on the Oroya railway line.

The latest authors on verruga peruana, Odriozola and Escomel, have carefully studied the clinical and pathological manifestations, and have described a bacillus which is to be found in the blood and to which they attribute the disease. The proofs brought forward in favor of the bacillus are not convincing, and the study of the etiological conditions in which the disease occurs brings out the most striking analogies with malaria.

The verruga occurs in certain valleys of Peru called quebradas; those which run perpendicularly to the coast and to the Andes are cool, well ventilated, and generally free from the disease, except in certain parts where a curve in the direction prevents proper ventilation. The verruga is common in the quebradas which are parallel to the coast and are hot and sultry. The infected valleys are all between 30 and 120 kilometers from the coast, and between 400 and 3000 meters altitude. Outside of these limits, in Lima for instance, are many imported cases, but the disease does not spread.

It must be remarked that it is exactly within the same limits and in the same valleys that malaria occurs most, except that malaria comes down a little nearer to the sea-level.

Verruga attacks especially newcomers, and the inhabitants of the infected valleys are generally immune or have only benign forms of the disease. Cattle and fowl are often attacked.

The disease is popularly ascribed to drinking the water of certain localities, and one of the torrents has so bad a reputation that it is called Agua de Verrugas; it was in a locality of that valley that during the construction of the Oroya railway thousands of men were attacked by the dangerous form

called "Oroya fever." Travellers going through these localities have taken the disease after a single night, or a few hours' sojourn, not having drunk a drop of the water of the place; others having drunk the water have remained immune. Moreover, it is difficult to explain how the water of a torrent could be dangerous in one place and not in another a few miles lower; how the water of the Rimac which goes through Lima can be safely drunk at Lima and be dangerous a few miles up stream.

The infected valleys are particularly dangerous in spring after the annual flooding of the torrents. The danger is increased by digging the soil, and the construction of the railway has been the circumstance which brought the Oroya fever into notice.

The verruga is not contagious and is not transmitted from man to man, except by inoculation, as in the case of Daniel Carrion. The numerous patients who come down to Lima to be treated have never given their disease to their neighbors and the malady can only be taken in certain localities.

All these etiological circumstances, carefully studied by Odriozola, are most strikingly similar to those of malaria, and may even be said to be identical. It is, therefore, most likely that the verruga peruana is caused by some parasite of the blood, apparently some protozoön which is carried from one man to another by some special sort of mosquito living in the hot valleys of the Andes, and breeding in the pools left by the torrents after their flooding.

The methods of work which have given so good results in the study of malaria, should be tried in the case of verruga.

THE OCCURRENCE OF A PROLIFERATING CESTODE LARVA (*SPARGANUM PROLIFERUM*) IN MAN IN FLORIDA

BY CH. WARDELL STILES, Ph.D., D.Sc.,

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Medical history of the case.—In June of this year, I received from Dr. H. Gates, of Manatee, Florida, specimens of worms, for identification, which he had taken from the skin of man. The following extracts from Doctor Gates's letters give all that is known to me regarding the medical history of the case. In connection with this history, it will be well to abstract in considerable detail an account of a very similar case recently reported by Ijima (1905)¹ in Tokyo, Japan.

Gates's case.—"Enclosed find specimens of worms from human flesh. They are inclosed in sacks deep under the skin in the connective tissue. My patient has thousands of them, all over the trunk; they can be seen and felt as nodules deeper in the connective tissue in the left groin and left breast, there seem to be large masses of them. I send some I obtained by cutting open the nodules and squeezing them out, and others still in the cyst as I found them."—From letter dated June 17, 1907.

"In reply to your request for history, etc., of patient (J. W. M.) infected with larval tapeworm, I would state that I first discovered the condition in April of this year. I was called in to treat him for dysentery. While examining over abdomen, I found a great many nodules in the skin, and also in the fascia between the skin and the muscles. Deep down in the abdominal cavity, I found large and small tumors, some movable and others fixed by adhesions. All the lymphatic

¹ Jour. Coll. Sci., Tokyo, v. 20 (7).

glands on the side most infected were enlarged and in masses as if they had formed close union with surrounding tissue.

"The muscles were exempt from nodules, but soft and flabby. I opened one nodule near the surface and obtained two worms. Most of the nodules on the skin are about the size and shape of grains of rice. When they first appear there is an itching produced. The cyst is filled with a clear watery fluid in which is found the small worm. In a few days a cyst wall is formed, surrounding the worm which lies in a jelly- or slime-like substance. After weeks or months the cyst wall becomes firm, and surrounds one or more worms. In some cysts I have found as many as three worms. In the course of a few months the cyst wall breaks and there is nothing left, but, sometimes, a blue spot showing a small hemorrhage; after this is absorbed, there will be only a spot of indurated tissue to mark the place. The places that have been infected the longest appear as a mass of indurated skin and fascia closely connected, so that the skin can be picked up only with the mass of worms and tissue.

"Patient is now forty-eight years old. He came to Florida in 1872 from Minnesota and settled with his father on a point on the Manatee River, now known as Mann's Point, which was accessible to fish and oysters.

"When twenty-three years old, while hunting in the woods about $1\frac{1}{2}$ miles from the coast, he noticed a small pimple on the left shoulder, which attracted his attention because of the itching. He thought the skin had been punctured by a thorn. He squeezed the lump, from which came a small flat worm about $\frac{1}{16}$ inch wide and $\frac{5}{8}$ inch long. One year after the first appearance on the shoulder, he noticed four or five small lumps on his chest; these he opened with a knife and he picked out the same kind of worms; these swellings also had produced an itching sensation. Patient was then living as fisherman on Sarasota Bay.

"While fishing, patient's diet consisted of smoked and dried fish, raw oysters, scallops, and clams. Up to five or six years ago he was a robust, healthy specimen of manhood, but lacked energy. At present he has a tired expression, has less energy, and becomes exhausted after little exertion.

"From the photographs (Plate xxix, Figs. 1 and 2), you will see enlargement of the left breast and shoulder, also of left groin and lumbar region. Spleen and liver are enlarged.

"The infection is slight on the right side.

"Patient has a wife and five children, all of whom are healthy.

"There probably was another case similar to this a few years ago, in this county. I have been trying to obtain a history of it, but have failed thus far. The man moved from here to California, where he died. The report was that he was eaten up with worms before he died."—Extracts from letter, August, 1907.

Japanese case.—The patient was a Japanese woman, Yae Tanaka by name, resident in Tokyo or immediate vicinity. Before her marriage to a dealer in old furniture, she was a weaver, "occupations which place her decidedly in the lower class of society."

At the age of thirty-three years, in the spring of 1904, she visited the University Hospital at Tokyo, for treatment for left inguinal hernia, entering the surgical wards of Dr. J. Kondo. This hernia was traceable to the presence of parasites in the region of ligamentum poupartii. In addition to the hernia, she presented a peculiarly swollen condition of the integument, which bore scattered spots of acne-like appearance. This abnormal condition extended over nearly the entire body, except on the face and upper extremities; it was most prominent on the left thigh, which was greatly swollen and presented very much the appearance of elephantiasis, although the skin and underlying tissues were quite soft, so that they hung down by their own weight and could be grasped in a flaccid mass by the hand.

When twenty-five years old, the patient had a tapeworm, the species of which is not known. The dermal affection was first felt when she was thirty-one years old, so that at time of entrance to hospital it was of about two years' standing. It had given no particular trouble beyond that imposed upon motion by the swollen thigh, and the itching of the skin in parts where a pimple-like hardening made its appearance; scratching with the nails, in order to allay the itching, had

led to breaking the skin, from which a soft whitish mass, together with some fluid, could be pressed out. A number of resulting recent scars, especially on the breasts, were visible.

From preparations made of skin taken from the left thigh, Ijima became convinced of the presence, in the connective tissue, of numerous encapsuled worms, the cestode nature of which was recognized from the calcareous corpuscles.

On each of two subsequent occasions, July 9th and 24th, 1904, a very large piece of skin, with the underlying connective tissue, was excised from the left thigh, in order to relieve the patient of the superfluous tissue. Altogether, several pounds in weight were removed during patient's stay at the hospital.

When freshly excised, the subcutaneous tissues presented an unusual appearance. At places several centimetres thick, they were moderately rich in panniculus adiposus and extraordinarily rich in lymph; the latter swelled the connective tissue between the panniculi, giving it a slimy or gelatinous appearance and consistency; the slimy character seemed more manifest in the deeper parts; lymph exuded copiously from the cut surfaces; numerous capsules, with the contained worm, were observable as whitish objects, isolated or in clusters, in all parts of the tissues. The thickness of tissues between the surface and the underlying tissue measures 30 to 60 mm., notwithstanding the fact that the hardening process has contracted the subcutaneous connective tissue, through loss of the lymph, into dense fibrous bundles, so that it no longer bears a resemblance to what it was in the fresh state. The corium in the same piece may be said to be 3 to 6 mm. thick; it seems to be on the whole considerably thicker than in the normal state.—Abstracted from Ijima, 1905, pp. 1-21.

Further medical details are not given by Ijima, but he states that Professor Kondo will publish a report of clinical and pathological observations. I have not as yet learned of the publication of the report in question.

From the foregoing abstracts, the suspicion immediately arises that in Florida we have a skin infection, hitherto unrecognized for the American continent, and similar to, perhaps identical with, an infection recognized only on one former occasion, namely in Japan.

It is interesting to note the following comparison in the cases, without laying too much stress upon these points at present:

Both cases occurred near the eastern shore of the continents in question (Old World, between 35° and 36° N.; and New World, between 27° and 28° N.); both patients lived in or near cities or towns located directly on the water, very near larger bodies of water (Pacific Ocean and Gulf of Mexico); both patients, though of different sex, were adult (twenty-three years male, thirty-one years female) when the infection was first noticed; both patients belonged to the poorer classes of society; one had a professedly fish diet, the other lives in a country where a fish diet is very common; both infections are of long standing (in one case over three years, in the other case about twenty-five years); in both cases the number of individual worms present was very great; both observers (Ijima for Japan, and Gates for Florida) independently call attention to the acne-like lesion resulting from the infection; each patient is a native of the country in which the case was found, and in neither case is there any history given of the patient's having visited the country of the other patient.

Nature of the parasite.—A microscopic examination of the worms forwarded by Dr. Gates showed them to contain calcareous corpuscles, hence the diagnosis of cestode infection was immediately established in this case on the same basis as was the diagnosis in the Japanese case. The cestode in question is a larval form, without suckers on the head, and, as far as seen, without any primordium of genital organs. The most striking feature of the worm is its irregular shape, with tendency to proliferation by forming supernumerary heads. These characters immediately bring up for consideration the question as to whether the worm found by Gates is identical with the parasite recently reported by Ijima (1905) for Japan. As the American and the Japanese parasites are very closely related, possibly specifically identical, it will be well to follow the two in comparison. In doing this, it will be advisable to abstract Ijima's paper rather liberally, more especially since it is published in a journal not generally accessible to dermatologists.

The worm capsule of Ijima's parasite.—Ijima (1905, 4-5) states that the worm capsules of various sizes occur in abundance in all parts of the subcutaneous tissues, and less abundantly in the corium. They were also observed in some numbers in the inter-muscular connective tissue, but not in the muscles themselves, so far as such observation could be made on parts incidentally exposed during the surgical operation. In the corium, the capsule may be situated so close to the epidermis that the latter is externally raised into an acne-like prominence. On a piece of the preserved skin, about two inches square, Ijima found at least four such prominences, which as seen on the surface, appear smooth and less pigmented than the surrounding parts. Capsules so superficially situated might easily be ruptured by force applied through the skin from without.

In shape, the capsules are generally subspherical or ovoid. While the smallest of them are considerably less than 1 mm. long, others measuring 1 to 2 mm. or more are of quite common occurrence; one of the largest seen was elongate, 2.5 mm. broad, by 8 mm. long; another measured 3 mm. by 6 mm. The larger capsules were found only in the subcutaneous parts, not in the corium.

The capsular wall, consisting of a dense felt-work of connective tissue fibres of the host, may reach nearly 0.33 mm. in thickness; in sections the capsules may appear not unlike a transversely cut blood vessel on account of the tough and compact-looking wall; under a hand-lens, the inner surface of the capsule appears smooth; in some of the larger cysts, the internal cavity is traversed by branching trabeculæ; microscopically, the wall either shows no special limiting structure or is lined with a deposit of granular coagulum or tissue debris.

Abundance of parasite.—In Dr. Gates's letter of June 17, he states that his "patient has thousands of" these parasites.

In the Japanese case, a section of about 11 sq. cm. showed nearly 60 capsules; in the most thickly infested portions of the thigh, there was 1 capsule to every 20 sq. mm. of cut surface, or to every 100 cu. mm. of infested tissue; this gives 1000 capsules per 100 cu. cm. of tissue. It was estimated that

there must have been considerably over 10,000 capsules in the left thigh alone.

Worms without capsules.—Scarcely any of the worms Gates forwarded to me bore any remnant of the cyst. Very probably most of these specimens were originally encysted and were freed from their cyst by Dr. Gates before he forwarded them.

Comparatively young, slender, worms were found by Ijima free in the connective tissue, that is, not surrounded by a capsule.—Ijima, 1905.

Movements of the worm.—Not having seen the worm alive, I can give no details regarding movements.

Ijima reports that the living worms, when taken from the patient, showed slow movements of extension and contraction, but effecting little or no change in position; upon cooling, the worms no longer exhibited such movements; in case of worms placed in salt solution, motion could be revived, up to a period of four hours, if the parasites were slightly warmed.

The head (narrow end) was the most motile, evaginating and invaginating at the apex, in addition to shortening and extending; the terminal, but inconstant, depression in some cases reminded the observer of a terminal sucker, such as seen in the fish bothrioccephalid *Cyathocephalus*. In addition to a motion as if feeling about, the head started a lively peristalsis, from before backward; such combined movements would aid the worm in penetrating and moving through tissues.

The broader parts of the body showed at most slow vermiform movements, with more or less constant indentation at the extreme hind end.

The head.—Ijima states that the head of his parasite is devoid of any definitely formed or permanent organ of attachment. This holds true also for the worm found by Gates. In some few specimens a slight apical depression is observed, but as the material is preserved in alcohol, this may be either an artifact or a depression due to sudden contraction on the part of the worm.

Encysted worms.—Gates writes that he found as many as three worms in one cyst. This condition is doubtless due, as Ijima explains also for his case, to the tendency of the worm to multiply by budding.

Ijima reports that the smaller capsules usually contained only a single worm; in the larger cysts, however, two or more worms or pieces were more frequently found; from one capsule, five worms were obtained, and from another, seven worms.

Size and shape.—The longest specimen I have observed is 12 mm. in length. Some of the worms are simple elongated bodies, either more or less flattened, or nearly round in transverse section. The larger specimens, however, assume all manner of bizarre and irregular shapes which cannot be well described. These variations in form may be reduced to a progressive but irregular formation of buds, the apex of each bud representing a structure similar to the cephalic end of the original worm; the form varies, of course, according to the number, position, contraction, etc., of the buds, and according to the contraction of the parent stock. (Plates xxx-xxxiii, Figs. 5 to 15), will give an idea of the great variety of forms found.

According to Ijima, many of the worms are small, filiform, about 0.3 mm. in diameter, 3 mm. in length; others attain, even when moderately contracted, 12 mm. long by 2.5 mm. broad. In some specimens, the body is flattened, dorso-ventrally, but there is no clew to which is dorsal and which is ventral surface. In its simplest form, the worm is plerocercus-like, or narrow at the head and broader caudad, when moderately contracted, or irregularly cylindrical when strongly contracted.

This simple plerocercus-like larva, when encysted, may assume a rather complicated structure, due to its ability to form buds or supernumerary heads, especially on the lateral edges of the flattened body in younger specimens, but quite irregularly in the more complicated older forms. When the heads detach themselves, they represent small independent plerocercus-like larvæ, and their method of formation explains the presence of several worms in one cyst.

The formation of heads, in the manner prescribed, naturally tends to give the worms a very irregular outline; this irregularity is increased by the formation of subcuticular bodies which Ijima interprets as food material. Ijima assumes that these younger heads leave the capsule and wander through

the connective tissue until they grow in size and then in turn form a capsule of their own.

Microscopic anatomy.—According to Ijima, the cuticula of the Japanese form may attain 8μ in thickness; the dermal musculature consists of external circular and internal longitudinal fibres. These statements are correct as applied to the Florida form also.

The *calcareous corpuscles* of the Japanese worm are described by Ijima as spherical or ellipsoidal, 7.5 to 12μ in diameter, and abundant in all parts of the parenchyma except in the head, in which they are lacking. In the Florida form, also, the calcareous corpuscles are abundant; they vary in size from 8.8μ to 17.6μ ; in shape they are spherical to ellipsoidal. Thus, in reference to the size of the calcareous corpuscles, there seems to be a slight difference between the American and the Japanese parasites.

Reserve food bodies.—Ijima has described as present in the parenchyma, certain bodies which he views as reserve food material. Usually they are roundish or oval, 100 to 300μ in diameter; but they may become very elongate.

In the Florida parasite, similar bodies are present, but in the specimens thus far examined microscopically they do not seem to be quite so numerous or quite so large and prominent as described by Ijima for the Japanese form. It is possible, however, that this is a matter of individual variation.

Excretory system.—The parasites as described by Ijima contain an extensive system of anastomosing excretory vessels. In this respect the Florida form agrees with the Japanese species. Some of the canals are quite large, others are smaller, some are very small. Ijima calls attention to the absence of excretory vessels in the peripheral zone of the posterior part of the body; he also states that he was unable to find any opening.

In sections of one of the Florida parasites, fine canals were found rather close to the cuticle, but because of the branched condition of the worm it is difficult to state just what portion of the body this was; it was not, however, a head. Likewise, in one case, sections of a pore (Plate xxxiv, Fig. 18) on the surface, with a centripetally directed canal, were distinctly seen. In

view of the absence of genital organs, one is naturally inclined to look upon this pore as belonging to the excretory system.

The longitudinal *muscles* of the Japanese worm are described as well developed, and in addition there is a less strongly developed set of muscle fibres running in different directions but mainly in the transverse plane. Near the head, these transverse muscles may be quite regular (some dorso-ventral, others crossing these at right angles), but in thicker portions of the body they may become very irregular. This description applies in a general way to the Florida form also.

Nervous system.—Ijima noticed a pair of longitudinal, lateral nerve trunks in the cephalic portion; they seemed to unite close to the tip of the head. In several sections of the Florida worms, nerves were distinguished, but details as to their topography were not studied.

Life cycle.—Experiments to raise the adult stage, by feeding the Japanese parasites to cats, dogs, and pigs, were negative.

As all of my own material was preserved, no experiments could be undertaken. The question as to the source of infection, life cycle, etc., must be left open for the present.

Systematic position.—From the general structure, especially from the presence of calcareous corpuscles, it is clear that both the Japanese and the Florida parasites are cestodes; the absence of suckers seems to place both forms in the old family Bothriocephalidæ, now known as Dibothriocephalidæ. Further than this, the exact systematic position is not clear at present and cannot well be determined until the adult stage is known.

So far as can be judged from the material thus far studied (prior to the meeting of the International Dermatological Congress in New York, Sept. 9, 1907), the Florida form must be considered as very closely allied to, perhaps specifically identical with, the Japanese form. The only anatomical point of difference thus far brought out is a difference in size of the calcareous corpuscles; the only biological difference known is the habitat—in two widely separated localities.

Ijima points out the structural affinities between the Japanese form and the bothriocephalid larval *Sparganium*

of Diesing; he refers also to the similarity between the Japanese form and the *Ligula mansoni* (= *Sparganum mansoni*).

Sparganum is an artificial collective group of worms, distinctly proposed, not as a systematic unit, but as a collective group of larval bothriocephalid cestodes. Under the International Code of Nomenclature (1907), such names may be proposed as a matter of convenience and may be used as if they were generic names; they do not require any type species and hence do not compete with generic names under the Law of Priority.

Both the Japanese and the American parasite may be temporarily classified in *Sparganum*.

The Japanese worm was originally published under the two names *Plerocercoides prolifer* and *Plerocercus prolifer*, but Ijima distinctly states that he uses the names as a matter of convenience, namely, not in a taxonomic sense. Certain objections arise, however, to the use of the names *Plerocercus* and *Plerocercoides* in this connection and on this account I transferred (1906a) the parasite to *Sparganum*.

The nomenclatural points involved are somewhat complex and it may be well to explain them in this place.

Under the original International Code, the names of larval cestodes, and of certain other forms, were for special reasons exempted from the Law of Priority. Later (1901), contrary to the judgment of helminthologists, this exemption was done away with.

To apply the Law of Priority consistently to all such larval names would be almost an impossibility. There are, in fact, many names which have been proposed, not in a generic sense, but as names of admittedly artificial groups, which were used simply as a matter of temporary convenience, and it was on account of a failure to distinguish between names of this category and names proposed for supposed genera, that the exception was rescinded. In 1907, at the Boston Congress, helminthologists proposed the following, which was adopted as part of the Code:

“Certain biological groups which have been proposed distinctly as collective groups, not as systematic units, may be treated for convenience as if they were genera, but they

require no type species. Examples: *Agamodistomum*, *Amphistomulum*, *Agamofilaria*, *Agamomermis*, *Sparganum*.”

As will be shown below, *Plerocercus* and *Plerocercoides* also now come under this paragraph. As matters now stand, it is necessary to show that a name was distinctly proposed to designate an artificial collective group in order to bring it under this provision. A name like *Cysticercus* or *Echinococcus*, originally proposed as generic, not distinctly to cover an admittedly artificial group, is subject, now as before, to the Law of Priority.

The term *Plerocercus* (πλήρης, full; κέρκος, tail) was proposed by Braun (1883a, 98) as designation for the parenchymatous cysticerci (namely, those the caudal portion of which contains no fluid) as distinguished from the bladder worms, or true cysticerci; thus, it is a descriptive term for a stage of development (larva) possessing certain characters, but not the designation of a systematic unit. As examples, Braun cited a *Plerocercus* (*Dithyridium lacertae* Val.) of lizards and a *Plerocercus* of *Tetrarhynchus*. This plerocercus of the lizards happens to figure in a true nomenclatural sense, namely in the genus—

DITHYRIDIUM Rudolphi, 1819.

- 1819: *Dithyridium* Rud., 1819a, 559 (*lacertae viridis*, *lacertae muralis*; Europe. Type by later absolute tautonymy *Piestocystis dithyridium* = *Dith. lacertae*).
- 1850: *Piestocystis* Dies., 1850a, 478, 494-496 (*Dithyridium* 1819, renamed; includes as valid species *P. crispa* Rud., *P. rugosus* Dies., *P. variabilis* Dies., *P. dithyridium* Dies. [for *Dithyridium* of Rud., namely, *D. lacertae* Valenciennes, 1844]).

This genus is based upon a larval tapeworm (a plerocercus) provided with four suckers, and is classified in the family *Taeniidae*; the type species occurs in Europe in lizards of the genus *Lacerta*.

In 1866, Baillet mentioned a parenchymatous cysticercus (namely, a plerocercus) from the abdominal cavity of the cat and dog. In 1882 or 1883, Blumberg described this form

as a new species under the name *Cysticercus elongatus*; the latter name, however, was already preoccupied (cf. *C. elongatus* Leuck., 1842). In 1885, Railliet renamed this form *Cysticercus bailleti*, and in 1893a, p. 314, he classified it in the genus *Dithyridium* as *D. elongatum*. In the meantime, however, Neumann (1892a, 537-539, Figs. 292, 293) referred to the same parasite as "*Plerocercoides bailleti*," clearly using a Latin binominal nomenclature.

The name *Plerocercoides* as used by Neumann is traceable to Braun (1883a, 100), who used a German term, "Plerocercoiden," to designate certain larval forms which differed from the cysticercoids by having parenchymatous tails; as examples Braun cites a form which occurs in the body cavity of *Trichodectis canis*, and the young (*Gyporhynchus*) of *Taenia macropeos* and *T. unilateralis*. Blanchard (1888a, 491) used a French form (*Plérocercoides*) of the word, while Neumann (1892a, 537) seems to have first used the Latin *Plerocercoides*. From Neumann's text, however, it is clear that he based his name on Braun's "Plerocercoiden," hence Neumann's *Plerocercoides* is not a generic name but the designation of an artificial collective group, hence also the type designation (*bailleti*) suggested by myself in 1906 is not necessary under the new (1907) Code.

As a plerocercus may be the larval form of species belonging to widely distinct families, even to different orders, it is wise not to use the combination *Plerocercus prolifer* in case a better designation is available; this point probably occurred to Ijima, for he used the combination only once. *Plerocercoides* is also open to the same objection, and in the only use of the term prior to Ijima, it was used for a *Dithyridium*.

It so happens that Diesing proposed a name which is open to fewer objections. This is the

Collective Group SPARGANUM Diesing, 1850.

DIAGNOSIS.—*Dibothriocephalidae*: An artificial collective group to contain larval stages of bothriocephalid worms, which have not reached a stage in their development that they can be determined generically.

Such groups do not require a type species.

In 1906, I placed Ijima's form in this group as the proliferating Japanese Tapeworm Larva—

SPARGANUM PROLIFERUM (Ijima, 1905), Stiles, 1906.

SPECIFIC DIAGNOSIS.—*Sparganum*: Larva may attain 1 to 12 μ in length and 2.5 μ in breadth; head narrower and more motile than posterior end, and may show an apical depression which, perhaps, serves as sucker; no true suckers or other organs of attachment present. Calcareous corpuscles spherical or ellipsoidal, 7.5 to 12 μ (Japanese worm) or 8.8 to 17.6 μ (Florida worm) in diameter, and situated in any part of body except head; irregularly distributed reserve food bodies present in older specimens, but they later undergo disintegration; genital organs not present; longitudinal muscles better developed than either dorso-ventral or transverse system; transverse fibres do not divide body into cortical and medullary layers; excretory system well developed, consisting of larger approximately longitudinal branches, with anastomoses. The larvæ possess the power of multiplying by transverse fission and of forming supernumerary heads which may become independent. Adult unknown.

HABITAT.—Encysted in subcutaneous tissue and elsewhere in man.

GEOGRAPHICAL DISTRIBUTION.—Found but twice; once by Ijima in Tokyo, Japan; once by Gates in Manatee, Florida.

Whatever results may be obtained from examination of further material, which I could not study prior to the meeting of this Dermatological Congress, at the present time I do not feel justified in separating the American form specifically from the Japanese species, despite the difference in geographic distribution and the slight difference in the calcareous corpuscles. That the adult stage may eventually prove the Florida form to represent a distinct species seems entirely possible; in fact, when we consider the seeming isolation of the two cases, this appears probable. At the same time, if it should eventually be shown that the infection was contracted from eating marine fish, the possibility would not be excluded that the two forms are identical, despite the wide difference in locality. In the



FIG. 1.



FIG. 2.



FIG. 3.



FIG. 4.



FIG. 8.

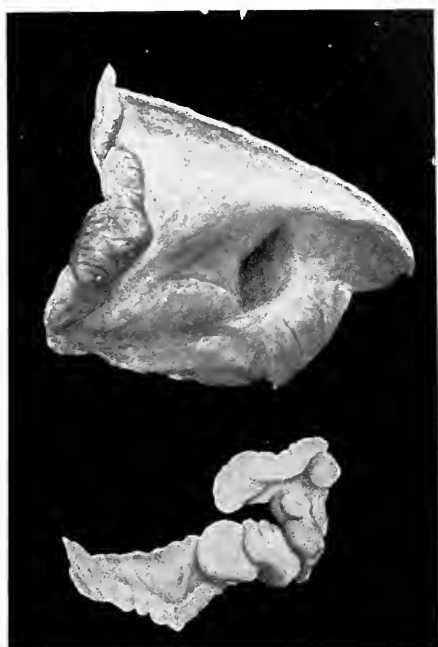


FIG. 9.



FIG. 10.

L. H. MILDOR, DEL.



FIG. 11.



FIG. 12.



FIG. 13.

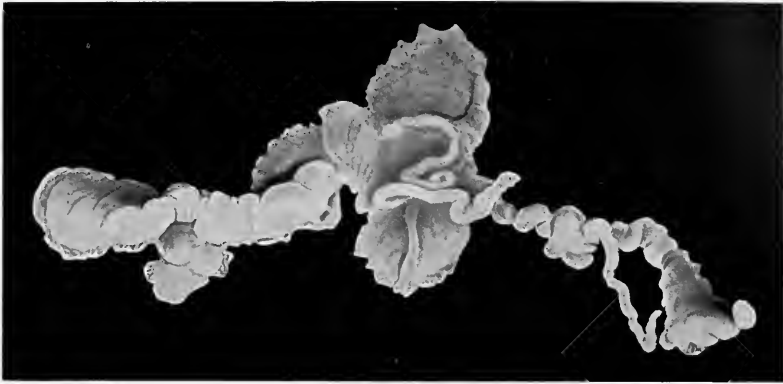


FIG. 14.



FIG. 15.



FIG. 16.

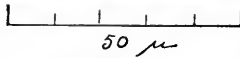
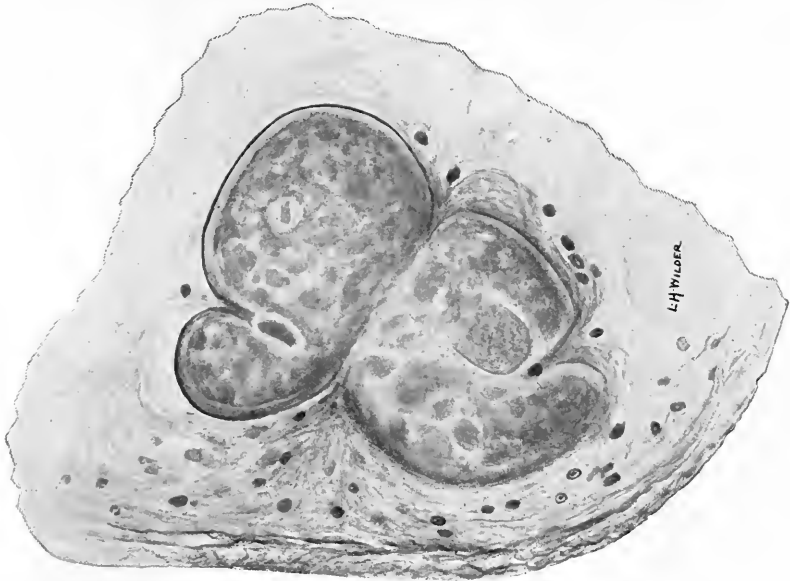


FIG. 17.

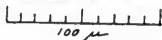
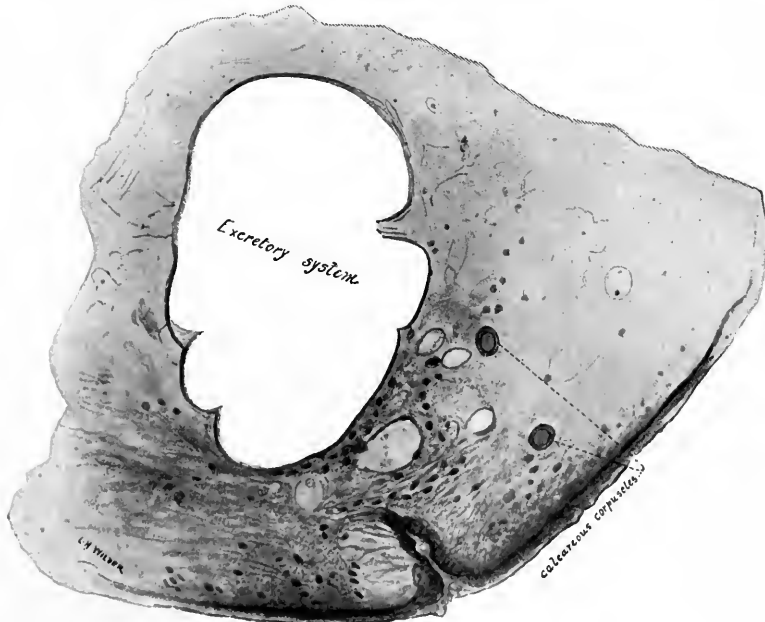


FIG. 18.

interest of conservatism, accordingly, I classify, for the present, the two in the same species.

In an earlier paper (1906a, 86) I called attention to the fact that because of the remarkable reproduction of the larval stage described by Ijima, a new genus would probably be justified. I hesitated somewhat to make the genus without seeing actual specimens. After examining the American specimens, I am further convinced of the probability that the worm in question represents a new genus.

The proposition of a new generic name at this time presents both advantages and disadvantages. To continue to call the worm *Sparganum* shows that the family position is recognized, but that the adult is unknown; the worm is, however, so different from the other forms of *Sparganum* that it seems advisable to bring out this difference in a generic name; further, as long as a new generic name seems almost inevitable, it would appear wise to introduce it as soon as possible, in order to reduce its competition (through homonymy) in the future. On the other hand, to introduce a new combination at present does not seem absolutely necessary; its introduction would destroy the advantages we have at present in the use of the name *Sparganum*.

There is, I believe, a conservative method by which the advantages of both plans may be united, namely, by the introduction of a new subgeneric name. This course permits the continuation of the use of the name *Sparganum*, and at the same time brings out the fact that the worm is very different from the other forms of *Sparganum*; further, it procures for the name any advantages in homonymy which may be gained by its proposal this year instead of later.

As such subgeneric name, I propose

GATESIUS¹ n. subg.

DIAGNOSIS.—*Dibothriocephalidae*, ? *Ligulinae*, classified temporarily in *Sparganum*: Adult unknown. Larva, in its simplest form, similar to the plerocercus of *Dibothriocephalus* except for suckers, which are not indicated; possesses the pro-

¹ Dedicated to Dr. H. Gates, of Manatee, Fla., who found the first American case.

perty of branching and of reproducing by budding, thus forming supernumerary heads which become free from parent and assume a simple plerocercoid form. Body contains numerous calcareous corpuscles, richly developed canal system, and may contain reserve food bodies.

TYPE SPECIES.—*Sparganum (Gatesius) proliferum* (Ijima, 1905) Stiles, 1908, from connective tissue of man; Japan.

It will be noticed that from the form of this proposal, the name *Gatesius* is proposed not as name for a collective group, similar to *Sparganum*, but as a true systematic name of subgeneric rank. When the adult form becomes known, the species should be taken out of the group *Sparganum* and this subgenus raised to generic rank.

PLATE XXIX, FIGS. 1-4.—Four photographs of Gates's patient in Florida, showing acne-like condition and enlarged breasts due to infection with *Sparganum proliferum*. Original; photos kindly furnished by Dr. Gates.

PLATE XXX, FIG. 5.—*Sparganum proliferum*, in part in a cyst. Original. $\times 10$.

PLATE XXX, FIG. 6.—*Sparganum proliferum*, escaped from the cyst. Original. $\times 10$.

PLATES XXX-XXXIII, FIGS. 7-15.—Nine specimens of *Sparganum proliferum*, showing various forms, buds, and supernumerary heads. Original. $\times 10$.

PLATE XXXIII, FIG. 16.—Section through a cyst (a), with the escaped *Sparganum proliferum* (b); x, reserve food particle. Enlarged. Original.

PLATE XXXIV, FIG. 17.—Section through a reserve food particle (see x, Fig. 16). Enlarged. Original.

PLATE XXXIV, FIG. 18.—Section showing: large excretory canal, smaller canals, calcareous corpuscles, and a pore. Enlarged. Original.

THE CLINICAL GROUPINGS OF TROPICAL ULCERS OF THE PHILIPPINES, WITH SOME NEGATIVE NOTES AS TO ETIOLOGY AND TREATMENT

BY SURGEON E. R. STITT, U. S. NAVY

During the first few months of my service in the Philippines the question of the nature of the various ulcerations so common among the natives interested me greatly.

The findings of Wright as to the presence of Leishman-Donovan-like bodies and the negative results regarding them obtained by Strong, together with his putting forward of a yeast-like organism as a possible causative factor, made the subject seem one that might offer great opportunities for investigation.

Keeping in mind the type of ulceration described under the various designations of Aleppo Evil, Delhi sore, and Bagdad boil, I was constantly on the lookout for ulcerations which would clinically correspond with the descriptions of these diseases.

Of the many articles describing these sores the most concise and satisfactory ones are:

I. *As Regards a Division into Stages.*—Where in an article on Aleppo Evil, Cazenave and Schedel quote from M. Guilhou, who, in 1835, described the condition in three stages: *first*—of eruption: a lenticular swelling which gradually increased during four or five months without general symptoms; *second*—of suppuration: in which deep and irregular ulcers were a prominent feature during the succeeding three to five months; *third*—a stage of desiccation: in which dry tenacious scabbing occurred for the remainder of the year.

II. *From a Clinical Standpoint.*—The description of the late Sir Joseph Fayrer (*The Practitioner*, 1875, pp. 264) is a most excellent one. He describes it as an indurated indolent sore at first papular, later encrusted and fungating. The small red papule gradually enlarges during several weeks, then becomes an indurated sore.

He notes that inoculation was only successful by the introduction of the specific cell matter and not the exuding pus.

After observing in the natives a number of chronic ulcerations, especially of the lower extremities, and finding that clinically they did not differ from ulcerations which might be expected from badly infected and neglected wounds, or from the infective granulomata, and that from a standpoint of history there was the single common statement of long duration, I came to the conclusion that the form of tropical ulceration as described in the books did not exist in the Philippines—at any rate in the hospitals.

Subsequently, in Guam, I observed the same thing. Many cases of most extensive and frightful ulcerations of the extremities were noted, in none of which could one eliminate the possible cause of tuberculosis or infected yaws when those due to leprosy were set aside. It was impossible to obtain a history of a papular, comparatively painless swelling, lasting

several weeks or months—in other words, there was nothing to connect such cases with oriental sore.

It is interesting to note that the Spanish of the island of Guam divided their quarantinable skin cases into three types: (1) the *gangosas*, when the ulceration was confined to oral and nasal cavities; (2) the *leprosos*, where in addition to face lesions there were the various leprotic lesions of the extremities; and (3) the *llagosos*, which would include those cases principally showing lesions of the lower extremities—possibly tuberculosis—possibly tropical ulcer.

That the confusion existing as to the clinical characteristics of oriental sore was due to mistaking cosmopolitan skin affections for the more geographically circumscribed oriental sore is clearly shown in a contribution by Dr. Gebers in the "*Archiv für Dermatologie und Syphilis*," 1874, where he takes issue with those calling all ulcerations about Aleppo, Aleppo Evil, when he, upon an examination of a series of so-called cases, found the greater proportion to be either syphilitic, tuberculous, or eczematous. Any one reading the classical descriptions on the subject of oriental sore in *Endemic Skin and other Diseases*, Tilbury Fox, 1876, must be convinced that the descriptions by various observers certainly refer to a variety of skin lesions.

The confusion as to clinical course and characteristics which had existed in my mind from my earlier observations of these skin lesions was in a measure cleared up by the opportunity of observing several cases among Americans—most of these coming from sailors under treatment in the Naval Hospital, at Canacao, P. I.

These cases were of two distinct types—the one more nearly conforming to the description as given by Fayrer—the latter to Jeanselme's description of tropical phagedena. As regards the first type: 1. A history of a red spot or lump coming generally on the outer surface of the lower extremities which had gradually enlarged as a painless swelling. While not subjectively painful and only slightly tender to pressure yet complaint was made of a stinging sensation of pain when the swelling was sharply struck. There is considerable itching at times and I am inclined to think that

some of the scaling described as preceding ulceration may be secondary to scratching. 2. After slowly enlarging for from four to eight weeks this circumscribed reddened glazed area of skin, giving about the sensation of a solid oedema on palpation, begins to exude from its summit a serum which quickly dries and crusts. Just prior to this it would be mistaken by the average practitioner for a blind boil. 3. Ulceration now proceeds under this encrusted secretion more or less rapidly. There is only a scanty discharge of a serum-like at times, sanious, secretion which tends to crust over. The ulcers are shallow with irregular, somewhat undermined edges. Later on the ulcers are more or less punched out and may show considerable induration. In some instances I am disposed to think that the induration was the result of frequent cauterization. 4. These remarkably painless chronic ulcers in a person whose health seems unimpaired continue for from three to six months, varying only as a result of the trial of some new form of treatment. In our most characteristic case where there were several of these ulcers the patient enjoyed robust health. 5. After from two or three months to a year these ulcerations show a tendency to heal under the crusts and eventually give rise to a pale, somewhat puckered, cicatrix with pigmented margins.

The shortest period in which the discharge showed itself—that is, in which ulceration set in—was twenty-two days. It is as a rule much longer.

These ulcerations when curetted failed to show any pyogenic organisms. The smears, as will be seen in the specimens exhibited, show practically an absence of polymorphonuclears, cells of the lymphocyte type predominating. There are many large cells, 20 to 30 μ in diameter, some of which look as if full of small circular bodies which, however, show no chromatin staining (Giemsa's method).

Now as to the second type of ulceration observed: These sores were observed in persons greatly debilitated. It is interesting to note that in one case the sore was attributed to the eating of mangoes, an idea which was advanced by some of the early Indian writers on this subject.

In the earliest stages these sores seem to resemble an area

which has been excoriated and inoculated with vaccine virus, there being a rather dry, angry-looking spot of erythema. This within a few hours may be surrounded by a circle of vesicles beyond which is an encircling inflammatory areola. There is marked subjective pain with tenderness. The serum from the vesicles fails to show any bacteria, and the cellular contents are made up almost entirely of polymorphonuclear leucocytes. Within a few hours to one or two days the area within the ring of vesicles is converted into a dark gray to black pultaceous diphtheroid membrane which when detached shows underlying fungating granulations covered with greenish yellow pus. This membrane, if stripped off, tends to reform with great rapidity (twenty-four to forty-eight hours), and in many respects resembles the membrane of diphtheria, except for its dark color.

These ulcerations extend with great rapidity and even when showing a tendency to heal may suddenly, from a point along the margin, proceed to form a new area of ulceration, extending somewhat as would a ringworm. When the original site of ulceration fails to heal during a period of several weeks, the edges become rather indurated but do not show the punched-out or undermined characteristics of the first type.

These cases last for months and are far more tantalizing than the former type of ulceration for the reason that from time to time they show a strong tendency to heal, the process clearing up almost entirely, when suddenly the former area of the ulceration is equalled or exceeded.

In the former type of ulceration there is rarely any tendency to healing so that a favorable prognosis is not given.

Smears made from the surface of the granulations underneath the diphtheroid membrane¹ show a profusion of polymorphonuclears with an abundance of a branching, irregularly staining organism which somewhat resembled diphtheria, but was larger and did not show parallelism or involution characteristics. There was a total absence of any cocci or other bacteria.

The organisms described by LeDantec as occurring in cases of tropical phagedena apparently were similar but of

¹ Specimen shown before the meeting.

larger size. James, in referring to Naga sores, states that he found polymorphonuclears in great numbers, but does not record the finding of any bacillus. It will be remembered that he found a striking absence of polymorphonuclears in the Delhi sores examined by him and in which he found parasites corresponding to the *helcosoma tropicum* of Wright or the Leishman-Donovan bodies.

Strong refers to a third type of tropical ulcers in which there were various clinical manifestations but in which there were found staphylococci. Such cases were frequently observed at Canacao and presented all types clinically from simple vesicles to pemphigoid lesions and from impetigo-like pustules to extensive erysipelatoid areas going on to necrotic processes and spreading ulcerations. In one case the abdominal muscles were involved. All of these cases showed in smears an abundance of a diplococcic organism which upon culture gave all the characteristics of the staphylococcus *pyogenes aureus*. Although culturally the same organism yet in its clinical manifestations of virulence and variations as to phagocytosis observed in stained films it would appear to be an organism of wide range of pathogenicity.

Wherry and Clegg described such an organism under the name of *diplococcus pemphigi contagiosi*.

Woolley (*J. A. M. A.*, March 2, 1907), considers that Dhobie itch is an important factor in tropical ulcer.

After a study of a large number of such cases in which at times I found various moulds of different types in profusion, and again, after repeated examinations, nothing whatever to account for the extensive erythema, I am very skeptical of the existence of any specific organism for this exceedingly common affection. In several of our cases of tropical ulcer there was no history of Dhobie itch and the large number of cases of the latter affection only furnished a very occasional case of tropical ulcer, so that I am sure the coexistence of the two diseases could only be of the nature of a coincidence.

There is one point about fulminating cases of Dhobie itch, however, which I have noticed and which I have never seen brought out, and that is that in such cases a symbiosis

seems to exist between an infecting mould and a coccus. In the midst of a mass of mycelium in a smear one would observe areas studded with staphylococci. These cases showed a virulence far surpassing those in which only a mycelium and its spores were demonstrated. Whether the symbiosis increased the virulence or whether the cocci facilitated the extension of the mould I am unable to conjecture.

The foregoing clearly brings out the negative character of the etiological consideration of tropical ulcer as observed by me in the Philippines. As regards therapeutical considerations, I feel constrained to follow the views of Osler as to whooping cough—in other words, I should sum up the treatment of tropical ulcer as four months of development, four months of ulceration, and four months of cicatrization. The French do well to call it the *bouton d'un an*.

It is needless to state that we tried every ordinary treatment that had ever been suggested. Among the special treatments which were tried and which at times appeared to give favorable results, but which again were without effect, may be mentioned:

1. Pepsin and hydrochloric acid locally (artificial gastric juice).
2. Ice bags.
3. Excision of the entire lesion. (In every instance in which this was practised additional lesions made their appearance.)
4. Thorough cauterization with pure carbolic acid and after one or two minutes neutralization with alcohol. (On the whole this gave the most favorable results.)
5. Bier's passive congestion method. (This was very painful and did not benefit in the least.)
6. Massive doses of potassium iodide combined with rest. (Apparently of benefit in some cases.)

I have to thank Assistant Surgeon H. W. Smith, U. S. Navy, for the use of the notes of some of his cases and for valuable suggestions in the preparation of this paper.

GANGOSA WITH ADDITIONAL NOTES

BY O. J. MINK AND N. T. McLEAN, PAST ASSISTANT SURGEONS,
U. S. NAVY

Since the publication of our original paper on this subject, (*Jour. A. M. A.*, Oct. 13, 1906), additional literature, not available at Guam, has been studied, and a few further facts regarding certain phases of the disease have been obtained. At the suggestion of Dr. Fordyce, we will present the facts of our original paper, modified by the recent work and observations.

Definition.—Gangosa, a Spanish word meaning muffled voice, is the name employed by the Spaniards in the Ladrone and Caroline Islands to describe a disease characterized by a destructive ulceration, usually beginning on the soft palate, pillars, or uvula, and extending by continuity to the hard palate and nasal cavity, larynx, and even to the face. Active ulceration is followed after a variable period by cicatrization or chronic ulceration. Mutilation always results. Constitutional symptoms are either slight or absent.

Synonyms.—Rhinopharyngitis mutilans (Leys). Ogo (Chamorro).

History and Geography.—The disease has existed in Guam for at least 150 years. In 1828 a Spanish Royal Commission, investigating conditions in the Ladrone Islands, recognized and named the disease and recommended the isolation of all patients. It exists throughout the Ladrone and Caroline Islands.

The case from Panama reported by Fordyce and confirmed by Arnold (*Jour. Cut. Dis.*, Jan., 1906) is undoubtedly true gangosa. Dr. Fordyce examined pathological material from two cases from Guam and reports the findings identical with those from the Panama case.

Surgeon J. F. Leys, U. S. N. (*Jour. Trop. Med.*, Feb. 15, 1906), has carefully studied the literature, and mentions reports of rhinopharyngeal ulcerations in Fiji, British Guiana, Jamaica, Italy, Dominica, and Nevis. Dr. Leys, who is familiar with the disease as it exists in Guam, has recently discussed the cases found in Dominica and Nevis with Dr. J. Numa Rat, the recorder of these cases, and believes the disease may exist in the West Indies as well as in Polynesia. We have not seen Dr. Rat's original report, but we understand that he reports in his cases an initial lesion resembling a tubercle. None of our cases in Guam showed this condition.

Branch (*Jour. Trop. Med.*, May 15, 1906) reports his cases in Nevis and St. Kitts. He considers them syphilis, and not a distinct disease. His report will be discussed later in speaking of syphilis.

In January, 1907, Musgrave found one case in the Philippines. This case was seen by Dr. McLean, who considered it a case of gangosa. Since then two other cases have been found in Manila. Dr. Musgrave believes there are many other cases, especially in the southern islands.

Etiology—General Prevalence.—Although only 125 cases have been examined in Guam, there are probably 200–250 cases on the island. The population of the island being about 11,000, the ratio is 18–22 per thousand. As the natives of the various parts of the island are intimately associated by religious, marital, and commercial relations, no topographical distinctions can be made.

Season.—The limited number of cases seen during the period of invasion makes it impossible to give any definite statement concerning the effect of season.

Age.—In a series of 80 cases, the ages at the time of invasion were as follows:

First decade.....	2
Second decade.....	38
Third decade.....	23
Fourth decade.....	13
Fifth decade.....	2
Sixth decade.....	2

The youngest ages at invasion were 3 and 9 years; the

oldest were 54 and 59 years. From these figures it appears that the majority of the cases start during the second and third decades.

Sex.—In the above series of 80 cases, 49 were in females, and 31 in males.

Immunity.—Surgeon E. R. Stitt, U. S. N. (*Nav. Med. Bull.*, July, 1907), reports a case in a United States marine, who had been in Guam for several years, and, while there, associated intimately with gangosa families. He developed the disease about four months after leaving Guam. This is the only known case of the disease in the white race. Dr. Fordyce's case was a negro. Cases in persons of mixed white and native blood are infrequent. The great majority of all our cases appeared in the pure blood natives. The relative immunity of the white and mixed races may be explained by the superior hygienic and dietetic surroundings of these races.

Heredity.—There is no evidence showing that heredity plays any part in the transmission of the disease.

Food.—The native theory and that held by the Spaniards, gives food a prominent place in the causation of the disease. They believe that such foods as decomposed or very salty fish, especially if eaten raw, uncooked taro, and native pepper are the direct causes of the disease. This theory seems improbable. The eating of tainted fish is not more frequent than in any other fish-eating community, and when eaten the usual symptoms of ptomain poisoning occur. Cases of gangosa rarely give a history of such poisoning. The eating of very salty fish, raw taro, and native pepper is not sufficiently frequent to explain the large number of cases. Furthermore, cases are seen in natives eating the same food as the whites.

A Manifestation of Syphilis.—The disease has been considered a late manifestation of syphilis. During a year and a half in Guam we did not see syphilis in any type among the native population, and do not believe it exists. Our observations agree with those of Leys,¹ who states:

“It [gangosa] appears in healthy and well developed

¹ Leys: *Report of the Surgeon General, U. S. Navy*, 1905, p. 93.

persons of all ages, and no signs of hereditary syphilis in their own persons or in their brothers and sisters, and with no signs of syphilis in their parents. . . . Acquired syphilis is a common disease in most races over nearly the whole world. It is an extremely rare disease here, and neither primary nor secondary syphilis has been seen in a native during the past year, among thousands of persons treated for other diseases, including several prostitutes. This disease is common here, and rare or unknown where syphilis is common. Dr. Daniels, who was in Fiji for years, states that there was no syphilis in Fiji at a time when the lesions of this disease were common. The appearance of the primary lesion of this disease in otherwise healthy children of healthy parents, at 3, 4, and 9 years of age, excludes acquired syphilis."

In the *Journal of Tropical Medicine*, May 15, 1906, Branch, in speaking of his cases in the West Indies, takes issue with Dr. Leys as to the advisability of considering this condition as a distinct disease, and classes it as a manifestation of syphilis. He offers no proofs, and in the main sums up his article as follows:

"Considering the incalculable importance to the human race of the recognition of syphilis and the difficulty, as yet, of confirming the diagnosis by any certain test, it is most inadvisable to claim independence for any condition which may reasonably be attributed to syphilis, until its etiological individuality can be established. Far better to treat everything as syphilis than to miss the diagnosis of half the cases of syphilis."

We cannot agree with Dr. Branch in this last statement in so far as Guam is concerned. Tolfree, Leys, Grieve, Bagg, and Stitt all agree that syphilis is practically unknown in Guam. During our tour of duty there, we saw no syphilis in the native population, although some twenty-five prostitutes were examined weekly.

Dr. Branch says in addition: "I noticed in a hospital report for 1902 (*Colonial Reprints Medical Reports*, 1904) that destructive rhinopharyngitis was exceedingly common on the leeward side of St. Vincent, while on the windward side destruction of the face took its place. Syphilis is equally

prevalent on both sides of the island, but the land conditions are very different. . . ." It would seem from this report that the facial ulceration is not a sequel to the rhinopharyngeal lesions, while this was always the case in our series and is, we think, one of the important points in the diagnosis of gangosa. Evidently in the above report two distinct conditions are included, occurring in different individuals and not in the same person as is the case in gangosa.

Dr. Branch does not state whether his cases reacted to specific treatment, but from the confidence with which he calls the condition syphilis, it is not improbable that this is the case.

A consideration of the above facts and a careful study of the description of the disease as seen by Dr. Rat (abstracted in Dr. Leys's article *Jour. Trop. Med.*, Feb. 15, 1906) might lead to a reasonable doubt that the conditions in Guam and the West Indies are identical.

A Sequel of Yaws.—Gangosa has been described as a sequel of yaws. Only one of our cases gave a history of this disease. While gangosa is limited to a few localities, yaws is a common disease in most tropical countries. We see no reason to consider it as an etiological factor.

Specific Infecting Agent.—Our observations lead us to believe that there is a specific infecting agent, the nature of which is as yet undetermined. It is believed that in the transmission of the disease flies are an important factor. The lesions of gangosa are so exposed that flies are attracted in great numbers, and, while feeding on the exudations, their legs, wings, and bodies are contaminated. They in turn may infect the patient directly or indirectly through the food. The use in common by all members of the family of such articles as towels, clothing, pipes, cigars, and betel-nut, with absence of dietetic hygiene, renders direct infection probable. The individual vital resistance is lowered by overcrowding, fifteen to twenty persons, as a rule, sleeping in a small, unventilated hut. The resistance being lowered by such environment, the disease is easily transferred.

Very few facts are available concerning the incubation period. In the case reported by Surgeon Stitt, the incubation period was at least several months.

Inoculation.—We saw no cases which would indicate that infection by inoculation occurs. Dr. Fordyce (*Jour. Cut. Dis.*) injected infected material subcutaneously into a guinea-pig. Within three months a superficial ulceration appeared, extending from the root of the tail, where inoculation was made, over the back, causing a loss of hair. The guinea-pig did not give the tuberculin reaction with 4 mg. of tuberculin, and sections and inoculations from the ulcer were negative.

Morbid Anatomy.—As the disease is not fatal, autopsy is only possible when death results from intercurrent disease. The gross lesions are superficial, and can be observed about as easily in the living as in the dead subject. In speaking of the pathological histology of his Panama case, Dr. Fordyce states (*Jour. Cut. Dis.*):

“The lesion was a granuloma, the nature of which could not be determined by the methods employed. It could be differentiated from others of this class, like blastomycosis, actinomycosis, rhinoscleroma, and lepra, by the absence of their specific micro-organisms; from mycosis fungoides, by the character of the infiltrate and the absence of fragmentation. The histological picture could be readily mistaken for tuberculosis, as the giant cells were numerous, with nuclei arranged peripherally, and, as is often seen in that type of inflammation, many independent foci containing three or four such cells were encountered deep in the corium. The epidermic hyperplasia was such as is met with in hypertrophic lupus and other forms of skin tuberculosis; but as it is seen also in blastomycetic dermatitis and other cutaneous inflammations, its presence is of slight diagnostic importance. The existence of a tuberculosis, however, would seem to be conclusively disproved by the failure of the inoculation and tuberculin tests, as well as by the absence of bacilli in the secretions and sections.

“It is also probable that the affection was distinct from yaws, as such vascular changes, giant cells, small number of leucocytes, and great disintegration of fibrous stroma are not characteristic of the latter. It is not unlikely that many of the so-called tertiary manifestations of yaws are in reality not due to that disease, but to another infection identical with the one under consideration.

"It was difficult to exclude syphilis microscopically, but the presence of many giant cells and the less definite perivascular sheathing might be considered in favor of another diagnosis."

Two specimens from Guam were sent to Dr. Fordyce. His findings correspond in all details with those of his Panama case.

SYMPTOMS

Onset.—We observed only three cases from the earliest stages of the disease. The majority of patients present themselves for treatment only after mutilation is marked. In the three cases above mentioned, the initial symptoms led to a diagnosis of tonsillitis, pharyngitis, and laryngitis of mild degree. The patients were between the ages of 12 and 15 years, and were in good physical condition. Prostration was slight or absent. All showed a slight rise of temperature and complained of soreness in the posterior nares and pharynx, with stiffness in the muscles of deglutition. In one case, a typical acute coryza was present. Inspection, at this time, showed mild congestion of tonsils, pillars, soft palate, and uvula. During the first week, the general condition was practically unchanged.

Local Symptoms.—The throat symptoms became localized, and on the third day a patch of yellowish-gray membrane was observed on the soft palate in the first case, the uvula in the second, and the right pillar in the third case. The membrane was elevated, thick, and tenacious. On removal, the denuded surfaces bled freely. Within twenty-four hours of the appearance of the membrane, the typical ulceration was established. On the area covered by the membrane, a number of small depressions appeared. The ridges between the depressions and the membrane were rapidly absorbed. The ulcer, now about one-half inch in diameter, had a punched-out appearance, with undermined edges and a deep, uneven floor, covered with a yellowish-white, very offensive discharge. It was surrounded by a zone of inflammation about one-fourth inch in width. The depth of the ulcer rapidly increased, until, in the cases of the uvula and soft palate, the

tissues were perforated by the seventh day. These cases are still under observation.

Course of the Disease.—After the first week, no marked changes occur in the character of the ulcer. It progresses steadily, the rapidity varying with the individual case, destroying the bony and soft parts with equal ease. This active stage may continue indefinitely, or may become arrested at any period. The average duration in those cases of our series, which later became quiescent, was about two years. The active stage in those cases varied from one to seven years in duration. In seven cases, which have never been quiescent, the disease has progressed slowly but steadily, the shortest having continued for ten and the longest for thirty-five years. At any time during quiescence, the disease may again become active. This activity may continue indefinitely or pass into a second stage of quiescence. These alternate periods of activity and quiescence may occur repeatedly. When inactive, the zone of inflammation is replaced by a more or less perfectly scarred area, from which an abundant and very offensive discharge pours. At no time during either stage is the patient's general health materially affected.

Fulminating Gangosa.—This type occurs in children under five years of age, and all cases seen have been in gangotic families. In some instances, two or three children in the same family have been attacked. The sudden onset, extreme prostration, extensive membrane, marked cervical adenitis, and rapidly developing toxemia and dyspnoea give a picture closely resembling diphtheria. Surgeon C. P. Bagg, United States Navy, states that cultures from the throats were negative for Klebs-Loeffler bacilli. Death occurs from toxemia rather than from dyspnoea. The great majority of these cases prove fatal within forty-eight hours, but if the patient survives this period the typical mutilation rapidly develops, and the case follows the usual course.

COMPLICATIONS

All complications result from the direct extension of the disease, and vary in severity with the extent of the ulceration (Plate xxxv). The principal parts which may be involved are

the nose, hard palate, and superior maxilla, larynx, eyes, face, and teeth.

Nose.—This organ may be totally destroyed. There was some degree of involvement in sixty-five out of eighty-one cases. The septum and the turbinates are attacked early. The supporting structure is destroyed, the external soft parts sink, and later may be destroyed, the organ being replaced by an opening. The sense of smell is destroyed early in the course of the disease.

Hard Palate and Superior Maxilla.—The hard and soft palate may be scarred, perforated, or entirely destroyed. It was involved in sixty-five out of eighty-one cases. The destruction of the hard palate starts at the juncture of the two superior maxillæ. This deformity produces the typical "cleft palate voice," from which the disease takes its name. The involvement may be of sufficient extent to cause loss and deformity of the upper teeth.

Larynx.—In eighty-one cases, the larynx was involved in thirty-three. Involvement varies from slight ulceration to total destruction, and as a result the voice is husky or absent.

Face.—Ulceration extends peripherally from the oral and nasal openings, or from the common opening when the upper lip is destroyed.

Eyes.—These become involved when facial ulceration destroys the lids. The eyes were involved in twenty-one cases. The sequence in destruction is conjunctivitis, corneal opacity, staphylomata, and finally blindness.

Tongue.—The tongue and muscles of deglutition were unaffected.

Hearing.—Hearing was affected in only two cases.

DIAGNOSIS

To those who have ever seen a case of gangosa, diagnosis offers no difficulty. The primary rapid ulceration, consequent mutilation, and subsequent chronic ulceration produce a picture seen during the active stage. During the quiescent stage, the ulceration is replaced by scar tissue.

Differential Diagnosis.—Gangosa is differentiated from (1) leprosy, by the sudden onset with immediate localization,

absence of fatal termination, and absence of *B. leprae*. (2) Lupus of the mucous membranes, by the sudden onset, local appearance of the throat symptoms, absence of tubercle bacilli, and absence of tuberculosis elsewhere. (3) Syphilis, by the absence of history and symptoms, and the failure of specific treatment.

Fulminating gangosa is diagnosed from diphtheria by the absence of Klebs-Loeffler bacilli and by the typical mutilation in those cases which survive.

PROGNOSIS

Except in the fulminating type, the disease *per se* is never fatal. The mutilations and complications are permanent, and cause corresponding disability. Intercurrent diseases follow a typical course and are not more severe than in those unaffected with gangosa.

PROPHYLAXIS

The contagiousness of the disease has been recognized by the Spaniards in Guam for almost a century. They established a colony for the segregation of these cases, which was discontinued at the time of the American occupation. There is good evidence showing that this abandonment of segregation has increased the prevalence of the disease in Guam. In view of the fact, the Governor of Guam, on April 9, 1906, issued an order providing for the segregation of cases of gangosa. This order went into effect April 18, 1906, and over sixty of the cases were isolated.

In the fulminating type, rigid quarantine should be established, the unaffected members of the family being removed and kept under observation.

Surgeon E. R. Stitt, U. S. Navy, in the Report of the Surgeon General, U. S. Navy, 1906, states: "To present briefly the gangosa problem, we have the following considerations: 1. Gangosa is a disease which results in the most frightful mutilation unless it can be checked by measures taken in its incipiency. 2. It is considered by all to be a disease which is contagious, affecting in many instances, a large proportion



of a family, and in authentic cases those occupying a house previously occupied by gangosa. It is believed to be less infectious than tuberculosis, but more so than leprosy. 3. In one undoubted instance, it has attacked a white man. 4. The liability of the disease to sudden recurrence after a period of quiescence makes it peculiarly dangerous. 5. The experience of the Spanish indicates that by methods of segregation the spread of the disease can be controlled."

TREATMENT

There is little doubt that treatment in the early stages limits the progress of the disease. The treatment is essentially local, and should aim to destroy the infected area. Tincture of iodine, applied freely, appears to be the best agent for this purpose. Lunar caustic, phenol, and chromic acid have been used. It is believed that in some cases the actual cautery would be the most effective agent. An antiseptic mouth wash should also be used. Tonic treatment, when indicated, should be given. Potassium iodide, even in large doses and long continued, appears to have no effect on the disease. Fordyce, Musgrave, and Stitt report the failure of specific treatment in their cases. In chronic cases, deodorants should be used. Potassium permanganate in one per cent. solution has proved the most advantageous. When possible, complications should receive their appropriate treatment. It seems reasonable to believe that the X-ray, Finsen light, and radiotherapy would be of service in the treatment of this disease, more especially in the chronic external ulceration. In the fulminating type, treatment should be symptomatic, combined with active local disinfection.

Discussion

DR. W. F. ARNOLD, United States Navy (Retired), said that he had been able to differentiate clinically, more by good luck than otherwise, the condition known as gangosa, that he had been the first American to describe it as an entity on the Island of Guam, and that he had had the good fortune to add slightly to the description of the case illustrating the condition, which was published in collaboration with Dr. John A. Fordyce,

of New York, in January, 1906, in the *Journal of Cutaneous Diseases*.

This admirable elucidation here of the subject of tropical diseases, especially those of the skin, contained in the papers of Drs. Radcliffe-Crocker and Stiles, and the researches of Surgeon Stitt, U. S. Navy, illustrated the scope as well as the importance and difficulty of the subject.

With reference to the relation of these diseases to syphilis, very much was still to be learned, in Dr. Arnold's opinion.

In order to correct the misapprehension that syphilis did not exist on the Island of Guam, Dr. Arnold said that during his short service there he had seen a native hospital attendant with distinct mucous patches, and subsequently he had found the native woman who had caused this man's infection. Those were the only two cases he knew of, not excluding any clear manifestation of distinct hereditary syphilis, for which he had looked in vain, with the exception of an Eurasian of some sort in one of the Navy ships there who was also infected. This last instance illustrated the certainty of its continuous importation. The speaker thought there was no doubt that syphilis had been introduced into the island, inasmuch as Guam was often visited by whaling vessels operating off the coast of Japan. What modification race and climate would effect, or had effected, remained to be shown.

Dr. Arnold said that recent investigations had made it clear that white men who were necessarily exposed to earth contaminated with hook-worm larvæ would certainly become victims to hook-worm disease, and he was inclined to believe that this was the cause of the epidemic that must have occurred among the Northern soldiers in prison at Andersonville, Ga.

He said that he was glad to accept Dr. Stiles's statement in the spirit in which it had been offered. Still, as a Southerner he was convinced, as General Lee had been convinced and as he had testified before a Committee on the Conduct of the War, that the Federal prisoners in the South had received the Confederate ration. He explained that he did not wish to commend that ration—of 1863-65—as a diet for sick soldiers, especially for hook-worm patients; but, he added, that he had no apologies to make for it beyond the bare statement of this fact. He said that he should always much esteem it, if anything that he had done, or that he could hereafter do, would alleviate the harshness of feeling on this subject or tend to soften its bitter memories.

NOTES ON CHRONIC ULCERS OCCURRING IN THE PHILIPPINES

BY DR. GEORGE C. SHATTUCK

From the Biological Laboratory, Bureau of Science, Manila, P. I.

Opportunity being afforded through the kindness of Dr. Strong to work in the Biological Laboratory of the Bureau of Science in Manila, I accepted it gladly. I became interested in the question whether or not Oriental sore occurs in Manila, and in the etiology of ulcerations in general occurring in the tropics. The authors of text-books hold very different views on the classification and definition of "tropical ulcers."

This paper is based on clinical notes and microscopical findings in thirty-four cases of chronic ulcerative processes. With the exception of one Chinaman, all the patients were natives of the Philippines. Fifteen cases lived in or near Manila,¹ and nineteen in the neighborhood of Catbalogan, on the Island of Samar. In the Manila cases smears were taken from the exudate on the surface of the ulcer and from the deeper tissues exposed by the curette. In four of these cases a piece of tissue² was removed and sectioned. Giemsa's new stain was used on the smears and a variety of stains were employed for the sections. In all the Catbalogan cases smears were taken from the exudate on the ulcer and from blood or serum expressed from a needle puncture close to the lesion.

Three weeks were spent on an expedition under Dr. Heiser, Director of the Bureau of Health, to collect lepers from the islands between Luzon and Mindanao. A great many ulcers

¹ Twelve cases are from Dr. Saleeby's clinic at St. Luke's Dispensary of the Episcopal Church, two from the service of Dr. Dudley at St. Paul's Hospital, and one from that of Dr. Edwin C. Shattuck at the Hospital of Bilibid Prison.

² Tissue was first put in alcohol and subsequently treated with acetone and embedded in paraffin. Thickness of sections 4 microns.

were observed among the patients brought in as suspected lepers. Twenty patients were taken on board our steamer at Catbalogan for more careful clinical study and repeated microscopical tests. They were all released a week later, as being non-leprous. Nineteen of them were added to this series. The aim has been to differentiate divergent clinical types and to trace their etiology. Oriental sore was searched for particularly.

Strong (1) described three very different types of ulcer found here in Manila exclusive of all those due to tuberculosis, leprosy, or syphilis. His first two cases can best be discussed in relation to the first and second cases described below. His third variety, observed in whites only, was not found in this series. The report of cases follows.

First type of ulceration: Native,¹ age 30, a laborer. Neither the patient nor his family have had anything of the sort before. He said that four years ago, without assignable cause, a small boil appeared on his foot, that it burst spontaneously, and did not heal. When he began coming to the dispensary, a month before I saw him, phthisis was diagnosed. When Dr. Saleeby went on service about that time he removed a stitch which was closing the lesion. (The patient denied that anything had ever been done except to apply dressings.) The patient was fairly well nourished, had no scars suggesting syphilis, and only one external lesion. Just below the external malleolus on the right foot was an ovoid swelling, $1 \times 1\frac{1}{2}$ in. in diameter with a gash across it that went down nearly to the periosteum. The walls of the gash were rather ragged and the lower side was undermined. A little yellowish slough was adherent to the bottom and sides. There was scarcely any discharge. The superficial skin over the swelling was thick and rough. The subcutaneous tissues were thickened. The swelling felt firm. There was no tenderness, redness, or pigmentation. The lesion was curetted and a small piece excised for examination. Under simple dressings the wound healed rapidly.

A smear from scrapings showed many polymorphonuclear leucocytes, a few large and small basophiles, and a rare plasma cell. A very few cocci were observed, but no other bacteria

¹ St. Luke's Dispensary, No. 14,319. First seen March 30, 1907.

or parasites. A smear from the exudate showed in addition a few round bodies identified as blastomycetes by double contour and budding. A section stained with hematoxylin and eosin showed all the layers of the skin and a little subcutaneous tissue. One side of the section showed ulceration, infiltration, and necrosis of the upper layers of the skin. There was an increase of dense fibrous tissue in the deeper parts of the sections, and strands of this tissue ran out to the edge of the ulceration. The tissue near the ulceration was œdematous. There were coagulation necrosis, deposit of fibrin, and considerable infiltration with small round and plasma cells and a few polymorphonuclear leucocytes. Other sections were stained for tubercle bacilli, and by the methods of Wright, Giemsa, Gram-Weigert, and silver impregnation. A few Gram-staining cocci were seen near the edge of the ulcer, but no blastomycetes.

This lesion corresponds pretty closely to Strong's description of his "ulceration of the first type." On the one hand, the scarcity of macroscopic pus is common to both, the mode of onset is much the same; on the other hand, Strong found an oval blastomyces in the tissues, whereas in this case a round one was found sparingly in the exudate. It must be borne in mind that this case was four years old when it came under treatment, and that probably the lesion had been thoroughly curetted before specimens were obtained (when the stitch was put in). Supposing it to be of parasitic origin, the parasites may either have died out or been scraped out. The duration is four times as long as is usual with Oriental sore. The finding in the exudate of blastomycetes which might have been secondary invaders renders the observation valueless; and yet the assumption of a blastomycotic origin would explain the chronicity and mildness of the lesion better than any other diagnosis that I can make.

Second type of ulceration: Native,¹ age 21. He says that five months ago he had swellings in both groins, which disappeared under treatment by a Chinese physician. There was also a sore on his penis. Then a small boil appeared in the right groin, resulting in an ulcer which spread slowly in spite of treatment. Another ulcer developed later between scrotum

¹ St. Paul's, No. 2697. First seen April 24, 1907.

and thigh. The patient was treated for a month in the out-patient clinic and was admitted to the wards a month ago because the ulcers were obstinate. At the time of entrance he had a large chancroid on the penis. The chancroid has done well, but the large ulcer has not improved in spite of vigorous anti-syphilitic treatment. On the other hand, several small ulcers have appeared recently near the anus.

The patient was fairly well nourished. He had no skin lesions other than those already mentioned. There was slight general glandular enlargement. The throat was negative and there was no periostitis. Extending from the base of the scrotum to the inner aspect of the right thigh was a smooth granulating area neither elevated nor depressed and measuring about 4 x 4 in. in greatest diameter. Its outline was made up of curves like the arcs of intersecting circles. The margin was clearly defined, a little raised, and slightly undermined. The granulation tissue was boggy and dark bluish-red in color. There was no slough visible. There were several round ulcerated papules near the anus. Their interior resembled the surface of the large ulcer. There was an ulcer of moderate size in the groin which evidently was improving. On the following day Dr. Dudley curetted the large ulcer and those near the anus. The granulations were so soft that they could almost have been wiped off. The fascia beneath looked healthy. A week later the ulcer was covered with healthy granulation tissue.

Smears from the ulcerated surface showed ordinary pus and a very few cocci, but no other bacteria. Smears from the depths showed no bacteria or parasites. Cultures from the base of the curetting were made on ordinary agar in the ordinary way and under anaërobic conditions. They remained sterile. A culture on blood serum showed one colony of *Staphylococcus citreus* and several colonies of a white mould. A section stained with hematoxylin and eosin showed a rounded edge covered with epithelium and undermined by ulceration. The fibrous tissue of the corium is much increased and infiltrated with a few small round cells. There is a fibrinous exudate on the surface of the ulceration having polymorphonuclear leucocytes and plasma cells in its meshes. Other sections were stained with eosin and methylene blue, by silver

impregnation, by Gram's method, and for tubercle bacilli, but no parasites or bacteria were found in the tissues.

Like Dr. Strong's second case this ulcer began without previous injury, spread slowly in spite of treatment, and did not improve until after curetting. This case differed clinically from his in smoothness of base and absence of slough, but the appearance was undoubtedly modified by two months' treatment at St. Paul's. The discoloration and bogginess of the surface recalls Scheube's (4) description of phagedenic ulcers. Against the supposition that this ulcer was due to the same organism as the chancroid, we have the fact that they reacted differently to treatment, one healing and the other not. Syphilis is ruled out by the failure to respond to energetic treatment with iodide and mercurials. The appearance and behavior of the ulcer were not like tuberculosis. It did not resemble venereal granuloma. In favor of phagedena are the obstinacy of the ulcer, the discoloration of the granulation tissue, and the fact that common causes can be excluded.

Third type of ulceration: Native,¹ age 37. He states that he had small-pox long ago, but no other illness or skin affection until two years ago, when he received a wound on the left leg from a board. A large ulcer developed from the wound, and about the same time ulcers developed spontaneously on the other leg. These healed, but the primary ulcer did not. The patient was unusually well developed and well nourished. There were no lesions in the throat, no glandular enlargement, and no anæsthetic areas or infiltrated nodules.

On the anterior surface of the left leg midway between knee and ankle was a smooth scar about 6 in. long and $\frac{1}{2}$ in. wide. The skin over the scar was pale and the hair along its margin was white. On the external aspect of the leg, surrounded by pigmented scar tissue, was a shallow granulating area. The edges were not elevated or undermined. The surface was clean. There was a small ulcer on the front of the leg covered with a viscid, purulent exudate and a brownish crust. Grouped around the right ankle were many similar pigmented scars. The man was put on small doses of iodide of potassium the day before I saw him and antiseptic dressings were used. When seen again six weeks later the large ulcer

¹ 6536—3—P. Bilibid Prison. First seen March 22, 1907.

had a border of new skin around the edge and the granulations in the centre looked healthy. Two smears from the exudate of the small ulcer were examined. None were taken from the large ulcer because it had been cleaned. They showed polymorphonuclear leucocytes in abundance, tissue fragments and very numerous cocci and bacilli lying some intra- and some extra-cellular.

The history and course of this case are typical of many others in which chronic ulcers developing after trauma have been followed by ulcerations in other parts of the body, particularly on the other leg. That lesions occurring in this manner are not all alike may be seen by referring to the second case described under the fourth type of ulceration. Some cases gave little indication of syphilis, but others had lesions suggesting it strongly. The second case described under the fourth type of ulceration is such a one.¹

Mense (3) states, from personal observation, that leg ulcers from trauma are very common in Africa among the negroes. He says that they heal without anti-syphilitic treatment, are often large, but *generally single*. In our case the balance seems to swing toward syphilis as the most probable diagnosis, but there is certainly much room for doubt. The bacteria observed were probably nothing more than secondary invaders. In favor of syphilis are the multiplicity of the lesions and their close resemblance to other lesions seen in undoubted syphilitics. Other characteristics are ambiguous.

Fourth type of ulceration: Native,² coachman, age 33. Patient denied having had any skin lesion until three years ago when he was scratched by harness. An ulcer developed at the site of the scratch and gradually increased in size. The patient looked healthy and showed none of the ordinary signs of syphilis. The lesion was roughly circular, 7-8 in. in diameter, and occupied most of the posterior surface of the right buttock. It extended a short distance across the median line to the left buttock. The skin around the lesion looked normal. The margin of the lesion was elevated and composed of a dense inelastic tissue covered with pink, scaling epidermis, which was adherent and immovable. The same sort of tissue covered

¹ St. Luke's, No. 14,584.

² St. Luke's, No. 14,612. First seen March 22, 1907.

the greater part of the lesion. The ulcers near the margin were small, deep, pit-like, and of uniform size. Their edges were firm, inverted, and slightly undermined. The ulcers contained sero-purulent exudate and there was a yellowish slough in the bottom of each. In the central part of the lesion the ulcers were deeper, larger, and serpiginous as if formed by confluence of smaller ones.

A smear showed polymorphonuclear leucocytes in fair numbers, a few large basophilic cells, and an occasional small lymphocyte and eosinophile. Rare diplococci were observed, but no other organisms. A section taken from the edge of an ulcer, stained with hematoxylin and eosin, showed thickening of the Malpighian and papillary layers of the epidermis and vacuolation of some of the cells of the upper stratum lucidum. The normal pigment in one place was wanting. The reticular stratum looked oedematous and showed a marked increase of connective tissue cells. The lymph spaces were wide and contained polymorphonuclear leucocytes and plasma cells. There was no small round cell infiltration about the veins and no endarteritis. At one end of the section the epidermis was undermined by ulceration. At this point traces only of the structure of the corium remained. There was much fibrinous exudate. Other sections stained by the Gram-Weigert method and for tubercle bacilli showed many diplococci and a few bacilli in the horny layer but none in the deeper tissues. No tubercle bacilli were found, and a section stained with silver showed no spirochætæ.

The patient was put on small doses of iodide of potash, and the lesion was cleaned and covered with a wet bichloride dressing. It looked much better after two days, and at the end of six weeks the remnants of ulceration were covered with a few scabs. The skin over the site of the lesion was still pink, but the subcutaneous induration had disappeared and the skin was soft.

Fourth type of ulceration—Second case: Native,¹ age 55. History unreliable. Patient states that he was kicked by a horse seven months ago on the left leg and that a chronic ulcer developed from the wound. The right leg became ulcerated at about the same time. The patient was poorly

¹ St. Luke's, No. 14,584. First seen March 20, 1907.

nourished. There were no scars in the throat or typical mucous patches. The inguinal glands were somewhat enlarged and hard, but the other glands were not. On the front of the left lower leg was a large pocketed ulcer. The pockets contained moist grayish slough and necrotic granulation tissue. The margin was indurated and bands of firm inelastic tissue covered with adherent skin intersected the ulcer. The left leg presented a few pigmented scars around the ankle. The ulcer was cleaned and dressed with an antiseptic. When seen again two days later the ulcer looked very much better. A piece of tissue was removed from one of the knobs in the base of the ulcer. The patient stopped coming and has not been seen since.

Smears from scrapings showed blood with a few polymorphonuclear leucocytes and many cocci and thick bacilli, the latter intra- and extra-cellular. One slide showed also a few blastomycetes. A section stained with hematoxylin and eosin showed hypertrophy of the middle and papillary layers of the epidermis. There were a few polymorphonuclear leucocytes and plasma cells in the corium but no lymphocytes around the vessels. No necrotic or ulcerated areas were shown. The silver stain and that for tubercle bacilli gave negative results. The Gram-Weigert stain showed many diplococci and bacilli in the horny layer (the former were positive and the latter negative to Gram).

Fourth type of ulceration—Third case: A young native woman.¹ The patient was weak and emaciated, the throat negative and the glands not enlarged. The lesions were confined to the lower legs and feet which presented an appearance suggesting elephantiasis. The knees could not be straightened completely. The left foot was firmly held in the position of equinus by contracted, atrophied muscles. The right foot and ankle were much enlarged and held immovable by the dense, woody character of the swelling. The skin was pink, unyielding, and immovable, with a macerated, scaling surface which merged into large ulcers that encircled both ankles. On the feet there were sloughing ragged ulcers of varying size and depth. The great and second toes of the

¹ No. 4 of Catbalogan series. Name Carmela Ducos. First seen April 10, 1907.

right foot were absent, but the bone was not exposed. On the legs there were many small, round, punched-out ulcers of equal size, having firm inverted edges and a yellowish slough at the bottom from which exuded a sero-purulent sticky fluid. The legs were bathed in this foul-smelling exudate. They were not anæsthetic. This patient was under observation for a week. The lesions improved under simple washing.

Smears from the exudate taken on two occasions showed semi-necrotic pus and enormous numbers of bacteria of many kinds. Spirochætæ were present in three out of four specimens and were very abundant in two of these. The fourth specimen showed blood with a little pus and only a few bacteria in it. Many of the spirochætæ could fairly be classed as *Spirochæta refringens* (Schaudinn), but the characteristics of the majority were midway between those of typical refringens and typical *Treponema pallidum* (Schaudinn). No typical examples of *pallidum* were seen. No. 17¹ is an excellent example of the same sort of hypertrophy and ulceration. The toes on the affected side are drawn up by contraction.

These four cases had two important common characters: first, a similar hypertrophic process affecting the skin in the same way, second, punched-out ulcers of the same type. These fundamental resemblances were noticeable at a glance. In his description of ulcerating gummata Stelwagon (11) says that an "elephantoid" condition with punched-out ulcers is common, that it has no clear limits, and that in a few months it takes on a violaceous hue, softens, and breaks down or is absorbed. The indications are that the hypertrophic condition in the first and third cases had lasted much longer than this. The process in the first case was pretty definitely circumscribed, but its limits in the third case could not be determined. Chronic inflammation is shown by the sections. They are not characteristic of syphilis or tuberculosis. The bacteria and spirochætæ found in the smears were probably all secondary invaders, for the most part saprophytic. Their absence in sections points this way. If we concede that the four cases have the same etiology we may say that they are due to a chronic but curable non-tuberculous disease causing

¹ No. 17 refers to table of which there was only one copy. There are several explanatory tables.

hypertrophy and ulceration, and that the disease is probably infectious. The diagnosis of syphilis is almost forced upon us. Blastomycetic infection and "tertiary lesions of yaws" are far less probable than syphilis. Elephantiasis does not require serious consideration as a possible diagnosis. Whether we do or do not concede that these cases have the same etiology, it must be recognized that they have many differences. The contraction and loss of toes in the third case and contraction in the fourth are not easily explained by syphilis alone. They may be the result of phagedenic ulcers occurring perhaps long before the hypertrophic process began. The present condition of the skin renders it difficult to judge of this by observation. Nerve leprosy seems less probable as an explanation in view of the careful consideration it was given and the negative verdict. Congenital defects and trauma are possible causes.

Table No. I of the Catbalogan cases shows (1) a strikingly large number of lesions on the legs, (2) multiplicity of lesions, (3), a marked resemblance in distribution of lesions, and (4) a considerable number of deformities. Clinically the resemblance between individual lesions in different cases and between individual cases themselves was very striking. This points to a common etiology.

Leprosy, tuberculosis, and syphilis require careful consideration. Against leprosy we have the absence of the following characteristic signs; loss of eyebrows, nodules, spots, anæsthesia, and also six or more negative smears taken from inside the nose, the lobes of the ears, and from the lesions in many places. Were the bone lesions tuberculous, sinuses, lupus vulgaris, or verrucous skin lesions would have been present in some of the cases. Nothing of this sort was found and no tubercle bacilli were seen in the smears made for leprosy.

The following lesions: destruction of soft palate, dactylitis, destruction of the phalanges, depressions in the bone of the forehead, "elephantoid" swellings of the legs with gumma-like ulcerations are in favor of syphilis. The microscopic evidence is negative. Syphilis, then, is a probable diagnosis, but syphilis uncomplicated rarely produces ulcerations deep enough to cripple limbs or amputate toes. According to

Scheube, tropical ulcerating phagedena does this very thing. It often invades unprotected lesions in the tropics. Therefore the diagnosis of syphilis complicated by phagedena might be made.

Table II, of the Manila cases, shows the preponderance of lesions on the legs as in Table I, and also that the number and variety of lesions in the Manila cases was much less than in the Catbalogan cases.

The spirochætæ seen present some interesting features. These organisms were found in five of the thirty-four cases (about fifteen per cent). There were several varieties which may all be divided into three classes.

Spirochætæ. Class A

Characteristics:

1. Outline wavy rather than spiral.
2. Curves very large and sweeping.
3. Curves few, rarely more than six.
4. Body wide and short.
5. Body as a whole nearly straight.
6. Ends tapered gradually to a point.
7. Stains dark blue with Giemsa.
8. Stains heavily.

Class B

1. Outline wavy rather than spiral.
2. Average length of curve is moderate.
3. Curves shallow.
4. Number of curves rarely more than ten.
5. Curves often of different sizes in same individual.
6. Body often bent, curved, or looped.
7. Body of medium thickness and medium length.
8. Both ends tapered as a rule; sometimes one end is truncated.
9. Stains blue or purple with Giemsa.

Class C

1. Outline wavy or spiral.

2. Curves very short.
3. Curves shallow.
4. Number of curves rarely more than fourteen.
5. Curves of nearly uniform size.
6. Body as a whole nearly straight.
7. Body very thin and long.
8. Ends tapered.
9. Stains light blue with Giemsa; sometimes purple.
10. Stains faintly.

Evidence of transverse division was observed in all three cases. It was indicated by a pale area (1) between two curves or at the top of a curve near the middle of the organism, or (2) at two points in the same organism dividing it into thirds. The pale area looked narrower than the rest of the body. This is particularly well shown in examples of Class A when the division, if such it be, is nearly complete. Against the idea that two individuals happening to lie end to end have produced a false impression, there are the facts that many instances can be found in a single specimen and that the line of the curve is unbroken. These appearances occur but are by no means as distinct in Classes B and C as in Class A. Similar appearances have been described by Goldhorn (13) and Fox (10) for *Treponema pallidum*, and by Novy and Knapp (12) for *Spirochæta Obermeieri*.

Classes B and C also show appearances suggesting longitudinal division or agglutination, or both. A very few examples were observed in which one end of the organism was distinctly forked. Two organisms intertwined were not uncommonly seen, but in many of these four separate ends could be distinguished so that the arrangement might have come about either by longitudinal division or by agglutination. One large bundle of organisms of Class C was observed. They were arranged nearly parallel to each other. One spirochæta projecting from the side of the bundle showed a forked extremity with the junction of the ends entirely clear of the bundle where it could be plainly seen. This datum on the question of multiplication of spirochætæ is not considered sufficient to prove the occurrence of either form of division, as the number of specimens examined is small.

SUMMARY OF WORK

Four different types of ulceration were studied. The first and second types were not definitely diagnosed. They were probably infections *sui generis*. In the third type the weight of evidence is slightly in favor of syphilis. Many examples of this type were seen. In the fourth type the probability of syphilis is strong. The remaining cases of the series seem to be variations of types three and four which might all be placed in one group. Together they would comprise ninety-four per cent. of the series (thirty-two cases). The diagnoses were all made clinically because the microscopical findings were all negative or ambiguous.

The cellular content of the exudates examined was nearly the same in all the cases. The same was true of the bacteria seen.

Blastomycetes were found in the exudate of two cases, but were not proved to be of etiological importance.

Spirochæta refringens and two other varieties of spirochætæ were observed, but they were not believed to bear a causal relationship to the ulcers. Evidence of division was seen among the spirochætæ.

CONCLUSION

Oriental sore, madura foot, and the typical phagedenic ulcers of Manson and Scheube were looked for in vain. No varicose ulcers were seen. The proportion of ulcers due to typical phagedena, blastomycetes, and infections *sui generis* is small. A very large proportion of the chronic ulcers are syphilitic. Owing to neglect the lesions are unusual in degree, if not in kind, and they become very destructive.

The view that *Spirochæta refringens* is a bacterium is supported by strong evidence of transverse division.

I wish to express thanks and appreciation for the kindness of those gentlemen who allowed me to use their clinical material, to Dr. Strong for his kind advice and for the opportunity to work in the Biological Laboratory of the Bureau of Science, and to Dr. H. T. Marshall for many helpful suggestions.

TABLE I

CATALOGAN CASES

Location of Ulcers and Scars

Other Lesions

No	Legs	Feet	Arms	Hands and shoulders	Other places	Other Lesions
1	Scar, r.	Scar, r.				
2	Scars, both; ulcer, r.	Scar, l.		Scars, shoulders; ulcer, hand, r.		Hypertrophic periostitis, tibia, r.; contracture of toes, r.
3	Scar, ankle, l.	Ulcer, l.				Amputation of second finger, r.
4	Ulcers, both	Ulcers, both				
5	Scars, both; ulcer, l.		Scars, wrists	Scars, shoulders and hands		Two toes amputated, r.; contractures, knees and foot, l. Finger amputated, r.
*6						
7	Scars, both; ulcers, both		Scars, both		Scar, nose	
8	Scars, both; ulcers, ankles		Scar, l.			Two toes amputated, r.

9	Scars, both; ulcers, both	Scars, both	Scars, elbows				Contracture legs.
10	Scars, ankle, l.; ulcers, ankle, l.		Scars, both; ulcers, elbow, l. Scar, l.			Scars, forehead	Bones of forearm half destroyed; l. epitrachlea.
11	Scars, both	Scars, both; ulcer, r.	Scars, elbow	Scars, shoulders		Scars, forehead	Bone destruction, forehead.
12	Scars, both; ulcer, r.		Scars, both; ulcer, wrist, l.	Scars, shoulders		Scars, forehead	Bone destruction, forehead.
13	Scars, both; ulcers, both	Scars, both	Scars, elbows	Scars, shoulders		Scars, forehead	Bone destruction, forehead.
14	Scars and ulcers, l.; scars, knees	Scars, r.	Scars, l., ulcers, l.	Scars shoulder, l.		Scars, cheek	
15	Scars and ulcers, ankle, r.; scars, l.						Contracture, foot, l.
16	Scars and ulcers, l.						Hypertrophic periostitis, tibia, l.; hand swollen and deformed.
17	Scars and ulcer, r.						Hypertrophic periostitis, tibia, l.
18	Scars and ulcers, r.						
19	Scars and ulcers, r.	Scars and ulcers, r.					

Note: r. = right; l. = left.

* No. 6 was not tabulated.

TABLE II

MANILA CASES

(To show location and character of lesions)

No.	Legs	Other Places	Miscellaneous.
14319 2697 ¹	Ulcer, ankle, r.	Ulcer, perineum, groins, penis	General glandular enlargement.
6536-3-P. ²	Scars, both; ulcer, l.	Ulcer, buttock, l.	
14612			
14584	Scars, both; ulcer r.	Inguinal glands	
1495 ¹	Scars, both; ulcer, r.	Scars, vulva	
14125		Scars, foot and arm, r.	
11778	Scars, both; ulcer, l.	Ulcer, palate	Hypertrophic perios- titis, tibia, r.
14413	Scars, both; ul- cers, both		
14518		Scars and ulcer, foot, l.	
13842	Scars, both; ul- cers, both		
12846		Ulcer, sole of foot	
14560	Ulcer, ankle		
13647	Ulcer, l.		
14581		Scars and ulcers, foot, l	

*Explanatory Note.*¹ = St. Paul's hospital number.² = Bilibid hospital number.

The other numbers are those of St. Luke's.

r. = right.

l. = left.

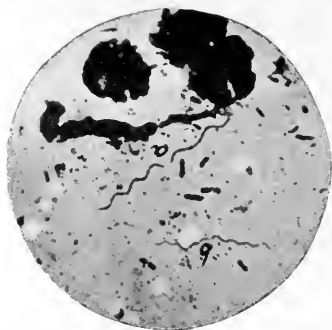


FIG. 1.

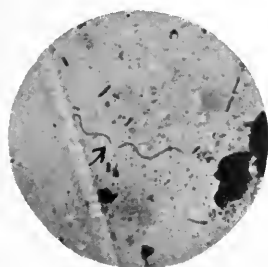


FIG. 2.

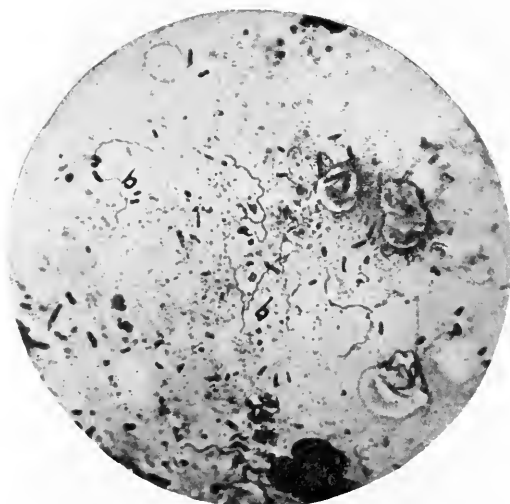


FIG. 3.

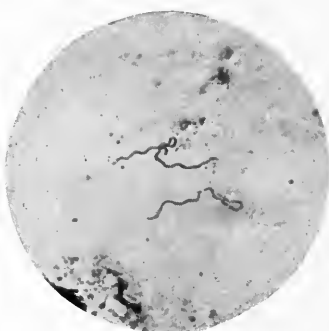


FIG. 4.

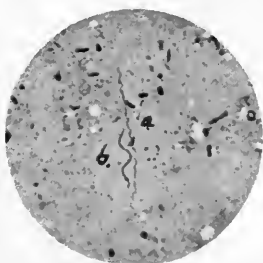


FIG. 5.

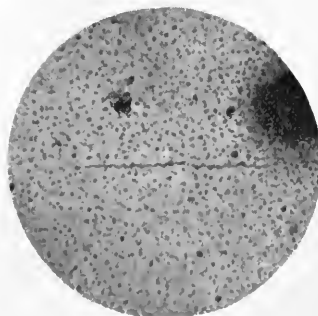


FIG. 6.

TABLE III

TABULAR SUMMARY OF ALL CASES

Location and Character of Lesions	Number of Each	Percentage of Each.
Lesions of lower extremity	32	94
Lesions of upper extremity	13	35
Lesions in other locations	14	41
General glandular enlargement	1	3
Hypertrophic bone lesions	4	12
Destructive bone lesions	4	12
Amputations	4	12
Contractures	5	15

TABLE IV

OCCURRENCE OF SPIROCHÆTÆ

Case No.	Class A.	Class B.	Class C.
4	Numerous	Abundant	Rare.
8	Few	Numerous	
14	Few	Few	
14560	Few	Numerous	
12846	Numerous	Abundant	Rare.

EXPLANATION OF PLATE XXXVI

- FIG. I. (a) *Sp. refringens* (Class A) showing transverse division nearly complete. (1000 diam.)
 (b) Class B. Unidentified spirochætæ.
- FIG. II. *Sp. refringens* (Class A) undergoing transverse division. (1000 diam.)
- FIG. III. (a) Forked end of spirochætæ (Class B). Suggests longitudinal division.
 (b) Spirochætæ of Class B. (1000 diam.)
- FIG. IV. Twisted examples of Class B. (1000 diam.)
- FIG. V. (a) Spirochætæ of Class C, which approaches *Trep. pallidum*. (1000 diam.)
 (b) *Sp. refringens*.

FIG. VI. Spirochætæ of Class C undergoing division. Separation incomplete. (1200 diam.)

Credit is due to Mr. Charles Martin who took the photographs.

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ÜBER FILARIASIS. BLUTBEFUNDE, HARNUNTERSUCHUNGEN UND NIERENFUNKTION

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Filariasis ist eine Art endemische Krankheit, die in gewissen tropischen und subtropischen Ländern vorkommt. Seit Demarquay in Paris i. J. 1863 in der durch Punktion entleerten Hydrocelenflüssigkeit eines Havanesen Embryonen der *Filaria* entdeckt hatte, wurde die Untersuchung in dieser Richtung immer lebhafter. Wucherer in Brasilien fand 1866 dieselbe in der Hämaturie, und Lewis in Calcutta in der Chylurie. Der letztere sah 1868 dieselbe wieder im Blut und lymphatischen Sekrete der Elephantiasis scroti und nannte sie *Filaria sanguinis hominis*. Endlich gelang es aber 1876 Bancroft in Brisbane (Australien), das Mutterkörperchen selbst anzutreffen, welches von Cobbold *Filaria Bancrofti* genannt wurde. Die *Filaria*embryonen, die ich untersuchte, sind durchschnittlich 0.26–0.265 mm. lang und 0.0055–0.006 mm. breit, manche mit Hüllhaut versehen, gehören der Gattung der *Filaria Bancrofti* an und sind eine Art der Manson'schen *Filaria*

nocturna. Diese Krankheit greift hauptsächlich das Lymphgefäßsystem an und verursacht eigentlich die Hämatochylurie, die Elephantiasis (Arabum), das Lymphscrotum und noch verschiedene andere Formen von Lymphektasien und Lymphorrhagien. Meine Fälle waren aber meistens Hämatochylurie und waren auch von Lymphocele, Varicocele, etc. begleitet, wie die erste Tabelle zeigt.

BLUTUNTERSUCHUNGEN DER FILARIASIS

1. Die Untersuchungsmethode der Filariaembryonen und Blutkörperchen im Filariasisblut.

a. Wenn man die Filariaembryonen im Blut leicht finden will, so muss man eine verhältnismässig grosse Menge Blut innerhalb eines kleinen Gesichtsfelds umfassen und beobachten. Ich bestrich also das Deckglas mit Blutstropfen aus der Fingerspitze des Kranken, trocknete das Ganze in der Luft und tauchte es wiederum ins Wasser, woraus ich es nach Verlauf von 15—60 Sekunden herausnahm. Auf dem Präparat war der Blutfarbstoff nun schon aufgelöst, und das ganze sah grau und halbdurchsichtig aus. Dann färbte ich das Präparat mit beliebigen Farbstoffen wie Methylenblau, Hämatoxylin-Eosin, etc., und nun konnte ich durch die mikroskopische Beleuchtung ganz leicht die Filariaembryonen wahrnehmen.

b. Wenn man aber die Filariaembryonen und Blutkörperchen zu gleicher Zeit zählen will, so muss man den Thoma'schen Blutkörperzählapparat benutzen. Beim Gebrauch dieses Apparats aber wendete ich die 0.1% Neutralrot und 0.3% Essigsäurelösung anstatt der Toisson'schen Gentianaviolettlösung an. Zunächst wird das Volumen des Kapillargefäßes bestimmt, und dann hat man die Zahl der Filariaembryonen und Weissblutkörperchen im Raum von 1 mm³ auszurechnen.

c. Was das trockene Präparat des Bluts anbelangt, so färbte ich es mit Ehrlich'schem Triacidgemisch und Säure Hämatoxylin-Eosin, oder mit Alumhämatoxylin-Eosin und Unna'schem Polychrome Methylenblau und zeigte die Prozentzahl der Arten von Blutkörperchen.

d. Für die Bestimmung des Hämoglobingehalts benutzte ich den Fleischl'schen Apparat.

2. Die Untersuchungsweise.

a. Die Beziehung der Weissblutkörperchen zu den Eosinophilzellen.

Wie die zweite Tabelle zeigt, hängt die Mehrheit der Weissblutkörperchen nicht immer mit der Mehrheit der Eosinophilzellen zusammen. Dass aber bei dem Reichtum der Eosinophilzellen die Neutrophilzellen immer geringer an Zahl werden, ist ja klar. Das ist der Grund, warum ich annehme, dass die Eosinophilzellen dadurch erzeugt werden, dass *das im Krankheitsherd oxydierte Produkt* von den Neutrophilzellen aufgenommen wird. Wenn man die Neutrophilzellen durch die Kernzahl unterscheidet, so ist die Binucleäre am zahlreichsten, wie der 7. Fall der zweiten Tabelle zeigt. Und das kommt daher, dass die Binucleäre sich so lebhaft bewegt, wie es z. B. in der Jugendzeit des Menschenlebens der Fall ist, um die Produktion des Krankheitsherds aufzunehmen.

b. Die Beziehung der Embryonen zu den Eosinophilzellen.

In dieser Beziehung gibt es nur wenige Fälle, die in meiner dritten Tabelle dargestellt sind. Im ersten Falle, in welchem die Embryonen 1 mm^3 Blut 10—209 betragen, enthalten die Eosinophilzellen durchschnittlich 25.3%. Im zweiten Falle aber betragen die Embryonen in 1 mm^3 Blut nur 6—28, u. die Eosinophilzellen durchschnittlich 8.0%. Und im ersten Falle enthält das Blut auch weit zahlreichere Embryonen als das Blut des zweiten Falls. So hat Gulland ganz recht, wenn er meint, dass das mit vielen Embryonen versehene Blut auch zahlreiche Eosinophilzellen enthält.

c. Die Beziehung der Embryonen und Blutkörperchen zu der Zeit. Diese Beziehung ist auch in der dritten Tabelle dargestellt. Wenn von einem und demselben Falle die Rede ist, so kommen die Embryonen erst nachmittags allmählich im Blut vor, vermehren sich nach und nach, erreichen gegen Mitternacht ihre grösste Zahl; dann wird ihre Zahl allmählich kleiner, und gegen 6 Uhr vormittags wird das ganze fast unsichtbar. Die Zahl dieser Embryonen steht

mit der Zahl der Weissblutkörperchen und Eosinophilzellen in keinem Zusammenhang. Die Ursache beruht auf der Tatsache, dass die Blutcirculation im menschlichen Körper sehr geschwind vor sich geht.

d. Die Beziehung der Embryonen zu den Bädern.

Diese ist in der vierten Tabelle dargestellt. Ich gab dem Präparat 10–15 Minuten lang das volle Wasserbad von 11 bis 14 Grad Celsius und konnte in 1 mm³ Blut wohl 38 bis 56 Embryonen sehen, während ich vor dem Bad im gleichen Volumen Blut bloss 7 bis 14 Embryonen wahrgenommen hatte. Mit dem heissen Bad von 40.5 bis 41°C, das 20 bis 40 Minuten dauerte, wurden die Embryonen wieder geringer an Zahl, und ich zählte diesmal bloss 14–17 Embryonen. Die Zahl ist mit der vor dem Bade fast gleich. Da bei der Anwendung von kalten Bädern auf die Körperoberfläche mit der Kontraktion der Blutgefässe und der Steigerung des Blutdrucks eine Konzentration des Blutes erfolgt (Grawitz), so kann die Zahl der Embryonen in einem bestimmten Volumen Blut also grösser werden. So wird das Aufkommen resp. Abgehen der Filariaembryonen in oder aus dem Blut wohl der Veränderung des Blutdrucks zuzuschreiben sein, welche durch die Veränderung der Körpertemperatur oder durch den Einfluss der Nerven verursacht wird. Wenn man aber diese Vermehrung der Embryonen im peripherischen Gefässe im weiteren Sinne ausschliesslich der Steigerung des Blutdrucks zuschreiben will, so ist die Erklärung der Erscheinung immer noch schwierig. Denn in dem Fall muss die Vermehrung der Embryonen mit der Steigerung des Blutdrucks in irgend einem ordentlichen Verhältnisse stehen, sei es eine arithmetische oder eine geometrische Progression. Jedoch ist in den obigen Fällen kein solches Verhältnis nachweisbar. Aber die Ursachen genügen noch nicht. Denn die Sache ist sehr kompliziert und lässt sich gar nicht leicht erklären. Die umfassende Erklärung lasse ich also auf eine andere Gelegenheit.

e. Die Beziehung der Embryonen zu dem Licht.

Auch nach der Einsetzung des Präparats in die von den Sonnenstrahlen unbeschienene Dunkelkammer sieht man weder eine Vermehrung noch eine Verminderung der Embryonen. Selbst dann, wenn die Einsetzung 2 bis 4 Stunden

dauert, bleibt die Embryonenzahl immer noch dieselbe. Wenn es aber durch die Röntgenstrahlen beschienen wird, dann mag die Embryonenzahl kleiner werden.

f. Die Beziehung der Embryonen zur Ruhe.

Wenn man auch die Kranken den ganzen Tag hindurch ruhig bleiben lässt, so wird doch die Zahl der Embryonen *weder vermehrt noch vermindert*. So scheint die Ruhe keinen nennenswerten Einfluss auf die Embryonen auszuüben.

DIE HARNUNTERSUCHUNGEN DER FILARIASIS

Der Harn der Filariasis ist meistens Hämatochylurie, öfters aber Chylurie und selten klarer Harn. Unter meinen 11 Fällen zeigten 7 Hämatochylurie, 2 Chylurie und 2 fast klaren Harn.

Die Reaktion des Harns ist schwach sauer oder neutral. Mikroskopisch kann man rote und weisse Blutkörperchen, Fettkörperchen, Epithelien, Cylinder, Filariaembryonen und sehr selten noch Filariaeier sehen. Mittels des Katheterismus sah ich auch Eier in der Chylurie.

Die Zeit, wo die Embryonen am zahlreichsten in den Harn ausgeschieden werden, fällt auf den Frühhorgen bis 8 Uhr vormittags, d. h. fast dieselbe Zeit, wo sie im Blut am zahlreichsten aufkommen. Diese Tatsache lässt sich vielleicht durch die Veränderung des Blut- oder Lymphdrucks erklären.

Über die Beziehung der Nahrung zu der Chylurie wird gesagt, dass der Chylus der Chylurie durch die Aufnahme der Milch vermehrt wird. In der Tat wurde im ersten Falle meiner ersten Tabelle die milchige Trübung durch die Aufnahme der Milch vermehrt, weil in diesem Falle das Blasen-geschwür mit den lymphatischen Gefäßen kommunizieren konnte. Wenn aber die lymphatische Stauung der Blase weggenommen wird, so wird die Harntrübung nicht mehr durch die Zugabe der Milch verursacht. Die übrigen Fälle wurden ebenfalls von der Aufnahme der Milch nicht beeinflusst.

Ich gab meinen Kranken einige Monate lang täglich eine bestimmte Quantität Speise, nämlich:

morgens: Brot (Halbpfund) und drei Eier (120 Gr.),

mittags: gekochten Reis (340 Gr.) und Sashimi (frischen Fisch 70 Gr.), ein Ei (40 Gr.) und Takuan (gesalzene Rübe, vier Stückchen),

abends: wie mittags; ausserdem 400 Gr. Wasser.

Ich untersuchte wochenlang wiederholt das Körpergewicht, den Stickstoffgehalt und Fettstoff im Harn. Das Resultat war folgendes:

Gesamte Eiweisse: 10.126%; Albumin und Globulin: 7.5220%; gesamte Fette: 0.3231%.

Den gesamten Stickstoffgehalt bestimmte ich durch die Kjeldahl'sche Methode. Die Fettbestimmung wurde mittels des Soxhlets und des Kumagawa-Suto'schen Apparats vorgenommen. Ich machte 0.5% HCl, 1% Pepsin (Langebeck)-Lösung, gab ihr kontinuierlich 40°C Temperatur und tauchte die den Fettstoff haltenden Substanzen 24 Stunden lang in diese Lösung ein, bis die Substanzen im Bad gelöst wurden. Das gelöste Fett extrahierte ich mit absolutem Äther.

Um den Gehalt des Stickstoffes zu dem des Eiweisses umzurechnen, multiplizierte ich die Quantität des Stickstoffes mit 6.25.

DIE NIERENFUNKTION DER FILARIASIS

Auf welchem Teile der Harnwege wird die Chylurie resp. Hämatochylurie der Filariasis zu stande gebracht? Hierüber herrschen verschiedene Meinungen der Autoren. Havelburg nahm wahr, dass der Chylus in den lymphatischen Sack eindringt, welcher an der oberen, linken Wand der Harnblase hängt. Dickinson und Siegmund vermuteten, dass Chylus und der Harn in der Blase zusammenfliessen. Grimm sagte, dass es direkt vom Chylus zum Harn kommt und dass es mit der Niere in keiner Beziehung steht, da die Speise, welche reich an Fettgehalt ist, ganz leicht den Fettstoff in der Chylurie vermehrt. In Japan entdeckte Baelz, 1877, zum ersten Male die Filariasis und fasste die Meinung, dass die Chylurie zwar durch die Speise beeinflusst werden kann, dass sie aber durch die Nierenfunktion zu stande gebracht werden soll. Lewis sah bei der Sektion keine merkwürdige Veränderung der Nierengewebe, aber doch zahlreiche Filarien in den Nieren—Arterien

und Venen. K. Murata sah bei der Sektion, dass die Kapsel der rechten Niere sich ausdehnt, die Nierenglomeruli und Harnkanälchen aber meistens degenerieren, ja fast zerfallen, dass sich die interstitiellen Bindegewebe gewöhnlich gut entwickeln und dass in den Nierengeweben Fettkörperchen sichtbar sind. In den Nierenbecken sah er grosse Gerinnsel, welche *Filaria*-embryonen enthalten, an dem Ureter und Blase sah er aber keine Veränderung.

Falls es eine Tatsache wäre, dass die Chylurie durch das Zusammenkommen des Chylus mit dem Harn oder der Lymphe mit dem Harn zu stande kommt, so sollte als die notwendige Folge die Nierenfunktion der Hämatochylurie-Patienten mehr oder weniger gestört worden sein. Als ich aber das spezifische Gewicht, die Erniedrigung des Gefrierpunkts, Elektroleitfähigkeit, Acidität und das Zuckerprodukt durch Phloridzindiabetes etc. des durch Katheterismus gewonnenen Harns untersuchte, merkte ich wohl, dass es kein Merkzeichen der gestörten Nierenfunktion gibt. Der milchig getrübe Harn sowohl wie der intakt klare Harn war nämlich ganz normal, wie es der IV., VIII. und X. Fall der sechsten Tabelle zeigen. Im sechsten Falle war die Erniedrigung des Gefrierpunkts des Harns an der kranken Seite etwas kleiner, der Zuckergehalt aber an beiden Seiten gleich ähnlich mit dem gesunden Zustande. Die Verminderung der Funktion im siebten Falle ist wohl dem Hinzukommen des Diabetes mellitus zuzuschreiben. So kann man annehmen, dass im Anfangsstadium der Chylurie der Harn und Chylus noch nicht in den Glomeruli, sondern in der Gegend der Harnkanälchen zusammenfliessen, dass aber später die Glomeruli auch angegriffen und schliesslich die Nierenfunktionsstörung verursacht wird. In den von mir behandelten Fällen kam es niemals vor, dass in den Nierenbecken und in dem Ureter die Chylurie zu stande kommt, wie ich es durch die Katheterisation feststellte. Im ersten Falle der sechsten Tabelle sah ich den Chylus und Harn an der Blasenschleimhaut zusammenfliessen, das kann aber eine seltene Erscheinung sein. Eine Anzahl lymphatische Säcke umgab das Blasengeschwür, und hieraus entrannt der Chylus sichtbar. Dieser Fall unterscheidet sich auch dadurch von den übrigen Fällen, dass die

milchige Trübung und der Fettgehalt durch die Aufnahme der Milch wirklich vermehrt wurden. Nachdem aber die Blasenbeschwerden einmal beseitigt worden waren, übte die Aufnahme der Milch auch keinen Einfluss mehr auf die milchige Trübung des Harns aus. Dieser Kranke schied auch aus der linken Niere milchig getrüben Harn aus.

Ich untersuchte mittels des Cystoskops, auf welcher Seite denn die Chylurie vorkommt. Das Resultat war folgendes:

Unter 10 Fällen: linke Seite 6, rechte Seite 2, beide Seiten 1, und beide Seiten klar 1.

Meine Fälle bezogen sich alle auf das männliche Geschlecht und zeigen, dass es die linke Seite ist, welche am häufigsten angegriffen wird. Betreffs dieser Pathologie bin ich der Meinung, dass die Embryonen der *Filaria* die Thrombose im Unterleibslymphgefäß und die Lymphstauung im Ductus thoracicus etc. verursachen, sodass auch im Nierengefäß die Stauung zu stande kommt und die Harnkanälchen und Lymphgefässchen kommunizieren, um die Chylurie zu stande zu bringen. Auch bei den Frauen kann wohl die Hämatochylurie vorkommen. Da aber bei ihnen die Urethra kürzer ist und das Blutgerinnsel durch die Erweiterung der Urethra leicht ausgeschieden wird, ist der Schmerz nicht so gross wie bei den Männern, und die Frauen besuchen nicht die Poliklinik.

BEHANDLUNG DER FILARIASIS

Als Behandlungsmittel der Filariasis wendete ich zunächst die Kalipikronitrit-, Thymol-, Methylenblau-, etc. an, aber erfolglos. Dann benutzte ich die Kali jodat., und in dieser Weise konnte ich mich bei jedem Falle des glücklichen Erfolgs erfreuen. Denn die Chylurie wird durch die lymphatische Stauung verursacht, welche wiederum der Thrombose zuzuschreiben ist. Durch die Kali jodat. aber wird die Viskosität des Bluts vermindert und die Stoffwechselfunktion gesteigert, sodass die Thrombose und Embolie beseitigt werden, die Stauung und Chylurie notwendiger Weise verschwinden und der Harn klar wird. Dass aber der *Filaria*embryo sich im Blut befindet, ist ganz natürlich. Ich sah auch in verhältnismässig klarem Harn *Filaria*embryonen schwimmen. Daher

bedeutet das Verschwinden der Hämatochylurie nicht gleich die Genesung von der Krankheit. Es ist aber klar, dass mit der Hämatochylurie zusammen auch die Urkrankheit allmählich abgeht.

Am Ende dieses Vortrages spreche ich dem Herrn Prof. Dr. Dohi meinen aufrichtigen Dank für seine liebenswürdige Unterstützung aus.

No.	Name.	Alter.	Geschäft.	Trinkwasser.	Anfang der Erkrankung.	Diagnose.	Datum.
I	Fall. J. Horino.	25	Bauer.	Flusswasser (Fuji).	Seit 8 Jahren Hämato- chylurie.	Hämatochylurie, linke Hoden- schwellung, Lymphom in der linken inneren Seite des rechten Oberschenkels, Nagel u. Haut u. starke Anämie.	13/VIII 1903
II	H. Kibe.	38	"	Flusschenwasser.	Seit 6 Jahren Hämato- chylurie.	Hämatochylurie, Hodenschmerz u. Hodenschwellung, starke Anämie.	2/X 1903
III	M. Kato.	32	Seidentuchhändler.	Flusswasser (Fuji).	Seit 6 Monaten Hämato- chylurie.	Hämatochylurie.	17/VIII 1904
IV	N. Takayama.	29	Methinhändler.	Flusswasser (Katsura)	Im 17. L. J. Harnverhal- tung u. starke Hämato- chylurie.	Hodentumor in der rechten Seite (hühnereigröss).	1/IX 1905
V	S. Kiyomiya.	58	Pferdehändler.	Brunnenwasser.	Seit 6 Jahren Hämato- chylurie.	Hämatochylurie, rechter Hoden- tumor (faustgröss), Varicöse Stauung in der inneren Seite d. rechten Oberschenkels.	11/VII 1906
VI	K. Kin.	28	Schüler.	Flusswasser.	Seit 7 Jahren Hämato- chylurie.	Hämatochylurie.	10/X 1906
VII	T. Kikuchi.	39	Lehrer.	Brunnenwasser.	Seit 9 Jahren Hämato- chylurie.	"	11/XI 1906
VIII	S. Komata.	21	Bauer.	Flusswasser (Fuji).	Seit Juni d. vorigen Jahres 2 mal Chylurie.	Chylurie u. Diabetes mellitus.	30/X 1906
IX	N. Asayama.	48	Lehrer.	Brunnenwasser.	Seit März d. vorigen Jahr- es 3 mal Hämatochy- lurie.	Sehr leichte Chylurie.	10/II 1907
X	S. Kurokawa.	22	Bauer.	Flusswasser.	Seit Sept. d. vorigen Jahr- es Chylurie.	Chylurie u. leichte Schwellung des rechten Hodens.	20/IV 1907
XI	M. Sawamura.	46	"	Brunnenwasser.	Seit 8 Jahren Hämato- chylurie	Leichte Hämatochylurie.	2/V 1907

TAB. II.

No.	Name.	Datum u. Zeit der Unter- suchung.	Häm- ogio- bin- ge- halt (Flei- schl.)	Rote Blut- korp. (Thoma- Zeiss).	Weisse Blut- körper- chen (Thoma- Zeiss).	W.:R.:X	Eosino- phile Zellen. %	Neu- tro- phile Zellen. %	Über- gangs- formen. %	Lympho- cyten. %	Baso- phile Zellen.	Zerfall- ende Leu- cocyten.	Andere Zellen:
I Fall.	J. Horino.	22/VII 1903	45	3360000	6000	1:560	47.0	43.0		10.0	einige.		
		22/XI 1903	50	5580000	9000	1:620	25.3	58.5	2.5	13.5	einige.		
II "	H. Kibe.	Mitternacht am 15/X 1903	45	4136000	14000	1:295	4.1	83.5	0.8	11.6		! wenige	
III "	M. Kato.	19-20/VIII 1904	72	5400000	10743	1:503	8.0	73.4	5.5	12.1	wenige.	"	Megalo- cyten.
		17/XII 1904	96	4140000	8000	1:518						"	
IV "	N. Takayama.	10 U. P. M. am 15/IX 1905	47	5944000	5600	1:1071	5.1	70.2	3.4	19.1		"	
V "	S. Kiyomiya.	10 U. P. M. am 8/XII 1905	95	7573000	5800	1:1305	2.2	78.5	3.6	15.7	wenige.	"	
VI "	S. Kurokawa.	10 U. A. M. am 20/IV 1907	109	5856000	8400	1:697	1.8	90.3	5.3	2.6	einige.	einige	
VII "	M. Sawamura.	11 U. A. M. am 9/V 1907	120	6000000	16400	1:366	11.9*	75.2	7.3	5.5		"	
	Maximum.						47.0	90.3	7.3	19.1			
	Minimum.						1.8	43.0	0.8	2.6			
	Mittel.						13.2	71.6	4.1	11.3			

TAB. III-IV.

Zeit der Untersuchung.	Name J. Hortio, 1903.										Mit- tel.					
	2 U.P.M. am 21/XI.	4 U.P.M.	6 U.P.M.	8 U.P.M.	10 U.P.M.	11 U.P.M.	12 U.P.M.	2 U.A.M. am 22/XI	4 U.A.M.	6 U.A.M.		8 U.A.M.	10 U.A.M.	12 U.A.M.	Max.	Min.
Weisse Blutkörper- chen in 1 mm. ³	10000	12000	13300	8000	10300	9000	8900	8900	8800	9700	9000	9000	9000	13300	8000	9000
Eosinophile Zellen %	34.3	33.5	32.7	22.9	18.3	18.5	22.5	28.1	30.0	31.5	10.1	14.3	32.8	34.3	10.1	25.3
Neutrophile Zellen %	57.1	58.2	60.0	65.7	66.7	67.4	60.3	52.4	50.7	49.4	62.3	57.2	53.7	67.4	49.4	58.5
Lymphocyten %	5.7	5.5	5.8	10.0	13.0	9.1	15.5	17.1	17.7	18.0	26.0	23.8	9.0	26.0	5.5	13.7
Übergangsformen %	2.9	2.8	1.5	1.4	1.7	5.0	1.7	2.4	1.6	1.1	1.5	4.8	4.5	5.0	1.1	2.5
Filariembryonen in 1 mm. ³ d. Blut.	14	49	70	75	111		209	104	21	10	0	0	0	209	0	
Zeit der Untersuchung	Name M. Kato, 1904.										Mittel.					
	6 U.P.M. 19/VIII.	8 U.P.M.	10 U.P.M.	12 U.P.M.	2 U.P.M. 20/VIII.	4 U.P.M.	6 U.P.M.	Max.	Min.							
Weisse Blutkörper- chen in 1 mm. ³	5800	8200	8400	16600	10200	14200	11800	16600	5800	10743						
Eosinophile Zellen %	3.4	7.8	9.1	6.6	6.0	12.3	10.5	12.3	3.4	8.0						
Neutrophile Zellen %	62.1	72.2	76.9	83.1	66.3	78.3	57.0	83.1	62.1	73.4						
Lymphocyten %	25.3	14.4	8.3	6.6	24.1	4.3	9.2	25.3	4.3	12.1						
Übergangsformen %	9.2	5.6	5.8	3.7	3.6	5.1	5.3	9.2	3.6	5.5						
Filariembryonen in 1 mm. ³ d. Blut.	0	0	0	28	6	20	14	28	6							

TAB. III.—IV.—Continued.

Methode d. Untersuchung u. Zeitdauer u. Datum.	Vor dem Kaltebad um ein u. p.m. 12/XI 03.	Im Kaltebad (12-14°c) in 1 u. 15 bis 25 p.m. 12/XI.	Im Warmebad (44°c) um 1 u. 40 bis 2 u. 25 p.m. 12/XI.	Vor dem Kaltebad um 1 u. 30' p.m. 20/XI 03.	Im Kaltebad (11-12°c) um 1 u. 40' bis 55' p.m. 20/XI 03.	Vor dem Warmebad um 1 u. 45' p.m. 19/X 03.	Im Warmebad (40,5°c) um 2 u. 10' bis 30' p.m. 17/X 03.											
Rote Blutkörperchen in 1 mm. ³ d. Blut.	4860000	7488000	6610000	9000	9800	10000	38.7											
Weisse Blutkörperchen in 1 mm. ³ d. Blut.	9000	10400	15200		25.6	34.3	50.7											
Eosinophile Zellen %.					54.4	57.1	8.0											
Neutrophile Zellen %.					17.8	5.7	2.7											
Lymphocyten %.					2.2	2.9	1.4											
Übergangsformen %.																		
Filariaembryonen in 1 mm. ³ d. Blut.	7	56	17	14	38	14	14											

Name J. Horton, 1903.

TAB. V.

Datum u. No.	Körpergewicht.	Gesamte Harnmenge in 24st.	Harnentleerungszahl.	Harnreaktion.	Harnfarbe u. Trübung.	Sp. Gewicht.	Eiw. nach Esbach 0/00	Gesamte Stickstoffe nach Kjeldahl (mittel)	Gesamte Eiweiss N X 6.25	Fällbare Eiweisse (Albumin u. Globulin.)	Gesamte Fettsäure Soxhlet, Kunitzawa u. Suto.
26-27 VI (1)	47100	800g	5	neutral.	leicht ziegelrot. u. milchig getrübt.	1010	8	GN/o. 11. 1.5764%	9.8525%	6.9788%	0.3744%
26-27 (2)	47450	1000	5	schwach sauer.	rosarot u. milchige Trüb.	1015	7	1.6778	10.4863	7.5075	0.2538
28-29 (3)	47800	1100	5	"	rötlich milchig.	1012	10	1.6408	10.2550	7.4375	0.2788
29-30 (4)	47900	1000	5	"	leicht rötlich milchig getrübt.	1012	8	1.6744	10.4650	7.8400	0.2346
30/VI-1/VII (5)	48000	1100	5	"	"	1012	8	1.6184	10.1140	7.0875	0.3762
1-2 (6)	47900	1100	5	"	"	1012	9	1.5715	9.8219	6.8250	0.3674
2-3 (7)	48000	900	5	"	"	1013	8	1.5820	9.8876	8.0775	0.3786
Harnanalyse von J. Horino. 26/VI-3/VII 1904.											
Mittelzahl											0.3231

TAB. VI.

No.	Name.	Schleimhaut der Blase.	Datum für Katherismus.	Nieren.	Farbe u. Trübung.	Acidität (Reaktion).	Eiweiss (Essbach) o/oo	Sp. Gew.	Gefrierpunkts-ermittlung.	Elektrifität.	Zucker-gehalt in Phloridza-diabetes %.	Embryo und Eier.
I Fall.	J. Horno.	Eine halbfingergrosse, hämorrhagische u. lymphatische Ausbuchtung, welche die linke Uretermündung umgebend sich nach oben u. hinten ausdehnt, wird teils mit Blutcoagula besetzt, teils von stagnierenden Lymphgefässen begossen. Am übrigen Teil der Wand zeigt sich gewisse Lymphstauung.	8/X 1903	l.	blutig milchig getrübt.	schwach sauer	3	1004				Embryo.
II "	H. Kibe.	Etwas anämisch, doch bei der Uretermündung zeigt sich kleine Erweiterung der Blutgefässe.	10/X 1903	l. r.	blutig milchig getrübt. leicht rötlich milchig.			1012				
III "	M. Kato.	Fast intakt, gewisse Erweiterung der Blutgefässe um die Uretermündung herum.	7/X 1904	l. r.	leicht milchig. gelblich klar.							
IV "	S. Kiyomiya.	Im allgemeinen anämisch, in der inneren Seite der rechten Uretermündung kleinfingerritzengrosse lymphatische Ausbuchtung. An der hinteren Wand entwickeln sich Balken stark.	4-8/VII 1906	l. r.	milchig. gelblich klar.	0.80 m.g. c.c. 0.5 m.g. c.c.m. Harn.	7.4	1017	-1.8°C	0.01575	1.22	Embryo.
				r.		0.58	0.5	1014	-1.16	0.01671	1.0	

V "	K. Kin.	Ein zeigefingerspitzengrosser Lymphsack an der inneren Seite der rechten Uretermündung.	10/X 1906	l. r.	gelblich klar. milchig.	0.292 0.292	4.8 spur.	1010 1007	-0.71 -1.90	0.01451 0.01440	1.67 1.51	Embryo u. Eier.
VI "	T. Kikuchi.	Eine papillomatöse lymphatische Cyste um Blasen Hals und starke Vorwölbung der Interureterzüge.	11/XI 1906	l. r.	gelblich milchig. gelblich klar mit wenig Nubecula.	0.29 0.29	10.0 0	1007 1008	-0.55 -0.56	1.03 (" 1.0 ")	1.03 (aus 0.15% f. Diab. mell.)	Embryo u. Eier.
VII "	S. Komata.	Intakt.	30/X u. 4/XII 1906	l. r.	milchig. leicht gelblich wasserklar.	1.62 1.09	0 0	1018 1015	-1.92 -1.65	0.01936 0.01828	1.4 1.84	
VIII "	N. Asayama.	Fast intakt.	10/II 1907	l. r.	gelblich klar. " "							
IX "	S. Kurokawa.	Im allgemeinen ödematöse Schwellung, besonders stark um die beiden Uretermündungen herum, namentlich um die linke.	23/IV 1907	l. r.	leicht rötlich milchig. gelblich klar.		4.5 0	1012 1013	-0.85 -0.97	0.01523 0.01587	0.806 (15'-17" nach Injektion.) 0.84, (17'-20' "-)	
X "	M. Sawamura	Etwas hyperämisch, u. empfindlich an der Uretermündung.	2/V 1907	l. r.	" " sehr wenig milchig.			1013 1012	-1.22 -1.31		1.84 1.52	

FRAMBŒSIA TROPICA (YAWS, PIAN, BOUBA)

BY DR. ALDO CASTELLANI, OF COLOMBO (CEYLON)

The disease was first called frambœsia by Sauvage in 1759, on account of the raspberry-like appearance of the eruptive elements. The colloquial name most frequently used in the British colonies is yaws; in French colonies, pian. Other synonyms are parangi (Ceylon), momba (Angola), dubi (Gold Coast), tetia (Congo Coast), framosi (Calabar), aboukone (Gaboon), gattoo (West Coast Africa), kuena (Burma), puru (Borneo, federated Malay States), patek (Dutch Indies), tonga (New Caledonia and Loyalty Islands), coco (Fiji), tona (Tonga Island), lupani tomo (Samoa). In Venezuela and other South American countries the name bubas is much used. Charlouis in 1882 suggested the term polypapilloma tropicum.

Geographical distribution.—Yaws is essentially a tropical disease, as few, if any, genuine cases have been reported from temperate zones. There are authors, however, who believe that yaws was in the past endemic also in temperate zones; for instance the so-called "button scurvy" disease which was common in Ireland about a century ago, is considered by some to have been a form of frambœsia.

The peculiar disease called sibbens or sivvens, an outbreak of which occurred in Cromwell's armies and in Scotland during the seventeenth century, has been also believed to be yaws.

At the present time cases of a skin disease resembling yaws have been reported by several writers in Greece.

Africa.—The disease is very rare in the northern regions of the continent; it is said to be occasionally met with in Algeria; it is apparently non-existent in Egypt, though, according to some writers, fairly common in some districts of the Soudan. Yaws is very common on the West Coast, Congo Free State, on the Gaboon River; it is also found in Mozambique,

Angola, Madagascar, and the Comoro Islands. In Uganda and the region of the great lakes it is occasionally met with. Recently Griffith has observed yaws among the kaffirs in South Africa near Kimberley.

Asia.—The disease is unknown in Japan, and in the central and western regions of the continent. It is also unknown in most parts of China. The affection is frequently met with in the Malay Peninsula, Assam, Upper Burma, Siam, Java, Batavia, and is extremely common in Ceylon, where it is known as parangi. The number of cases treated in the Government hospitals in Ceylon during the last seven years was as follows: 3646 in 1900; 3117 in 1901; 3434 in 1902; 3254 in 1903; 3501 in 1904; 3535 in 1905; 3606 in 1906.

In India cases of yaws are very rare, though small outbreaks of the disease have been described by various observers.

Australasia.—The disease is not present in Australia, Tasmania, and New Zealand—while it occurs frequently in many of the Pacific Ocean islands.

It is extremely common in Fiji, British Guinea, Loyalty Islands, Samoa, New Hebrides, and New Caledonia.

America.—In the West Indies and French Antilles yaws is very common. In Cuba some cases occur. It is known in British Guiana, Venezuela, and Brazil. Cases have been occasionally reported from the Southern United States, but never from the Northern States, or from Canada.

History.—It has been suggested by some authors (Hume, Adams), that frambœsia is the disease from which the Israelites suffered during their emigration from Egypt, and that the word "saraat," occurring in the thirteenth chapter of Leviticus, really means frambœsia rather than leprosy, as usually translated.

In the works of Avicenna and Ali Abbas of the tenth century there is mentioned a disease called *safat* or *sahafati* with symptoms somewhat similar to frambœsia; most authors, however, are of opinion that the disease referred to by the two Arabian physicians was syphilis.

The study of the disease first began to engage the attention of European physicians after the discovery of America. Ovedio y Valdez (1478-1557) describes the malady in his

work *La Genera y Natural Historia de las Indias*. Pison (1648) refers to the disease in his work *De Medicina Brasiliensi*. Rochefort (1656), Raymond Breton (1665), and Labat (1694) relate in their publications that the inhabitants of the West Indies (Caribs) frequently suffered from a peculiar disease called by the natives *pyans* or *yaya*. Bontius in 1718 proved that framboesia was endemic not only in the West Indies of Africa, but also in Java, Sumatra, and other Dutch colonies of the East, where the disease was known under the name of "anboyna pox or pimple."

In the slave-trading days outbreaks of yaws frequently occurred on the crowded ships carrying African slaves to America; special hospitals for the isolation and treatment of slaves suffering from yaws were built on all the important estates in the West Indies. Occasionally in the countries in which it is endemic the disease has spread in such a way as to give rise to true epidemics; an example of such an epidemic occurred in Dominica in 1871, when two special segregation hospitals had to be built for yaws patients.

In 1694 an outbreak of a peculiar disease occurred in Scotland, called sibbens or sivvens (*sivvi*, Celtic for raspberry), imported apparently by Cromwell's soldiers; it is believed to have been yaws by some authorities, while others consider it to have been syphilis.

The so-called *button scurvy* of Ireland, endemic there in the eighteenth century and in the beginning of the nineteenth century; the "radesyge" which appeared in Sweden and Norway in 1710, when it was imported into Finland; and the "mal de Chicot" in Canada have been considered by some writers to have been forms of yaws.

Attempts have been made by several authors—among the moderns, Breda—to distinguish between yaws, parangi, pian, and boubas; those, however, who have had the opportunity of studying the disease in different countries have all come to the conclusion that yaws, pian, parangi, and boubas are simply synonyms referring to the same malady, *viz.*, framboesia.

Since the time of Labat there have always been a few writers who have believed that framboesia is a form of syphilis;

this theory has been supported by so high an authority as J. Hutchinson.

In modern times the disease has been investigated clinically and experimentally by a large number of observers.

Of great importance were the researches, carried out in 1882 by Charlois, who experimentally proved that syphilis and yaws are two different diseases; the clinical investigation of the disease by Numa Rat also was most complete; his report on the malady, written in 1891, has become classical.

Among the more recent observers who have investigated yaws in various parts of the tropics are Manson, Neisser, Daniels, Jeanselme, Powell, Branch, Martin, Halberstadter, Von Prowazek, and many others.

Symptoms.—For convenience's sake the course of the disease may be divided into three periods:

1. A primary stage comprising the development of the primary lesion.
2. A secondary stage during which the characteristic framboetic granulomatous eruption appears.
3. A tertiary stage in which the late manifestations of the disease develop: deep ulcerations, gummatous-like nodes, etc.

This division into three periods is somewhat arbitrary as tertiary symptoms may appear during the secondary stage.

It is often stated that the whole course of the disease varies between three to six months in children, and six to twelve in adults; in my experience, however, the duration of the malady is often much longer, and, when the infection does not become extinct after the secondary stage, may extend to many years. In fact I believe that in a certain number of cases,—although there are periods during which the organism is apparently free from symptoms, the infection is simply dormant and sooner or later gives rise to renewed attacks.

The primary lesion.—After an inoculation period varying in length between two to four weeks, characterized often by signs of malaise, rheumatoid pains, headache, and irregular rises of temperature a primary sore appears at the seat of inoculation, which is generally extragenital. The primary sore is a papule which after about a week becomes moist, developing

a yellowish secretion which dries into a crust; often at the place of inoculation several papules appear which become moist and fuse together into a single element covered by a thick crust. If after some days the crust is removed the primary sore will appear as an ulcer,—not rarely of rather large dimensions,—with clean-cut edges and a granulating fundus.

This ulcer may heal, leaving a whitish scar,—or in other cases it may develop into a granulomatous mass, not dissimilar to the granulomata of the secondary eruption which appear later on, but frequently much larger. This large single projecting nodule is called “mother yaw” or “maman pian” in French patois. Occasionally round it, before the general eruption begins, several smaller granulomata develop like satellites. The primary sore is often painful during the first stage of development; later it may be quite painless; occasionally there may be pruritus.

The proximal lymphatic glands may become enlarged and hard, but do not come to suppuration.

The seat of the primary sore is generally extragenital. It often develops on an old ulceration, an itch pustule, an itch bite, a wound, a vaccination mark; the smallest erosion is sufficient for the entrance of the virus.

Most of my female patients had the primary sore on one of the mammæ, developing on some crack or abrasion of the nipple and areola. In several other women the primary lesion was found on the skin of the trunk, just above the hip, this being due to the custom the Ceylon women have of carrying their child astride of the hip; any yaws element present on the scrotum or nates of the child will therefore be continually rubbed against the skin of the mother, and infection will take place through any slight abrasion already present or that may be caused by the friction.

In men and children the primary sore is often found on the arms, hands, and legs, but it may develop on any region of the body. The primary sore may heal before the general eruption begins,—but as a rule is still present when the secondary eruption appears. I had a case in which the primary sore was still present six months after its first appearance, and

when the secondary eruption had nearly undergone complete involution. The duration of the primary sore, therefore, may vary between a few weeks and several months. The primary sore leaves a whitish scar which later on may become pigmented; in some cases the scar is small and smooth, in others it is large and very thick. It is to be noted, however, that in Ceylon the disfiguring scar so often found is partly due to the custom the natives have of cauterizing the sore energetically and with very primitive methods; in other cases the large disfiguring cicatrix is due to the primary sore having developed on an old ulcer which in healing leaves a coarse scar.

The secondary stage.—The general eruption usually begins between one and three months after the first appearance of the primary sore. Before the general eruption appears the patient often complains of malaise, headache, severe pains in the muscles, joints, bones. In some cases fever is present of an intermittent or remittent type; the patients, however, are ordinarily able to attend to their work.

The general eruption develops, in my experience, as follows: Minute roundish papules the size of pinheads appear on various parts of the body; some papules soon show a yellow point or minute yellow crust at their apex. Most of the papules remain of practically the same size for many weeks and disappear, leaving occasionally some furfuraceous patches; others become larger, several often coalescing, and frequently acquiring a dark areola in natives, a reddish one in Europeans. Some of the larger papules increase in size, and develop into large granulomatous-looking nodules, covered with a crust, honey-yellow or brownish, formed of desiccated secretion. If the crust covering the granulomata be removed there will be seen a raw surface throwing up coarse red or yellowish fungoid granulations secreting a thin, slightly purulent secretion, which soon dries into a crust again. These yaws granulomata are of various size, and may be found on practically any part of the body; they are extremely common on the upper and lower limbs, and on the face; on the scalp they are very rare; they may form rings round the mouth or anus and may enclose sound skin. They may remain of the same size and appearance for months; often after a few weeks the

secretion diminishes, and a process of hyperkeratosis sets in; they become of much harder consistency, and some of them, especially those of the feet, may be covered with numerous hard, verrucose-like, small protuberances. In the majority of cases within three to six months in children, and six to twelve months in adults, the yaws dry up, shrink, and disappear, leaving dark, hyperpigmented spots on their site which are very persistent. In some cases the granulomatous eruption is very persistent, lasting for several years, new crops of granulomatous nodules appearing from time to time in succession. Each framboetic granuloma generally undergoes involution within two to four months, leaving behind a dark area; occasionally, however, the framboetic granuloma does not involute so soon. I have among my patients a boy of eleven who two years ago had a general eruption of yaws; all the granulomata disappeared excepting one on the right knee, which is still present.

The granulomata are seldom painful unless when developing between the toes, on the soles of the feet, or round the nails; they often cause itching.

Patients affected with yaws often exhale a peculiar offensive odor which has been variously described as sour or musty; this is probably due to the growth of various bacteria representing secondary infections, under the crust of the granulomata; I have more especially noticed this offensive odor when the secondary infection is due to bacilli of Vincent's type, and coarse spirochætes. In such cases if the sores are well washed with perchloride solution for two or three days, the bacilli of Vincent's type and coarse spirochætes disappear and the smell is no longer noticeable, though the granulomata do not undergo any change.

Though the framboetic granuloma is the characteristic eruption of the secondary stage, there are during this stage eruptions of different types, papular, scaly, and ulcerative.

An average ordinary case will present at the same time several typical yaws granulomata, numerous small reddish papules with the epidermis intact, other papules which have become moist and are covered by a tiny yellow crust; several furfuraceous patches here and there, and spots of increased

pigmentation at the place of previous granulomata. Occasionally some granulomata break down and large irregular ulcers with central reddish papillomatous masses develop, which in my experience do not usually heal spontaneously.

At times in the later period of the secondary stage peculiar, roundish, or irregularly outlined whitish patches are present, especially on the back and arms, with a nutmeg-grater-like surface; on closer observation these patches are seen to consist of numerous hard, conical papules, containing in their centre an epidermic plug, which is easily removed, leaving a depression in the papule; sometimes the plugs are spiny, and in this case the eruption closely resembles lichen spinulosus.

Eruptions on the palms and soles.—The granulomatous eruption very often attacks the soles of the feet; at first dark-brownish or livid intense spots, very painful, appear; their thick epidermis is gradually broken away and is pierced by framboesial nodules similar to those found on the other regions of the body. This framboetic affection of the soles is very painful, and is called by natives of Ceylon "dumas."

The same lesions, but generally not so severe, may be found on the hands. The granulomatous infiltration may attack the matrix and margins of the nails (framboetic onychia and paronychia). The nails become thickened, dry, brittle, and may be cast off entirely, though later they grow again.

After the granulomata have disappeared—occasionally at the same time—peeling whitish patches may be found on the palms and soles of the feet, closely resembling the syphilitic psoriasis palmaris et plantaris.

Peculiar pitted appearance of the palms.—In several cases, in the latter part of the secondary stage, I have observed on the palms and wrists hard, roundish, flattened papules or small nodules, having a thick, hard, epidermic plug in their centre; this plug falls off spontaneously or is easily pulled out; a deep depression remains,—the papules gradually disappear, but the depressions remain and the palms take on a peculiar pitted appearance.

This condition of the palms may remain unchanged for several years after every symptom of framboesia has disap-

peared. A somewhat similar appearance of the soles of the feet is occasionally met with.

Lesions of the hair and nails.—I have never noticed any change in the appearance of the hair, nor alopecia. A few hair follicles may be destroyed when the granulomata develop on the scalp; which, however, very seldom happens.

Mucous lesions.—These are not very common; during the secondary stage small granulomatous nodules may develop at the base of the tongue, also whitish patches closely resembling syphilitic leukoplakia. Small granulomata may develop on the nasal mucosa.

Constitutional symptoms: Fever.—As already stated, fever is frequently present, of intermittent or remittent type, before the general secondary eruption begins. During the secondary stage proper fever is absent unless complications supervene.

Lymphatic glands.—In a number of cases various groups of lymphatic glands are found to be enlarged. The enlarged glands are roundish or spindle-shaped, hard, painless, and never come to suppuration unless a secondary pyogenic infection be present; the cervical and inguinal glands are those most frequently enlarged.

Alimentary system.—As a rule the digestive functions are not disturbed. In children slight diarrhoea may be occasionally noticed preceding the general eruption. The spleen and liver are very often found enlarged in children, but this is probably due to progressed or concomitant malaria infection. The microscopical examination of the fæces of yaws patients will often reveal ova of various worms; *Ascaris lumbricoides*, *Trichocephalus dispar*, and occasionally *Anchylostoma duodenale*; but this is of frequent occurrence also in normal natives.

Respiratory system.—The small granulomatous ulcers occasionally met with in the nasal mucosa have already been mentioned; similar ulcerations are to be found, though very rarely, in the larynx. As a rule the respiratory, as well as the circulatory, system is not affected.

Locomotory system: Joints.—Arthritis; pseudo-rheumatism.—In some yaws patients several of the large articulation may become swollen and very painful. The condition is often of an acute character and may be accompanied by fever, so

that an attack of articular rheumatism supervening on the framboëtic infection might be suspected. Sodium salicylate, however, is not beneficial, while the administration of large doses of potassium iodide speedily reduces the temperature to normal, and causes the swelling of the articulations to disappear. At other times one articulation only is involved and the symptoms may become so serious as to suggest purulent arthritis—as shown by the following case:

Podyhanny, female, æt. forty, was admitted to the clinic on December 9, 1906, showing a typical general eruption of yaws. After a week, during which time no specific treatment was given, she began to complain of malaise, vague muscular pains, and severe pain in the left knee and in the right shoulder, the temperature rising to 101° . Salicylate of sodium was given in large doses. The following day the pain in the shoulder and the muscular pains had disappeared and there was no fever in the morning, but at night the temperature rose to 103° ; the knee was very painful and there were clear signs of effusion. During the next few days the condition became worse, the fever ranging between 99° to 100° in the morning, and 103° to 104.2° at night. The patient often had shivering in the morning, while at night she perspired profusely. Examination of the blood for malaria negative; well marked leucocytosis (22,000 leucocytes per c. mm.) present. Spleen not palpable. The knee became greatly swollen and extremely painful, the skin very tense; no movement of the articulation was possible. On the sixth day I tapped the articulation with a sterile syringe expecting to find pus, but only clear fluid was drawn. Large doses of potassium iodide were then given, and all the symptoms disappeared in four or five days.

In many cases the smaller articulations become involved; the symptoms in such cases are not acute and there is usually no fever.

Bones.—Inflammation of the periosteum of various bones is of common occurrence. Very frequent is a form of multiple periostosis of the digital phalanges, the cause of the "multiple dactylitis" so often seen in yaws patients.

Muscles.—Contractures of various groups of muscles may

be observed; fairly common is a contracture of the flexor muscles of the forearm; this contracture is often permanent, and, in my opinion, is probably due to pathological alteration of the peripheral nerves, rather than of direct muscular origin.

Nervous system: Neuritis.—Neuralgic pains are often observed; but also a true form of neuritis must be admitted; I have seen in several cases clear symptoms of neuritis of the sciatic nerve, with severe pain along the course of the nerves and signs of motor and trophic disturbances.

Hyperidrosis.—In several of my patients I have noticed hyperidrosis. The phenomenon was limited to the face in some cases, to the hands and soles of the feet in others; it never extended to the whole body, and always affected symmetrical regions. Hyperidrosis is more frequently observed in children than in adults. In one case—a boy of fourteen—presenting a general eruption of yaws, the hyperidrosis of the face was so marked that large drops of perspiration were continually dropping down. I treated him with potassium iodide; after a month the yaws granulomata had disappeared and the hyperidrosis was no longer noticeable. In some cases the hyperidrosis ceases suddenly without treatment; the condition may last, however, for some weeks or months.

Cerebro-spinal fluid.—In the three cases of typical yaws I have performed lumbar puncture, collecting in each case about 22 cc. of fluid. The liquid was in all cases perfectly clear, like distilled water. The pressure was not increased. The physical and chemical characters were alike in all cases and apparently did not show much variation from what is found in normal condition. The density varied between 1.003 and 1.005.

A certain amount of globulin was present and a substance (dextrose?) reducing Fehling's liquid. This reducing substance was, in two cases, distinctly in excess of what is observed in the normal fluid. No cholin was found. The reaction of the fluid was alkaline. In two cases the centrifuged liquid, examined microscopically, did not contain any cellular elements; in the third case a few, extremely rare mononuclear cells were found. The liquid was sterile; no spirochætes could be detected.

The eyes.—Granulomatous and papular eruptions may develop on the eyelids. A slight periostitis of the orbital margin is not rare, the margin becoming thickened and very painful on pressure. The occurrence of iritis is denied by most authors. I have seen two typical cases occurring during the general granulomatous eruption; in both cases the affection was of moderate severity; there were photophobia, ciliary congestion, discoloration of the iris; pupillary reaction was almost absent. Both cases recovered on large doses of potassium iodide without any local treatment.

The genito-urinary system.—The primary lesion is rarely found on the genital organs; in fact in all the cases I have seen, which amount to several hundred, the primary lesion was always extragenital. Eruptions of the secondary stage, papular and granulomatous, frequently involve the skin of the penis and of the labia; granulomatous ulcerations may be found on the vaginal mucosa.

The urine, as a rule, does not contain anything abnormal; only when there is fever, as, for instance, when the articulations are acutely involved—then a slight amount of albumin may be present.

The blood.—In all my cases in which the blood was examined a certain degree of anæmia, never very severe, was present. The number of red blood corpuscles varied from 3,000,000 to 4,000,000; the hæmoglobin index (Fleischl), from 50 to 75. The red blood corpuscles did not show anything abnormal in their shape. On several occasions I noticed a comparatively large number of polychromatic erythrocytes staining blue instead of pink with Leishman's method. Many of these basophile red cells are micro-erythrocytes.

The leucocytes varied from 7000 to 11,000 per c. mm. In the majority of cases an increase was noticeable in the number of the large mononuclears, even when there was no sign and no history of malaria. In almost all the cases the eosinophiles were increased, this being possibly due—in part at least—to the presence of intestinal worms, as revealed by the microscopic examination of the stools, which showed frequently ova of *Ascaris lumbricoides*, *Trichocephalus dispar*, and in a few instances of *Anchylostoma duodenalis*.

Tertiary stage.—The disease often terminates with the secondary stage; in some cases, however, the infection does not become extinct, and tertiary lesions appear. Sometimes the secondary and tertiary stages merge into each other, but frequently the tertiary symptoms appear after the lesions of the secondary stage have undergone complete involution. The interval of time varies considerably in length and may extend to many years.

The characteristic lesions of the tertiary period are gummatous-like nodules and deep ulcerative processes. These gummatous nodules may develop in any tissues. When developing in the skin and subcutaneous tissues they are indolent, and by their softening and breaking down ulcers are produced which may present clear-cut margins and a granulating fundus; when several contiguous nodules break down, serpiginous ulcers are left. In other cases deep irregular-shaped ulcerations, with very thick and undermined edges, are seen; in others large fungative ulcers are present. On healing, these various ulcers leave whitish scars which, when unbroken, run a very chronic course, and when healing leave frequently very thick and disfiguring scars which often undergo retraction, and cause thereby permanent contractures and disfigurements.

Lesions of the osseous type are very frequent, painful nodes developing under the periosteum of several bones—ribs, sternum, etc. In other cases a diffuse chronic periostitis is present, altering the normal shape of the bones. Contractures of various groups of muscles are frequently seen.

Tertiary affections of the internal organs and of the central nervous system have not yet been described; I believe that future investigation will prove that they do occur in some cases. It is also probable that further research will show that framboesia may be hereditary—though it is worth noting that, in contrast to syphilis, parents generally contract the malady from their children.

Cases illustrating the occurrence of tertiary symptoms in yaws.—As several of the modern authors deny the occurrence

of tertiary symptoms, I may quote a few of my cases clearly showing the existence of such lesions.

CASE 1. Young Singhalese girl of about fourteen years of age. No history of syphilis, either congenital or contracted; she is a strong-looking girl, her teeth, eyes, and ears normal; her genital organs are intact; five years ago suffered, together with all the other members of her family, from yaws, and was treated in a Government hospital, from which she was discharged cured a few months later. She remained in good health till four months ago, when she noticed a slight indolent swelling on her right leg. The swelling increased in size and finally broke down, leaving a rather large ulceration. Two months later, when I examined her, several ulcers were present on both legs, of irregular shape, thick margins, rather deep, and without much secretion; the left tibia was arching forward; moreover, on one of the ribs an indolent gummatous-like swelling was present. In the secretion of the ulcers no spirochætes were found. The girl has been treated with potassium iodide, and the ulcers have healed leaving large whitish irregular scars (Plate xlii, Fig. 12).

CASE 2. Singhalese girl of about eleven years of age, sister of the previous patient. No history of syphilis; genital organs intact. Five years ago suffered from yaws at the same time as her sister. She recovered and remained in good health till three months ago, when an ulcerative process developed on the soft palate which, at the time I examined her, had already destroyed the uvula. The patient presented thickenings of the metacarpal bones and phalanges which had caused a certain distortion in the right hand. The potassium iodide treatment was begun some months ago, and the patient is rapidly improving, the ulcerative process of the palate being already arrested and healed. No spirochætes were found in the ulcer.

CASE 3. Singhalese boy nine years old; strongly built, with no signs of hereditary or contracted syphilis; was treated by me for a general eruption of yaws in June and July, 1905. The boy is living near the clinic, and it has been very easy, therefore, to keep him under observation. After having been discharged at the end of July, 1905, he was well for eight

months; only the dark spots at the site of the granulomata and a scurfy condition of the skin of the back could be seen. In March, 1906, he suffered from a mild form of "dumas," a few small granulomatous nodules being present on the left foot. This condition disappeared in a few weeks under the action of large doses of potassium iodide; and the boy remained in good health till May of this year (1907), when several gummatous-like nodules developed on both legs; the nodules broke down, leaving serpiginous ulcers. At the same time a painful node appeared on the left clavicle. Large doses of potassium iodide were again given, with the result that the ulcers have healed, leaving whitish scars, and the node on the clavicle has become absorbed.

Pathology.—The histo-pathology of the disease has been thoroughly investigated by Unna, Jeanselme, MacLeod, and Plehn. I have come to the same conclusions. The typical lesions of yaws must be considered to be granulomata. There is a very diffuse plasma cell infiltration, the plasma cells retaining their original type better than in any other granulomata. The proliferative changes are very well marked; the papillæ are much elongated, their blood vessels being dilated but rarely thickened.

When the yaws have reached a certain stage a very well-marked hyperkeratosis is noticeable. I would call attention to the appearance of the films, taken in the usual way from yaws granulomata and stained according to Leishman's method. In such films it is interesting to note the presence of a large number of polychromatic red blood cells of very different size; some much larger than the normal erythrocytes, some much smaller. They are stained deep or light blue instead of pink, and sometimes have a granular appearance. The leucocytes present in the films frequently contain in their protoplasm, and sometimes in their nuclei, roundish or oval, more or less deeply stained bodies, which I believe to be probably polychromatic micro-erythrocytes engulfed by phagocytes.

Etiology. Historical.—Various bacteria have been described in yaws; Eijkman found some peculiar bacilli; Pariez

observed numerous micrococci; Powell, in 1896, cultivated in two cases a yeast which was present in the granuloma and also between the epithelial cells. Breda in several cases found a bacillus which he named the "Framboesia bacillus."

Nicholls and Watts, in 1899, found in the granulomata a coccus, which they cultivated in pure cultures. The same coccus was found once in the lymphatic glands. Inoculations into animals did not succeed.

In February, 1905, an extremely delicate, almost invisible spirochæta, or spirillum, as I thought at that time, was observed by me in a case of yaws. Schaudinn's discovery of a spirochæta in syphilis, published soon after, induced me to work on the subject in a systematic manner. A preliminary note on the presence of spirochætes in yaws was published by me on June 17, 1905, in the *Journal of the Ceylon Branch of the British Medical Association*; another communication was made by me at the meeting of the British Medical Association, Leicester, July, 1905. I described several more cases of yaws showing spirochætes in the *British Medical Journal* of November 18 and 24, 1905; at that time I had eleven positive cases out of fourteen. My results were confirmed by Wellman in one case (*Journal of Tropical Medicine*, December 1, 1905), and by Powell in another (*British Medical Journal*, December, 1905). Further researches of mine appeared in the *Journal of Tropical Medicine*, January 1, 1906, and *Deutsche medizinische Wochenschrift*, No. 3, January, 1906. Recent publications by various authors confirm the presence of spirochætes in yaws; among these publications, one of the most important is by Borne, who has found spirochætes in nine cases out of eleven (*Geneeskundig Tijdschrift*, 1906). Recently Borne has informed me by letter that he has been able to detect spirochætes in forty-nine cases out of fifty-two. Halberstadter has very recently confirmed the presence of the spirochæte in human yaws as well as in monkeys inoculated with the disease.

SPIROCHÆTE PERTENUIS (CASTELLANI). JUNE, 1905¹

The Spirochæte pertenuis is an extremely delicate, motile,

¹In the *British Medical Journal* of November 26, 1905, I suggested the name *Spirochæte pallidula* for the yaws spirochæte on account of its resem-

spiral-shaped organism; its length varies from a few microns to eighteen and twenty microns and even more. It is extremely thin; some individuals are, however, thicker than others. The yaws spirochæte is stained with difficulty. Good results are obtained by Leishman's method, provided the alcoholic solution is allowed to act for five minutes and the subsequent admixture with distilled water for from one-half hour to several hours. Giemsa's stain also gives good results. Using either of these methods the spirochæte stains purplish; occasionally a few chromatoid points may be seen in the body of the organism.

The extremities of the organism are often pointed, but, due, possibly, to the manipulation of the films, forms may be met with, presenting blunt extremities, or one extremely blunt and the other pointed.

In a few individuals one of the extremities may present a rather large pear-shaped expansion, or a loop-like formation. The number of waves varies (six to twenty and more), but they are generally rather numerous, uniform, and of small dimensions. Occasionally a portion of the spirochæte shows numerous narrow uniform waves, while the rest of it has no waves at all. Sometimes two spirochætes may be attached together, or apparently twisted one on the other.

As regards the minute histological structure I have not so far been able to detect an undulating membrane, though the presence of such an undulating membrane has been admitted by other observers (Blanchard). Occasionally in preparations stained by Löffler's method of flagella staining, it has seemed to me that some of the organisms present an extremely delicate flagellum at one end. According to my results, therefore, the organism should be considered a *treponema* rather than a spirochæte. Further investigation, however, is necessary to settle this point.

From the description I have given it will be seen that the yaws organism shows, morphologically, resemblance to the

blance to the spirochæte found in syphilis; according, however, to the laws of nomenclature, the correct zoological name is *Spirochæte pertenuis*, which form I had used some months before. (*Journal of the Ceylon Branch of the British Medical Association*, June 17, 1905.)

organism of syphilis. In fact I was for a long time of the opinion that the two germs differ biologically rather than morphologically. According to Blanchard, Mesnil, and others, however, slight morphological differences can be made out. Martin in a recent very interesting publication in the *Deutsche medizinische Wochenschrift* states that the yaws spirochæte is even more delicate and more difficult to stain than the *Spirochæta pallida* of Schaudinn. Rivas states that the *Spirochæte pertenuis* is thinner than the *Spirochæta pallida*, and has narrower waves. In non-ulcerated lesions the *S. pertenuis* is the only germ present.

Bacteriological flora found in open sores of frambæsia.—While in the non-ulcerated lesions the *S. pertenuis* is the only germ found, the ulcerated lesions of frambœsia are invaded very quickly by all sorts of germs. Besides innumerable bacteria, often spirochætes of various kinds are present; one form is rather thick, and takes up the stain easily; it is morphologically identical with the *Spirochæta refringens* of Schaudinn. Another form is thin, delicate, with waves varying in size and number, and with blunt extremities; I proposed for this variety the name of *Spirochæte obtusi*. A third form is also thin and delicate, but is tapering at both ends; I named it *Spirochæte acuminata*. The *Spirochæte pertenuis*, as found in non-ulcerated lesions, may also be present.

INOCULATION EXPERIMENTS OF YAWS IN MAN

Paulet (1848) inoculated fourteen negroes with the secretion taken from yaws granulomata. All of them developed yaws, the inoculation period varying from twelve to twenty days, when at the place of inoculation, in ten cases, the first nodule of yaws appeared, soon followed by a typical general eruption. In two cases apparently the eruption did not start from the seat of inoculation.

The investigation of Charlois (1881) is most important. He inoculated thirty-two Chinese prisoners—who had never suffered from the disease—with crusts and scrapings of a yaws case. In twenty-eight cases the disease developed, beginning always at the seat of inoculation.

Moreover, Charlouis inoculated a native, suffering from typical yaws, with syphilis. The inoculation was quite successful, a primary syphilitic sore developing, followed by all the usual types of secondary eruption. That yaws patients are not immune against syphilis is proved also by Powell, who described two very interesting cases of syphilis supervening on yaws.

PERSONAL EXPERIMENTAL INVESTIGATIONS

Inoculation of yaws in monkeys.—My first experiments, made at the beginning of 1905, on a "purple-faced monkey" (*Semnopithecus cephalopterus*), were negative. In February and March of 1906 I made some more experiments of inoculation on three monkeys of the genus macacus, with positive results in one case. The monkey which was successfully inoculated with yaws was later successfully inoculated with syphilis.

In the meantime Neisser, Baermann, and Halberstadter published, in the *Münchener medizinische Wochenschrift* (November 28, 1906), a complete report of their results on the inoculation of yaws in monkeys, coming to the conclusion that monkeys of a high as well as of a low type are susceptible to infection with yaws; and that monkeys immunized for syphilis do not become immune for yaws.

I have continued the investigation on numerous monkeys of the genera macacus and semnopithecus. In both genera the positive results are fairly numerous, provided the scarifications on which the yaws material is inoculated are made as deep as possible. I quote two of the experiments which gave positive results.

Monkey No. 4 (*Macacus pileatus*), November 10, 1906. The scrapings taken from a non-ulcerated yaws papule were rubbed thoroughly into the scarified spots over the left eyebrow. The slight local inflammatory artefacts caused by the scarification subsided in three days. Nineteen days after the inoculation a very small flattened papule surrounded by an infiltrated zone appeared at the seat of inoculation. The lesion soon became enlarged and moist, the secretion drying

into a thick crust. On removing this crust a granulating raw surface was seen. Two months later, the first element being still present, four more papules appeared, two on the lower part of the forehead close to the primary lesion, and two just over the upper lip. One of these elements disappeared after a few days; the others became moist and a yellowish crust formed on each of them. These papules remained always small and disappeared within three months, leaving tiny dark marks. The eruption was evidently very pruritic, as the monkey was continually scratching. It is possible that the papules observed two months after the first lesion appeared may represent facts of auto-inoculation by scratching rather than a true secondary eruption.

Monkey No. 17 (*Semnopithecus priamus*), October 15, 1906. Scrapings taken from a non-ulcerated papule of a yaws patient were well rubbed into deep scarifications over the left eyebrow. Forty-five days after, three slightly elevated spots appeared which soon fused together into an infiltrated mass, covered by a thick crust. The lesion is still present and of much larger size. It was examined for the Spirochæte *pertenuis* on three different occasions, with positive results twice. Altogether eight monkeys of the genus *macacus* and eleven of the genus *semnopithecus* have been inoculated by me with scrapings taken from the eruptive elements of yaws patients; the inoculation was successful in five monkeys of the first genus and nine of the second. The incubation period has varied from a minimum of sixteen days to a maximum of ninety-two. The appearance of the lesion developing at the seat of inoculation was practically the same in all cases, viz., an infiltrated spot slowly increasing in size and soon becoming moist, the secretion drying into a thick crust. When the crust was removed a raw, granulating red surface was seen. With the exception of three cases the eruption remained localized at the point of inoculation, and no other eruptive elements appeared. In the three cases in which eruptive elements developed some time after the primary lesion, in one, as I have already mentioned (monkey No. 4), two small papules appeared on the lower part of the forehead in vicinity of the

primary lesion, and two others above the upper lip. Of the other two monkeys, in one a rather large moist papule appeared on the lower lip three months after the primary sore had developed; in the other, three small papules, which soon broke and became covered with a crust, developed on the lower part of the forehead close to the primary lesion, two and a half months after the first lesion had appeared.

INOCULATION OF MONKEYS WITH THE BLOOD OF THE GENERAL CIRCULATION FROM A YAWS PATIENT

About five cubic centimetres of blood were withdrawn (September, 1906), with all aseptic precautions, from a vein at the bend of the elbow of a patient suffering from a typical yaws eruption on the legs, back, and face, but not on the arms; the needle, therefore, could be inserted through a perfectly normal skin without touching any yaws element. One cubic centimetre of the blood was well rubbed into deeply scarified spots on the right eyebrow of a macacus. Thirty-three days later a small deeply raised brownish papule appeared. Before the papule became moist a scraping was taken and stained with Leishman's method according to the directions already given by me. Numerous individuals of the *Spirochæte pertenuis* were present. The papule slowly enlarged and became covered with a crust. The lesion disappeared within three months; no other elements developed.

This experiment shows that:

1. Monkeys can be successfully inoculated with the blood of a yaws patient.
2. The *Spirochæte pertenuis* is, at least temporarily, present in the blood of the general circulation, though, so far, I have not been able to detect it microscopically.

INOCULATION OF MONKEYS WITH THE SPLENIC BLOOD DERIVED FROM A CASE OF YAWS

About one cubic centimetre of splenic blood was obtained by puncturing the spleen of a patient affected with typical

yaws. Films showed that the Spirochæte pertenuis was present, though very rare. The splenic blood was inoculated in two monkeys of the genus macacus (*Mac. pileatus*) with the usual technique. Result positive in one monkey, a framboetic papule developing after an incubation period of thirty-six days; in the other monkey the result was negative.

INOCULATION OF MONKEYS WITH THE CEREBRO-SPINAL FLUID
OF YAWS PATIENTS. NOVEMBER, 1906

Four monkeys (two *Macacus pil.* and two *Semnopithecus priamus*) were inoculated with cerebro-spinal fluid derived from three different patients affected with yaws. The cerebro-spinal fluid was in all the cases perfectly limpid; on centrifugation did not show any sediment, and the Spirochæte pertenuis could not be found, though it was present in the skin lesions of the same patients. Up to date (July 15, 1907), eight and a half months after inoculation, the result has been negative.

INOCULATION OF FILTERED YAWS VIRUS. SEPTEMBER 14, 1906

The scrapings from non-ulcerated human papules containing the Spirochæte pertenuis in such abundance as is seldom the case—and no other germs which could be detected microscopically or by cultural methods—were mixed and well triturated with normal saline solution. Preparations made from this mixture showed many individuals of Spirochæte pertenuis. Part of the mixture was then inoculated, with the usual technique, into two monkeys of the genus macacus (*Mac. pileatus*). The rest of the mixture was filtered through a Berkefeld filter (12a); preparations made from the filtrate did not show the presence of the spirochæte. The filtrate was inoculated into three monkeys of the same species (*Mac. pil.*) and one *Semnopithecus priamus*. Both monkeys inoculated with the unfiltered material developed—one after twenty-five days, the other after forty days—framboetic papules at the seat of inoculation, covered by a thick crust. Films made from the scrapings of the framboetic lesions of

both monkeys contained the *Spirochæte pertenuis*. The four monkeys inoculated with filtered material have not shown any eruptive element, either at the place of inoculation or in any other region of the body, though ten months have elapsed since the inoculation. This experiment tends to prove that the *Spirochæte pertenuis* is the true cause of yaws, as when it is removed from yaws material the latter is no longer infective.

INOCULATION OF SYPHILIS IN MONKEYS PREVIOUSLY INOCULATED WITH YAWS

Monkey No. 4 (*Mac. pil.*). This monkey was successfully inoculated with yaws in February, 1906. On June 16, 1906 the scrapings from a primary sore of a syphilitic patient were well rubbed into scarified spots on the prepuce of the monkey's penis. On the twenty-sixth day after inoculation, a small vesicle surrounded by a reddish halo appeared. The vesicle broke, leaving an erosion surrounded by infiltrated tissue. The glands of both groins became enlarged and hard, and could be easily felt. No secondary eruption appeared, but, as shown by Metchnikoff and Roux, this is almost always the case when experimenting with monkeys of a low type.

Monkey No. 11 (*Mac. cyn.*), September 10, 1906. Inoculation of human yaws, taken from a non-ulcerated papule, on the left eyebrow, and of human syphilitic virus on the right eyebrow. The syphilitic material was taken from the primary sore of a man. After thirty-two days the left eyebrow, inoculated with yaws, showed three small flattened papules which fused together into an elevated mass the size of a pea, covered by a thick crust. The right eyebrow, inoculated with syphilitic material, thirty-nine days after inoculation, presented a tiny brown crust, which soon broke and became covered with a slight crust. As regards the appearance of the yaws and the syphilitic lesions, the yaws lesion was larger, more elevated, and covered by a much thicker crust. The syphilitic lesion disappeared after two months, while the framboetic one is still present.

TRANSMISSION OF YAWS FROM MONKEY TO MONKEY

Monkey No. 21 (*Mac. pil.*) was inoculated on the left eyebrow with human yaws virus taken from a non-ulcerated papule, on September 19, 1906. From the infiltrated spot which appeared four days later, and which contained the Spirochæte pertenuis, a scraping was taken and inoculated on November 22, 1906, in three monkeys of the same genus and species, and four monkeys of a different genus (*Semnopithecus priamus*).

Of the three monkeys of the same species, the results were in two cases positive, the incubation period being thirty-one days in one and forty-two in the other. Of the four monkeys of a different species, one only gave a positive result, after an incubation period of sixty-seven days.

INCIDENCE OF THE SPIROCHÆTE PERTENUIS IN MONKEYS INOCULATED WITH YAWS, IN COMPARISON WITH THE INCIDENCE OF THE SPIROCHÆTE PERTENUIS IN MAN SUFFERING FROM YAWS

The results of the investigation are collected in the following two tables.

TABLE I.—INCIDENCE OF THE SPIROCHÆTE PERTENUIS IN MONKEYS INOCULATED WITH YAWS

MATERIAL INVESTIGATED.	NO. OF MONKEYS EXAMINED.	NO. OF MONKEYS IN WHICH POSITIVE RESULTS WERE OBTAINED.
Primary lesion at the seat of inoculation.	16	15
Framboetic papules which appeared some time after the primary lesion..	3	2
Spleen juice.....	4	3
Bone marrow.....	4	1
Blood, general circulation.....	15	nihil
Smears from liver.....	4	nihil
Lymphatic glands.....	6	3
Brain substance.....	4	nihil
Cerebro-spinal fluid.....	4	nihil

TABLE II.—INCIDENCE OF THE SPIROCHÆTE PERTENUIS IN YAWS PATIENTS

MATERIAL INVESTIGATED.	NO. OF CASES EXAMINED.	NO. OF CASES IN WHICH POSITIVE RESULTS WERE OBTAINED.
Primary lesion.....	6	6
Unbroken papules of the general eruption.....	76	75
Ulcerated papules of the general eruption.....	76	52
Blood of the general circulation.....	20	nihl
Spleen blood.....	5	3
Cerebro-spinal fluid.....	6	nihl
Lymphatic glands.....	11	6

Comparing Table I. with Table II., it will be seen that the incidence of the Spirochæte pertenuis is practically constant in the eruptive elements both in man and in inoculated monkeys.

In the monkeys I have experimented with, the eruption does not become general as in man; notwithstanding this, we must admit that in monkeys also we have to do with a generalized infection, as is proved by the presence of the Spirochæte pertenuis in the spleen and lymphatic glands

THE HISTO-PATHOLOGY OF EXPERIMENTAL YAWS

Monkey No. 4 (*Mac. pil.*).—In this monkey, nineteen days after inoculation, as already described, a small infiltrated spot appeared at the point of inoculation over the left eyebrow; the lesion became moist, the secretion drying into a thick crust and attaining the size of a sixpenny-piece in about two weeks. Two months later, the first lesion being still present of the same size and with the same characters, four more papules appeared, two close to the first lesion, and two just above the upper lip. These papules remained always of small dimension and disappeared within three months. It is possible that these four papules were due to auto-inoculation by scratching; it cannot be excluded, however, that they might represent a partial secondary eruption comparable to the general secondary eruption which appears in man; it must be remembered that though the skin lesions in experimental

yaws—with the monkeys I have used—are generally localized at the point of inoculation, the infection is general, as is clearly proved by the presence of the *Spirochæte pertenuis* in the spleen of the animals.

On the 1st of June, 1906, the crust from the primary lesion was removed; from the raw elevated granulating surface a piece of tissue was cut, divided into small portions, and fixed in various ways (alcohol, sublimate, etc.); then imbedded in paraffin. Sections were stained with various methods (Pappenheim's, etc.). The two papules which appeared above the upper lip were also removed and investigated by the same methods. The results of the histological examination are briefly the following:

1. *Primary lesion.*—(a) A well-marked proliferation of the interpapillary processes.

(b) A cellular infiltration consisting of: (1) numerous typical plasma cells, found diffusely with no definite arrangement; (2) some extravasated polymorphonuclear leucocytes; (3) small mononuclear leucocytes, connective tissue cells, and a few mast cells. No true giant cells were observed. The fibrous stroma is very delicate and scarce.

2. *Papules removed from lip.*—Practically the same result, only the proliferation of the interpapillary processes is much less marked.

Comparing these results with those found by MacLeod, Unna, Nicholls, Plehn, and myself, in man, it would seem that the histological structure is practically the same in human yaws as well as in experimental yaws.

THE BORDET-GENGOU IN YAWS

I have applied to yaws this reaction following the technique used in syphilis by Wassermann, Neisser, and Bruck (see *Deutsch. med. Woch.*, May 10, 1906).

As is well known the principle of the reaction is this: when complement is mixed with the complex antigen + immune body, and afterwards some sensitized red cells are added, no hæmolysis takes place, as the complement has been already taken up by the complex antigen + immune body, and cannot, therefore, get fixed to the hæmolytic receptors.

If the complex antigen + immune body is absent, or only antigen or only immune body is present, then the complement will remain free, and, on addition of the sensitized red cells, will get fixed to the hæmolytic receptors and hæmolysis will take place. From the absence or presence of hæmolysis we can, therefore, detect the presence or absence of the complex antigen + immune body. As the following experiments prove, it is possible to demonstrate the existence of specific yaws antigen and antibodies.

Experiment I.—To the extract of non-ulcerated yaws papules, containing abundantly the Spirochæte pertenuis, some serum (heated to 55° C.) is added, derived from a monkey which has been successfully inoculated with yaws, and which had been afterwards treated at intervals with subcutaneous inoculations of yaws material. Then some fresh guinea-pig serum (complement) is added, and after a certain time some sensitized red cells, in my case goat red cells, treated with inactivated serum from a rabbit which had been inoculated several times with goat red cells.

Result: No hæmolysis.

The investigation is repeated, using the extract of papules taken from six other different cases of yaws.

Result: Constantly the same, viz., no hæmolysis.

Experiment II.—Same procedure as in Experiment I., using, instead of the extract of yaws papules, the extract of leprosy nodules.

Result: Well-marked hæmolysis.

Experiment III.—Same procedure, using the extract of nodules taken from a case of pseudo-granuloma pyogenicum.

Result: Hæmolysis.

Experiment IV.—Same procedure, using instead of the extract of yaws papules the extract of syphilitic condylomata.

Result: Hæmolysis.

Experiment V.—Same procedure, using the extract of a syphilitic primary sore which presented numerous individuals of Spirochæta pallida of Schaudinn.

Result: Hæmolysis.

Experiment VI.—Extract of yaws papules containing the Spirochæte pertenuis, + serum (heated to 55° C.) of a

monkey immunized for syphilis, + fresh guinea-pig serum, + sensitized red cells.

Result: Hæmolysis.

The experiment is repeated, using the extract of papules from six different cases of yaws, always with the same result, viz., hæmolysis. It is to be noted that the serum of the monkey contained with certainty syphilitic antibodies, as by inactivating it and then adding to it the extract of a primary syphilitic sore, then fresh guinea-pig serum (complement), then sensitized red cells, no hæmolysis takes place.

Experiment VII.—Extract of yaws papules, + serum (heated to 55° C.) derived from a normal monkey, + fresh guinea-pig serum (complement), + sensitized red cells.

Result: Hæmolysis, well marked.

Experiment VIII.—Extract of spleen juice obtained by puncture of a case of typical yaws, + inactivated serum of a monkey immunized for yaws, + complement, + sensitized red cells.

Result: No hæmolysis.

Experiment IX.—Same procedure as in Experiment VIII., using, instead of the serum of a monkey immunized for yaws, the serum of monkeys immunized for syphilis.

Result: Hæmolysis.

The above experiments show that it is possible to detect specific yaws antigen in the yaws papules and in the spleen of cases of yaws; specific yaws antibodies in the blood of monkeys treated with inoculations of yaws material.

The Experiments IV., V., VI., IX., show also that yaws antibodies and antigen are different from syphilis antibodies and antigen, and therefore syphilis and yaws can not be the same entity.

COMMUNICABILITY OF YAWS. DO INSECTS PLAY A RÔLE IN THE TRANSMISSION OF THE DISEASE?

As is well known, the disease is in most cases conveyed by direct contact from person to person, usually by absorption of the virus through some pre-existing abraded surface or small wounds or ulcerations which are frequently present on

the skin of natives. The simple contact of the virus on normal skin is not sufficient to cause the infection; but very slight abrasions—as, for instance, those due to scratching—are sufficient for the entrance of the virus.

Women are frequently infected by their children, the primary lesion appearing often on the mammæ. In the native women of Ceylon the primary lesion frequently develops on the skin of the trunk just above the hip. This is due to their habit of carrying the child astride of the hip, as shown in Plate xxxviii, Fig. 3. Any yaws element present on the scrotum and nates of the child will, therefore, be continually rubbed against the skin of the mother and infection will take place through any slight abrasion already present, or that may be caused by the friction.

In my opinion, however, there can be little doubt that, in certain cases, insects may carry the disease.

It is very noticeable that flies eagerly crowd on the open sores of yaws patients. In the hospitals, as soon as the dressings are removed, the yaws ulcerations will become covered with flies, sucking with avidity the secretion, which they may afterwards deposit in the same way on ordinary ulcers of other people. Ants also are occasionally seen to go on the yaws ulcerations as well as on ordinary ulcers.

In Nuttall's classical work on the rôle of insects as carriers of parasitic diseases, several authors are quoted (Alibert, Hoish, Cadet, Wilson) who believe that the infection may be conveyed from one individual to another by flies. Wilson states that this belief prevails also among the natives of the West Indies.

I may quote some of the experiments I have made to prove that flies are instrumental in the dissemination of the disease:

Experiment I. (November 10, 1906).—Some scraping was collected from slightly ulcerated papules of a yaws patient. The Spirochæte pertenuis was present, together with various other thicker spirochætes (*S. obtusa*, *S. acuminata*), but no bacteria. The scraping was placed in a sterile petri dish. Ten flies (*Musca domestica* and allied species), caught in the rooms of the Bacteriological Institute, were placed inside the petri dish and left there for half an hour. They fed greedily

on the material; then the proboscis and buccal organs as well as the legs were examined for spirochætes, making extracts and films; in nine flies the spirochætes of the thicker type were found; in two also the *Spirochæte pertenuis*. As control, five flies were caught the same day, in the same room, and examined at once, with negative results as regards the presence of the spirochætes.

Experiment II. (January 12, 1907).—Twenty flies were collected from the rooms of the Bacteriological Institute. The buccal apparatus and legs of five of them were removed and examined by making extracts and films; no spirochætes of any kind were present. The other fifteen flies were divided into several groups, and placed on various semi-ulcerated papules of three yaws patients presenting the *Spirochæte pertenuis*, and spirochætes of the thicker kind such as are often found in semi-ulcerated lesions. The flies were kept in place by covering the papules with a piece of gauze made to adhere to the skin by means of collodion all round the margin. All the flies fed greedily on the ulcerated papules. After two hours the proboscis and other parts of the mouth organs, as well as the legs, were removed, extracts and films made and stained. Out of the fifteen so examined, in fourteen it was possible to detect the coarse spirochætes, and in two the *Spirochæte pertenuis* as well as the thicker ones.

TRANSMISSION OF YAWS TO MONKEYS BY MEANS OF FLIES FED ON YAWS MATERIAL

Experiment III. (November 15, 1906).—Thirty flies were fed in a sterile petri dish for half an hour on scrapings taken from non-ulcerated papules of a case of yaws containing only the *Spirochæte pertenuis*. Three monkeys of the genus *semnopithecus* (*S. pria.*), and two of the genus *macacus* (*Mac. pil.*) were inoculated in this way: over the left eyebrow of each monkey very numerous deep scarifications were made; then five flies, deprived of their wings, were applied to the scarified spots and kept there by means of a piece of gauze smeared with collodion at the margins. The monkeys had their legs tied together to prevent their removing the gauze. After

two hours the gauze and the flies were removed. Of these monkeys, one, *Semnop. pria.*, after forty-five days developed a small infiltrated spot, which soon became enlarged and covered with a thick crust. The microscopical examination of the lesion showed the presence of the *Spirochæte pertenuis*. The other five monkeys gave negative results.

Experiment IV.—Twenty-eight flies (*Musca domestica* and similar species) were caught in one of the rooms of the Bacteriological Institute. The legs and buccal organs of five were removed and examined for spirochætes, making numerous preparations with negative results. The remaining flies, deprived of their wings, were placed on two slightly ulcerated elements of a yaws patient. The flies were kept on the ulcers by means of a piece of gauze, the margins of which were made to adhere to the skin with a little collodion. The flies sucked readily the secretion of the ulcers. After one hour the flies were removed; meanwhile seven monkeys of the genus *semnopithecus* (*Semnop. pria.*) had deep scarifications made over their eyebrows. Several flies which had fed on the ulcerated yaws lesions were placed on the scarified spots of each monkey and kept in place there for two hours by means of the device already mentioned.

One of the monkeys forty-six days after developed a slightly infiltrated spot which slowly enlarged into a framboetic nodule covered by a thick crust; the microscopical examination of films taken from this nodule showed the presence of the *Spirochæte pertenuis*. In another monkey, sixty-seven days after inoculation, three tiny papules developed at the place of inoculation; they soon fused together into an infiltrated mass covered by a thick crust. Films made from scrapings of the lesion contained the *Spirochæte pertenuis*.

The remaining five monkeys so far (March 15, 1907) have given negative results.

RESULTS OF THE INVESTIGATION

1. Monkeys are susceptible to yaws. The skin eruption in the monkeys I have experimented with (*Semnop. pria.*, *Mac. pil.*) is, as a rule, localized to the seat of inoculation, but

the infection is general, as is proved by the presence of the Spirochæte pertenuis in the spleen and lymphatic glands; these experiments confirm the results obtained by Neisser and his co-workers.

2. The extract of yaws material from which the Spirochæte pertenuis has been removed by filtration becomes inert.

3. The extract of yaws material containing the Spirochæte pertenuis, and, so far as our present methods of investigation permit us to say, no other germ, is infective to monkeys.

4. The inoculation into monkeys of blood of the general circulation and splenic blood taken from yaws patients, may give positive results.

5. The inoculation of the cerebro-spinal fluid of yaws patients is negative.

6. Monkeys successfully inoculated with yaws do not thereby become immune for syphilis.

7. Monkeys successfully inoculated for syphilis do not thereby become immune for yaws.

8. By means of the Bordet-Gengou reaction, it is possible to detect specific yaws antibodies and antigen.

9. Yaws antibodies and antigen are different from syphilitic antibodies and antigen.

10. The presence of the Spirochæte pertenuis in monkeys experimentally inoculated, as well as in yaws patients, is practically constant in the unbroken eruptive elements. It is frequent in the spleen and lymphatic glands.

11. Yaws is generally conveyed by actual contact, but under certain circumstances it may be conveyed by flies, and possibly by other insects.

PREDISPOSING CAUSES

Dirt and insanitation favor to a certain extent the development and spreading of yaws as well as any other infectious disease; the malady is extremely rare among Europeans and better-class natives who live in good sanitary surroundings, while it is very common among villagers and low-caste natives who live in uncleanly and overcrowded huts. Sex does not exercise any influence, nor does age to

a great extent, though the disease is somewhat more frequently met with in children and young people.

Food is mentioned by some Ceylon native practitioners as a very important predisposing cause; some inculcate a sort of fish called *balla malu*, others a fruit known as *rattadel* (breadfruit) and a kind of grain known as *kurrakkan* (nutcherry).

DIFFERENTIAL DIAGNOSIS

Verruga peruviana.—This disease is strictly limited to certain valleys of the Andes at an elevation of from three thousand to ten thousand feet. It is far more mortal than yaws, the mortality rising to thirty and forty per cent. It is often accompanied by severe fever of long duration; the eruptive elements of *Verruga peruviana* often attack the various mucosæ and bleed with great facility.

Bubas.—In Brazil and other South American countries, frambœsia is known under the name of bubas. A few authors (Breda) are of the opinion that bubas is a different disease from frambœsia. Rivas, after a complete investigation of the disease, has come to the conclusion that bubas is identical with yaws, and that it is caused by the same organism, viz., the *Spirochæte pertenuis*.

Syphilis.—The theory according to which yaws is a form of syphilis has now only an historical interest. The results of experimental investigations on yaws and syphilis prove clearly that the two diseases are different, inasmuch as:

1. Monkeys successfully inoculated with yaws do not thereby become immune for syphilis, and *vice versa*.
2. The yaws antigen and antibodies have been proved to be different from syphilis antigen and antibodies.

Syphilis is practically pandemic; yaws, on the other hand, is localized to some parts of the tropics. Yaws is extremely common in Ceylon, extremely rare in India. Syphilis is common in both countries. In Samoa, according to Turner, syphilis was unknown up to at least 1880, while yaws has been endemic there ever since the group was discovered. In Fiji, too, up to a few years ago, syphilis was not present,

while yaws was almost universal. Daniels has made the interesting observation that in British Guiana yaws of late years has disappeared, while syphilis is still rampant. As regards clinical features, yaws presents the following symptoms in contrast to syphilis: primary lesion generally extragenital, principal type of eruption a papule which proliferates into a papillomatous growth; extremely well-marked pruritus.

The histo-pathology of yaws and syphilis, as pointed out by MacLeod, Unna, etc., is somewhat different; in yaws the proliferative changes of the epidermis are much more marked, the yaws granulomata present a more diffuse plasma-cell infiltration, and their blood vessels have no tendency to thickening; naturally these differential histological details must be considered collectively, as there is no individual histological character which, exceptionally, might not be present both in syphilis and yaws.

PROGNOSIS OF YAWS

The prognosis is not serious *quoad vitam*. In Ceylon, in 1905, 3535 cases were treated, with 25 deaths; in 1904, out of 3591 cases, 16 died; in 1903, out of 3254 cases 10 only died. The prognosis is much more serious in children than in adults.

When the disease ends fatally it is generally due to the ulcerated lesions becoming phagadenic, and to septicæmic and pyæmic processes. Though frambœsia rarely terminates in death, its long duration and great contagiousness make it a serious complaint. The patients suffering from it are not able to attend to their work; epidemics of yaws, therefore, acquire great importance in plantations of tea, sugar, etc., as they greatly reduce the supply of labor.

Prevention of yaws.—The slightest abrasions of the skin should be taken care of and properly treated with antiseptics in countries where yaws is endemic. The yaws patients should be prevented from mixing with the rest of the population, and should be isolated in special hospitals till the disease is cured; their huts and belongings should be thoroughly disinfected.

TREATMENT

The natives treat the disease in various ways; in Samoa

the patient is rubbed down with sand and washed in the sea, and then the yaws are scraped with a shell. In the West Indies boiled and beaten-up leaves of the "physic nut" are applied, or powdered alum and sulphur used.

In Ceylon, the *vederellas* (native doctors) apply concoctions of various herbs, and give decoctions of sarsaparilla and other roots. They use also mercury disguised in various ways. The majority of European practitioners use mercury and potassium iodide; others affirm these drugs to be quite useless, and believe that cleanliness and good and abundant food are quite sufficient to bring about a cure.

In the Colombo Clinic for Tropical Diseases I have made some experiments on the various treatments, and I have convinced myself that the potassium iodide treatment is the most effective of all. I do not deny that some mild case may recover spontaneously, but this is certainly the exception, not the rule. I kept, purposely, four typical cases of frambœsia without any treatment for a certain time; one remained stationary, the other three became worse and worse. In one of these—a woman—I had, for humanity's sake, to give up the experiment after four weeks, numerous large fungoid ulcerations having developed. The symptom of which she complained the most, and for which she was continually begging some remedy, was the unbearable pruritus. As soon as the potassium iodide was administered, this symptom decreased remarkably in intensity, and finally disappeared, the eruption also getting better.

The potassium iodide should be given in large doses (at least three to four gms. daily); I have little doubt that many reported failures of the treatment are due to the insufficient quantity of iodide administered, though occasionally cases are met with refractory to potassium iodide or to any other treatment. The yaws patients bear large doses well; when severe symptoms of iodism set in, the doses should be temporarily decreased or the treatment may be stopped altogether for a few days. Mercury is useful in many cases, especially in children, but it is as a rule less efficient than the iodides.

Local treatment consists chiefly in keeping the skin scrupulously clean, washing the eruption twice daily with a per-

PLATE XXXVII.—To Illustrate Dr. A. Castellani's Article,
‘*Framboesia Tropica*.’



FIG. 1.



FIG. 2.



FIG. 4.



FIG. 3.





FIG. 6.



FIG. 5.



PLATE XL.—To Illustrate Dr. A. Castellani's Article,
"Framboesia Tropica."



FIG. 7.



FIG. 8.

PLATE XLI.—To Illustrate Dr. A. Castellani's Article,
"Framboesia Tropica."



FIG. 10.



FIG. 9.

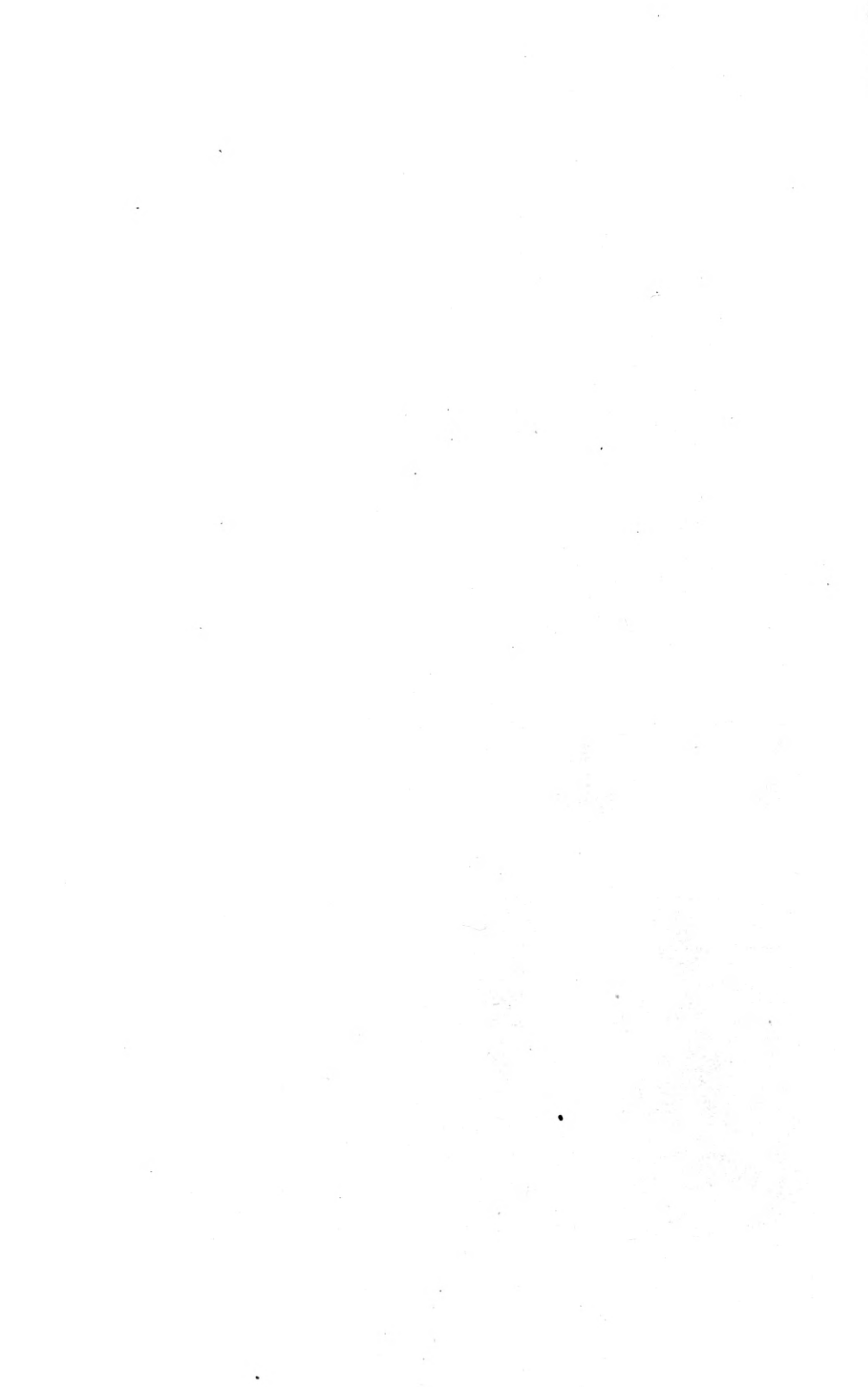


PLATE XLII.—To Illustrate Dr. A. Castellani's Article,
"Frambœsia Tropica."



FIG. 11.



FIG. 12.



PLATE XLIII.—To Illustrate Dr. A. Castellani's Article,
"Framboesia Tropica."

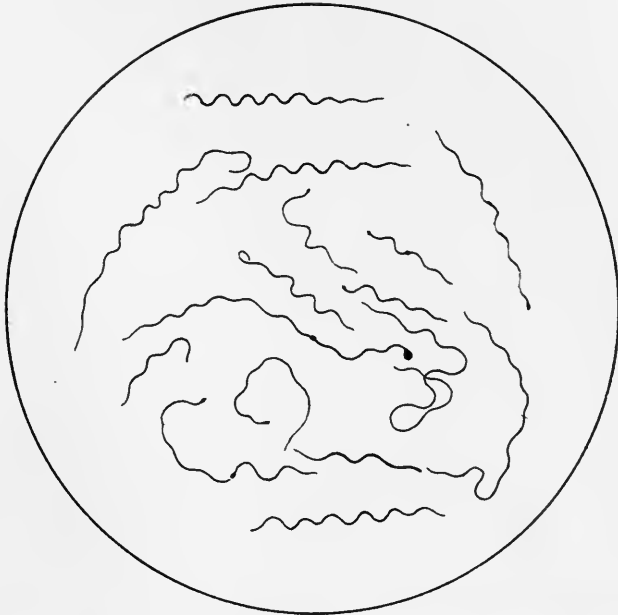


FIG. 13.



FIG. 14.

chloride of mercury solution (1 to 1000) which greatly allays the itching. The ulcerated lesions may be dusted with iodoform, boracic acid, etc. Mercury ointments may be beneficial, but in my experience are not sufficient to hinder secondary pyogenic infections.

Caustics are not called for unless the ulcers become phagadenic; in such cases pure carbolic acid is best. Though the external treatment may be useful, one must bear in mind that it is not, as a rule, sufficient alone to cure the disease.

DESCRIPTION OF PLATES

- Plate xxxvii. Fig. 1. Primary lesion of frambœsia on the thumb. General eruption on the face.
 Fig. 2. Primary lesion under the nipple.
- Plate xxxviii. Fig. 3. Showing how Ceylon women carry their children.
 Fig. 4. Frambœsia, general eruption.
- Plate xxxix. Figs. 5 and 6. Frambœsia, general eruption.
- Plate xl. Fig. 7. Frambœsia, general eruption.
 Fig. 8. Palmar eruption, showing peculiar pitting.
- Plate xli. Fig. 9. Frambœsia, general eruption.
 Fig. 10. Frambœsia. Eruption of the soles of the feet, which is called "dumas" by the natives of Ceylon.
- Plate xlii. Fig. 11. Frambœsia, tertiary eruption on heel. Note pitting of skin.
 Fig. 12. Frambœsia, tertiary lesions of legs.
- Plate xliii. Fig. 13. Spirochæte pertenuis.
 Fig. 14. Experimental frambœsia. Initial lesion on left eyebrow. General eruption on upper lip.

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NOTE ON A PALLIATIVE TREATMENT OF ELEPHANTIASIS

BY DR. ALDO CASTELLANI, OF COLOMBO (CEYLON)

In elephantiasis, as shown by the histological researches of Crocker, Virchow, Unna, and others, the subcutaneous tissue is enormously hypertrophied from increase of fibrous tissue in various stages of development; most of it being in fibrous bands and networks, while other portions are gelatiniform with fine fibres, numerous nuclei, and cells. Given these anatomical features of the disease, I thought that thiosinamin, which has been used by Hebra and others with success in cases of benign fibrous tumors, scars, etc., might be of some use in the treatment of elephantiasis, especially in cases of old standing.

As injections of thiosinamin are very painful, I have always used fibrolysin (Merck), which is a water-soluble combination of thiosinamin with sodium salicylate, and can be obtained in sterile glass ampullæ, each containing two cubic centimetres of liquid—corresponding to 0.2 grains of thiosinamin.

Method of treatment.—Before beginning the injections I keep the patient in complete rest in bed for a week, bandaging the affected parts with flannel bandages, or india-rubber bandages, and massaging them regularly twice daily. After

these manipulations the affected parts do not show much improvement as regards size, but become much softer, and thus the injections are made with much more facility. I make the injections in various parts of the affected regions, using the ordinary antiseptic precautions. I use an antitoxin syringe supplied with a strong needle. A sterile pad of gauze is applied to the place of the injection and the part is firmly bandaged. The injections are almost painless; after two or three hours there may be a little local pain, and the following day the part may feel harder than before, but in the successful cases after two or three days, the spot where the injection was made and the parts surrounding it become much softer. As regards dosage, I generally inoculate two cubic centimetres of fibrolysin every day or every other day according to the features of the case, for about a month; then I stop the injections for a week, during which time I continue the use of india-rubber bandages, or begin it if I have been using ordinary bandages hitherto. This india-rubber bandaging is most useful in cases of verrucose elephantiasis; it has no action on the deep lesions of the disease, but it renders the skin much smoother, the hard verrucose-like projections disappearing or becoming smaller. After a week or ten days a second course of thirty or more injections is given; then again a week's rest with rubber bandaging, followed, when necessary, by another course of injections.

After this treatment the affected parts—in successful cases—are of much smaller size; the skin becomes softer, elastic, and can be pinched up in folds; the enlargement of the bones, however, so frequently found, does not decrease. After the treatment is over I advise the regular wearing of puttees or elastic stockings; if this precaution is not taken, in a few days the affected parts again become enlarged; it is to be noted, however, that this enlargement is due, apparently, simply to an œdematous infiltration—as a day or two of rest and proper bandaging are sufficient to make the swelling disappear.

To remove the superfluous skin which remains after most of the subcutaneous tissue has been absorbed, and which facilitates the œdematous infiltration, I have suggested, when the disease affects the legs, the removal of long elliptical strips of skin, stitching up together the margins of the wounds; this

would not be practicable before the medical treatment, as the skin being enormously thickened and inelastic the coaptation of the opposed surfaces could not be obtained.

I have not observed any serious symptoms due to the thiosinamin: on one occasion a patient after the injection of a double dose (four cubic centimetres fibrolysin) complained of severe frontal headache, slight nausea, and general malaise which lasted for a few hours.

CASE I. *Elephantiasis verrucosa of the right leg*.—Ganegada Singhappu, Singhalese lad of eighteen years of age; admitted to the clinic June 2, 1907. First symptoms of the disease appeared twelve years ago, when he suffered from repeated attacks of fever accompanied by painful temporary swelling of the right leg. Later on the enlargement of the leg became permanent, increasing gradually to such an extent that the patient had to give up his work; he was an indoor servant.

At the time of admission the whole limb below the knee was greatly enlarged, the skin being thickened, hard, and rough; on the dorsum of the foot and toes numerous horny prominences were present. The limb measured round the ankle $23\frac{1}{2}$ inches; round the calf, $25\frac{1}{2}$ inches; the inguinal glands were not enlarged, the scrotum and the left leg were not affected.

No filaria were found in the blood.

The patient was first kept in bed for two weeks with the right leg slightly elevated and tightly bandaged with flannel bandage. Massaging was done twice daily. At the end of the two weeks the parts were slightly softer, but the dimensions of the leg were practically the same. The thiosinamin treatment was then begun, using the precautions already mentioned.

The patient received altogether sixty-two injections; during the last period of treatment the limb was very tightly bandaged for one hour three times daily, with a Martin rubber bandage.

At the end of the course of injections the condition of the affected leg was strikingly improved; the circumference round the ankle being reduced to 9 inches; round the calf to 12 inches.

Moreover the skin had become soft and of almost normal elasticity.

The patient, finding himself so much improved, able to walk easily—whereas when admitted he could scarcely move without help—asked to be allowed to leave the clinic for a short time as he had some business to transact in the village. I told him to use a flannel bandage continuously and to return to the clinic at the earliest date. He came back two weeks later, confessing that he had never used the bandages given to him. The lower part of the leg and foot were much enlarged (circumference round the ankle 12 inches), œdematous, soft. After twenty-four hours of complete rest in bed and rubber bandaging, the swelling disappeared and the measurements of the limb gave the same results as when he left the clinic.

The patient remained in the clinic; he was not given any more thiosinamin injections; he was allowed to walk; for one hour in the evening and one hour in the morning the use of rubber bandages was continued regularly; the limb did not enlarge. A short time ago I suggested that long elliptical strips of the redundant skin should be removed, and I asked Dr. Paul, surgeon to the General Hospital, to perform the operation. Dr. Paul very kindly consented and on July 24, 1907, it was done. The patient was put under chloroform and an elliptical portion of the skin and subcutaneous tissue was removed; the maximum longitudinal diameter of the portion of skin excised was 11 inches; the maximum transverse diameter $3\frac{1}{2}$ inches. The edges of the wound were brought in contact by means of an interrupted suture.

Since the operation the patient has complained for three days of some local pain; no fever. The stitches have not yet been removed.

CASE 2. *Elephantiasis verrucosa of the right leg.*—The patient—a private case—consulted me in October, 1906. He was suffering from elephantiasis of the right thigh, leg, and foot, of twenty years' duration. The skin of the lower part of the leg and foot was extremely hard, inelastic, and covered with numerous small wart-like protuberances.

Measurements: Thigh, 25 inches; calf, 27 inches; ankle, $24\frac{1}{2}$ inches. The patient underwent a treatment of ninety

thiosinamin injections combined with complete rest in bed, and the use of flannel bandages at first, and india-rubber bandages later. The case improved greatly, the skin becoming softer, more elastic, and much smoother. The circumference round the thigh was reduced to 21 inches; round the calf to 16 inches; round the ankle to 14½. The patient was able to walk with much greater ease.

I saw the patient again recently, nearly five months after the injections were stopped. The dimensions of the affected limb now are: thigh, 22 inches; calf, 17½ inches; ankle, 16½ inches. The patient, following my instructions, has been wearing puttees, and has continued regularly the use of rubber bandaging twice daily for an hour. He states that if he stops the bandaging and the wearing of puttees even for two or three days, the leg becomes swollen and œdematous; the swelling disappears, however, after a few hours' rest and bandaging.

CASE 3. *Elephantiasis of the left leg.*—The patient—a private case from India—had elephantiasis of fifteen years' duration localized to the lower part of the left leg and foot. He underwent a course of fifty-six thiosinamin injections, combined with rest, massage, and the use of rubber bandages. The improvement was very slight; the skin became somewhat smoother, but the dimensions of the affected parts remained practically the same. I think that rest, massage, and bandaging alone, without the injections, would have induced the same improvement.

CASE 4. *Elephantiasis of the left leg.*—Singhalese woman; fifty-six years of age; admitted to the clinic April 2, 1907. The disease is of fifteen years' standing and is localized to the lower two-thirds of the left leg and to the foot, the skin thick and inelastic, but not so rough as in the other cases. Circumference round the ankle 19 inches. The woman was kept in bed for ten days and the parts were bandaged with flannel bandages; skin softer, but dimensions of the limb practically unchanged. I then began giving the thiosinamin injections. She had thirty-five injections and she then left the clinic, wishing to visit her family, in a distant village. She was much better, the dimensions of the limb round the ankle being 11 inches. When the patient was admitted to the clinic

she could not move her toes; on leaving, such movements were easily made.

CASE 5. Bennet Gregory, Singhalese boy, æt. ten. Admitted to the clinic on June 25, 1907. Three years ago the patient began suffering from attacks of fever with contemporary swelling of the left leg and lymphatic inguinal glands of the left side. On admission the left leg and foot were greatly enlarged, the skin being thick and hard but with a smooth surface. Lymphatic inguinal glands of the left side were slightly enlarged and hard.

The measurements were as follows: Round the ankle, 12 inches. Treatment was begun on June 28, 1907. He received twenty-five injections and the limb was regularly tightly bandaged with flannel bandages, and for one hour every other day with rubber bandages.

On July 23d the injections were discontinued; they were resumed on the 29th of the same month. During the interval only massage and the use of india-rubber and flannel bandages were continued.

After the first twelve injections a distinct improvement was noticeable, the parts becoming softer and the size of the limb smaller. On the 15th and 16th of July, however, the affected part again became enlarged and very hard, though there was no fever. This condition lasted for three days.

TROPICAL FORMS OF PITYRIASIS VERSICOLOR

BY DR. ALDO CASTELLANI, OF COLOMBO (CEYLON)

In the *British Medical Journal*, November 11, 1905, I published a preliminary note in which I stated that in the tropics there are found several forms of pityriasis versicolor. I described two principal varieties: one yellow, under the name of pityriasis flava, the other black, under the name of pityriasis nigra. Further investigations have enabled me to confirm and enlarge these observations.

Pityriasis versicolor flava.—This is the commonest form, and in my opinion there are several sub-varieties of it. The affected parts are yellowish, of much lighter color than the surrounding healthy skin; the yellow color may be of various tinges, from dark, deep, orange-yellow in some cases, to very light canary-yellow in others. The patches are of various sizes; generally roundish, smooth, sharply defined, with margins not elevated, or only slightly so. Sometimes the patches are irregularly festooned, and may encircle areas of healthy skin (Plate xlvi, Fig. 6). Occasionally the encircled healthy skin appears to be intersected by many yellowish, ribbon-like lines originating from the surrounding yellow patch. The regions most frequently affected are, in order of frequency, the face, neck, chest, and abdomen. Large portions of the body may be involved. There is no pruritus. The patches are not desquamating, or only very slightly so. The course of pityriasis flava is very chronic. In the natives of the lower classes it appears in childhood as tiny spots on the face and chest, spreading slowly during years; they may coalesce, covering practically the whole of the face and chest. One is occasionally surprised to see a native whose face and chest are quite light in color; on closer examination it may be found that this lighter appearance is due to a diffuse, very light-colored form

of pityriasis flava, covering the whole of the face, neck, and chest. In native women, when the patches of pityriasis flava are small, light, and situated on the face, they are considered as beauty spots, and are highly appreciated by the ladies and their admirers. Such patches are called in Singhalese, "alu-hama," which means ashy skin (*alu*, ash, *hama*, skin). There is also another word used by native poets for such conditions, "gomera," which means skin dotted with beauty spots.

The disease in Ceylon and India usually affects natives only (Singhalese, Tamils, etc.), more rarely Burghers. I have seen one case among Europeans. The patient has been in the island for twenty years, and is a planter on a tea estate. He noticed the first light yellowish spots on the skin of the right arm six years ago: the eruption spread, slowly but continuously, to the neck and trunk; some spots are to be seen on the legs also. He has no pruritus whatever. The patient thinks he has been infected by some coolie affected with the disease.

Peculiar variety of pityriasis flava.—I have recently come across a peculiar variety of pityriasis flava characterized by a reddish-yellowish, or copper-colored tint. The fungus is microscopically indistinguishable from the fungus of the typical pityriasis flava, and cannot, likewise, be grown. I have seen several cases among natives of lighter complexion, and a most interesting one among Europeans. In the European the eruption was of four months' duration; he was sent to me with a diagnosis of seborrhœa corporis. The eruption was localized to the skin of the chest; numerous reddish spots, with perhaps a yellowish tinge, were present; some of which had coalesced in larger patches; no pruritus. The microscopical examination of scrapings from the eruption in liquor potassæ revealed the presence of a fungus microscopically identical with the fungus of pityriasis flava.

The fungus was very abundant.

Pityriasis versicolor alba.—This might perhaps be considered as a variety of pityriasis lutea. The color, however, is extremely light, occasionally altogether white; and the fungus found, as described later, is quite different from the

one found in pityriasis lutea. Pityriasis alba is oftener seen on the arms and legs than on the face and chest. The patches are frequently slightly elevated and are not so smooth as those of pityriasis lutea generally are; a slight degree of very fine pityriasic white desquamation is often present. The fungus is very abundant. The infection in contrast to pityriasis flava is very easily cured with the ordinary antiparasitic substances.

Pityriasis versicolor nigra.—The affected parts are of a dull black, lusterless color, much darker than the surrounding dark, healthy skin of the native. The patches may be small, roundish, and separated from each other, or may coalesce; they are often very slightly elevated, and may present a slight desquamation. Little, if any, pruritus is present. The face is not usually affected in this type of pityriasis, though the eruption may be found on practically any other region of the body. The neck and upper portion of the chest are apparently the regions most frequently affected. Pityriasis nigra usually attacks natives only. I have seen, however, an identical or similar form in a European. This European went for a pleasure trip to Burmah, where he remained for about a month. On coming back to Ceylon he noticed a small, roundish, very slightly elevated, non-desquamating black patch on the palm of his left hand. There was no pruritus. The patch spread slowly for two months, reaching the size of a sixpenny-piece. It disappeared after a single application of formalin; three months later it reappeared in the same place as a tiny black dot, which slowly spread. Another application of formalin caused it to disappear. From the patch a fungus was grown apparently identical with the one found in the usual form of pityriasis nigra.

Mixed infections.—It is not at all rare to find different varieties of pityriasis versicolor in the same patient; a mixed infection of pityriasis nigra and flava, for instance, is somewhat frequently met with. Several of my patients had on the neck a few round patches of pityriasis versicolor nigra, and on the face and chest some smooth yellow roundish patches of pityriasis flava. (Plate xlv, Fig. 1).

DESCRIPTION OF THE FUNGI FOUND IN THE VARIOUS TROPICAL FORMS OF PITYRIASIS VERSICOLOR

Microsporium tropicum.—I suggested this name (1905) for the fungus found in the pityriasis versicolor flava (Plate xlv, Fig. 2). The mycelial threads are generally thick with numerous swellings, constrictions, and other irregularities in their shape; they may occasionally contain specks of pigment. The spores are roundish or oval, 3.5 to 4.5 microns, and may have a double contour. In fresh cases the fungus is abundant with plenty of mycelium and spores which occasionally run into clusters; in old chronic patches the fungus becomes very scanty; the spores are not numerous, and generally do not collect in clusters; the mycelium is very scanty, and is even more irregular in shape than in fresh patches (degeneration forms of the fungus). I have not been able to grow this fungus.

M. macfadyeni.—This name was given by me to the fungus found in pityriasis alba (Plate xlv, Fig. 5). The fungus is very abundant, mycelium and spores are of small dimensions, much smaller than in the *M. tropicum* and *M. mansoni*. The mycelial tubes are often short and thin; regular in outline and often straight. The spores are small, 3 to 3.5 microns, oval in shape, sometimes forming large clusters. I have been able to grow the fungus on two occasions only, using Sabouraud's maltose agar. The fungus grew extremely slowly, giving rise to yellowish colonies which coalesced into a raised yellow mass, deeply pitted, very firmly and deeply rooted into the medium. Subcultures have never succeeded.

M. mansoni.—I suggested this name (1905) for the fungus found in pityriasis nigra (Plate xlv, Figs. 3 and 4). The fungus is abundant; the mycelial threads are rather short, 18 to 20 microns in length, and 2.5 microns in breadth. Sometimes they may be irregular in outline, bent, banana-shaped, etc. The spores are globular and most of them very large, 5 to 7.5 microns. They are frequently arranged in clusters. This fungus is easily cultivated by inoculating scrapings of the affected patches on maltose agar plates and tubes. The principal cultural characters are as follows:

Maltose agar.—The growth, especially in subcultures, is

comparatively rapid. After two or three days, roundish, hemispherical colonies appear (Plate xlvii, Fig. 7); they are black, sometimes with a dark greenish tint at first and may present at the periphery some radiating delicate pale greenish hyphæ. They soon coalesce into a jet-black knobby mass, deeply rooted into the medium.

Common agar.—The growth is similar to that found on maltose agar, only much less abundant and less rapid.

Glucose, saccharose, mannite agar.—Same characteristics as found in maltose cultures, though the growth is less abundant.

Broth and peptone water.—The fungus grows very slowly at the bottom of the tube, forming a black, or greenish-black sediment.

Milk.—Very slight growth; the milk is not rendered acid nor clotted.

Gelatine.—The fungus grows very slowly; for the first three or four weeks there is no liquefaction of the medium, then a very slight liquefaction generally takes place.

Temperature.—The fungus grows best at a temperature varying from 30° to 32° C.; over 35° and under 25° the growth is much slower.

Fructification of M. mansoni.—The fructification has been studied by making impression preparations and hanging drops. It takes place by formation of sprouts and clusters of spores and by endoconidia; aspergillar fructifications have never been observed.

Diagnosis.—The difference in color between pityriasis flava and pityriasis nigra is so characteristic that the two affections cannot be confused.

The diagnosis between pityriasis flava of a light variety, and pityriasis alba may sometimes be difficult; in pityriasis alba, however, there is always a fine whitish, pityriasic desquamation, the patches are slightly elevated and not so smooth; the face and chest are not the regions most frequently affected. The microscopical examination will reveal the presence of a fungus with thin, straight mycelium, and small oval spores; different from the irregularly shaped fungus found in pityriasis flava.

Pityriasis versicolor of temperate zones.—Of the various forms of pityriasis existent in the tropics, pityriasis flava *only* might be confused with the European form as regards color of the patches and the microscopical appearance of the fungus, which in neither form can be grown on artificial media.

The pityriasis of temperate zones, however, is generally not of so light a tinge, never attacks the face, and is curable with the greatest facility; while pityriasis flava affects the face more frequently than any other part of the body, and is curable only with great difficulty. It has been stated by Powell and others that the reason why pityriasis versicolor is in the tropics so commonly found on the face is due to the fact that natives seldom wash the face. This, in my opinion, is not so; natives of Ceylon, at least, wash often and are very fond of bathing. Moreover, I have been able to make this observation: three of my attendants, Singhalese, shave regularly every other day, using plenty of strong shaving soap. I have had them under observation for nearly three years. The patches of pityriasis which were present on their cheeks three years ago are still there—in fact they have spread.

Pinta.—The various forms of pityriasis met with in the tropics might be confused with pinta, of which, as is well known, there are several varieties, black, white, etc. The microscopical examination will clear the diagnosis at once: the fungus in all the various forms of pinta has the characters of an aspergillus; but in the various forms of pityriasis versicolor, the characters of a microsporon.

Leukoderma.—Only on very superficial observation can patches of pityriasis be mistaken for patches of leukoderma. Leukoderma patches have a characteristic dead-white color which is not found in any form of pityriasis, not even in pityriasis versicolor alba, in which there is, besides, frequently a fine whitish desquamation which is never present in leukoderma. In case of doubt the microscopical examination would establish the diagnosis at once.

Circumscribed scleroderma (Morphœa).—In this disease the patches may present a peculiar yellowish tinge, which in colored patients may resemble some varieties of pityriasis

flava. In pityriasis flava, however, there is no change in the texture of the skin, which is still pliable and does not exhibit the peculiar parchment-like feeling of scleroderma. The microscopical examination will clear the diagnosis in any doubtful case.

Seborrhæa corporis.—The peculiar reddish-yellowish variety of pityriasis flava I have described might, on superficial observation, be mistaken for a form of seborrhœa corporis, very common in the tropics among Europeans. The microscopical examination will clear the diagnosis.

Prognosis and Treatment.—None of the tropical forms of pityriasis versicolor show any tendency to spontaneous cure. All the forms are very chronic and may last for life. The forms that yield most readily to treatment are pityriasis nigra and pityriasis alba; the most obstinate is pityriasis flava. For pityriasis nigra and alba the usual antiparasitic lotions and ointments answer well; a salicylic spirit lotion (4 per cent.) followed by a mild mercurial ointment as, for example, white precipitate, grs. x to xv to the ounce of vaseline, gives good results.

Pityriasis flava is much more difficult to deal with; turpentine, applied every day and followed by a betanaphthol or epicarin ointment is often successful; but the treatment must be continued for months. It is to be noted that in several cases of pityriasis flava the fungus has apparently a deep, permanent disturbing action on the pigmentation processes of the skin, as even when the fungus has been destroyed the patches remain of a lighter color than the surrounding skin for a long time, though ultimately they become again normally pigmented.

PLATE XLIV.—To Illustrate Dr. Aldo Castellani's Article, "Tropical Forms of Pityriasis Versicolor."



FIG. 1.—Patient affected with Pityriasis Flava (face) and Pityriasis Nigra (neck).



PLATE XLV.—To illustrate Dr. Aldo Castellani's Article, "Tropical Forms of Pityriasis Versicolor."

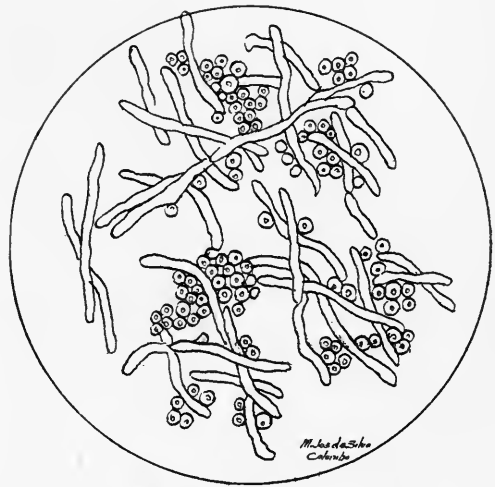


FIG. 2.—*Microsporon Tropicum* (Castellani).
Fresh preparation in liq. potassæ from
an old case of pityriasis flava.

FIG. 3.—*Microsporon Mansoni* (Castellani).
Drawing taken from a fresh prepara-
tion in liq. potassæ.

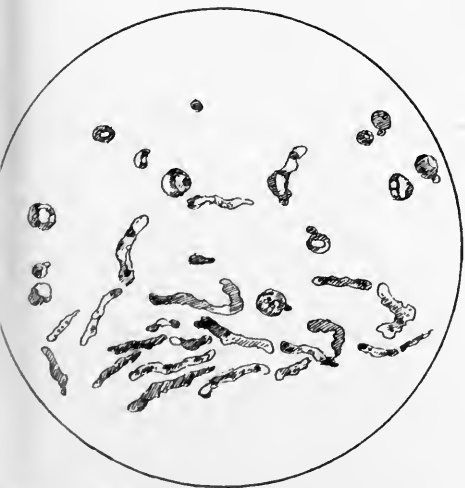


FIG 4.—*Microsporon Mansoni* (Castellani).
Preparation stained with fuchsin.

FIG. 5.—*Microsporon Macfadyeni* (Castellani).
Parasite stained with fuchsin.

PLATE XLVI.—To illustrate Dr. Aldo Castellani's Article, "Tropical Forms of Pityriasis Versicolor."



FIG. 6.—Patient affected with Pityriasis Flava.

PLATE XLVII.—To Illustrate Dr. Aldo Castellani's Article, "Tropical Forms of Pityriasis Versicolor."



FIG. 7.—*Microsporon Mansoni* (Castellani), young culture on Maltose-agar.

TINEA INTERSECTA

BY DR. ALDO CASTELLANI, OF COLOMBO (CEYLON)

I have had the opportunity to investigate, in Ceylon, two cases of a peculiar dermatomycosis, which, so far as I know, has not yet been described, and for which I suggest the name of *tinea intersecta*. Both patients were Tamil; in one the eruption developed while he was convalescent from typhoid fever. It showed identical characters in both patients and ran the same course. Small oval or roundish, very slightly elevated, pruritic spots appeared on the skin of the arms (Plate *xlviii*, Fig. 1), chest, and back; in the second patient on the legs also; the margins of these patches were occasionally slightly raised. The latter were dark brown, much darker than the surrounding skin, and presented a smooth tense surface at first; they increased in size slowly and some coalesced. After a certain time the surface of the patches was no longer tense; it became somewhat shrivelled and dry; superficial cracks appeared, so that white lines were visible intersecting the brown surface of the affected areas; later the cracks became deeper, the epidermis split, and several flaky curled-up scales, whitish inside and dark on the outer surface, were seen; the scales were often removed by friction, etc., and whitish patches only remained.

The eruption never develops in concentric rings like *tinea imbricata*; the patches remain isolated or fuse together, forming irregular larger ones. Some may disappear spontaneously after a time. The general health of the patients does not seem to be affected; in both my cases a slight degree of eosinophilia, 8 per cent. in one case and 6 per cent. in the other, was present. The eosinophilia, however, may have been due to the intestinal worms which both patients harbored—as shown by the examination of the stools which

contained ova of *Ascaris lumbricoides* and *Trichocephalus dispar*.

Transmission of the disease.—I made one of the patients scratch with his nails some of his patches and then scratch a healthy Tamil coolie, who volunteered for the experiment, on the arms and upper part of the chest. On the arms nothing developed; on the chest at the inoculated place there was—on the second and third day—much itching; on the fourth day two tiny, dark, very slightly elevated, roundish spots appeared; these enlarged slowly and a few days later their surface showed several whitish cracks. Unfortunately at that time the coolie—who was complaining of great pruritus—scrubbed himself thoroughly with sand soap, with the result that the patches disappeared.

The fungus.—If a portion of one of the brown patches or a scale is removed and treated with liquor potassæ, the fungus is easily detected. It grows apparently between the superficial and the deep strata of the epidermis, and is present on the inner surface of the scales, but not on the external surface (Plate xlvi, Fig. 2).

The fungus presents the general characters of a trichophyton; what is very remarkable is the extreme rarity of free spores, in fact in none of my preparations have I been able to detect any. The mycelium is fairly abundant, though far from being so abundant as in *tinea imbricata*. It is composed of long straight articulated threads which are sometimes dichotomous, the breadth being between 3 and 3.5 microns. Endospores are present as well as endoconidia. No aspergillar fructifications nor clusters of spores are to be seen. So far I have not succeeded in growing the fungus.

Diagnosis.—When the eruption is in the very first stage it might be mistaken for a form of tropical pityriasis versicolor. In pityriasis, however, the epidermis does not split; moreover, in *tinea intersecta* the fungus is not found on the surface—it grows between the superficial and deep layers of the epidermis.

Tinea imbricata.—In contrast to *tinea imbricata* the eruption never develops in concentric circles; is far less severe, as patches may disappear spontaneously; and is cured without

PLATE XLVIII.—To Illustrate Dr. Aldo Castellani's Article,
"Tinea Intersecta."



FIG. 1.—Forearm of patient affected with Tinea Intersecta.

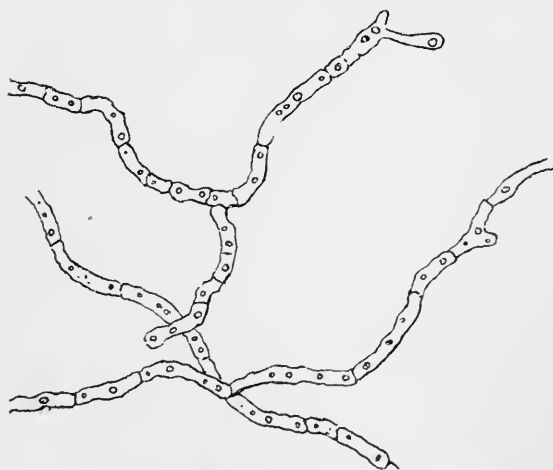


FIG. 2—Fungus of Tinea Intersecta.
Drawing from a fresh preparation in liq. potassæ.

much difficulty. At the time I had in my clinic the two cases of tinea intersecta, I had also two cases of tinea imbricata; the two eruptions could not possibly be confounded.

Treatment.—Tr. iodine and the usual antiseptic ointments answer well.

NOTE ON TINEA IMBRICATA AND ITS TREATMENT

BY DR. ALDO CASTELLANI, OF COLOMBO (CEYLON)

As a small addition to the present knowledge of the geographical distribution of tinea imbricata (Manson), it may be desirable to put on record the cases of the disease I have seen in Ceylon, in which country as well as in India it is stated to be non-existent.

Eleven cases have come under my observation during the four years I have been in Ceylon. The first of these was briefly described by me in the *Brit. Med. Journal*, Nov. 26, 1905. All the cases have come from villages near Colombo, with the exception of one—a Tamil coolie coming from Southern India—and most of them have been treated as out-patients. They were all typical cases; in all of them Manson's fungus was easily detected. I will limit myself to giving a brief clinical history of the patient whose photograph and sketch are attached in this paper—.

James—, Singhalese villager, twenty-six years of age; entered the clinic on March 20, 1906. No disease of importance in the past. The present eruption, according to the patient, had begun eighteen months before on the right shoulder, and from there spread slowly but steadily; he was treated without receiving any benefit by several *vederallas* (native medicine men). The disease did not cause any disturbance in the general health, but he complained of the disfigurement and the unbearable pruritus. At the time of admission the eruption was found to extend over practically the whole of the body (Plate xlix) with the exception of the scalp; the palms, soles of the feet, lower part of the face, and the axillary

regions were affected, though it is generally stated that the disease does not affect either the face or the axilla, and is rarely found on the palms and soles. The eruption was most typical on the chest, back, and axilla. Several round patches were present, each presenting concentric scaly rings. The scales were flaky, very dry, of a dirty grayish color, and slightly curled; they were of various dimensions and if removed rings of concentric circular dark lines could be seen.

The number of rings forming the patch varied; in some patches eight or ten could be seen, though Tribondeau states there are generally not more than four.

On the abdomen, arms, and legs, the patches had coalesced and their disposition in rings could not be seen. The thin flaky, curled scales were, however, quite typical. On the forearms and hands numerous warts were present; the nails were thickened, having a rough surface and cracks; scrapings taken from them show the fungus. Infection of the nails is against the experience of most authors.

Physical examination.—Negative for all organs.

The urine, slightly alkaline, and loaded with carbonates, this being probably due to the vegetarian diet of the patient.

Stools, ova of *Ascaris lumbricoides* and *Trichocephalus* dispar present.

Blood, hemoglobin 70% (Fleischl).

Number of red blood cells.....	4,100,000
Leucocytes.....	9,000

Differential Count:

	PER CENT.
Polymorphonuclear.....	50
Large mononuclear.....	10
Small mononuclear.....	20
Eosinophiles.....	18
Transition forms.....	2

A certain degree of eosinophilia was also present in four other patients. I am inclined to think that the eosinophilia

is partly due to the numerous intestinal worms present in all patients.

The fungus.—Fresh preparations of scales in liquor potassæ were made and also stained preparations, using Walker's modification of Morris's method (Plate 1). In all the cases Manson's trichophyton (*T. concentricum* Blanchard) was found to be very abundant. The characters of the fungus corresponded much more closely to the descriptions given by Manson, and recently by Pernet, rather than to the descriptions given by Tribondeau and others.

Fresh preparations of scales show a diffuse mass of interlacing mycelium. The segments of the mycelium vary greatly in length. They are generally straight and of regular outline, not showing swellings and constrictions. The spores are rather large, oval, or rectangular. Aspergillar fructifications, which have been described by several authors, have never been observed by me. In two cases I tried to grow the fungus, using various media, but failed. My experiments, however, on the growth of the fungus were very few, and it is to be noted that Tribondeau and others have succeeded in growing it in several cases.

Treatment.—Every medical man practising in the tropics well knows how difficult is the treatment of tinea imbricata; it is easy to obtain temporary improvement, and even an apparent disappearance of the eruption; but as soon as the treatment is discontinued the eruption, as a rule, begins afresh.

In the Colombo clinic I have made various experiments to test the efficacy of the various medicaments by applying contemporaneously different liniments, ointments, etc., to symmetrical parts of the body and comparing the results. The medicaments employed by me were sulphur, calomel white precipitate, red precipitate, turpentine, etc.

Sulphur has practically no effect whatever on the fungus.

Turpentine induces generally a slight improvement, some scales disappearing and the skin becoming smoother; the improvement, however, is not permanent, and as soon as the turpentine application is discontinued, the typical scales reappear.

Calomel, white precipitate, and other ointments of mercurial preparations do not induce any improvement in the eruption.

Thymol and naphthol ointments may cause a slight improvement.

Carbolic acid and epicarin ointments have no effect whatever.

Cyllin ointment (20 to 50 per cent.) may induce a temporary improvement.

Formalin is very effective for localized patches. The usual 40 per cent. solution is applied with care, treating each time a small portion of the eruption. Formalin often causes severe pain and a certain degree of inflammation, which is best relieved by applications of iced water. Soon after the application of formalin the patches become dark brownish, which color lasts for a few days, when they clear. Care must be taken not to apply the formalin to too large portions of the skin and not to repeat the application too often, otherwise a peculiar form of depigmentation similar to leukoderma patches may appear later on, to which disfigurement colored patients strongly object.

Tinctura iodi and Linimentum iodi.—Tr. iodi freely applied induces a very marked improvement, which, however, is not permanent. Strong linimentum iodi, as recommended by Manson, is most effective; it cannot be used freely, however, on patients with a delicate skin, such as women and children.

Chrysarobin.—The repeated application of chrysarobin in ointment (gr. xxx to one ounce of vaseline) may induce a strikingly rapid improvement in cases which are not of long standing; in my experience, however, the eruption recommences a few days or weeks after its apparent disappearance. Chrysarobin is a very toxic medicament—the patient must be watched and the urine regularly examined; in one of my cases symptoms of absorption appeared after a single application.

Salicylic acid and methyl salicylate have very little, if any, action on the fungus.

Resorcin and Tr. benzoini.—Resorcin alone, or mixed with salicylic acid, in alcoholic solution and ointments, has very little efficacy. If, however, resorcin is dissolved in Tr.

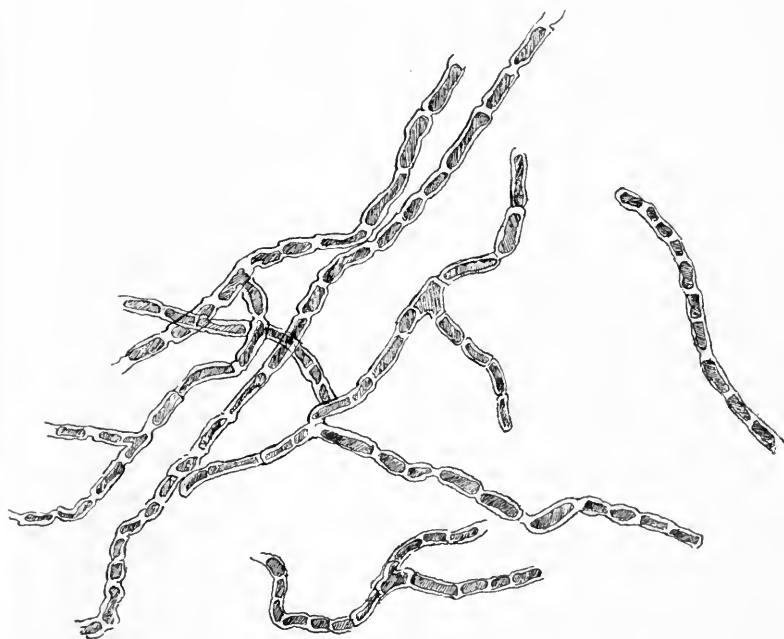
PLATE XLIX.—To Illustrate Dr. Aldo Castellani's Article,
"Tinea Imbricata."



Patient affected with Tinea Imbricata.



PLATE L.—To Illustrate Dr. Aldo Castellani's Article,
"Tinea Imbricata."



Fungus of Tinea Imbricata,
From a preparation stained by the Morris-Walker method.

benzoini co. (gr. xxx to lx of resorcin, to one ounce of the Tr. benzoini) very good results are obtained; it is now my routine treatment for tinea imbricata.

It is to be noted that Tr. benzoini without resorcin has very little action on the eruption. I generally apply freely the resorcin dissolved in Tr. benzoini once or twice daily on the affected regions; if the whole body is affected, one day one half is painted and the other day the other half, alternately. The treatment must be continued for several weeks.

Once or twice a week the patient is given a very hot bath and scrubbed all over with sand soap. I have treated in this way five cases, all of whom left the clinic apparently cured. I have had opportunity to see three of them again after four months: two remained well; in one, two small patches had reappeared on the right shoulder. So far I have not observed symptoms of absorption; in fact the patient who showed symptoms of absorption after chrysarobin, stood the resorcin treatment well. It is always prudent, however, to proceed at first with care, as it is well known that individuals may be met with, though rarely, showing idiosyncrasy for resorcin.

Conclusions.—1. The geographical distribution of tinea imbricata is more extensive than was hitherto supposed, as it includes Ceylon and probably some parts of India.

2. The treatment of tinea imbricata is very difficult; the best results perhaps are obtained by using strong Lin. iodi as suggested by Manson; or resorcin dissolved in Tr. benzoini co., as suggested by myself.

DEMONSTRATION OF THE USES OF LIQUID AIR IN DERMATOLOGY

BY DR. CHARLES T. DADE, OF NEW YORK

Before showing the cases I have here to-day may I say a preliminary word or two? Seven years ago last spring liquid air was first used in dermatology on a case of most rebellious erythematous lupus. The result was most surprising. The patient is here to-day that you may see the permanency of the cure resulting from a single application. Since then I have made use of liquid air principally in the treatment of all the varieties of *nævi*, in erythematous lupus, and in the superficial epitheliomata of the face to the extent and with such uniformly good results that, at the Vanderbilt Clinic, these lesions are now, and have for some time past been treated with liquid air to the exclusion of all other methods. I have not as yet published anything on the subject, waiting until I have completed some experiments on animals undertaken to find out just what takes place in the tissues during and after healing, more especially in regard to the vascular *nævi* in which the results are so peculiarly good, both in respect to obliteration and beauty of subsequent scar obtained. The failure of liquid air to affect lupus vulgaris as yet has been most disappointing,—apparently the lesion is too deep-seated to be affected. In the so-called scrofulodermata, however, following broken-down glands, the results are excellent, as a case here to-day will show. From the success, then, in erythematous lupus and failure in true lupus, it would seem that liquid air has but little effect when the lesion is a deep-seated one.

Liquid air is 312° F. below zero. It is applied with a cotton swab with firm pressure until the part is thoroughly frozen—a time varying from twenty to thirty seconds. There

is considerable pain on application and as thawing out takes place, but this feature is very variable; some do not complain at all of any great pain, and I have repeatedly seen babies quietly take the bottle or nurse and shortly afterwards go to sleep. In from two to four hours after application a bulla is formed arising like a true pemphigus bulla without surrounding inflammation of the neighboring skin. This bulla is either allowed to be absorbed, to dry up and form a crust which in from ten days to three weeks falls, showing as a rule a smooth white cicatrix level with the skin and often hardly to be noticed, or it is opened, the contents expressed, aristol powder dusted on, and the whole left to form the crust, under which healing goes on. It is to the protection of this primary crust *in situ* until it falls spontaneously that the excellence of the scar is due. In loose tissue, as around the eye, there is much œdema, which however soon subsides, but as it is often formidable-looking it is just as well to give warning of what to expect to allay possible alarm. I have never known hemorrhage to occur when the liquid air is applied to the unbroken skin or mucous membrane, even after its use on the most formidable-looking protuberant cavernous nævi which look at times as if they would burst as the child cries. On open lesions, such as ulcers, naturally there is some oozing as the blood returns after thawing out takes place, but this never is of any moment.

With your permission I will now show you some of the cases that have already been treated and cured, and apply the air to one or two cases for the first time and to some now in course of treatment.

S. R., 5 years old. Four applications in 1903 for a vascular nævus over entire back of right hand, spreading into palm. Complete removal—smooth white soft scar barely noticeable.

R. T., seven applications in 1904, when 6 months old, for large protruding cavernous nævus on forehead and overhanging right eye almost closing it. As you see, the eye is normal in opening and a smooth white scar level with the skin surface.

A. R. Cavernous nævus on mucous membrane of lower

lip, left side, size of half a cranberry. A surgical operation would have destroyed half the lip and hot needles, as formerly used in such cases, would have made an ugly scar. One application of liquid air was made; the contour of the lip is preserved and it is difficult to see where the lesion was formerly located as the red of the mucous membrane of the lip is normal. This baby also had a protruding cavernous nævus on the forehead the size of a five-cent piece, standing out a quarter of an inch. It took but two applications to reduce this to the level of the skin surface with the resulting smooth white scar.

M. G. Cavernous nævus on forehead, one inch in diameter and raised a quarter of an inch. Smooth white scar almost level with the skin.

E. C. Cavernous nævus on right cheek—same result as in all such cases.

A. Mc. Cavernous nævus above and below left eye, extending down side of the nose on to upper lip; eye was partly closed by the mass. Forehead shows the white scar level with the skin where mark is completed; the eye can be opened much better already, and I expect the result when treatment is completed to be as good as in the second case shown, which was similar to this case but less extensive.

The next two cases I show through the courtesy of Dr. Gold of Bridgeport, Conn.

(A) A pigmented hairy mass on right cheek, one inch by two inches standing out one eighth of an inch. Dr. Gold made but two applications, treating one half the lesion at the first sitting, and when the crust fell in two weeks the other half. As you see, there is no sign of pigmentation or hairs and the scar is smooth and level with the skin surface. I venture to say no other process could have produced such a result, whether as regards time involved, the amount of pain, or cosmetic effect.

(B) Dr. Gold's second case, a most extensive one of cavernous nævus taking in almost the entire left side of the face, head, and neck. He has not yet completed the work, but what has been done on the eye, forehead, cheek, and ear shows, in comparison with the character of what remains to be done, what superb results have already been accomplished. The

mother of the child tells me that before applications were made the eye was closed and the ear pushed forward by the cavernous mass overhanging it. It is certainly the most extensive cavernous nævus I have ever seen and I think you will agree that Dr. Gold's results are fairly astonishing.

J. Y. Erythematous lupus. This case is the one referred to as the first to which liquid air was applied seven years ago. The forehead, cheeks, and nose are as free to-day as when the crusts fell after the first application in 1900.

A. B. Epithelioma of nose. Treated three years ago. No trace to be seen to-day.

M. D. Erythematous lupus of the nose and scalp. Scalp has not yet been treated. The nose, as you see, is entirely free and smooth

M. B. Epithelioma of nose—extensive case. Treated four years ago. No recurrence.

¹ J. B. Epithelioma, size of five-cent piece, on left temple, to which I will make an application now.

A. B. Tuberculosis verrucosa cutis of the dorsum of foot and instep. The lower part was treated five years ago and has remained cured. He was prevented from returning to the clinic until lately. I will apply the air to the lesion on the instep. This patient also has a patch of lupus vulgaris on the right arm, and several attempts have been made with the liquid air without avail.

² J. M. Scrofuloderma of right side of neck following broken-down glands. Three years ago this patient had two applications of the liquid air made and the whole area healed in six weeks. Previously over a period of four years she had had three operations on the neck by scraping or cutting, none of which proved successful. She has just returned to the clinic showing a tuberculous ulcer on the left knee below the patella, the result of the breaking through of a tuberculous bursitis. The surgeon who was consulted advised, in view of the quick and lasting result obtained on the neck lesions three years ago, that liquid air be applied to the knee and if not

¹ This case healed in three weeks.

² Since the liquid air was applied to this case the knee lesion has entirely healed.

successful that a cutting operation be done. In the hope that it may be successful, I will apply the air to-day. To save time, I will not bring before you any more of the cases, but those you have not seen will remain and you can inspect them at your leisure. I will only say that the cases shown have not been at all selected ones, but just the regular clinic patients I have been able to secure for this occasion. If in presenting the cases to-day I seem to have sounded the personal note too much, or held down the loud pedal too long, please forgive it in the enthusiasm I feel for a very definite means toward very real results.

End of Fourth Day

FIFTH DAY, FRIDAY, SEPTEMBER 13TH.

PROF. WOLFF, of Strassburg, DR. HERMANN G. KLOTZ and DR. ROBERT W. TAYLOR, of New York, Vice-Presidents, in the Chair

THEME III.—(a) THE POSSIBILITY OF IMMUNIZATION AGAINST SYPHILIS. (b) THE PRESENT STATUS OF OUR KNOWLEDGE OF THE PARASITOLOGY OF SYPHILIS

PRESENTED BY PROF. ERICH HOFFMANN, DR. A. BUSCHKE, AND DR. OSCAR T. SCHULTZ

PARASITENBEFUNDE BEI MENSCHLICHER SYPHILIS

VON PROF. ERICH HOFFMANN, BERLIN

Unsere Kenntnisse über die Ätiologie der Syphilis habe ich in einer Broschüre, welche den Inhalt meines im September 1906, in Bern gehaltenen Referats erweitert wiedergab, ausführlich zusammengestellt und die Geschichte und den damaligen Stand der Spirochätenforschung eingehend erörtert und durch einen kurzen Nachtrag vom Dezember vorigen Jahres ergänzt. Bei dieser Gelegenheit habe ich aus den neuen ätiologischen Forschungsergebnissen auch schon eine Reihe von *Schlussfolgerungen* für die Diagnostik, Pathogenese, Prognose und Therapie der Syphilis gezogen und zugleich die Frage ihrer Bedeutung für die Lehre von der Infektiosität und Vererbung dieser eigenartigen Krankheit kurz besprochen. Dem Referat konnte ich schon damals ein Verzeichnis von 750 Publikationen beifügen.

Seitdem sind natürlich wieder zahlreiche Arbeiten erschienen, die allerdings grösstenteils nur das damals bereits

Bekannte bestätigen und in Bezug auf Einzelheiten vielfach erweitern. Es kann nicht meine Aufgabe sein, Ihnen noch einmal in aller Ausführlichkeit all die Tatsachen vorzutragen, die ausser in meiner Broschüre inzwischen auch von R. Kraus, Sobernheim und Lévy-Bing zusammenfassend dargestellt worden sind, sondern ich glaube in Ihrem Interesse zu handeln, wenn ich mich darauf beschränke, nur die wesentlichsten Punkte kurz hervorzuheben und auch von den neuen Forschungen nur das wirklich Wertvolle zu berichten und dafür das Hauptgewicht auf eine Demonstration aller wichtigen Befunde lege, die Ihnen besser als lange Beschreibungen ein Bild der Syphilisspirochäte und ihrer Beziehungen zu den erkrankten Organen und Geweben zu geben vermag.

Wenn ich in diesem Referat *nur über die Spirochäta pallida* berichte und andere Befunde wie die Siegels nicht näher berücksichtige, so glaube ich dazu berechtigt zu sein, weil die ätiologische Bedeutung der Spirochäta pallida ja unzweifelhaft erwiesen und so gut wie allgemein anerkannt ist, und die Befunde Siegels durch sorgfältige Nachprüfungen besonders von Hartmann und Mühlens widerlegt worden sind.

Ich will nun zunächst die morphologischen und biologischen Eigenschaften der Spirochäta pallida schildern, um im Anschluss daran die Parasitenbefunde in den verschiedenen Krankheitsprodukten der erworbenen und angeborenen Syphilis und ihre Bedeutung für die Pathogenese der Krankheit zu besprechen und endlich noch einige Bemerkungen über die Vorteile, die uns die Spirochätenforschung für die Diagnose und Therapie gebracht hat, anzuschliessen.

Auf die bereits früher von mir zusammengestellten *Methoden* für den Nachweis der Spirochäta pallida will ich hier nicht näher eingehen und nur sagen, dass für die klinische Untersuchung gewöhnlich am schnellsten und sichersten die *Dunkelfeldbeleuchtung* (nach Reichert oder Zeiss) zum Ziel führt, welche in dem durch Reiben gewonnenen "Reizserum" oder in dem durch Aspiration mit kleinen Klappschen Glocken¹

¹Man setzt auf die Papel oder den Primäraffekt (nötigenfalls nach vorsichtigem Abschaben der Hornschicht bei geschlossenen Efflorescenzen) einen Klappschen Saugkopf und aspiriert unter Kontrolle des Fingers, bis leicht blutig tingiertes Serum hervorsickert; nach wenigen Minuten erhält man

hervorgelockten "Saugserum" oder endlich in dem durch Punktion oder Abstreifen von excidierten Krankheitsherden erhaltenen "Gewebsaft" die Auffindung auch spärlicher Exemplare in kürzester Zeit ermöglicht. Ausgezeichnetes leistet aber auch die früher von mir bevorzugte *Ausstrichmethode und Färbung nach Giemsa* (entweder eine Stunde oder noch besser wenige Minuten bei Erwärmung über der Flamme (Róna-Preis), ja mitunter hat sich mir z. B. bei der Untersuchung der Cornea oder innerer Organe diese Methode, wenn das Material im Mörser gut zerrieben wurde, sogar der Dunkelfeldmethode überlegen gezeigt. Für das Studium der Pathogenese sind die *Silbermethoden* unentbehrlich; sie sind dem pathologischen Anatomen in erster Linie zu empfehlen, da sie allein über die Lagerung der Parasiten zu den einzelnen Gewebsbestandteilen Auskunft geben, ihre Auffindung wesentlich erleichtern und sie gewöhnlich auch in weit grösserer Zahl zur Anschauung bringen.

Die Behauptung, dass alle mittels der Silbermethoden dargestellten Spiralen Gewebsbestandteile seien, ist gänzlich grundlos; bei einiger Übung und Kritik wird jeder die dunkelschwarzen charakteristisch gewundenen Spirochäten von den grösseren meist unregelmässig gewellten mehr bräunlich tingierten Gewebsfasern gewöhnlich unschwer unterscheiden können.¹ Neuerdings ist ja auch die *Färbung der Parasiten mit Giemsalösung in Gefrierschnitten* formalinfixierter Organe (Schmorl) sowie die Versilberung in Ausstrichpräparaten (Stern) einwandfrei gelungen. Die Unterscheidung feiner Zahn- und Darmspirochäten von der Spirochäta pallida und pallidula dürfte in Silberpräparaten oft recht schwierig, ja bisweilen unmöglich sein.

Die *morphologischen Eigenschaften* der Spirochäta pallida hat Schaudinn in unseren ersten Arbeiten bereits so treffend geschildert, dass seitdem wenig Neues hinzugefügt werden konnte. Die Syphilisspirochäte (Sp. luis) stellt bekanntlich eine äusserst feine schwach lichtbrechende und daher ohne

so gewöhnlich ein spirochätenreiches Material, welches auch zu Impfungen sehr geeignet ist.

¹Dass deformierte Spirochäten von geschwärzten Gewebsbestandteilen nicht immer unterschieden werden können, habe ich nie bestritten; das gelingt auch in Giemsa-Ausstrichpräparaten nicht immer.

Dunkelfeldvorrichtung im frischen Zustand nur schwer erkennbare Spirale mit zahlreichen steilen, tiefen und regelmässigen ("korkzieherförmigen") Windungen dar. Die grosse Länge (durchschnittlich 8 bis 15 μ) ihres oft spitz auslaufenden Fadens im Vergleich zu seiner äusserst geringen Dicke (ca $\frac{1}{4}$ μ), das Verhältnis der Windungstiefe zur Länge (1-1.5:1.2 μ), die verhältnismässig geringe Variabilität ihrer Form, die auf der grossen Elasticität der schwer deformierbaren Spirale beruht, die Art ihrer Bewegung im frischen und der rötliche Farbenton in dem nach Giemsa gefärbten Präparat ($\frac{3}{4}$ Stunde) sind Eigenschaften, von denen jede einzelne zwar nicht absolut charakteristisch ist, die aber in ihrer Gesamtheit massgebend und ausreichend für die Artdiagnose sind. Schwierigkeiten kann besonders ihre Unterscheidung von manchen Formen der Zahn- und Darmspirochäte bereiten, und ihre Trennung von der Spirochäte pallidula Castellani's (*Sp. frambæsiæ*) erscheint mir, obwohl v. Prowazek einige geringfügige Unterschiede heraus gefunden hat, zur Zeit noch nicht mit einiger Sicherheit möglich.

Was den *feineren Bau* der Spirochäte pallida betrifft, so besitzt sie häufig lange spitz auslaufende Endfäden (Schaudinn's "Geisseln"); eine undulierende Membran, deutliche Kerne oder ein axialer Kernstab, die bei grössern Spirochäten vorkommen, konnten bisher nicht dargestellt werden; vermutlich ist die Kernsubstanz in Form feinsten Körnchen (Chromidien) durch die ganze Länge der Spirale verteilt. Mitunter finden sich sowohl im Giemsa- wie im Silberpräparat knotige Auftreibungen des Fadens gewöhnlich in Gestalt zweier manchmal symmetrisch gelegener Körnchen, die vielleicht durch eine Ansammlung des Chromatins bedingt sind.¹ Die Enden der Syphilisspirochäte können in kleine kugelige Gebilde verwandelt sein, die sog. Endkörperchen, welche mitunter auch schleifenförmig erscheinen. Oft sieht man ganz deutlich, dass es sich dabei um eine Einrollung des Fadens handelt, während in anderen Fällen davon nichts erkennbar ist.

Von einigen Autoren wird angenommen, dass eine gradlinige Form für die Produkte der Spätluës charakteristisch ist.

¹Häufiger fand ich diese Bildungen bei der *Sp. pallidula*, welche übrigens nach meinen Erfahrungen noch schwerer färbbar als die *Sp. pallida* ist.

Diese Meinung ist indessen nicht berechtigt, da solche Formen, die in Schnitten häufiger und besser als in Ausstrichen erkennbar sind, nicht nur bei älterer, sondern auch bei frischer Syphilis vorkommen. Zerfall in einzelne Segmente bis zur Auflösung in eine Reihe von Körnchen ist ebenfalls in Schnitten der verschiedensten Krankheitsprodukte häufig festzustellen.

Über die Art der *Fortpflanzung* sind die Ansichten der Autoren noch weit auseinandergehend; die einen, denen ich mich angeschlossen habe, nehmen mit Schaudinn Längsspaltung, die andern mit Metchnikoff und Levaditi Querteilung an; in der Nachlassarbeit Schaudinns findet sich die bestimmte Angabe, dass er die mit Verdoppelung des einen Endfadens beginnende Längsteilung an lebenden Exemplaren (denselben Vorgang habe ich bei der Spirochäta balanitidis im frischen Präparat gesehen) mehrmals beobachtet hat. Entwicklungs- (Ruhe-) Stadien sind bisher nicht mit genügender Sicherheit nachgewiesen worden; einige Autoren wie v. Prowazek sind der Meinung, dass die oben erwähnten kugeligen Endkörperchen als Übergang zu Ruhestadien anzusehen seien; die Annahme, dass während der Latenzperioden und in tertiären Produkten eine andere Entwicklungsform vorkäme, ist nachdem auch hier die Spirochäte selbst gefunden worden ist, jedenfalls nicht mehr notwendig.¹

Alle Zuchtungsversuche sind bisher fehl geschlagen, nur die Anreicherung in Gewebstücken scheint Volpino gelungen zu sein.² Als Ersatz der Reinkultur kann die besonders bei Serienimpfung regelmässig zu erzielende reichliche Anhäufung in der lebenden Kaninchencornea einstweilen angesehen werden. Was die weiteren biologischen Eigenschaften der Syphilisspirochäte betrifft, so bleibt sie im luftdicht abgeschlossenen frischen Präparat gewöhnlich nur wenige Stunden lebhaft beweglich. Schwächere Bewegungen lassen sich mitunter mehrere Tage lang noch nachweisen; ob aber, wie ich zuerst für andere Spirochätenarten an einzelnen Exemplaren festgestellt habe und Beer, Paschen u. a.? es auch bei der

¹ Bezüglich der unbestätigten Angaben von Krzystalowicz und Siedlecki über geschlechtliche und ungeschlechtliche Entwicklungsformen vergl. meine "Aetiologie der Syphilis," Berlin, 1906.

² Levaditi ist angeblich die Züchtung in Collodiumsäckchen (allerdings nur neben andern Bakterien!) gelungen.

Syphilisspirochäte zuweilen gesehen haben wollen, eine gewisse Beweglichkeit noch nach 2 bis 3 Wochen erhalten bleiben kann, scheint mir nach meinen neuen auch mit der Dunkel-feldmethode angestellten Untersuchungen nicht zweifelfrei erweisen, ja unwahrscheinlich zu sein. So viel aber ist sicher, dass in derartigen Präparaten Exemplare der Syphilisspirochäte ebenso wie solche anderer Spirochätenarten nach unsern Beobachtungen sich Monate lang in ihrer Form gut erhalten können. Die Art der Bewegungen entspricht der in unsern ersten Arbeiten gegebenen Schilderung; hinzuzufügen ist, dass die seitlichen und bohrenden Bewegungen besonders kurz nach der Entnahme aus der Tiefe von Primäraffekten und recenten Papeln ausserordentlich kräftig sind, und dass völlige Aufrollungen und kranzförmiges Zusammenlegen mit nachheriger Rückkehr in die frühere lebhaft bewegliche Form von uns nicht in diesen Präparaten, sondern auch im Blut congenital-syphilitischer Kinder nicht selten beobachtet werden konnten. Spontane Agglutination konnten wir ebenso wie Landsteiner und Mucha im Reizserum von Papeln und Sklerosen einige Stunden nach der Entnahme beobachten; die genannten Autoren glauben diese Erscheinung auf lokale Agglutininbildung zurückzuführen zu sollen, da das Serum solcher Kranken keine derartige Wirkung zeigte. Landsteiner und Mucha fanden ferner, dass normales menschliches Serum ebenso wie solches von syphilitischen Kranken in gewisser Weise hemmend auf die Beweglichkeit wirke. Die alte Beobachtung von v. Prowazek und mir, dass das Serum unbehandelter Syphilitiker bei 6–8 Monate alter Erkrankung zuweilen bewegungshemmend wirkt und zu einem Agglomerationsphänomen (Häufchen- und Sternbildung) Anlass geben kann wollen Zabolotny und Maslakowetz neuerdings mehrfach haben bestätigen können; sie geben an, dass sie nach Zusatz des Serums von lange an Lues leidenden Personen zunächst die Bildung kleiner, dann grosser Sterne und nach 3–4 Stunden vollständige Agglutination beobachtet haben, wobei zugleich im Zentrum grosser Haufen ein Zerfall der Spirochäten sich nachweisen liess, und sind der Meinung, dass es sich hier wirklich um eine spezifische agglutinierende Wirkung des Serums und nicht um die oben erwähnte, mit-

unter zu beobachtende spontane Agglutination gehandelt hat. Dass ich auch in Schnittpräparaten grössere Sterne und Haufen, z. B. in den Lumina von Lymphgefässen und bei congenitaler Syphilis auch in der Lichtung von Venen, nachweisen konnte, sei hier nur kurz erwähnt.

Landsteiner und Mucha prüften das Verhalten des Saponins, v. Prowazek dasjenige des taurocholsauren Natrons gegenüber der Syphilisspirochäte und fanden, dass diese Stoffe, welche Protozoen auflösen, die meisten Bakterien dagegen nicht angreifen, auch lösend auf die Spirochäta pallida einwirken.

Was nun das Vorkommen der Spirochäta pallida in den verschiedenen Krankheitsherden anbetrifft, so ist jetzt als sicher festgestellt anzusehen, dass sie in allen Produkten, welche überhaupt noch das Virus enthalten und überimpfbar sind, in grösserer oder geringerer Zahl vorhanden und nachweisbar ist.

Bei acquirierter Syphilis gelingt ihre Darstellung gewöhnlich leicht im Gewebssaft, Reiz- oder Saugserum von Primäraffekten und Genital-, Anal- und Schleimhautpapeln und Erosionen, ziemlich regelmässig auch in pustulösen, krustösen und papulösen Hautsyphiliden der Frühperiode und im Punktionsaft geschwollener Lymphdrüsen; seltener ist der Nachweis in frischen Roseolen und ganz besonders schwierig im strömenden Blut, das die Parasiten nur in geringer Zahl enthält, zu führen. Vereinzelt ist die Spirochäte im Urin bei syphilitischer Nephritis und in der Spinalflüssigkeit, nicht aber im Sperma und in der Milch gefunden worden.

Wie häufig die Spirochäta pallida bei erworbener Syphilis während der Frühperiode in *innern Organen* vorkommt, lässt sich nach den spärlichen bisher vorliegenden Untersuchungen noch nicht sagen; einstweilen kann hier nur erwähnt werden, dass sie in vereinzelt Fällen in der Milz, Nebenniere, Leber und Lunge dargestellt worden ist.

Die Angabe einzelner Autoren, dass die Spirochäte pallida bei maligner Syphilis nicht nachweisbar sei, ist durch eine Reihe positiver Befunde widerlegt worden; in den ulcerösen Produkten, die auch aus andern Gründen als die Folge einer besondern Reaktion (Widerstandslosigkeit) des Organismus

gegenüber dem syphilitischen Gift angesehen werden müssen, findet sie sich nur in geringer Zahl. Die Produkte der *Spätperiode* enthalten gewöhnlich nur sehr spärliche Spirochäten; bisher gelang der Nachweis in Spätpapeln und tuberösen Syphiliden, in Gummen der Haut, der Leber und Knochen, bei schwieliger Hepatitis, in der Wand Spezifischerkrankter Hirnarterien und bei der Heller'schen Aortitis.

Anders als bei der erworbenen liegen die Verhältnisse bei der *congenitalen Syphilis*, wo man oft geradezu von einer Überschwemmung des Organismus mit Parasiten sprechen kann; hier lassen sich, zumal bei schwereren Fällen die Spirochäten nicht nur in den Haut- und Schleimhautefflorescenzen und Lymphdrüsen, sondern nicht selten auch im strömenden Blut nachweisen und finden sich in den verschiedensten innern Organen oft in ungemein grosser Zahl sowohl bei Föten als auch bei frühzeitig an Syphilis sterbenden Kindern; Maceration selbst hohen Grades hindert ihre Erhaltung und wohl auch ihre Vermehrung meist nicht. Die grössten Spirochätenmengen enthält gewöhnlich die Leber, sehr zahlreiche oft auch Lunge und Nebenniere, während in den lymphoiden Organen ihre Zahl meist geringer zu sein pflegt. Besonders bemerkenswert ist das Vorkommen der Spirochäta pallida bei der für die pathologisch-anatomische Diagnose so wichtigen Osteochondritis und im Auge (z. B. Cornea, Chorioidea, Iris, Nervus opticus) sowie ihr Übergang in die verschiedenen Se- und Exkrete (Harn, Meconium bezw. Fäces, Bronchial- und Nasensecret, Schweiß) und in Exsudate, wie z. B. Ascitesflüssigkeit.

Bei congenitaler Syphilis konnte die Spirochäta pallida von Beer und mir mehrfach im Blut lebender Kinder mit Dunkelfeldbeleuchtung nachgewiesen werden und zwar nicht nur bei Kindern, die bald darauf zu Grunde gingen, sondern auch bei solchen, die später durch Quecksilber geheilt wurden. Einzelne Autoren haben sie bei tödlich verlaufenden Erkrankungen in solchen Mengen gefunden, dass sie geradezu von einer Spirochäten-Septikämie sprechen; in den Blutgefässen lassen sich dann, wie bereits erwähnt, mitunter ganze Knäuel von Syphilisspirochäten auffinden.

In der Placenta und Nabelschnur sind die Spirochäten in

einer grösseren Reihe von Fällen nachgewiesen worden, allerdings meist in spärlicher Zahl und gewöhnlich nur im fötalen Teil der Placenta.

Ihre *Verteilung* in den erkrankten Geweben und Organen ist keine gleichmässige; das zeigt sich schon in Primäraffekten, Lymphdrüsen und Hautsyphiliden, noch mehr bei den Spätprodukten der Syphilis. Im allgemeinen kann gesagt werden, dass sie in der Randzone und in der nächsten Umgebung der Krankheitsherde gewöhnlich am reichlichsten vorhanden sind, während sie an den am stärksten und längsten erkrankten Stellen spärlicher zu sein pflegen und oft gänzlich verschwinden; dabei bevorzugen sie das Lumen und die Wände der Lymphbahnen, das Bindegewebe und die Wandungen der Blutgefässe (Capillaren und Venen); aber auch die lymphergefüllten interepithelialen Spalträume suchen sie mit Vorliebe auf und gelangen, das Epithel durchwandernd, an die Oberfläche der Schleimhaut oder der von der Hornschicht entblössten Haut, wo sie sich den Sekreten und Excreten beimischen. Auch in das Innere gewisser Parenchymzellen, z. B. der Ovula, Leber- und Nebennierenzellen vermögen sie einzudringen. Bei ihrer Vernichtung spielt die Phagocytose eine gewisse Rolle.

Die Beziehungen zwischen der *Spirochäta pallida* und den Gewebsveränderungen und ihr Verhalten gegenüber den das Infiltrat zusammensetzenden Zellen lassen sich am besten im syphilitischen Primäraffekt studieren. Über die Veränderungen während der ersten Inkubationsperiode habe ich einige Untersuchungen an Affen und Kaninchen begonnen, über die zur Zeit noch nichts berichtet werden kann. Die Befunde von jüngeren und älteren Primäraffekten will ich nach meinen eigenen und den Untersuchungen von Ehrmann im Folgenden etwas eingehender darstellen.

Die Spirochäten liegen auch hier recht unregelmässig und finden sich mitunter im Verlauf bestimmter Lymphgefässe, wie ja auch klinisch und histologisch die Erkrankung diesen Bahnen folgt; sie liegen im Lumen der Lymphgefässe, und zwar zuweilen in grösseren Haufen, finden sich zwischen den Endothelien, in dem adventitiellen Gewebe und schliessen sich ganz besonders jungen Blutgefässsprossen an, welche in das noch unveränderte Bindegewebe ziemlich weit vordringen

und von Spirochätenfilzen oft geradezu durchsetzt sind. Auch im dichten syphilitischen Infiltrat sind die Spirochäten stellenweise in grosser Zahl vorhanden, werden aber im allgemeinen umso spärlicher, je älter das Infiltrat ist. Sehr interessant ist ihr Verhalten zu den Zellen und die Beobachtungen über den Zerfall von Spirochäten innerhalb und ausserhalb der Zellen. Besonders Ehrmann hat darauf aufmerksam gemacht, dass innerhalb von Leuko- und Lymphocyten sich mehr oder weniger deutlich erkennbare Spirochätenbüschel finden, und zwar sowohl in Primäraffekten, wie auch in einem von ihm untersuchten dorsalen Lymphstrang des Penis. Ähnliche Bildungen habe ich in Primäraffekten nachweisen können. Daneben finden sich zum Teil noch normal gewundene, zum Teil körnig zerfallene Spirochäten vereinzelt oder mitunter in knäuelartigen Haufen innerhalb von ein- und mehrkernigen Leukocyten.

Am eklatantesten habe ich derartige Bilder in Leukocyten innerhalb der Alveolarlumina der Lunge bei weisser Pneumonie in einem mir von *E. Gierke* überlassenen Präparat studieren, ähnliche Bilder, wenn auch seltener, aber auch in Primäraffekten nachweisen können. Auch die Angabe *Ehrmann's* dass im Innern von geschwollenen, mehrere Kerne aufweisenden Fibroblasten und adventitiellen Zellen Spirochäten nicht selten gelegen sind, kann ich nach meinen Erfahrungen an einigen ausserordentlich reichlich spirochätenhaltigen Primäraffekten bestätigen und hinzufügen, dass ich auch in Plasmazellen und riesenzellartigen Gebilden intracelluläre Spirochäten habe auffinden können.

Für die Initialsclerosen der Affen gilt nach meinen Erfahrungen etwa dasselbe, nur sind die Spirochäten im allgemeinen weit spärlicher als bei menschlichen Primäraffekten.¹

Was die regionäre Lymphdrüsenanschwellung anbetrifft, so habe ich meinen früheren Untersuchungen, in welchen ich

¹ Ob das durchweg der Fall ist, möchte ich noch nicht bestimmt entscheiden; in der syphilitischen Kaninchenkornea können ja bekanntlich Myriaden von *Sp. pallida* vorkommen; auch die Initialaffekte der südamerikanischen Seidenäffchen (*Hapale Jacchus*), welche nach meinen Erfahrungen sehr empfänglich und auch zu Serienimpfungen gut geeignet sind, enthalten öfters (ebenso wie die Hoden dieser Tiere) reichlichere "Syphilisschraubchen."

über das Vorkommen der Spirochäten hauptsächlich im Lumen der Lymphbahnen und in den Wandungen kleiner Blut- und Lymphgefässe der Rindenschicht berichtet habe, nur hinzuzufügen, dass ich auch da mitunter intracelluläre Parasiten nachweisen konnte.

Über die secundären syphilitischen Exantheme liegen einige neue Untersuchungen vor, welche beweisen, dass bei den makulösen Syphiliden die Spirochäten hauptsächlich in den erweiterten Blutgefässen, in deren Wand und nächster Umgebung gelegen sind, während sie bei gewissen papulösen Syphiliden sich besonders reichlich in den tieferen Schichten der gewucherten Retezellen bis dicht an das Stratum granulosum finden. Bei den circinären oder orbiculären Syphiliden sind sie ebenfalls im Rete und in der Papillarschicht in verhältnissmässig grosser Zahl aufzufinden. Auch bei diesen Formen hat Ehrmann Bilder nachweisen können, welche dafür sprechen, dass ein Teil der Spirochäten durch Phagocytose seitens der Endothelien, Fibroblasten und der Lympho- und Leukocyten vernichtet wird.

In einem tuberösen Spätsyphilid konnte ich ganz vereinzelt intracelluläre und z. T. deformierte Spirochäten nachweisen. Die Phagocytose spielt demnach bei der erworbenen Syphilis, aber auch bei der congenitalen, wie aus den Beobachtungen Levaditis, Gierkes und meinen eigenen hervorgeht, eine grosse Rolle, kann aber meiner Ansicht nach nicht allein den Untergang der Spirochäten in den Krankheitsprodukten bewirken, da auch ausserhalb der Zellen, zum Theil in den Gefässlumina nicht nur einzelne, sondern auch büschel- und sternförmig angehäuften Spirochäten mitunter alle Zeichen des Zerfalls aufweisen. Zur Erklärung dieser Erscheinungen kann nur die Wirkung von im Serum vorhandenen Antikörpern herangezogen werden.

Durch die geschilderten *Abwehrvorrichtungen* von seiten des Organismus werden aber keineswegs immer alle Parasiten in den Krankheitsherden vernichtet, einmal weil die beweglichen Spirochäten den nachhinkenden Infiltratzellen vorauszuweichen vermögen, und zweitens weil sie an gewissen Orten gegen Phagocyten und Antistoffe anscheinend Schutz finden können. Hierzu gehören nach den bisherigen Erfahrungen

die interepithelialen Räume speziell des Rete Malpighii, die collagenen Bündel der Cutis und vielleicht auch der Gefässwände. So vermochte ich in älteren Schankernarben ziemlich reichliche Spirochäten aufzufinden und Pasini konnte in einem atrophischen und pigmentierten zwei Jahre nach einem papulösen Syphilid (Lues congenita) zurückgebliebenen Fleck die Spirochäten nicht nur zwischen den Zellen des Rete Malpighii, sondern auch besonders reichlich innerhalb der äusseren Wurzelscheide des Haares zwischen den Schweissdrüsenzellen und zum Teil auch im Bindegewebe nachweisen. Bei congenitaler Syphilis scheinen die Spirochäten auch in manchen Parenchymzellen, wie denen der Leber einen Unterschlupf finden zu können.

Das *Blut* bietet der Spirochäta pallida keine günstigen Existenzbedingungen; sie ist vielmehr meiner Meinung nach ein "an die engen Räume des bei Syphilis zunächst und mit Vorliebe betroffenen Lymphgefässsystems angepasster Parasit" und höchstwahrscheinlich *anaërob*. Dementsprechend ist ihr erster Ansiedlungsort wohl das Lymphspaltenetz der tieferen Epithelschichten, wo sie am besten gegen Phagocyten geschützt wäre; hier vermehrt sie sich dann und wandert in den Lymphgefässen, deren Wand sie zugleich ergreift, bald bis zu den regionären Drüsen; frühzeitig aber dringt sie auch in die Bindegewebsbündel und Blutgefässwandungen (speziell der Capillaren und Venen), aus welchen einzelne Exemplare oft schon sehr bald in den Blutkreislauf gelangen können. Die Reaktion von Seiten des Organismus folgt dem Vordringen der Spirochäta pallida erst nach längerer Zeit und "hinkt ihr beträchtlich nach"; hieraus erklärt sich, die lange erste Incubation und die Tatsache, dass Spirochätenschwärme im ganz gesunden, noch unveränderten Gewebe gefunden werden können.

Wo die Spirochäten während der *Latenzperioden* gelegen sind, ist noch nicht näher erforscht; sicher ist, dass sie sich in Residuen (auch Narben) von Schankern und Exanthenen noch spät finden können; die Bindegewebsbündel, Gefässwandungen, die interepithelialen Spalten auch der äusseren Wurzelscheide der Haare und vielleicht auch gewisse Parenchymzellen (besonders bei congenitaler Syphilis) mögen ihnen

als Schlupfräume gegenüber den Abwehrkräften des Organismus dienen. Das Quecksilber bringt die Mehrzahl der Spirochäten in den Krankheitsprodukten gewöhnlich schnell zum Verschwinden, indess bleiben einzelne Parasiten während der Kur mitunter lange Zeit nachweisbar; über die Art seiner Einwirkung wissen wir noch nichts Bestimmtes. Während der Atoxylkur haben wir die Spirochäten oft in grosser Zahl im Papel- und Sklerosensekret nachweisen können.

Die von zahlreichen Klinikern, Pathologen und Parasitologen beim Menschen erhobenen Befunde, welche ich hier nur kurz skizziert habe, sind allein schon ausreichend, um die *ätiologische Bedeutung der Spirochäta pallida* so gut wie sicher zu beweisen; die Tatsache, dass die bei Affen in den Initialaffekten, selten auch in Lymphdrüsen, Hoden, Milz und Knochenmark gefundenen und die in der spezifisch erkrankten Cornea von Kaninchen, Hunden und Schafen dargestellten Spirochäten—auch nach zahlreichen (13) Passagen—völlig den im menschlichen Organismus vorkommenden entsprechen, beseitigt in dieser Hinsicht jeden Zweifel.

Andere Mikroorganismen kommen für die Ätiologie der Syphilis nicht in Betracht.

Die Spirochäta pallida hat eine *grosse diagnostische Bedeutung*. Dem Kliniker ist durch ihren Nachweis die Erkennung junger Primäraffekte vom ersten Tage ihres Auftretens an, verdächtiger Erosionen der Genitalien und Schleimhäute, suspekter Drüsenschwellungen (Punktion) und anderer unklarer Krankheitsfälle (z. B. Schankernarben und Residuen von Exanthenen) möglich; bei congenitaler Syphilis ist ausserdem die Untersuchung des Bluts (besonders mit Dunkelfeldbeleuchtung) von grosser Wichtigkeit. Der *positive* Befund ist entscheidend, während negative Resultate nur mit Vorsicht verwertet werden dürfen.

Auch dem pathologischen Anatomen ist sie bereits ein unentbehrliches und ausschlaggebendes Hilfsmittel zur Feststellung der Syphilis zumal bei Föten und Kindern, aber auch zur Erkennung der spezifischen Natur mancher Spätläsionen (z. B. der Gefässe) geworden.

Für die Therapie ist durch die Möglichkeit der Erkennung und Excision ganz junger Primäraffekte viel gewonnen; die

frühzeitige Beseitigung des ersten, die grösste Giftmenge einschliessenden Krankheitsherdes und die Verhütung oder Beschränkung der infektiösen Sekundärererscheinungen ist auch in *prophylaktischer* Hinsicht von grosser Bedeutung.

Meiner Meinung nach darf man in solchen Fällen die Quecksilberbehandlung nicht unterlassen, da die Spirochäten nach allen unsern Erfahrungen schon frühzeitig in die Lymph- und Blutbahnen wandern, und selbst bei monate- und jahrelangem Ausbleiben deutlicher Allgemeinerscheinungen niemand die Garantie geben kann, dass nicht doch irgendwo im Körper (z. B. Gefässwandungen oder Nervensystem) das Gift sich schleichend entwickelt. Ob man die erste Kur, wie das besonders Thalmann fordert und wie auch ich es in einer Reihe von Fällen durchgeführt habe, sogleich einleiten soll (Frühbehandlung) oder erst beim Ausbruch von Sekundärererscheinungen oder, falls sie ausbleiben, zu der Zeit, wo sie durchschnittlich aufzutreten pflegen, beginnen soll, ist eine Frage, die, wie ich schon mehrfach betont habe, erst durch weitere über Jahre ausgedehnte Erfahrungen entschieden werden kann. Die völlige Unterdrückung der Allgemeinerscheinungen gelingt, wie ich auf Grund meiner Beobachtungen schon jetzt sagen kann, durch die Frühbehandlung gemeinhin nicht.¹

Für die congenitale Syphilis verspricht die Möglichkeit der frühzeitigen Erkennung durch Blutuntersuchung und sich sofort anschliessenden Behandlung ebenfallseinen wichtigen Fortschritt.

Über den Wert der neuerdings vorgeschlagenen *Atoxylbehandlung* lässt sich gegenwärtig Folgendes sagen:

Die Ergebnisse der zuerst von Uhlenhuth und mir, später von Metchnikoff angestellten Tierexperimente lehren, dass dem Atoxyl für Affen und Kaninchen eine schützende (präventive) Wirkung zukommt und dass es bei Affen allem Anschein nach auch die Heilung befördert. Unsere Versuche beim Menschen haben ebenso wie diejenigen Salmons, Lassars und anderer gezeigt, dass das Atoxyl eine unverkennbare Wirkung auf die meisten syphilitischen Krankheitserscheinungen besitzt und dass es besonders bei frühulcerösen Haut-

¹ In der Mehrzahl der von mir frühbehandelten Fälle ist auch die Wassermannsche serodiagnostische Reaktion positiv geworden; ich werde darüber später genauer berichten.

syphiliden und hartnäckigen Erkrankungen der Zunge selbst dann nützlich sein kann, wenn Quecksilber und Jod versagt haben. Für solche Fälle und bei Idiosynkrasie gegen die beiden genannten hauptsächlichen Medikamente darf es als neues wertvolles Heilmittel begrüsst werden; allerdings darf dabei nicht vergessen werden, dass es häufig nicht nur unangenehme, sondern auch gefährliche Nebenwirkungen hat und in grösserer Menge verabreicht, Erblindung herbeiführen kann. Die Meinung einiger französischer Autoren, dass es dem Quecksilber gleichwertig oder gar überlegen sei, muss ich nach meiner Erfahrungen als viel zu weitgehend bezeichnen.

Am Schluss des Vortrages wurden zahlreiche mikroskopische Präparate gezeigt und mittels des Epiaskops die Tafeln des Atlas der experimentellen und ätiologischen Syphilisforschung demonstriert.¹

SPIROCHÄTEN BEI SYPHILIS

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I. MORPHOLOGIE UND METHODIK

Die von Schaudinn und Hoffmann, in ihren ersten Publikationen gegebene morphologische Characterisierung der Spirochäte pallida haben wir in unseren Untersuchungen vollkommen bestätigen können. Dabei möchte ich bemerken, dass wir den Nachweis der geisselartigen Verlängerung, von der es keineswegs feststeht, dass es sich um eine Geissel handelt, besonders bei Löffler'scher Beizenfärbung, aber auch bei der ursprünglich modifizierten Giemsa-Tinktion häufig genug haben nachweisen können.

Für den praktisch diagnostischen Zweck ist sie nicht nennenswert verwertbar. Im übrigen ergaben sich als die wichtigsten, diagnostischen Merkmale die Tiefe, Steilheit und Starrheit der Windungen, die durchschnittlich grosse Zahl derselben, die Zartheit des Mikroorganismus, die nahezu regelmässige rötliche Färbung gegenüber der bläulichen, an-

¹ Dieser dem Andenken F. Schaudinns von mir gewidmete Atlas ist inzwischen erschienen (Berlin, F. Springer, 1908).

derer in Betracht kommender Spirochäten bei Giemsa-Färbung.

Was die Länge der Mikroorganismen betrifft, so haben wir häufig genug auch kurze Exemplare mit wenigen, 3-4 Windungen mit im übrigen deutlichen Merkmalen besonders bei acquirierter seltener bei ererbter Syphilis gefunden. Ob es sich hier um degenerierte oder um in Entwicklung begriffene Exemplare oder um zufällige Erscheinungen handelt, liess sich nicht feststellen. Keineswegs halten wir es für erwiesen oder auch nur für wahrscheinlich, wie das von mehreren Seiten behauptet wurde, dass es sich gewissermassen um eine Verkümmernng von Spirochäten infolge von Quecksilberbehandlung hierbei handelt. Irgend einen Schluss auf die Rückbildung des Krankheitsprozesses oder auf seine geringe Virulenz ist aus dem Vorhandensein solcher Exemplare, die im übrigen natürlich gelegentlich auch durch die Präparation entstandene Kunstprodukte sein können, nicht zu ziehen.

Von weiteren morphologischen Besonderheiten haben wir in vier Fällen von acquirierter Syphilis—und zwar handelt es sich hierbei um Primäraffecte, nässende Papeln und Schleimhaut-Plaques—die besonders von Herxheimer u. a. beschriebenen knopfartigen endständigen Körperchen nachgewiesen. Dieselben färben sich bei Giemsa-Tinktion meist nur randständig, sind fast immer kreisrund; gelegentlich haben wir sie auch bei diesen Fällen nicht am Ende sondern in der Mitte oder nahezu der Mitte des Spirochätenkörpers gefunden, wie das bereits beschrieben worden ist. Bemerkenswert war, dass wir in mehreren Efflorescenzen desselben Falles diese Veränderung fanden, die wir sonst immer vermissten und bei hereditärer Lues nie sahen. Dass es sich hier etwa um eine Schlingenbildung handelt, halte ich für unwahrscheinlich; man gewinnt vielmehr den Eindruck, dass hier ein solides dem Spirochätenkörper angehörendes Gebilde vorliegt, dessen Bedeutung aus den sonstigen klinischen und anatomischen Befunden nicht zu erschliessen ist.

Anscheinende Teilungsfiguren, so dass zwei Spirochäten-Exemplare in der Längsrichtung mit dem spitz zulaufenden Körperende zusammenhängen oder in der Querrichtung ganz oder teilweise (evtl. y-förmig) aneinander hängen, haben

wir häufig, sowohl, in Ausstrich- wie in Schnittpräparaten gesehen. In wieweit es sich hier wirklich um Fortpflanzungsvorgänge handelt, und ob eine solche Teilung in der Längs- oder Querrichtung erfolgt, ist meiner Meinung nach aus diesen rein histologischen Beobachtungen kaum festzustellen.

Was nun die Agnoszierung der Spirochäte pallida im gefärbten Ausstrichpräparat und ihre Abgrenzung gegenüber anderen ähnlichen Mikroorganismen betrifft, so ist zuzugeben, dass die Spirochäte einen morphologisch gut charakterisierten Mikroorganismus darstellt, dessen Erkennung dem geübten Untersucher besonders, wenn mehrere Exemplare da sind, gelingt; dagegen ist es zweifellos, dass besonders an den für die Praxis am häufigsten in Betracht kommenden Lokalisationen, nämlich an den Geschlechtsorganen und in der Mundhöhle so ähnliche Spirochäten garnicht so selten sich finden — ohne dass, wie die weitere klinische Beobachtung ergibt, Lues vorliegt — dass eine absolut sichere Abgrenzung gegenüber der Spirochäte pallida schlechterdings unmöglich oder schwierig ist. Ueber die Beobachtung des lebenden Parasiten bei einfacher und Dunkelfeldbeleuchtung habe ich keine sehr ausgedehnten Erfahrungen; ich glaube aber nicht dass diese Untersuchungsmethode, welche wissenschaftlich natürlich von sehr grosser Bedeutung ist, für praktische Zwecke das Ausstrichverfahren völlig ersetzen kann.

Zur Färbung im Ausstrichpräparat hat sich uns am besten die ursprünglich angegebene modifizierte Giemsa-Färbung in vier und zwanzig Stunden bewährt, aber auch die später von Giemsa selbst angegebene Schnellfärbung gibt gute Resultate. Von den zahlreichen anderen Färbemethoden, welche empfohlen wurden, haben wir keine als zweckmässig gefunden, teils weil die Resultate unsicher sind, teils weil hierbei gerade die bis zu einem gewissen Umfang wenigstens färberische Differenzierung gegenüber anderen Spirochäten verloren geht. Auch die neuerdings von Löffler angegebene Färbung, die an sich sehr gute färberische Resultate liefert, erscheint uns nicht empfehlenswert, weil vielfach hierbei die Spirochäten massiger und verbreiteter erscheinen, und ihre Abgrenzung gegenüber anderen Formen erschwert wird.

Für den Nachweis in Schnitten hat sich uns besonders die erste Levaditi'sche Methode bewährt; sie gibt die klarsten Bilder, während die zweite Pyridinmethode doch zu schwereren Zerstörungen des Gewebes führt, und Täuschungen leichter möglich sind. Das ältere Bertarelli'sche Verfahren, welches den Ausgangspunkt der Schnittimprägnationen darstellt, erschien uns nicht so praktisch, weil die Ergebnisse unsicher sind, und häufig zahlreiche Niederschläge störend wirken. Ich glaube nun, dass der grössere Teil der mittelst Levaditi-Färbung in syphilitischem Gewebe imprägnierten Gebilde Spirochäten darstellen, dass aber zweifellos gar nicht so selten feinste Nervenfibrillen und besonders kollagene Fasern, seltener anscheinend elastische Fibrillen so täuschend ähnlich Spirochäten sein können, dass sie schlecht oder garnicht von ihnen zu differenzieren sind; das haben wir besonders im Centralnervensystem und in Lymphdrüsen, seltener in inneren Organen gefunden. Auf diese Täuschungsmöglichkeit muss bei allen wissenschaftlichen und praktischen Untersuchungen zweifellos Rücksicht genommen werden. Hierbei möchte ich gleich erwähnen, dass auch in Ausstrichpräparaten von Sekreten wenn auch hierbei für den Geübten seltener ganz besonders aber bei Untersuchungen des Blutes mit Giemsa-Färbung den Spirochäten täuschend ähnliche Gebilde erscheinen, welche erst bei genauster Untersuchung als indifferente faserige Elemente aber auch als der Rand roter Blutkörperchen sich erweisen; und ich möchte auch nach unseren Blutuntersuchungen jetzt annehmen, dass abgesehen von der hereditären Syphilis, wo besonders kurz vor dem Tode, wie wir das ja schon in unserem ersten Falle nachgewiesen haben, zahlreiche Spirochäten sich finden—eine Anzahl die am Anfang der ganzen Forschung erhobener Blutbefunde bei acquirierter Lues auf solchen Täuschungen beruhen dürften.

2. FUNDSTÄTTEN

Ich habe hier den zahlreichen in der Literatur niedergelegten Befunden nichts Nennenswertes hinzuzufügen und will nur in Bezug auf die acquirierte Syphilis Folgendes be-

merken. Nahezu regelmässig lässt sich die Spirochäte in genitalen und extragenitalen ausgebildeten, aber nicht zu alten Primäraffekten, in nässenden Papeln der Genitalorgane, weniger häufig in Plaques muqueuses, nässenden Körperpapeln, seltener in einfachen geschlossenen Rumpf- und Extremitäten-papeln und in Roseolen in Ausstrichpräparaten nachweisen, anscheinend sind sie wiederum etwas häufiger in circinären papulösen Syphiliden. Auch im Punktionsaft dem Primäraffekt benachbarter Drüsen haben wir sie etwa in der Hälfte der Fälle nachweisen können. Niemals gelang uns der Nachweis bisher in punktierten sekundären Drüsen. Bei häufiger Untersuchung derselben Efflorescenzen hatten wir den Eindruck gewonnen, dass die Befunde wechseln. Die Schnittuntersuchung hat uns ziemlich analoge Resultate geliefert; hervorheben möchten wir aber, dass wir jüngere, aber ganz besonders ältere Primäraffekte in Serienschnitten untersucht haben, ohne in ihnen Spirochäten nachweisen zu können. Von inneren Complicationen der Frühsyphilis waren wir einmal in der Lage, eingehend eine ausgedehnte ganz frische typische Arteriitis des Circulus arteriosus Willisii zu untersuchen mit negativem Resultat. In tertiären Herden und bei frischer, schwerer typischer maligner Syphilis ist uns in Ausstrichpräparaten und im Schnitt bisher der sichere Nachweis der Spirochäte nicht geglückt, worang wir zuerst hingewiesen haben, ebensowenig haben wir im kreisenden Blut bei acquirierter Lues und im Herzblut einer an Sepsis zu Grunde gegangenen frisch syphilitischen Frau Spirochäten nachweisen können.

Bei hereditärer Syphilis konnten wir die Spirochäte, wenn es sich um Kinder handelte, die an frischer Syphilis zu Grunde gegangen waren, die Mikroorganismen zum Teil in recht erheblicher Zahl in den meisten von uns untersuchten Organen nachweisen, und zwar nicht nur in erkrankten Partien, sondern auch in zweifellos anatomisch gesundem Gewebe, wie wir das bereits in einer unserer ersten Publikationen hervorgehoben haben. In erster Linie stehen hier Leber, Milz, Pankreas, Lunge, Haut, Cornea, ferner Schilddrüse, Thymus, Knochenmark, Epiphysenknorpel. In Bezug auf letzteren ist bemerkenswert, dass wir bei Osteo chondritis

Spirochäten im Erkrankungsherde, aber auch im benachbarten Knochenmark und Knorpel auffanden; ferner konnten wir sie in bronchialen, portalen, mesenterialen, cubitalen und hals-Lymphdrüsen auffinden, in der Nasenschleimhaut, in den Alveolar- und Bronchialwandungen, im Lumen der Bronchien, in der Darmwand, in der Wand der Gallenblase, in der Galle selbst, im Urin, welcher durch Punktion der gefüllten Blase der Leiche gewonnen war, im Mekonium, in Testikeln, im Ovarium, im Herzmuskel, während wir in der Wand der Aorta selbst bei einem genau untersuchten Fall keine Spirochäten fanden und nur vereinzelte Mikroben im Lumen der Vasa vasorum sahen. In grosser Menge finden sie sich in erkrankten und auch gesunden Nebennieren, und zwar wesentlich in den Bindegewebssepten, spärlicher in den Nieren. In den von uns allerdings nicht sehr genau untersuchten Placenten, im Nabelgefässblut und in der Nabelwand in einem Fall von Phlebitis fanden wir sie nicht. Ebensowenig ist es uns gelungen, sie im Centralnervensystem nachzuweisen. Bei der Untersuchung lebender Kinder konnten wir sie regelmässig und meistens in grösserer Zahl in geschlossenen Hautpapeln, auch in ausgedehnten, secundären Infiltraten der Haut, wie sie bei Kindern ja häufig vorkommen, nachweisen. Im kreisenden Blut, das an intakten Hautstellen gewonnen war, fanden wir sie mehrere Male, aber erst bei sehr ausgebreitetem Exanthem resp. kurz vor dem Exitus.

3. LAGERUNG DER SPIROCHÄTEN IM GEWEBE

Die Hauptlokalisationsstätte der Mikroorganismen sind die Wandungen kleinster und mittelgrosser Blutgefässe häufig auch mittlerer Lymphgefässe. Auch in den Lymphdrüsen selbst sind es gewöhnlich die Blutgefässwandungen, welche die Mikroorganismen enthalten, dann besonders die Wandungen der Lymphsinus. Im Lymphdrüsenewebe selbst vermissten wir sie entweder bei erkrankten Drüsen ganz oder wir fanden relativ wenig Exemplare unregelmässig zerstreut und gerade hier sehr häufig deutlich in körnigem Zerfall begriffen. Eine Hauptlokalisationsstelle stellen die interzellulären und interfibrillären Saftspalten dar. So finden

sie sich zwischen Epithelien der drüsigen Organe, besonders deutlich zwischen den Epithelzellen des Rete Malpighii der Haarfollikel, Talg- und Schweissdrüsen, ferner in den Saftspalten grösserer Bindegewebsbalken sowohl in der Haut, als auch beispielsweise im Bindegewebe der Portalgefässe, der Milz, der Nebennieren. Hervorzuheben ist und das gilt in erster Linie für die erworbene Syphilis, trifft aber auch für nicht zu weit vorgeschrittene Fälle von hereditärer Lues zu, dass die Lokalisation der Mikroorganismen meistens nicht diffus, sondern herdweise stattfindet, so dass bei selbst ausgiebiger Untersuchung erkrankter Organe, Lymphdrüsen, Primäraffekte, Leber, Milz, etc., man grosse Partien frei finden kann und dann plötzlich auf eine grössere Parasiten-Ansammlung stösst. Bei fortgeschrittenen Fällen von hereditärer Lues pflegt allerdings die Verbreitung eine diffuse zu werden, wobei aber trotzdem häufiger noch herdweise Ansammlungen sich finden. Im Gegensatz zu einer Reihe anderer Autoren muss ich auch heute auf meinem ursprünglichen Standpunkt bestehen bleiben, dass das Wachstum der Mikroorganismen im wesentlichen nicht in den Zellen, sondern in den Körpersäften stattfindet, dass ein Eindringen der Spirochäten in Epithelzellen nur ganz ausnahmsweise vorkommt und dann vielfach unter Verhältnissen, wo postmortale oder prämortale Vorgänge nicht ausgeschlossen sind. Aber auch ein Eindringen in Lympho- und Leukocyten findet nur in geringem Umfange statt. Wir haben nur selten teils anscheinend wohl erhaltene, teils deutlich in Zerfall begriffene Spirochäten in grossen mononukleären Lymphocyten gefunden.

Was nun die Beziehungen der Spirochäten zu den pathologischen Veränderungen betrifft, so müssen wir hier die erworbene und die vererbte Syphilis auseinander halten. Bei der erworbenen Syphilis findet man die Mikroorganismen im Wesentlichen im Anschluss an die spezifischen Infiltrate, aber auch hier zeigt sich, dass der Lieblingssitz nicht die Hauptveränderungen des Gewebes darstellen, wenngleich sie auch hier zwischen den Lymphocyten gelegentlich meist in geringerer Zahl und häufig in Zerfall sich finden, sondern dass die Peripherie, die Saftspalten grösserer nicht veränderte Bindegewebszüge und das gesunde Gewebe der nächsten

Nachbarschaft die meisten Mikroorganismen enthält. Auch im Lumen von Blut- und Lymphgefässen in und am Erkrankungsherde findet man garnicht so selten, wenn auch meistens nicht zahlreiche Spirochäten. Besonders interessant ist das sehr häufige Auftreten zahlreicher Spirochäten im normalen Epithelüberzug von Primäraffekten.

Bei hereditärer Lues finden wir zwar auch die Mikroorganismen im Anschluss an pathologische Veränderungen des Gewebes, allein in viel grösserer Ausdehnung, als bei der erworbenen Syphilis zeigen sich Mikroorganismen in morphologisch intaktem Gewebe in sehr grosser Zahl in den verschiedensten Organen; und zwar finden sich die Mikroben nicht etwa nur in der näheren oder weiteren Umgebung spezifischer Veränderungen, sondern auch in Gewebsbezirken, wo weit und breit bei genauer Untersuchung von anatomischen Veränderungen nichts nachzuweisen ist. Es würde zwecklos sein hier die einzelnen Gewebe aufzuzählen, weil in der Tat in manchen Fällen nahezu der ganze Körper von Spirochäten durchsetzt zu sein scheint, anscheinend mit Ausnahme des Centralnervensystems, in dessen Geweben wir auch in fortgeschrittenen Fällen Spirochäten mit Sicherheit nicht nachweisen konnten. Als besonders bemerkenswert möchten wir hervorheben den Nachweis zahlreicher Spirochäten in der Haut von Kindern, die an Syphilis gestorben waren, wo klinisch und histologisch nichts nachweisbar war und die Haut aus Bezirken entnommen wurde, die weit ab von syphilitischen Veränderungen gelegen waren. Hier war besonders bemerkenswert das Eindringen der Spirochäten in die Haarfollikel zwischen die Schweiss- und Talgdrüsenepithelien und bis in die obersten Schichten der Epidermis. Im übrigen verhielt sich die Lokalisation und Ansiedelung der Mikroorganismen in Beziehung zu den einzelnen Gewebsbestandteilen analog der erworbenen Lues. Während wir nun wie vorher schon erwähnt bei Spätsyphilis und deren gummösen Veränderungen Spirochäten nicht nachweisen konnten, finden sich dieselben bei den ja sehr häufigen gummösen und stark infiltrativen Veränderungen der inneren Organe hereditärer syphilitischer Kinder häufig in sehr grosser Zahl aber meistens nicht in nennenswerter Zahl im Gebiet der stärksten Verän-

derung und niemals im Zerfallsgebiet sondern in der Peripherie resp. im benachbarten gesunden Gewebe. Auch konnten wir uns niemals davon überzeugen, dass im Zerfallsgebiet mit Sicherheit Reste von Spirochäten nachzuweisen waren. Nach der allmählichen Aufsaugung dieser gummösen Gewebsveränderungen und der dann eintretenden Narbenbildung verlieren sich die Mikroorganismen, aber wir haben sie doch gelegentlich z. B. in den Narbenzügen einer in Ausheilung begriffenen Pankreatitis spärlich gefunden. Ganz anders verhält es sich mit mazeriertem Gewebe; hier kann man häufig enorme Mengen von Spirochäten finden, und das trifft auch für vollkommen mazerierte Föten zu. Bei hereditär syphilitischen Kindern, die minder schwer erkrankt oder in Heilung an interkurrenter Krankheit zu Grunde gehen, scheint die Ansiedlung der Mikroorganismen auch mehr herdförmig stattzufinden ähnlich wie bei acquirierter Syphilis.

4. BIOLOGISCHES

Wie aus den vorherigen Auseinandersetzungen hervorgeht, habe ich auf Grund meiner eigenen Untersuchungen die Anschauung, dass die Spirochäte vorwiegend in den Zellsäften wächst, dass sie in dem toten mazerierten Gewebe besonders gut sich zu entwickeln scheint, und dass bemerkenswerterweise das spezifische Infiltratgewebe und dessen Zerfallsprodukte für den Mikroorganismus keinen guten Nährboden abgeben. Auch der Untergang der Spirochäten vollzieht sich nach unseren Untersuchungen im wesentlichen in den Zellsäften, wo die Mikroorganismen anscheinend körnig zerfallen und resorbiert resp. dann häufiger anscheinend von Phagocyten aufgenommen werden. Wenn man nun auch—allerdings nicht häufig—wohlerhaltene Spirochäten innerhalb von Phagocyten antreffen kann, so ist bei der Seltenheit dieser Beobachtung wenigstens nach unseren Erfahrungen ein Beweis dafür nicht gegeben dass die Phagocytose für die Vernichtung und Elimination der Mikroorganismen eine nennenswerte Rolle spielt. Noch viel weniger kommen, wie ich das auch schon vorher erwähnt habe, Epithelzellen in Betracht, in welche wahrscheinlich—und das nur selten—

Spirochäten erst post- oder prä mortal eindringen; überhaupt ist als bemerkenswert hervorzuheben, wie wenig Epithelzellen auf in der Nachbarschaft befindliche selbst grössere Spirochätenmengen reagieren, sie sind meistens sowohl in Bezug auf das Protoplasma als auch den Kern normal auch tinktoriell, und erst bei Auftreten interstitieller Infiltrate pflegt ein Untergang von Epithelzellen sich zu entwickeln, sodass ich bis jetzt keinen durch morphologische Untersuchungen begründeten Eindruck davon gewonnen habe, dass von den Spirochäten aus irgend eine besondere Giftwirkung gegenüber benachbarten Epithelien stattfindet. Bezüglich der Lebensdauer und Beweglichkeit der Spirochäten nach ihrer Entfernung aus dem Körper resp. nach dem Tode des erkrankten Individuums sei hervorgehoben, dass wir in einem Falle von hereditärer Lues aus der Leber zehn Stunden nach dem Tode entnommene Spirochäten noch beweglich fanden. Was nun schliesslich den Einfluss der Quecksilberbehandlung auf die Spirochäten betrifft, so haben wir sowohl bei hereditärer Syphilis, soweit dies an Hautefflorescenzen verfolgt werden konnte, als auch bei acquirierter Lues nicht den Eindruck gewonnen (und nur von einem Eindruck kann man ja hier sprechen, weil derartige Untersuchungen keinen Anspruch auf Exaktheit erheben können) dass die Quecksilberbehandlung auf die Mikroorganismen in nennenswerter Weise vernichtend einwirkt; denn selbst bei starkem Rückgang der klinischen Erscheinungen und relativ weit vorgeschrittener Allgemeinbehandlung konnten wir garnicht so selten noch zahlreiche Spirochäten in Papeln nachweisen. Eine etwas grösseren aber auch keineswegs völlig überzeugende deletäre Wirkung scheint die lokale Quecksilberbehandlung auf die Mikroorganismen zu haben.

Eine wichtige wenn auch keineswegs ausschlaggebende Frage für die nosologische Beurteilung der Spirochäte ist das Verhältnis zwischen Spirochätenzahl im Krankheitsherd und Infektiosität des betreffenden Krankheitsproduktes. Hierzu ist zu bemerken, dass im Allgemeinen in der Tat ein gewisser Parallelismus zwischen Zahl der Spirochäten und Infektiosität vorzuliegen scheint, und dass besonders mit denjenigen Krankheitsprodukten, welche erfahrungsgemäss

zahlreiche Spirochäten enthalten, am leichtesten Haftung bei Affenimpfung sich erzielen lässt; aber es gibt zweifellos Ausnahmen hiervon. Wir selbst haben einen Fall beobachtet und bereits publiziert, bei dem eine positive Impfung mit ausserordentlicher Intensität und Schnelligkeit (bereits nach achtzehn Tagen) bei einem kynomorphen Affen zu erzielen war mit Ausgangsmaterial, indem wir bei genauestem Suchen in Ausstrichpräparaten und in Schnitten Spirochäten nicht nachweisen konnten, also wahrscheinlich sehr wenig oder gar keine Mikroorganismen vorhanden gewesen sind. Es handelte sich um eine grosse der Therapie hartnäckig trotzen- de auch nach scheinbar radikaler Excision recidivierende Ulzeration bei einer siebzehn Jahre alten Lues von malignem Character. Auf der anderen Seite haben wir bei Impfungen von drei frischen Fällen von maligner Lues und Herden, in denen wir ebenfalls keine Spirochäten fanden, nur relativ geringgradige, schnell sich zurückbildende Impfffecte bei Affen erzielt. Eine vollkommen befriedigende Erklärung für diese anscheinende Ausnahme von dem zuerst erwähnten anscheinenden Parallelismus zwischen Menge und Infektiosität können wir nach dem zeitigen Stande der Kenntnisse nicht geben. Es ist zweifellos wünschenswert, dass grade nach dieser Richtung hin noch ausgedehntere Untersuchungen angestellt werden, um diesen ja für die gesamte Beurteilung der Frage wichtigen Punkt zu klären. In Bezug auf die von uns allerdings nicht in sehr grosser Ausdehnung an niederen Affen vorgenommenen Impfungen will ich nur noch bemerken, dass wir relativ selten und spärlich Spirochäten im Ausstrich und in Schnitten bei den Impffacten gefunden haben.

Meine Herren! Ich habe im Vorhergehenden in aller Kürze im Wesentlichen über meine eigenen Erfahrungen und Untersuchungsergebnisse auf diesem jungen Forschungsgebiet berichtet, ich habe Ihnen auch im Wesentlichen nur das mitgeteilt, was mir nach unseren Untersuchungen wenigstens gesichert zu sein scheint. Ein kritisches Eingehen auf die ungeheure Literatur dieses Gegenstandes, die ich ja gelegentlich in Publikationen mit meinem Assistenten W. Fischer in den Kreis unserer Besprechungen gezogen habe, kann ich nicht

für meine Aufgabe halten, da ich mich ja nur in sehr geringem Grade activ an der Bearbeitung dieser Frage beteiligt habe; deshalb werden Sie begreifen, dass mein Gesamturteil über die nosologische Bedeutung der Spirochäte pallida zögernder und unsicherer ausfallen muss, als bei denjenigen Autoren, die in verdienter Weise in viel grösserem Umfang auf viel breiterer Basis diesen Gegenstand bearbeitet haben und demgemäss auch über bedeutend grössere Erfahrungen verfügen. Was zunächst das von mehreren Autoren bekämpfte Vorkommen der Spirochäte pallida und ihrer Characterisierung betrifft, so werden sie aus meinen ganzen Ausführungen entnommen haben, dass ich diese Einwände nicht für stichhaltig ansehe. Zwar gebe ich zu, wie ich das ja schon in meinen ersten Arbeiten über diese Frage und auch oben mehrfach ausgeführt habe, dass nicht alles was für Spirochäten erklärt worden ist und wird—auch von uns—solche darstellt, und Irrtümer bei der Deutung fraglicher Gebilde selbst dem allergeübtesten und noch vielmehr demjenigen, der weniger Erfahrung auf diesem Gebiete besitzt, vorgekommen sind und auch jetzt noch vorkommen. Allein ich glaube, dass selbst nach Ausschaltung dieser Fehlerquellen genug übrig bleibt um das Vorhandensein einer—soweit ich es zoologisch beurteilen kann—von anderen Spirochäten bis zu einer gewissen Grenze wohl abzutrennenden Spirochäte in syphilitischen Krankheitsprodukten anzunehmen.

Was nun die nosologische Beurteilung der Spirochäte und ihr Verhältnis zur Lues betrifft so sprechen gewiss eine Anzahl Gründe für die Möglichkeit, dass die Spirochäte pallida in ätiologischer Beziehung zur Syphilis steht. Das ist vor allem die grosse Zahl der Befunde, der wenn auch wie oben erwähnt anscheinend nicht ausnahmslose Parallelismus zwischen Infektiosität und Zahl der Parasiten, die Befunde bei Syphilis hereditaria, die morphologische Characterisierung des Mikroorganismus, eine gewisse Ähnlichkeit in der Vererbung mit einzelnen anderen Spirochätenkrankheiten besonders im Tierexperiment, das Vorhandensein in experimentell erzeugten Affenläsionen. Wenn ich trotzdem noch nicht bedingungslos vom Erreger der Syphilis spreche, so tragen hierzu bei die Verhältnisse bei der malignen Syphilis wenigstens nach meinen

Erfahrungen, das nicht völlig conforme Verhalten wenigstens häufig zwischen pathologischer Läsion und Mikroorganismenansiedelung, ferner auch die klinischen Verhältnisse bei anderen uns bekannten Spirochätenkrankheiten einerseits und bei der Syphilis andererseits, sowie die Biologie mancher Spirochäten überhaupt, von denen wir wissen, dass sie als absolut regelmässige Begleiter bestimmter Krankheitsprozesse auftreten, ohne doch—wenigstens wahrscheinlich nach unseren heutigen Kenntnissen—ätiologisch zu sein, vergleiche die Vincent'sche Angina, bestimmte Gangränformen, bestimmte Darmkatarrhe,—ein sonst in der Pathologie wenigstens in dieser Regelmässigkeit für andere Mikroorganismen nicht bekannter Vorgang. Allerdings handelt es sich ja hierbei um total verschiedene Verhältnisse, um offenliegende Krankheitsherde. Im übrigen kommt wiederum gegenüber diesen Einwänden der Umstand zur Geltung, dass es fraglich ist, ob überhaupt die Spirochäte pallida eine Spirochäte ist und biologisch mit diesen homologisiert werden darf. Alles in allem so will ich dieses nur anführen, um zu begründen, dass es in exakt wissenschaftlicher Weise zur Zeit nicht möglich ist, klipp und klar ein sicheres Endurteil über diese Frage abzugeben. Nicht nur die Reinkultivierung der Spirochäte und ihre Uebertragung auf Tiere, sondern auch die Impfung und Rückimpfung auf den Menschen und die Erzeugung einer wirklichen konstitutionellen Syphilis, die eingehendste zoologische und biologische Bearbeitung des Problems, an dessen Anfang wir erst stehen, kann diese ganze Frage zum Schluss führen. Aber bei der grössten Vorsicht im Endurteil werden wir gewiss alle dankbar zugeben, welch grosser Fortschritt in theoretischer Hinsicht erzielt worden ist, und damit befriedigt sein, dass nach langer Stagnation die Syphilisforschung wieder in Fluss gekommen ist.

Wie steht es nun mit den praktischen Konsequenzen aus den bisher erzielten Ergebnissen?

Da nach meinen obigen Auseinandersetzungen ich die ätiologische Bedeutung der Spirochäte als noch nicht mit Sicherheit für erwiesen halte, so ist es selbstverständlich, dass ich den Mikroorganismus für praktische Zwecke nur mit grosser Vorsicht verwerte. Hinzukommt, was ich vorher

mehrfach betont habe, dass die mikroskopische Differenzierung besonders im Ausstrichpräparat bei Vorhandensein weniger Parasiten selbst für den Geübten, zumal an den Genitalorganen und in der Mundhöhle von ähnlichen Spirochäten doch Schwierigkeiten machen kann. Auf der anderen Seite gestattet die Häufigkeit des Vorkommens des Mikroorganismus und seine in typischen Exemplaren ausgeprägte Form, morphologische Beschaffenheit und Färbung für den Geübten positive Befunde als Direktive zur Unterstützung der klinischen Diagnose in vorsichtiger Weise zu verwenden. Erstens handelt es sich zunächst um die Frühdiagnose. Wir verfügen ebenso wie andere Autoren bereits über Beobachtungen, wo wir im beginnenden Primäraffect Spirochäten fanden, und die weitere Entwicklung die Diagnose Syphilis verifizierte. In nahezu allen Fällen allerdings war auch klinisch der Verdacht eines beginnenden Primäraffectes bereits vorhanden; es scheint der Nachweis des Mikroorganismus doch erst im Stadium der beginnenden Infiltration zu gelingen. Immerhin halte ich es nach diesen meinen Erfahrungen für wohl möglich, jetzt die Frühdiagnose Syphilis in manchen Fällen eher zu stellen als es früher möglich war. Ich will hier gleich anschliessen den Nachweis von Spirochäten in dem durch Punktion gewonnenen Saft primärer Lymphdrüsen. Es ist uns bei technisch exakter Ausführung und sorgfältiger mikroskopischer Untersuchung bei doch nunmehr genügender Übung etwa in der Hälfte der Fälle gelungen, Spirochäten nachzuweisen, wobei allerdings sowohl Drüsen wie Primäraffect klinisch genügend charakterisiert waren. Immerhin kann gelegentlich dieses Verfahren zur Unterstützung der Diagnose verwertet werden. Auf dieselbe Weise ist nun der Nachweis von Spirochäten in sekundären Lymphdrüsen—ich habe hierbei besonders grosse Nackendrüsen im Auge—niemals geglückt.

Es fragt sich nun, welche praktische Bedeutung für die Therapie der Syphilis hat dieser diagnostische Fortschritt im Gefolge. Es wird hier auf den therapeutischen Standpunkt des Syphilidologen ankommen. Was zunächst die Coupierung der Lues durch Exstirpation der Primärläsion betrifft, so brauche ich in diesem Kreise wohl erst nicht darauf hinzuweisen, dass hier durch den erzielten Fortschritt der

Frühdiagnose ein irgendwie greifbarer therapeutischer Fortschritt sich nicht ergibt. Denn sowohl unsere klinischen Erfahrungen wie auch die besonders von Neisser gewonnenen experimentellen Versuchsergebnisse zeigen, dass selbst die frühzeitigste Exstirpation wohl höchstens ausnahmsweise, wahrscheinlich aber garnicht im Stande ist das Eindringen des Giftes in den Organismus zu hindern. In den allerersten Stunden aber, wo diese Hoffnung eine grössere wäre, dürfte aber schon nach unseren bisherigen Untersuchungs-Erfahrungen der Nachweis der Spirochäte wahrscheinlich überhaupt nicht gelingen. Im übrigen verfare ich in praxis so, dass ich jede verdächtige, im Anschluss an einen suspecten Koitus entstandene Läsion, wenn sie gut gelegen ist, excidiere oder sonst zerstöre ganz gleich, ob ich Spirochäten finde oder nicht. Ich tue es eben, um alles versucht zu haben, wobei ich aber immer gleich dem Patienten bemerke, dass es wahrscheinlich zwecklos ist. Dass hierdurch der Verlauf der Krankheit gemildert wird, ist selbstverständlich möglich, einen Anhaltspunkt dafür aus meinen Erfahrungen habe ich aber nicht. Nun stehen einige Autoren auf dem Standpunkt, dass man für die Allgemeinbehandlung die beschleunigte Frühdiagnose therapeutisch verwerten soll. Ich halte es aber prinzipiell für vorteilhafter, die Behandlung möglichst erst bei Ausbruch der secundären Symptome zu beginnen vor allem und in erster Linie aus biologisch-therapeutischen Gesichtspunkten, weil ich den Eindruck habe, dass erst dann das Quecksilber seine volle, segensreiche Wirkung entfaltet. Auch ist es ja eine bekannte Erfahrung, dass bei der Frühbehandlung in einer grossen Zahl von Fällen so schnell ein Rezidiv eintritt, dass man dann gezwungen ist, den Körper mit Quecksilber zu überladen. Dass in der Tat die sehr früh einsetzende Quecksilberbehandlung keine Coupierung der Krankheit, aber auch allem Anscheine nach keine wesentliche Milderung ihres Verlaufes im Gefolge hat, dafür sprechen klinische Erfahrungen und auch die von Neisser ausgeführten therapeutisch experimentellen Untersuchungen. Eine möglichst frühe Behandlung würde im wesentlichen ja auch nur dann prinzipiell begründet sein, wenn das Quecksilber das Contagium direkt zu vernichten imstande wäre. Das ist aber allem Anscheine nach nicht

der Fall. Es gibt selbstverständlich einzelne dringende Gesichtspunkte wie Gravidität, Strikturbildung durch Primäraffect, manche extragenitalen Primärläsionen, wo auch ich die Behandlung häufig vor Ausbruch der secundären Symptome einleite; auch in der Hospitalbehandlung ist man häufig gezwungen vorher zu traktieren, weil die Patienten sonst ungeduldig das Krankenhaus verlassen und sich dann womöglich garnicht zweckmässig behandeln lassen. Aber auch dann halte ich das Einsetzen der Behandlung in der allerfrühesten Periode d. h. wenn der Primäraffect klinisch noch nicht einmal gesichert ist, nicht für zweckmässig, sondern warte auch dann nicht aus diagnostischen, sondern aus allgemein therapeutischen Gründen möglichst lange, damit wenigstens der Primäraffect und die regionären Drüsen vorhanden sind, sodass mir auch nach dieser Richtung hin die klinische Diagnose meistens ausreichend ist. Immerhin gebe ich zu, dass gelegentlich der Spirochätennachweis in der Primärläsion oder im aspirierten Drüsensaft, mitunter auch in secundären Efflorescenzen wie z. B. zweifelhaften Syphiliden des Skrotums, etc., ein willkommenes Hilfsmittel sein kann; aber nach dem heutigen Stande unserer Kenntnisse ist und bleibt für diagnostische und therapeutische Gesichtspunkte die klinische Untersuchung das Wesentliche.

Für den Effect der Behandlung kann nachdem was ich oben über das Schwanken des Spirochätenbefundes überhaupt und das Verhalten der Mikroorganismen gegenüber dem Quecksilber gesagt habe, der Spirochätenbefund noch viel weniger verwertet werden. Negative Spirochätenbefunde sind für diagnostische Zwecke selbstverständlich vollkommen wertlos. Aus diesem Grunde leistet die Untersuchung auf Spirochäten nichts für die Frage: Wann ist ein Syphilitiker geheilt?

Wir haben auch Versuche darüber angestellt und bereits früher berichtet, den Spirochätennachweis für die Frühdiagnose der hereditären Syphilis zu verwerten. Bei der ererbten Syphilis verhält es sich mit der Therapie etwas anders als bei der erworbenen. Diese Kinder haben ja immer schon Erkrankungen der inneren Organe mehr oder weniger lange vor Auftreten der sicht- und diagnostizierbaren Haut- und

Schleimhauteruptionen; und es würde gewiss segensreich sein, wenn man vor Ausbruch der letzteren bereits diagnostizieren und behandeln könnte. Wir haben nun versucht durch Blutuntersuchungen und durch Untersuchung des Inhalts von Kantharidenblasen eine Frühdiagnose zu ermöglichen; die letztere Methode hat uns vollkommen im Stich gelassen. Man findet hier nur Spirochäten wenn bereits Exanthem vorhanden ist; und die Blutuntersuchung fiel auch erst positiv aus, wenn bereits klinische Erscheinungen wie Koryza, Exanthem die klinische Diagnose ermöglichten, noch häufiger, wenn das Kind bereits dem Tode verfallen war, sodass auch in Bezug auf die hereditäre Syphilis der Spirochätennachweis zwar gelegentlich zur Unterstützung herangezogen werden kann, für die Frühdiagnose aber nichts Nennenswertes leistet. Dagegen halte ich es für möglich, dass gelegentlich die Schnittuntersuchung von Organen gestorbener Kinder resp. Föten für die retrograde Diagnose der Syphilis der Eltern etwas leisten kann, wenn—was ja nicht allzu häufig der Fall sein dürfte—Anamnese und Klinik völlig im Stich lässt.

Auch zur Lösung der Frage ob die anscheinend immunen Mütter hereditär syphilitischer Kinder nur immun oder syphilitisch sind, kann die Untersuchung auf Spirochäten verwertet werden. Wir haben seiner Zeit über einen Fall berichtet, bei dem es uns gelang in der geschwollenen Leisten-drüse einer solchen Frau, die auch bisher keine manifesten Symptome der Krankheit darbot, Spirochäten nachzuweisen. Dieser Befund ist aber vereinzelt geblieben. Auch wir selbst haben in einem zweiten analogen Falle in sorgfältiger Schnittuntersuchung einer geschwollenen Drüse und in Ausstrichpräparaten nichts gefunden, auch die Affenimpfung mit einem Teil der Drüse verlief negativ, sodass auch dieses Problem zu seiner Lösung weiterer Untersuchungen bedarf.

THE PRESENT STATUS OF OUR KNOWLEDGE OF THE PARASITOLOGY OF SYPHILIS

BY DR. OSCAR T. SCHULTZ, OF CLEVELAND

In the two years and four months that have elapsed since the publication of Schaudinn and Hoffmann's first paper, there has appeared an immense literature dealing with the etiology of syphilis. The great majority of the references are confirmatory of Schaudinn and Hoffmann's announcement of the presence of *Spirochaeta pallida* in certain of the lesions of lues. A small fraction of the work attacks the correctness of this finding, while a still smaller proportion deals with Siegel's *Cytorrhycles luis*. Enough time has gone by and enough work has been done to make possible a summary of results, and an attempt at determining what conclusions one may draw concerning the present status of our knowledge of the parasitology of syphilis.

CYTORRHYPES LUIS

Whatever may be one's views as to the correctness of Siegel's work upon the relationship of *Cytorrhycles luis* to syphilis, it does deserve some commendation, because the attempt to confirm or disprove it resulted in the discovery of *Spirochaeta pallida*. Further than this, little can be said in favor of a possible etiological relationship between *Cytorrhycles* and syphilis, or of the protozoan nature of *Cytorrhycles*. In neither respect has Siegel's work received confirmation by any large proportion of the number of investigators who have busied themselves with syphilis.

Bodies which answer to Siegel's description of *Cytorrhycles luis* are in part blood platelets, in part cell granulations and cell degenerations. They do not exhibit true motility or

undoubted evidences of multiplication. Similar bodies are seen, not only in syphilis, but also in a number of other conditions, as well as in the blood of lower animals.

OTHER ORGANISMS

Lustgarten's bacillus, DeLisle's bacillus, the numerous other bacilli described in association with syphilis, as well as the parasites of Doehle, of Clarke, of Schüller, and of Horand, may safely be dismissed without discussion.

SPIROCHÆTA PALLIDA

There remains, then, for serious consideration, only *Spirochæta pallida*. And of the factors in favor of its relationship to syphilis the first to deserve review is the question of morphology.

FACTORS IN FAVOR OF THE ETIOLOGICAL RELATIONSHIP OF SPIROCHÆTA PALLIDA

MORPHOLOGY

Has *Spirochæta pallida* morphological characteristics sufficiently marked to permit the experienced observer to distinguish between it and other spiral organisms? I think it has. Its extreme fineness, the looseness and regularity of its spirals, and its peculiar staining reaction, which makes it, at first, so difficult to see in Giemsa-stained preparations, are not shared by any other organism thus far described. Further distinguishing characters are the peculiar motility and the lack of refractility in the living condition.

From *Spirochæta refringens*, with which *Spirochæta pallida* is perhaps most often associated, the latter is readily enough distinguished. In the case of the small *spirochæta* described by several observers (Mulzer, Kiolemenoglou and v. Cube, Loewenthal) in ulcerated carcinomata, there may be more difficulty. All such organisms, however, exhibit more irregularity than does *Spirochæta pallida*, and stain more readily. The spiral organism which has given me most uneasiness in making a differential diagnosis is the small

spirochæta, probably *Spirochæta dentium*, so frequently present in the mouth cavity. In the examination of buccal mucous patches and ulcerations, it is often apt to be confusing. It is very narrow, its spirals are fairly regular, and it takes a reddish tinge with the Giemsa stain. Examined in the living state, its rotating forward and backward locomotion, the bending and extension of its body and the peculiar wave-like undulations which pass along the body, give it a type of motility much like that of *Spirochæta pallida*. But when both organisms are present in the same smear, one becomes convinced of differences which are marked enough to permit a differential diagnosis. The small mouth organism is not quite so fine as *Spirochæta pallida*, it is much more easily seen both in stained and in fresh preparations, it is much more readily stained, and interposed between several small regular spirals will be a larger irregular one.

CONSTANT OCCURRENCE IN SYPHILIS

Granting that it is possible to differentiate *Spirochæta pallida* from other spiral organisms, there arises the question of its frequency in the lesions of syphilis. In earlier reports, a certain percentage of undoubted primary lesions examined gave negative results. With increased experience this percentage has constantly decreased, until to-day the results of competent observers are positive in as large a proportion of cases as are the examinations for the tubercle bacillus in undoubted tuberculous lesions. The results of one of Schaudinn's series, as published after his death, are striking. In smears made from twenty-six genital lesions, twenty-two were positive. These twenty-two cases later developed the clinical manifestations of syphilis. The four negative cases proved to be chancroid. One is justified in concluding that *Spirochæta pallida* is constantly present in the hard chancre, no matter whether the latter is genital or extra-genital.

In condylomata, in buccal patches, and in the early lesions of the cutaneous eruption, the results are equally constant. As the skin manifestations become older, the organism is less frequently found. This may be due, in part, to the thera-

peutic treatment which the patient has received; in part, to a disappearance of the causative agent after the lesion is well established. That the organism does, however, occur in the late skin manifestations cannot be doubted. In one of my own cases, of almost two years' duration, sections of a silver-impregnated portion of the excised rupial eruption showed the spirochætæ, although in very small numbers.

In the still later lesions, those of the tertiary stage, the findings are even more inconstant. The presence of the organism in Heller's syphilitic mesaortitis has been reported.

If one excepts two or three doubtful reports, the gummata of acquired syphilis have yielded uniformly negative results. This is not surprising. Although such gummata have been shown to be infectious, large quantities of material are required for successful inoculations. One is justified in believing that the etiological agent, if present at all, is present in very small numbers. I have no doubt but that silver impregnation of early small gummata, which will permit of serial sections through the entire lesion, will reveal the syphilis spirochæta. Furthermore, an entire absence of spirochætæ in old necrotic gummata is to be expected. There is an exact parallel in the failure to find tubercle bacilli in old, encapsulated, caseous tubercles. An encapsulated gumma is no longer an essentially syphilitic lesion. The specific vascular change and the action of the spirochæta have resulted in caseation. If, in this necrosis, the organisms are also completely destroyed, there results a chronic inflammatory formation of connective tissue, due not to living organisms, but to the presence of the necrotic material.

In the gummata of the congenital form of the disease the findings have been more encouraging. Previous to a positive case reported by me in May, 1906, before the American Association of Pathologists and Bacteriologists, I had been able to find only one other case in the literature. A considerable number of cases has been reported since. There seems, however, to be a tendency on the part of many to consider the gummata of congenital syphilis as in a group apart, and as having little in common with the gummata of the acquired disease. Such a view appears to have little in its favor. In

their histology and in their genesis the congenital gummata must be considered identical with the tertiary lesions of acquired lues. The former differ only in being more rapid in production and shorter in duration. For these very reasons they offer most excellent material for a study of the presence of spirochætæ in gummata.

The question of the constant occurrence of *Spirochæta pallida* has received its most brilliant answer in congenital syphilis. Here the organism has been uniformly found.

One may conclude that *Spirochæta pallida* is uniformly present in the primary and in the early secondary lesions, as well as in those of congenital syphilis. Furthermore, it has been found often enough in the late manifestations to justify the statement that it is associated with every possible lesion that may properly be considered essentially syphilitic. The constant occurrence of an organism, sharply enough characterized morphologically to permit the experienced observer to certainly recognize it, in the manifestations of a disease so varied as are those of syphilis, is a most important point in favor of the etiological relationship of the organism. It is a point which can be invalidated only by the finding of the same organism in other diseases.

OCCURRENCE ONLY IN SYPHILIS

Reference has already been made to the presence of spirochætæ, morphologically so much like *Spirochæta pallida* as to cause some difficulty in differentiation, in ulcerated carcinomata. Further investigation, however, has shown that such spirochætæ can be differentiated. None of the reported cases of diseases other than syphilis, in which the syphilis spirochæta was supposed to be present, has stood, and one may conclude that *Spirochæta pallida* occurs only in lues.

RELATION TO LESIONS

The most important addition to our knowledge of syphilis and its spirochæta, after Schaudinn and Hoffmann's earlier work, was the silver impregnation method, since it rendered

possible a study of the relationship of the organism to the histological changes. And this study has shown, in the most conclusive way, that there is a definite relationship. Congenital material has yielded most fruitful results, and the localization of the spirochæta in hereditary syphilis satisfactorily explains the cellular degeneration, the vascular changes, the connective tissue proliferation, and the lymphoid infiltration that one considers characteristic of the disease. A similar close relationship exists between the organism and the lesions of the acquired disease. The cellular parasitism of the organism and its predilection for epithelial and endothelial cells can no longer be doubted. The cellular degeneration thus produced is the beginning of the lesion. The degeneration is followed by proliferation of connective tissue and of endothelium and by lymphoid infiltration. It is particularly the endothelium of the perivascular lymphatics which becomes involved, because it is here that the spirochætæ seem to multiply most readily. The perivascular change must of necessity lead to changes in the blood vessel wall itself. The narrowing and obliteration of the lumina of vessels and the destruction of cells by the spirochætæ lead to the necrosis which finally occurs in the skin lesions and in those of the internal organs.

Not only does *Spirochæta pallida* bear a relationship to syphilis, expressed by the localization of the organisms in and about the lesions, but there is also, as a rule, a relationship between the type and the severity of the disease on the one hand and the number of spirochætæ present on the other. This can be illustrated best by a comparison of the findings in three cases of congenital syphilis. In one, a child born dead in the seventh month of pregnancy, the lungs, liver, spleen, and bones showed advanced lesions, and in one lung there was a gumma. Spirochætæ were fairly numerous. The mother of this case was admitted to the hospital with the copper-colored remains of an old rash. It seems reasonable to suppose that her infection occurred at conception or even before this time, while the child probably became infected very early in pregnancy. In a second case, the child died on the fourth day after birth. The lesions in the internal organs were of a more acute type, with only a slight grade of connective tissue proliferation.

Spirochætæ were astonishingly numerous, producing the condition best described by the German word "Überschwemmung." In this case the mother developed secondary manifestations after the birth of the child, and it would appear that the infection of both the mother and the child occurred late in pregnancy. The infection of the child was so heavy that death resulted before the establishment of advanced changes. In the third case, the child began to show evidences of illness a few days after birth, but lived for four weeks. Any facts relative to infection of the mother could not be determined. The internal organs showed the characteristic changes, which were not very extensive, but of a chronic type. Spirochætæ were present in very small numbers. These three cases represent the three types of the disease that one sees most often clinically. In the first group belong cases in which the changes are extensive and chronic and death occurs in utero. In the second belong the clinically acute cases, characterized by comparatively recent changes. In the third group we can place those cases in which the disease has a more chronic course after the birth of the child. Here belong the cases that are apt to last for months or even years. The lesions are chronic, and are not so extensive as to lead to the rapid death of the child. The infection does not seem to be a very heavy one. The varying number of spirochætæ in the three cases mentioned indicates a relationship between the number of organisms—that is, between the intensity of the infection and the pathological and clinical type of the disease.

THE ACTION OF MERCURY

There is some discrepancy in the reports dealing with the effect of the mercurial therapy upon the spirochætæ. According to Wechselmann and Loewenthal, the treatment causes the organism to break up into a number of short individuals. Pollio and Fontana, Scholtz and others state that mercury causes a gradual disappearance of the parasites, without the production of any involution forms. Still others report the persistence of spirochætæ for some time after treatment. My own experience in this side of the subject has been too

limited to be of much value. In four cases, in which treatment had caused a beginning amelioration of the papular eruption, no spirochætæ were found in sections of the excised inguinal lymph glands or of the excised skin lesions. The localization of the spirochætæ in the skin lesions being such as to indicate that they are the immediate cause of the pathological changes, one would expect a disappearance of the organisms as soon as the treatment begins to influence the eruption. The disappearance of the eruption under the action of mercury would indicate some action of the drug upon the organism itself.

Certain facts would seem to indicate a chemical affinity on the part of the spirochæta toward mercury and the other heavy metals. In material which certainly contains spirochætæ, and which has been fixed in mercury-containing fluids, it is impossible to impregnate the organisms with silver. One may theorize that some group or side-chain, which has an affinity for the heavy metals, has its affinity satisfied by the mercury of the fixing fluid and is consequently unable to take up any of the silver. Of tissue from one of my earlier cases of congenital syphilis, portions were fixed in formalin, other portions in Zenker's fluid. The formalin material, by the Levaditi method, was exceedingly rich in spirochætæ. Some of the Zenker material was then treated with silver nitrate in the same way, but no spirochætæ could be found. Believing that the failure of the silver impregnation was due to a saturation by mercury, attempts were made to reduce the mercury and thus bring the spirochætæ into view. The results were again negative. This would seem to indicate that the action of the mercury of the fixing fluid was a destructive one, causing a complete dissolution and disappearance of the spirochætæ. Further evidence in favor of the direct taking up of mercury by the spirochætæ is the fact that syphilitics are able to take mercury in larger amounts than are non-luetics. It seems justifiable to suppose that the union of parasite and mercury results in an organic mercurial compound which is much less toxic to the tissues of the syphilitic than are the salts and more ordinary albuminates of mercury to the tissues of the non-

syphilitic. Because of my failure to find spirochætæ in the lesions of four cases of syphilis which had been under treatment, and because of the theoretical considerations outlined above, I am prone to find, in the beneficial therapeutic action of mercury in syphilis, further evidence of the etiological relationship of *Spirochæta pallida* to lues.

THE PRESENCE OF SPIROCHÆTA PALLIDA IN THE LESIONS OF EXPERIMENTAL SYPHILIS

There will always be some who will demand for the absolute proof of the causation of a disease by a living organism, the growth of the latter in pure culture upon artificial media and the fulfilment of all of Koch's postulates. While such absolute proof is, of course, much to be wished for, there does not seem to be much hope of its attainment in a number of diseases. We have not even been able to successfully apply Koch's laws in a number of conditions of bacterial origin. Yet very few will deny the rôle of *Bacillus lepræ* in leprosy. In the diseases of protozoan origin, the problem is even more difficult. Although a few of the protozoa—trypanosomes, amœbæ, and some spirochætæ—have been grown upon artificial media, similar successful results cannot be expected for those animal parasites which must spend a part or all of the life-cycle within living host cells. In the case of *Spirochæta pallida*, although cultures have thus far failed, successful inoculations into lower animals deserve as much weight as does the ability to grow *Bacillus typhosus* upon agar. The work of Metchnikoff and Roux and of Neisser and his associates has demonstrated beyond a doubt that many of the monkeys, particularly the higher ones, are susceptible to syphilis when inoculated with material from human cases, and that the disease can be transmitted from one monkey to another by inoculation. In such experiments it has been shown that *Spirochæta pallida* is present in the original material, in the lesions of the animal inoculated with that material, as well as in the lesions of other animals inoculated from the first. Such results tend strongly to indicate that the organism is transmitted and propagated and that it sets up the experimental

lesion. The production of a chronic interstitial keratitis in rabbits and the presence of the spirochætæ in the inflamed tissue add further proof to the same effect.

SUMMARY OF POINTS INDICATING AN ETIOLOGICAL RELATIONSHIP

The factors in favor of an etiological relationship between *Spirochæta pallida* and syphilis may be summarized thus:

1—*Spirochæta pallida* has characteristics sufficiently marked to permit its differentiation from other spiral organisms.

2—It is present in all the various manifestations of the disease.

3—It is found only in syphilis.

4—It bears a definite relationship to those histo-pathological changes which are characteristic of syphilis.

5—After the use of mercury, the amelioration of the cutaneous lesions and the disappearance of the spirochætæ go fairly well hand in hand.

6—In the lesions of experimental syphilis of lower animals, *Spirochæta pallida* is present and has the same characteristics as in the human disease.

AGAINST SPIROCHÆTA PALLIDA AS THE CAUSE OF SYPHILIS

The majority of the published observations justify such conclusions as those just enumerated. A number of writers, however, for reasons which deserve consideration, hold a contrary opinion.

NEGATIVE RESULTS

One objection which has been brought forward is the failure to find *Spirochæta pallida* in a certain proportion of cases. It is asking too much to demand positive results to the extent of one hundred per cent. There will always be some failures in the making of microscopic diagnoses, no matter how gifted the worker. And the chances for failure are more than ordinarily great when working with an organism so difficult to see as *Spirochæta pallida*. In extended series there has been a progressive improvement in results as the technic

became better, and as the eye became more accustomed to the object sought, until the positive percentage finally reaches one hundred, as in Schaudinn's series referred to above. In undoubted cases of syphilis, there will always be some negative results, because of the liability of human methods to err. This chance for error decreases as the experience of the observer increases. Many of the early negative results reported were due to lack of experience and to faulty technic.

Some of the failures to find the spirochætæ in supposed cases of syphilis are no doubt due to mistaken clinical diagnoses. The dermatologist, who deals chiefly with the external manifestations of acquired syphilis, is much less apt to be wrong in his diagnosis than is the practitioner who is dealing with the internal lesions of the acquired and congenital forms of the disease. The clinical diagnosis of hereditary lues is often wrong. The greater part of the supposedly syphilitic material with which I have worked came from a maternity hospital where a large proportion of the births are illegitimate. In such cases one is apt to take a syphilitic history on the part of the parents for granted, and the clinician is not to be blamed for making a probable diagnosis of syphilis. Most of the cases, in which the diagnosis rested largely upon the possibility of infection in the parents, did not show the histological changes upon which the pathological diagnosis of congenital lues must rest. In these, *Spirochæta pallida* was, of course, absent. When one remembers how difficult the histological diagnosis of syphilis often is, it is easy to understand why some cases of so-called congenital lues should fail to show spirochætæ. In a number of my cases, in which death occurred in from several days to three or four weeks after birth, there was present in the lungs a chronic interstitial pneumonia almost impossible to distinguish histologically from pneumonia alba. In fact, only the absence of syphilitic lesions in the other organs prevented a diagnosis of syphilitic inflammation of the lung. Cases of this type, which do not show spirochætæ, might easily be reported as cases negative for *Spirochæta pallida*. I am no longer willing to make a diagnosis of congenital lues unless I am able to demonstrate the spirochætæ in the tissues.

The comparatively small number of cases in which *Spirochæta pallida* has been found in the blood during the secondary stage is advanced by some as a reason for doubting the etiological relationship of the organism. The production of the rash in syphilis is the same sort of a process as the formation of rose-spots in typhoid fever. Every one knows how difficult it is to prove the presence of typhoid bacilli in the circulating blood. Large amounts of blood are required and the small number of bacilli in this amount of blood must be allowed to grow out upon artificial media. It is impossible to find the bacilli in smears made directly from the blood. It is almost equally difficult to find *Spirochæta pallida* in the circulating blood, because of the small number of organisms present in the blood at any one time.

“SILVER SPIROCHÆTÆ”

Most persistent in their objections have been W. Schulze, Friedenthal, Siegel, and Saling, and they have given rise to a considerable literature dealing with the so-called “silver spirochætæ.” Their chief attack has been against the structures brought to view by the silver method. They deny the identity of the organisms present in smears and the spiral structures seen in sections after impregnation. The latter are nothing more than nerve fibrils, elastic fibrils, and cell boundaries. While all the writers mentioned cover practically the same ground, Saling’s paper is the most detailed. That the spirochætæ are nerve fibres, he attempts to show chiefly by copies of drawings of undoubted nerve fibres taken from the work of others. That these nerve fibres have anything in common with the structures that an experienced observer would designate *Spirochæta pallida*, or that there is even any close morphological resemblance, must be denied by any one who has busied himself with the study of syphilitic material. The characteristic spiral arrangement, so different from any nerve fibres hitherto described, Saling attributes to the technic, to maceration, and to the change which he supposes syphilis causes in the nerves. His attempts to parallel the changes produced by intra-uterine autolysis with the putre-

faction of the bodies of animals in air and in water are ludicrous. Control examinations of macerated and non-macerated non-syphilitic foetuses have completely disproven Saling's contention. In fifty-three foetuses and newborn infants examined by the Levaditi method, I have never seen anything in those that were certainly not syphilitic, whether maceration was present or not, that could be at all confused with *Spirochæta pallida*. In the skin, where the Levaditi technic usually impregnates the nerve fibres better than anywhere else, the latter and spirochætæ can be seen in the same field, and I am not willing to admit that there are any grounds for confusion. In the internal organs, the Levaditi method is an even more unsuccessful means of demonstrating nerve fibres than the more commonly used histological methods of nerve-impregnation. Occasionally some of the perivascular fibres are brought into view. But here again, just as in the skin, they have none of the appearances of the spirochætæ seen in luetic tissues. Saling is right in so far as he contends that most of the structures that he has illustrated are not spirochætæ. And in those illustrations which reproduce structures with small regular spirals he is very probably dealing with true spirochætæ.

BIOLOGICAL POSITION OF SPIROCHÆTA PALLIDA

A few words may be permitted concerning the biological nature of *Spirochæta pallida*. Direct observation has availed little, because of the extreme smallness of the parasite. One must depend, in great measure, upon a comparative study of other spirally shaped organisms. Some of these, because of their dual nuclear structure and their undoubted longitudinal division, are certainly protozoa. Others, whose body form is fixed and for which transverse division has been described, seem to belong more properly among the spirobacteria. How large this latter group is remains to be determined. I am convinced of the longitudinal division of at least two of the species of spiral organisms commonly met with in the mouth. In the living condition, and in smear preparations, I have never seen undoubted evidences of the

longitudinal division of *Spirochæta pallida*. Appearances which are often spoken of as intertwinings, but which seem more properly to be end stages of longitudinal divisions, are frequently seen. In sections of silver-impregnated tissues, one sees appearances which cannot be interpreted otherwise than as stages of longitudinal division. In the living state the flexibility of the body and the peculiar motility are further evidences of the protozoan nature of the organism.

DIAGNOSTIC VALUE OF SPIROCHÆTA PALLIDA

I have attempted to bring together the more important factors which indicate that *Spirochæta pallida* is the cause of syphilis. As the etiological agent the organism must be of extreme importance from the diagnostic standpoint.

In the matter of pathological diagnosis, I feel sure that the presence or absence of *Spirochæta pallida* will clear up many points in the histology of syphilis, just as the finding of the tubercle bacillus in the tissues has, in many ways, revised the pathology of tuberculosis. I have already referred to the chronic interstitial pneumonia of marasmatic infants, which is often not to be distinguished from syphilitic pneumonia except by the absence of spirochætæ.

In doubtful clinical cases the presence of the organism in smears made from primary and secondary lesions would likewise render possible a certain and positive diagnosis. Just as is the case with other microscopic diagnoses, a negative result in an individual case may be valueless. The value of a negative finding will depend, in great measure, upon the experience of the microscopist and upon the technic employed by him. Furthermore, it is well enough known that the organism may be absent entirely, or present in very small numbers, in smears, whereas tissue from the same lesion will show the spirochætæ readily. For this reason the removal of tissue and its impregnation with silver are imperative, if smears are negative. In the case of multiple secondary lesions, the removal of tissue for diagnostic purposes ought to be the routine procedure.

The presence of undoubted examples of *Spirochæta pallida*

in smears from early primary lesions ought to influence the treatment and the clinical course of the disease. Heretofore the clinician has been dependent upon the appearance of secondary manifestations in order to establish a certain diagnosis, and, as a rule, treatment is delayed until this period. If, however, an early positive diagnosis of a primary lesion can be made with the microscope, immediate excision of the chancre and the beginning of treatment ought to materially reduce the time required for a cure, since the removal of the chancre in its early stage will remove the chief breeding-ground of the causative agent.

SUMMARY

The presence, in the various manifestations of syphilis, of a characteristic spiral organism, *Spirochæta pallida*, has been confirmed by the vast majority of those who have busied themselves with the subject.

The negative observations thus far reported are of value only in so far as they show the amount of patience and experience required for the finding and the identification of the organism.

Comparative study and direct observation lead to the belief that the parasite is protozoan in nature.

The finding of *Spirochæta pallida* in a doubtful clinical case is of the greatest diagnostic value to the clinician. Its presence in pathological material is of equal importance to the pathologist.

Because it has thus far been impossible to obtain and grow the organism in pure culture, Koch's postulates are not susceptible of proof. However, the constant presence of the parasite in the lesions of syphilis, its presence only in syphilis and not in other diseases, its definite relationship to the pathological changes, its morphological characteristics, and its presence in the lesions of experimental syphilis of lower animals, furnish sufficient evidence to establish the etiological relationship of *Spirochæta pallida* to syphilis.

Discussion

DR. CH. WARDELL STILES, of Washington, D. C., said there was

only one point in particular that he wished to bring out in connection with the parasitology of syphilis. He had noticed that in the literature and also in the papers presented to-day considerable stress was laid upon the question as to whether this organism reproduced by longitudinal or transverse division, with the idea that if the division was longitudinal it must be a protozoön, whereas, if it was transverse, it must be a bacterium. Dr. Stiles said this was no absolute test of the question at issue. There are many animals that reproduce by transverse division, and in spite of the fact that so much stress was laid upon this test in deciding the question as to whether the *Treponema pallidum* was a protozoön or not, the test was not final. If it reproduced by longitudinal division, then the probabilities were in favor of the organism's being a protozoön, but if the division were transverse it might be either a bacterium or a protozoön.

Another point referred to by Dr. Stiles was the correct name of this parasite. On the program of this Congress it appeared under two names—*Spirochæta pallida* and *Treponema pallidum*. In adopting a name for such an organism, the speaker said, we should be governed by the international code of nomenclature, and under that ruling the name *Treponema pallidum* was preferable to *Spirochæta pallida*.

DR. ALEX. RENAULT, de Paris, a dit:

À propos des considérations thérapeutiques, par lesquelles M. le Prof. E. Hoffmann avait terminé sa très remarquable communication, il désirait présenter quelques observations.

M. le Prof. Hoffmann avait dit que la découverte du Spirochète, permettant le diagnostic précoce de la syphilis, il y avait lieu de recourir à l'excision et de prescrire ensuite la médication mercurielle.

Le Dr. Renault a demandé la permission de dire qu'il considérait l'excision comme une mauvaise opération.

Elle ne comportait, à son avis, que deux indications, subordonnées à la localisation du chancre, situé, soit à l'extrémité d'un long prépuce, soit au bord d'une petite lèvre exubérante. Il était clair que dans ces deux cas, lorsqu'on enlevait le chancre, on se trouvait en présence d'une plaie simple, dont la cicatrisation était plus rapide que celle de l'accident primaire.

Mais, en dehors de ces exceptions, si on extirpait le chancre, on le voyait se reproduire avec accompagnement d'une induration énorme en étendue aussi bien qu'en profondeur, et supérieure assurément à celle qui sous-tend le chancre habituel.

M. le Prof. Jadassohn est d'avis, a-t-il ajouté, après l'excision, d'attendre, pour prescrire le traitement mercuriel, l'apparition des accidents secondaires; il ne l'a pas contredit. S'il était rationnel, lorsque le diagnostic est ferme, de prescrire d'emblée l'hydrargyre, ce mode de procéder pouvait avoir des inconvénients en cas d'incertitude. Il ne fallait pas oublier que le traitement spécifique pouvait masquer les accidents secondaires. Le spécialiste ne savait plus alors quelle conduite tenir. Allait-il abandonner le malade et peut-être l'exposer à tous les risques du tertianisme, ou, au contraire, le soumettre à tort, pendant plusieurs années, à une médication, que l'on ne saurait considérer comme inoffensive? Il était inutile d'insister sur la perplexité de son esprit, en définitive, le médecin traitant aurait le devoir de n'agir qu'en pleine connaissance de cause.

Quant à l'atoxyl, les essais avaient été tentés simultanément dans son service et dans celui de M. Hallopeau par leur ancien assistant commun, M. le Dr. Salmon.

Il lui fallait déclarer que les résultats obtenus avaient été contradictoires.

Le plus grand nombre des malades traités étaient atteints d'accidents secondaires. Eh bien! lorsqu'on s'adresse aux manifestations de cette période, il était très difficile de se rendre compte de l'action d'un médicament nouveau. Les lésions secondaires ayant tendance spontanée à la guérison, et il n'avait pas remarqué qu'avec l'atoxyl leur durée ait été sensiblement diminuée.

Selon lui les accidents tertiaires, les syphilides ulcéreuses en particulier, qui ne se modifient promptement que sous l'influence d'une médication mixte énergique, étaient seules capables de fournir un champ d'expérience concluantes.

Or les résultats acquis ne l'avaient pas convaincu. Ils avaient été, a-t-il répété, contradictoires, et plusieurs cas avaient nécessité, après l'atoxyl, l'emploi de la médication spécifique ordinaire.

Il y avait lieu cependant, à son sens, de continuer l'essai du nouveau médicament; mais de poursuivre cet essai en silence. Le bruit de la prétendue infailibilité de l'atoxyl s'étant beaucoup trop promptement répandu dans le public et en raison des préjugés, absurdes, qui ont régné et règnent encore sur les méfaits imputés au mercure, on trouvait aujourd'hui des malades qui refusaient le remède dont l'expérience des siècles avait consacré l'efficacité.

Aux spécialistes, a-t-il-dit de réagir contre cette tendance désastreuse et à ne pas laisser transpirer au dehors, ce qui devait se passer exclusivement dans le domaine scientifique.

DR. H. HALLOPEAU, de Paris, a dit qu'il désirait présenter quelques observations à propos de la belle communication de M. Hoffmann.

1. En premier lieu, il se demandait s'il agissait en bon père en donnant à son enfant le nom de Spirochète; sur l'avis de zoologues des plus compétents, le Dr. Hallopeau l'appelait depuis plus d'un an le *Tréponéma pallidum*. Il était heureux de se trouver d'accord à cet égard avec l'éminent collègue M. Stiles, d'une si grande compétence en ce qui concerne la nomenclature médicale et la zoologie.

2. Le second point sur lequel il désirait appeler l'attention, était la grande utilité que présenterait l'étude du *Tréponéma* aux différentes périodes de son évolution; il n'était pas possible que le générateur du chancre induré et le roséole fût identique à celui des néoplasies gommeuses.

3. À propos des localisations du *Tréponéma*, il était essentiel de considérer qu'on le chercherait en vain dans ce qu'il avait appelé les deutéropathies syphilitiques qui étaient d'origine, mais non de nature, spécifique; par exemple, dans les cas de leucoplasie buccale, ce n'était pas dans les épithéliums agglomérés mais dans les lésions sousjacentes initiales qu'il fallait chercher le parasite; de même dans le tabes, ce n'était pas dans les altérations secondaires du névraxe que *jazet lupus*; on *pourrait* exclusivement trouver le parasite, ou ses reliquats, dans les néoplasies initiales qui étaient le point de départ de ces lésions médullaires, il en était de même pour la paralysie générale.

Il pensait être, de tous les médecins, celui qui avait employé le plus largement l'atoxyl; les premiers résultats obtenus dans son service par les doses élevées qu'employait son ancien interne M. Salmon avaient été si favorables, si surprenants, qu'il avait cru pouvoir généraliser cette médication. Les premières doses avaient toujours été bien supportées, mais presque constamment, il était survenu, après une pratique de 6 à 10 injections, des phénomènes d'intolérance d'ailleurs passagers. Ces injections avaient été faites exclusivement avec l'atoxyl de fabrique française. Il a dit que l'atoxyl allemand était beaucoup plus dangereux et que notamment, il avait provoqué, à sa connaissance, cinq cas de lésions rétiniennes qui avaient abouti en quelques jours à une cécité complète. M. Duret avait constaté dans le produit allemand qu'il avait d'abord fourni comme pharmacien, la présence d'anilarsinates libres, c'est-à-dire, toxiques. En présence de ces faits, malgré la tolérance observée en ce qui concernait l'atoxyl français le Dr. Hallopeau avait réduit les doses et il donnait alors

chez un sujet de stature moyenne, d'abord 75 centigrammes, deux jours après 60 centigrammes, puis, trois jours après, à deux reprises, 50 centigrammes du médicament. Il était encore, dans ces proportions restreintes, très actif, et il croyait indiqué de s'en servir pour donner, à plusieurs reprises, à des intervalles dont l'analyse des urines permettra de fixer la durée, des coups de massue.

DR. BOLESŁAW LAPOWSKI, of New York, said the conclusions presented by the readers of the papers were far-reaching, and before they could be accepted it was advisable to examine the statements from which they were drawn. The statement had been made that the *Spirochæta pallida* was the cause of syphilis, as it was present only in syphilitic lesions and, besides, in all the lesions of syphilis: first, in the smears obtained from superficial lesions, such as primary lesions; second, in all early manifestations and in sections from foetal organs affected with hereditary syphilis; and also that it was present in animals inoculated with syphilis. Some of these statements were open to question.

That a structure called *Spirochæta pallida*, with morphological characteristics, is present in smears of superficial primary lesions, papules, and mucous patches is unquestioned, but the statement that this same structure is found in sections of syphilitic tissues is doubtful, as many observers consider that the supposed *Spirochæta pallida* can not be distinguished from tissue elements or nerve fibres, and in some cases from plain spirilla. That in all probability they are tissue elements was best proven by the fact that when a specimen was shown at a meeting of the Medical Society of Berlin one of the readers of the paper who was present at the meeting recognized a structure in the lumen of a blood-vessel as a typical *Spirochæta pallida*. Yet the specimen in question originated from the macerated skin of a pig-fœtus; the mother pig when slaughtered was in perfect health, thus demonstrating that, if this structure was *Spirochæta pallida*, then it was present also in non-syphilitic tissue, and if the structure was a tissue element, then we can not always distinguish between *Spirochæta pallida* and tissue elements. Furthermore, that the structures in tissues accepted by many as *Spirochætæ pallida* are tissue elements and not *spirochætæ* is supported by the fact that in syphilitic fœti aborted in the second or third months of pregnancy—that is, at the time when no differentiation of tissues had yet taken place—no structures like supposed *Spirochæta pallida* had been demonstrated because there were no tissue elements.

As to the statement that *Spirochæta pallida* was present in animals inoculated with syphilis, Dr. Lapowski said that a spirochæte had only been found in superficial lesions, while in the internal organs of such animals, which, according to Neisser's investigations, contained the living, active syphilitic virus, these organisms had as yet not been demonstrated. The statement of one of the speakers that he saw a spirochæte in the testis of an inoculated animal was only a passing remark, and we would have to await a fuller publication before it could be taken into consideration.

Before we could accept the theory that the *Spirochæta pallida* is the cause of syphilis, at least two requirements are to be fulfilled: First, to demonstrate the presence of structures which are considered as *Spirochæta pallida* in tissues of a syphilitic foetus before it reached the third month; second, to demonstrate the presence of the *Spirochæta pallida* in the internal organs of apes inoculated with syphilis, the organs being in a fresh condition (absence of mixed infection).

Owing to the foregoing reasons, the statement that the *Spirochæta pallida* is the cause of syphilis could not be accepted, and the practical conclusion advanced by the speakers regarding any lesion, even the most superficial, as being syphilitic when the *Spirochæta* were demonstrated, could not be admitted. We still must rely upon clinical symptoms in making a diagnosis of a primary lesion. The presence of the *Spirochæta pallida* could only be regarded as a double warning to be more careful and to watch our patient for a longer period than usual.

DR. T. TANAKA, Tokio, bemerkte Prof. Dohi und er selbst hätten auch die *Spirochæta pallida* in allen syphilitischen Exanthenen gefunden, besonders in der Cerebrospinalflüssigkeit von einer syphilitischen Frau, welche in der Analgegend die *Condyloma lata* hatte. Sie hätten auch Tierversuche gemacht, und es sei ihnen gelungen, dem Auge eines Kaninchens die Syphilis mit *Condyloma lata* einzuzimpfen.

PROF. ERICH HOFFMANN, Berlin, bemerkte zum Schluss, der Name *Spirochæta pallida* habe sich in der medizinischen Literatur so eingebürgert, dass er nicht glaube, dass man ihn fallen lassen werde; auch träfen die von Schaudinn zwischen *Treponema* und *Spirochæta* aufgestellten Differenzen bezüglich der Geisseln nicht zu.

Bezüglich der Stellung der *Spirochæta pallida* im System

können er nur wiederholen, dass mehr Gründe dafür sprechen, dass sie zu den Protozoen gehöre, bes. auch die Beobachtung und Verfolgung des ganzen Vorgangs der Längsteilung im frischen Präparat (lebenden Zustand).

SUR LES LOCALISATIONS SYSTÉMATISÉES DU TRÉPONÉMA PALLIDUM

PAR MM. LES DRs. H. HALLOPEAU ET GASTOU, PARIS

Une des tâches qui appartiennent à nos grands congrès internationaux est l'exposé de questions de pathologie générale sur lesquelles il importe que l'accord s'établisse entre les dermatologues des différentes écoles: c'est dans cette idée que nous y avons étudié les *toxines en dermatologie*, les *toxines en syphiligraphie*, les *deutéropathies syphilitiques*, les *proliférations locales dans la syphilis*, les *infections associées à la syphilis*, les *tuberculides d'origine toxinienne*, etc.

L'ordre de faits dont nous allons nous occuper aujourd'hui nous paraît, comme les précédents, de nature à intéresser simultanément les cliniciens et les biologistes.

Si l'on jette un coup d'œil d'ensemble sur les éruptions syphilitiques considérées dans leurs localisations, on peut remarquer que, bien souvent, au lieu d'être disséminées sans ordre apparent, elles affectent exclusivement certains organes ou certaines régions: ce sont ces localisations systématisées que nous nous proposons d'étudier aujourd'hui dans leurs caractères généraux. On sait, depuis Schaudinn et Hoffmann, qu'elles sont subordonnées rigoureusement aux localisations du tréponéma qui en constitue la cause prochaine.

Nous les classerons ainsi qu'il suit:

I° *Systématisations organiques* (squelette, centres nerveux, muscles, articulations, vaisseaux, téguments, ongles, organes des sens, glandes);

II° *Systématisations régionales*;

III° *Systématisations à des territoires nerveux*;

IV° *Systématisations par auto-inoculations qu'il y a lieu de diviser en intra-inoculations et extra-inoculations*;

V° *Systématisations par milieux de cultures d'origine microbienne; ces microbes peuvent être des habitants pour ainsi dire normaux de l'organisme ou être spécifiques;*

VI° *Systématisations par irritations toxiques répétées (leucoplasies buccales);*

VII° *Systématisations par défaut d'élimination et de thérapie du tréponéma (syphilides palmaires et plantaires);*

VIII° *Systématisations dans l'hérèdo-syphilis.*

Nous étudierons successivement ces diverses systématisations.

I.—SYSTÉMATISATIONS ORGANIQUES.—Elles se localisent exclusivement dans tel ou tel tissu; on ne peut se les expliquer qu'en considérant les milieux de culture constitués par ces tissus comme particulièrement favorables, chez certains sujets, au développement du tréponéma; il appartient aux chimistes et aux bactériologues de déterminer en quoi consiste cet état des milieux et comment il agit.

Nous allons voir que la plupart des tissus peuvent être ainsi frappés isolément en foyers multiples et distants.

1° *Systématisations dans les os.*—Il n'est pas rare de voir, le plus souvent dans la période tertiaire, parfois dès la période secondaire, des exostoses ou des périostoses se développer en différentes parties, parfois fort éloignées, du squelette, alors que les autres tissus restent indemnes.

C'est ainsi qu'actuellement, dans notre pavillon Bazin, un de nos malades présente simultanément des exostoses d'un tibia, d'une côte et du crâne, sans autre manifestation apparente; nous avons observé, dans ces derniers temps, plusieurs faits analogues. En toute évidence, le tissu osseux offre, chez ces malades, un milieu de culture favorable au développement du tréponéma: en effet, ces localisations multiples supposent nécessairement un transport des agents infectieux par les voies circulatoires; or, s'ils ne s'arrêtent, ne se développent et ne donnent lieu à une réaction que dans les os, cela ne peut être que par le fait d'un milieu de culture

pour les tréponémas tertiaires ou secondaires constitué exclusivement chez le sujet par le tissu osseux.

2° *Systématisations exclusives et multiples dans les centres nerveux.* Les foyers isolés qui constituent, suivant nous, le point de départ du tabes et de la paralysie générale, peuvent se multiplier, se développer de nouveau à distance et coïncider avec des altérations analogues des nerfs optiques.

3° *Autres systématisations organiques.* On peut voir de même *des muscles, des articulations, des artères, des veines, les ganglions lymphatiques, les poumons, certaines glandes telles que les parotides, les ovaires, les mamelles, les reins, les testicules*, et enfin *les matrices unguéales*, devenir le siège de manifestations concomitantes.

Ces faits sont susceptibles de la même interprétation.

II.—*SYSTÉMATISATIONS RÉGIONALES SYMÉTRIQUES.*—Elles peuvent être rapportées, tout au moins dans la plupart des cas, à des *actions réflexes*. Nous avons publié¹ deux faits qui établissent la réalité de troubles trophiques réflexes; dans l'un, nous avons vu une eschare, provoquée par l'électrisation galvanique de la partie interne du genou droit, être suivie, quinze jours après, d'une escharrification semblable dans la partie symétrique du membre opposé; dans l'autre, il s'est agi d'une dermite suppurative provoquée par l'application d'un vésicatoire sur le côté gauche de la partie antérieure du thorax qui a été suivie, douze jours après, d'une éruption semblable dans la partie symétrique.

Or, il semble bien que les *localisations régionales du tréponéma* puissent constituer les *parties symétriques des téguments ou de différents organes en un milieu favorable à son développement*. C'est ainsi que l'on peut s'expliquer nos observations personnelles de localisations successives et exclusives de syphilides serpigneuses dans la portion externe des deux régions rétro-scapulaires; il en est de même pour celles de syphilomes au niveau des coudes ou d'autres parties du corps; un de nos malades présente actuellement deux groupes serpigneux de tubercules syphilitiques en voie de

¹ Hallopeau.—*C. R. de la Société de Biologie*, 1878 (avec Neumann) et 1880.

régression dans des parties symétriques des cuisses; or, celui de droite est bien plus fortement pigmenté que celui de gauche; on doit donc admettre qu'il s'est développé le premier et invoquer, pour la production de son congénère, l'action trophique réflexe, constituant un *locus minoris resistentiæ*.

De même, dans les syphilides papuleuses disséminées, on peut remarquer que les confluences symétriques se produisent à quelques jours d'intervalle.

On peut faire intervenir ce même mécanisme pour expliquer les apparitions successives de syphilomes, soit aux extrémités digitales, soit dans les deux reins, les deux testicules, les deux poumons, les deux parotides, les deux nerfs optiques. Nous avons déjà signalé ces systématisations parmi celles que peut expliquer la structure de l'organe affecté: c'est que si, d'une part, les organes de même structure anatomique, de mêmes fonctions ou de même composition chimique peuvent constituer, chez certains sujets, des milieux de culture plus particulièrement favorables à la prolifération des spirochètes, d'autre part, les actions trophiques réflexes, par l'intermédiaire des métamères, peuvent se trouver mises en jeu concurremment pour engendrer ces systématisations symétriques.

Enfin, il y a lieu de faire intervenir l'évolution elle-même de la syphilis, qui comprend schématiquement une phase lymphatique primitive, une phase à prédominance capillaire et veineuse secondaire, une phase artérielle tertiaire (Gastou).

—L'agent pathogène de la syphilis semble être anaérobie au début de son existence, pour devenir ensuite aérobie (Gastou).

III.—SYSTÉMATISATIONS LOCALISÉES A DES SPHÈRES DE DISTRIBUTION NERVEUSE.—Elles sont contestables. Nous avons vu, à diverses reprises, des syphilides papuleuses se localiser dans le domaine de certains nerfs, particulièrement des intercostaux: faut-il y admettre alors l'existence d'un trouble nerveux de nutrition ou de vascularisation qui en favoriserait le développement? On peut objecter à cette interprétation que ces territoires nerveux sont en même temps

des territoires de vascularisation et de nutrition, de telle sorte que ces localisations n'ont pas, par elles-mêmes, de signification précise. Si l'on remarque, d'autre part, qu'en règle générale les syphilides ne se développent pas avec une prédilection marquée dans les régions innervées par des nerfs malades, qu'on ne les voit pas, par exemple, envahir les régions auxquelles se distribue un sciatique atteint de névrite ou un membre anesthésié par le fait d'une lésion médullaire, bien qu'il existe alors des troubles de l'innervation vaso-motrice qui sembleraient pouvoir jouer le rôle de causes adjuvantes, on est conduit à admettre que les systématisations d'origine primitivement nerveuse ne sont pas nettement établies; de nouvelles recherches devront être entreprises dans cette direction.

IV.—SYSTÉMATISATIONS PAR AUTO-INOCULATIONS.—C'est dans ces dernières années seulement que ce mode de multiplication des foyers syphilitiques a été reconnu et étudié. Jusquelà, l'insuccès constant des tentatives d'inoculation, aussi bien du chancre que des syphilides secondaires ou tertiaires, avait conduit à poser en dogme l'impossibilité de transmettre par cette voie la syphilis à un sujet préalablement infecté, et, lorsque l'un de nous a soutenu au sein de la Société française de Dermatologie une opinion contraire, il a reçu de ses collègues la qualification de "révolutionnaire." Depuis lors, la clinique en premier lieu, puis l'expérimentation sont venues démontrer la réalité et l'importance prépondérante de cette interprétation pathogénique.

Ainsi que nous l'avons établi dans un article du 19^{me} fascicule de la publication intitulée: *Musée de l'hôpital Saint-Louis*, dans diverses communications à la Société française de Dermatologie et au Congrès de Liège, la prolifération locale des syphilomes, se produisant constamment dans chaque élément éruptif depuis l'induration chancreuse jusqu'à la tumeur gommeuse et à son pourtour, ne peut s'expliquer que par une multiplication de l'agent infectieux que l'on sait aujourd'hui être le tréponéma, et les réactions qu'il provoque ne sont pas nécessairement, comme chez les sujets vierges de syphilis, des indurations chancreuses, mais bien des syphilomes analogues, dans leurs caractères cliniques et biologiques, à

ceux dont ils émanent; cette manière de voir a été confirmée, en ce qui concerne le chancre, par les belles expériences de M. Queyrat, et, en thèse générale, par les expérimentations de M. Finger; on doit en effet au professeur Viennois d'avoir mis en fait l'auto-inoculabilité des syphilomes tertiaires, et ce sont des réactions identiques à celles des syphilomes générateurs qui sont provoquées par ces tréponémas tardifs, aussi, est-ce à juste titre que nous avons formulé aux récents congrès de Lisbonne et de Lyon la conclusion suivante: *le tréponéma évolue dans l'organisme; ses fonctions diffèrent aux différentes périodes de la maladie: ces diversités d'action ne peuvent s'expliquer que par une modification du parasite;* elle est d'ailleurs peu profonde puisqu'il suffit de l'inoculer à un sujet vierge pour qu'il reprenne ses caractères initiaux. Si nous ne nous trompons, ces notions constituent un progrès dans l'étude pathogénique et biologique de la syphilis.

Nous diviserons ces *auto-inoculations* en *intra-inoculations* et *extra-inoculations*.

(A) *Systématisations par intra-oculations*.—On doit à Lang d'avoir établi que l'agent infectieux émané du chancre induré se propage directement de proche en proche, soit par les lymphatiques, soit par les interstices des tissus; nous avons montré, d'un autre côté, par de nombreuses observations, dont plusieurs se trouvent relatées dans notre mémoire de 1905 au Congrès de Liège sur *les proliférations locales dans la syphilis*, que ces syphilomes par transport et greffes locales présentent, dans leur intensité, dans leur multiplicité, dans leur saillies, dans leur tendance à devenir ulcéreux ou végétants, toutes les marques d'une suractivité nutritive qui ne peut s'expliquer que par une *exaltation de la virulence des tréponémas directement émanés de l'accident initial*: le volume considérable et l'induration du ganglion initial témoignent dans le même sens: ces tréponémas générateurs émanent directement de ceux de l'accident primitif et possèdent, de ce chef, une activité supérieure à celle des générations qui se développent ultérieurement et donnent lieu à la pléiade secondaire.

Il se produit ainsi une systématisation de syphilomes re-

marquables par leur puissance de développement dans toute la région qui environne le chancre sur un rayon que l'on peut évaluer à 12 ou 15 centimètres.

(a) Cette localisation peut se traduire par des dépôts de tréponémas dans les parois des troncs lymphatiques et se propager dans leur voisinage: c'est ainsi que, chez un de nos malades du pavillon Bazin, à la suite d'un chancre du frein, une traînée de papules confluentes a envahi toute la partie médiane de la face inférieure du fourreau, sous la forme d'un ruban qui en occupait les quatre cinquièmes antérieurs dans une largeur d'environ 6 millimètres; partout ailleurs l'éruption était des plus discrètes. Cette systématisation ne peut s'expliquer que par une localisation des tréponémas dans les parois du tronc lymphatique médian et la prolifération des syphilomes dans son voisinage immédiat.

La systématisation péri-chancreuse serait plus prononcée si le ganglion inguinal directement en relation avec l'accident initial ne venait former un obstacle à la propagation locale des tréponémas à virulence exaltée qui en proviennent directement: la photographie que nous avons l'honneur de mettre sous vos yeux vous en fournit un témoignage que nous croyons pouvoir qualifier de saisissant; elle représente une éruption secondaire qui a envahi avec une intensité exceptionnelle toute la région inguinale gauche et son pourtour sur une largeur d'environ 15 centimètres et une hauteur d'à peu près 5 centimètres; formant une masse confluite et saillante, elle dépasse en dedans la ligne médiane où elle surmonte le pubis et elle s'élargit à sa partie interne qui forme comme la base d'un triangle; on trouve des papules isolées à son pourtour; partout ailleurs, l'éruption est discrète et modérément abondante; or, voici dans quelles conditions s'est développée cette systématisation inguinale: le malade a eu d'abord un bubon suppuré à la suite d'un chancre simple, affection actuellement très commune à Paris; ultérieurement, il a contracté un chancre induré: or, au lieu du ganglion direct que l'on pourrait appeler le ganglion barrière, il s'est développé, par le fait de la destruction partielle de cet organe, cette éruption d'une activité excessive qui s'est étendue sur tout le pourtour de l'ulcération ganglionnaire et s'est propagée rapidement à toute la région inguinale; les tréponémas, au

lieu de rester limités au ganglion direct et d'y engendrer des produits moins virulents, se sont ainsi inoculés aux parois de l'ulcération chancreuse et de là se sont multipliés de proche en proche avec l'activité exubérante qui appartient à ces premières générations du parasite; telle est du moins l'interprétation que nous croyons pouvoir formuler en raison des notions que nous possédons actuellement sur la pathogénie des syphilomes.

(b) *Les accidents secondaires peuvent être également systématisés dans leurs localisations par la voie d'intra-inoculations*: nous citerons comme exemple les adénopathies secondaires des régions inguinales, épitrochléennes, cervicales; elles sont dues manifestement au retour, par la voie lymphatique, de tréponémas qui ont été centrifugés par la circulation artérielle.

(B) *Systématisation par extra-inoculations*.—Si les syphilomes peuvent se propager par la multiplication dans les tissus des tréponémas en évolution intra-organique, ils doivent pouvoir être également transmis par l'introduction, dans les téguments, du même parasite; autrement dite *l'intra-inoculation suppose l'extra-inoculation*. On peut s'expliquer partiellement ainsi les proliférations systématisées des syphilomes dans certaines régions telles que, en première ligne, la vulve, l'anus et leur pourtour ainsi que la cavité buccale.

Déjà, dans notre mémoire sur *les proliférations locales impliquant l'auto-inoculation de la syphilis*, nous avons fait ressortir les arguments qui militent en faveur de ce mode de multiplication; nous avons montré que l'abondance, l'exubérance et la tendance à l'ulcération des syphilides qui surviennent dans les parties de la surface cutanée et des muqueuses qui se trouvent en contact avec des parties similaires ne doivent pas être attribuées essentiellement, comme on le fait généralement, à la malpropreté et au séjour de liquides septiques; on les voit, en effet, souvent se manifester dans des parties qui se trouvent en dehors de celles qui peuvent être ainsi contaminées, par exemple, au sommet des grandes lèvres, aux régions sous-inguinales et au pubis; si l'on considère, d'autre part, que ces syphilomes se trouvent souvent, par

rapprochement de parties symétriques, en contact immédiat, autrement dit, que les manifestations présentent, des deux côtés, des localisations exactement semblables, que, de plus, Queyrat a prouvé que les chancres indurés peuvent se multiplier et que Finger a obtenu l'auto-inoculation de produits tertiaires, on est amené à penser qu'il *s'agit bien là de localisations systématisées par auto-inoculations*: pourquoi ces inoculations ont-elles échoué jusqu'ici lorsqu'elles ont été pratiquées avec la lancette de l'expérimentateur? c'est parce que les conditions ne sont plus les mêmes: il y a loin, en effet, de l'introduction, à l'aide de l'instrument, d'une parcelle de tissu morbide, au contact incessant d'une surface ulcérée et de ses produits de sécrétion. Si ces syphilomes par auto-inoculation présentent, dans la région vulvaire et à son pourtour, une intensité que l'on ne retrouve pas dans ceux qui peuvent se produire dans les creux axillaires ou les plis sous mammaires, c'est sans doute encore parce que leurs tréponémas générateurs sont émanés directement du chancre induré et possèdent, de ce chef, une suractivité.

V.—SYSTÉMATISATIONS PAR MILIEU DE CULTURES D'ORIGINE MICROBIENNE.—Ces microbes peuvent être des habitants pour ainsi dire normaux de l'organisme ou être spécifiques.

(a) *Systématisations par microbes de nature banale*.—Il est d'observation journalière que les syphilides se développent avec une prédilection des plus marquées, et parfois exclusive, dans certaines régions parmi lesquelles il faut citer en première ligne la cavité buccale, les parois vulvaires et le prépuce des phimoses; viennent ensuite les espaces interstitiels des orteils; on ne peut attribuer cette prédilection à la structure histologique des tissus, car il s'agit aussi bien de surfaces cutanées que de muqueuses, et, d'autre part, il est nombre de muqueuses qui ne sont pas fréquemment envahies par la maladie.

La malpropreté, invoquée pour certaines de ces systématisations, n'intervient que d'une manière secondaire; les soins les plus minutieux de la bouche n'empêchent pas l'invasion des amygdales et de la face interne des lèvres.

Le seul caractère commun qui appartienne à ces diverses régions est une flore microbienne d'une extrême richesse; sans doute, les toxines qui en émanent constituent un milieu de culture favorable à la prolifération des tréponémas.

On a attribué à cette même cause, c'est-à-dire à l'envahissement des syphilides par d'abondantes colonies de microbes associés, la tendance des syphilides vulvaires à devenir exubérantes dans leurs saillies et leurs dimensions: c'est à tort, suivant nous, car on n'observe rien de semblable en ce qui concerne les manifestations intra-buccales et interstitielles des orteils. Ainsi que nous l'avons dit déjà, cette exubérance des lésions de la vulve est, comme celle des éléments péri-chancroïques dans les deux sexes, l'apanage des tréponémas à virulence exaltée qui proviennent directement du chancre.

(b) *Systématisations par associations avec des microbes spécifiques.*—Entre autres, on peut citer les associations avec le bacille de Koch, avec les fins bacilles des lésions séborrhéiques, avec l'agent inconnu du psoriasis. Il n'est pas très rare de voir, chez les syphilitiques, des adénopathies multiples qui se comportent comme des ganglions tuberculeux. Il y aura lieu de rechercher si l'on y trouve des tréponémas associés au bacille de Koch.

Il existe des cas authentiques de lupus compliqués de syphilomes.

Les localisations de syphilides dans les régions occupées par les affections séborrhéiques, et particulièrement dans les espaces intra-scapulaires, le cuir chevelu, les parties rétro-auriculaires et les sillons naso-jugaux sont fréquentes: les toxines engendrées par le fin bacille de Unna fournissent en toute évidence un milieu de culture des plus favorables au tréponéma.

À propos du psoriasis, nous avons plusieurs fois signalé la coexistence de placards mixtes d'éruptions psoriasiques et de syphilides.

VI.—SYSTÉMATISATIONS PAR ACTIONS IRRITATIVES TOXIQUES RÉITÉRÉES.—Il a été établi par M. le professeur Fournier que les leucoplasies linguales se produisent exclusivement

chez les syphilitiques qui font usage du tabac: l'action irritante de ce produit vient donc ici s'ajouter à l'action spécifique du tréponéma pour engendrer ces deutéropathies.

VII.—SYSTÉMATISATIONS PAR DÉFAUT D'ÉLIMINATION ET DE THÉRAPIE DES TRÉPONÉMAS.—Il est fréquent de voir des syphilides palmaires et plantaires persister avec une étonnante opiniâtreté pendant de longues périodes, parfois indéfiniment, malgré une médication énergique; ces faits s'expliquent par l'épaisseur que présente l'épiderme dans ces régions: les tréponémas, issus des capillaires, se multiplient dans les interstices cellulaires et sans doute aussi dans les cellules elles-mêmes et s'y trouvent comme emprisonnés, car il n'y a pas dans ces tissus de voies circulatoires, et, d'autre part, la couche cornée s'oppose à la sortie des parasites par la surface cutanée; le défaut de circulation empêche les agents thérapeutiques de venir les influencer et l'on se trouve hors d'état de les faire pénétrer à travers l'épiderme.

VIII.—SYSTÉMATISATIONS DANS LA SYPHILIS HÉRÉDITAIRE.—Elles s'observent dans les phases initiales ou tardives de cette syphilis.

Dans les phases initiales, il faut considérer séparément, 1° la syphilis congénitale, 2° la syphilis héréditaire précoce.

Dans la *syphilis congénitale*, qui souvent ne se manifeste pas cliniquement, la systématisation est diffuse, vasculaire ou glandulaire. On trouve, en effet, le tréponéma dans les parois et autour des vaisseaux ainsi que dans les cellules parenchymateuses des organes. Un point important à signaler est sa localisation ovarienne (Levaditi et Sauvage) ou testiculaire (Fouquet).

Dans la *syphilis héréditaire précoce*, on voit s'altérer concurremment les deux cavités nasales, les deux régions palmaires et plantaires, les deux bosses frontales: la structure histologique ou l'origine voisine, dans la vie embryonnaire, de ces diverses régions y expliquent la localisation des manifestations. Les *systématisations tardives* dans les dents, les oreilles, les yeux, le squelette, les téguments, les muscles, sont susceptibles de la même interprétation.

On voit combien sont multiples et diverses les localisations systématisées des syphilomes et notre tableau n'est sans doute pas complet; nous avons voulu seulement, dans cette courte étude, appeler l'attention sur ces faits, en élargir le cadre et essayer d'en donner l'interprétation pathogénique ainsi que la signification biologique.

Nous serons heureux si ce travail devient le point de départ de nouvelles recherches dans cette direction, en montrant quel puissant intérêt présentent ces systématisations au point de vue de la pathologie générale et du traitement de la grande maladie vénérienne.

BEITRÄGE ZUR SPIROCHÄTENFRAGE

VON DR. ALBERT DREYER, CÖLN

Wenn ich den Beobachtungen, die ich an Spirochäten machen konnte, ein negatives Ergebnis vorausschicken darf, so möchte ich zuerst einigen anderslautenden Befunden gegenüber mitteilen, dass ich bei der Vaccine des Kalbes in den nach *Levaditis* Methode hergestellten Schnitten keinerlei Spirochäten aufzufinden vermochte.

Zur Technik der Spirochätenfärbung im Gewebe erwähne ich für die gewiss mehr principiell als praktisch wichtige Giemsa-färbung nach *Schmorl*, dass sie sich vorzüglich an Refringentes enthaltenden Schnitten einstudieren lässt, da diese dickeren Mikroben sich sehr deutlich damit tingieren.

Zur Morphologie der Spirochäten gehe ich über, um über die Y-Formen einige Worte zu sagen. Dieselben sind zum wenigsten teilweise als sichere Längsteilungen zu deuten. Man sieht nicht bloss im Ausstrichpräparat, sondern vielfach auch im Gewebe ein gemeinsames dickeres Ende, von dem die feineren Abzweigungen ausgehen. Da ich im Gewebe eine Aneinanderlagerung und Verknäuelung ausser in Gefässen niemals beobachtet habe, so scheint mir eine fast zwingende Notwendigkeit vorzuliegen, diese Formen als Teilungsformen anzusehen.

Ob die von *Herxheimer* in den Spirochäten beschriebenen runden Körperchen zu der Teilung in Beziehung stehen, ob

sie vielleicht Ruhestadien darstellen, ist immer noch nicht entschieden. Sie können aber in zweifacher Hinsicht eine Bedeutung beanspruchen, einmal in differentialdiagnostischer Richtung, weil ähnliche bei der Refringens vorkommende Körperchen stets ovale, bezw. ∞ -Form besitzen, und zweitens, weil diese Körperchen, die sich gerade dort häufig finden, wo die Spirochäten scheinbar in Teilung begriffen sind, und die ich entsprechend verkleinert auch im Gewebe sah, bei der Verschiedenheit ihrer Gestalt bei Pallida und Refringens ein weiteres Moment dafür abgeben, dass es sich um wirkliche Teilungsformen und nicht um Zusammenlagerungen handelt.

Die Differentialdiagnose der Spirochäte pallida kann nicht immer aus einem einzelnen Exemplar gestellt werden. Zwar gibt es Spirochäten von solcher Steilheit und Enge der Windungen, dass ohne weiteres die Diagnose gesichert ist. Aber auch die Pallidae sind nicht stets typisch, ihre Windungen sind nicht immer so eng, und es kommen besonders in Condylomen die sogenannten Übergangsformen vor, welche nach Zartheit und Farbe schwer von der Pallida zu differenzieren sind. Freilich sind sie stets mit einer Menge typischer Refringentes vergesellschaftet, so dass bei einiger Vorsicht im Urteil nach der Durchsicht des Präparates die richtige Diagnose zu stellen ist. Ohne die bakteriologische Diagnose der Syphilis stets für leicht zu halten, ist sie doch mit geringerer Erfahrung möglich als beispielsweise die Erkennung *einzelner* Gonokokken (auch bei Gramfärbung) bei gewissen Gonorrhoeformen. Am schwierigsten erscheint sie mir in breiten Condylomen. Dort kommen die Refringens- und Pallidaformen stark gemischt vor und zwar stets mit Vorwiegen der Refringens. Diese Befunde ändern sich nach meinen Erfahrungen auch dann nicht, wenn man die Präparate der Tiefe des Gewebes entnimmt, etwa durch Abkappen der oberflächlichen Schichten. Wenn eine Anzahl Autoren im Anfang den Nachweis der Pallida im breiten Condylom für besonders leicht erklärten, so mögen hier zuweilen Verwechslungen vorgekommen sein. Wenigstens darf man dort, wo solche nahe liegen, nur typische Exemplare der Pallida für diagnostisch verwertbar halten.

Ich fand die Spirochäte pallida bisher in harten Schankern in 50 verschiedenen Fällen, in Schleimhautpapeln in 20 Fällen, in 11 Fällen in breiten Condylomen, in 9 Fällen in trockenen lenticulären Papeln, in Pusteln in 3 Fällen, in 2 Fällen im orbiculären papulösen Syphilid und je einmal im Chancre mixte, in der planen und in der folliculären Form des Lichen syphiliticus, im Speichel bei bestehenden Plaques und im Urin bei syphilitischer Nephritis. Das Alter der Syphilis schwankte zwischen einem Tag—es handelte sich um einen Patienten, der sich sehr scharf beobachtete, da zwei Freunde bei gleicher Gelegenheit inficirt, vor ihm erkrankt und bereits von mir behandelt waren—und drei Jahren. Den Wert der Untersuchung für die Praxis halte ich für ungemein gross. Unter den 99 Fällen, bei denen ich Spirochäten fand, war 13 Mal eine Diagnose nur bakteriologisch möglich (12 völlig uncharacteristische Schanker, 1 isolirte Pappel). In 36 weiteren Fällen lag zwar ein begründeter Verdacht auf Syphilis vor, ohne dass die Diagnose völlig gesichert werden konnte (31 Schanker, 1 Chancre mixte, 1 Lichen syphiliticus (folliculäre Form) mit starkem Jucken und Mangel anderer syphilitischer Symptome, 2 x vereinzelt lenticuläre Papeln, 1 x rhagadiforme Plaque der Zunge).

Die überwiegende Bedeutung der frühzeitigen Erkennung von Primäraffekten wurde durch die immer wieder konstatarite Tatsache noch beleuchtet, dass der Nachweis der Spirochäten in den ganz frischen Primäraffekten am allerleichtesten war. Hier war die Anzahl der Spirochäten zuweilen eine enorme. Mit seltenen Ausnahmen liess sich das Gesetz aufstellen, dass der bakteriologische Nachweis der syphilitischen Schanker um so leichter war, je schwerer die klinische Diagnose sich gestaltete. Auch als Polizeiarzt wurde ich zweimal durch den gelungenen Nachweis der Pallida in der Erkennung der vorliegenden Affektion (Erosionen) gefördert, und ich zweifele nicht daran, dass in Zukunft bei Vermehrung der ärztlichen Kräfte für die polizeiärztlichen Untersuchungen sich mancher Vorteil auch aus dieser neuen bakteriologischen Untersuchung für die Prostituirtencontrolle ergibt. Mir selbst verbot der Umfang der übrigen dort zu leistenden Arbeit, ausgedehntere Erfahrungen zu sammeln.

Auf den Nachweis der Infektiosität des Urins bei syphilitischer Nephritis glaube ich hinweisen zu sollen. Auch für die Behandlungsart hat bei vorhandener Nephritis der Nachweis von Spirochäten im Urin natürlich Einfluss, und eine von vornherein zielbewusste Hg-Behandlung wird hier durch die bakteriologische Diagnose an Stelle des bisherigen empirischen Tastens und Versuchens treten.

Für die theoretische Betrachtung möchte ich kurz 2 Tatsachen aus meinen Befunden hervorholen. Die grosse Menge der Spirochäten in den syphilitischen Pusteln und die nicht unbeträchtliche Zahl derselben im Lichen syphiliticus seien kurz erwähnt. Besonders betont sei das Vorkommen der Spirochäten in einem Fall von Mundpapeln bei gleichzeitigem Bestehen tertiärer Hauterscheinungen (ausgebreitetes tuberöses Syphilid). Ich unterlasse es vorläufig, aus dieser *einmal* konstatierten Tatsache einen Schluss zu ziehen.

Mit zwei Worten will ich auf die Menge und die Lagerung der Spirochäten in den Schnittpräparaten eingehen. In den harten Schankern schwanken ihre Mengen in ganz ausserordentlicher Weise, und es schien mir, als ob zwischen der Schwere des Falls und der Menge der Spirochäten ein direktes Verhältnis bestände, namentlich wenn der Vergleich unter Berücksichtigung der zeitlichen Entwicklung der Lues stattfand. In einem Fall von Lichen syphiliticus (folliculäre Form)—ich demonstriere die Präparate—fand ich die Spirochäten ausschliesslich in der äusseren Epithelscheide und der inneren Bindegewebsscheide der Haare und zwar in erheblicher Anzahl.

Etwas ausführlicher wende ich mich den als Saprophyten des Smegmas, der Mundhöhle, etc., beschriebenen, aber auch bei verschiedenen krankhaften Processen vorkommenden Spirochäten zu, über deren Biologie, Identität und Bedeutung noch grosse Uneinigkeit besteht. Bei Dunkelfeldbeleuchtung mit der einfachen von *Zeiss* angegebenen Sternblende kann man sie vortrefflich und leicht beobachten. Sie zeigen typische Contraktionen, wobei die Körnelungen, die sie vielfach characterisiren, verschwinden. Dass diese Körnelungen in Beziehung zu einer Querteilung stehen, glaube ich nicht. Man sieht niemals kurze Formen, wie sie den eventuel-

len Räumen zwischen den Körnelungen entsprächen. Wohl aber glaube ich typische Längsteilungen beobachtet zu haben und zeige ein bezügliches Photogramm. Die kleinen als Geisseln betrachteten Anhänge, welche auch diese Spirochäten besitzen, liessen sich am besten und schnellsten mit der Argentum-Methode *Sterns* zeigen. Nachdem *Schaudinn* und *Hoffmann* schon in ihrer ersten Publikation auf das Vorkommen der Spirochäte refringens an der Oberfläche und im Gewebssaft von spitzen Condylomen hingewiesen hatten, war es ein leichtes, diese Befunde zu bestätigen. Bei allem Wechsel der Anzahl der auch im Gewebssaft der Condylome gefundenen Spirochäten war dieselbe zuweilen eine so massenhafte, dass die Vermutung eines ätiologischen Zusammenhangs dem Untersucher sich aufdrängte. In Schnittpräparaten von Condylomen, welche nach den Methoden von *Levaditi* (ältere Methode) und *Bertarelli-Volpino* (jüngere Methode) behandelt waren, habe ich in 13 Fällen 10 mal Spirochäten mit unregelmässigen, flachen mal relativ dicken Windungen nachgewiesen. Auch hier ist es gerade so wie bei der Untersuchung syphilitischer Efflorescenzen nötig, Serienschnitte anzulegen. Dann auch hier finden sich die Spirochäten zuweilen nur in einem kleinen Teil der Schnitte. Dadurch erklärt sich vielleicht, dass unter den drei negativen Fällen sich gerade meine beiden zuerst untersuchten befanden, von denen nur eine kleine Anzahl Schnitte angefertigt und untersucht wurden. Der dritte erfolglos untersuchte Fall ist allerdings in langen Serien verfolgt worden. Immerhin darf man bei der grossen Anzahl negativer Ergebnisse bei der Untersuchung von Schankern und anderen syphilitischen Gewebstücken auch hierin keinen schweren Einwand gegen die Bedeutung der Refringens für die Ätiologie der Condylome erblicken. Denn die Zahl der vorhandenen Spirochäten schwankt hier wie dort ausserordentlich, und wenn es bei der Pallida die ausserordentliche Feinheit und die Schwierigkeit der Sichtbarmachung ist, die einzelne Exemplare in den Schnitten auch dem gewöhnlichen Auge entziehen kann, so ist es bei der dickeren Refringens die Schwierigkeit der Unterscheidung von Gewebselementen, namentlich Nervenfasern, die, sobald es sich um wenige

Exemplare handelt, die Entscheidung gelegentlich unmöglich machen kann. Wenn die typische Körnelung der Spirochäten allerdings in den Schnittpräparaten ausgesprochen ist, so kann auch bei einzelnen Exemplaren zuweilen die Diagnose hierdurch gesichert werden. Über die Unterscheidbarkeit der einzelnen Spirochäten in den Schnittpräparaten, ist es nicht nötig, heute noch ein Wort zu verlieren. Die kompetentesten Beurteiler: *Bertarelli, Rona, Müller, Scherber, Sakurane, Beer* und *Hoffmann* sind hierin nur einer Ansicht, und auch *Stern* scheint seinen ursprünglichen Widerstand aufgegeben zu haben. In sämtlichen von mir untersuchten Fällen von spitzen Condylomen bestand übrigens nur einmal gleichzeitig eine Balanitis erosiva circinata und ein anderes Mal eine gewöhnliche Balanitis. Auch diese Fälle glaubte ich nicht ausschalten zu sollen, da geschwürige Prozesse fehlten und ich in Fällen von Balanitis erosiva Spirochäten in der Gewebstiefe nur in geringerer Menge und anderer Lagerung zu finden vermochte. Die Lagerung der Spirochäten in den Condylomen betrifft sämtliche Gewebsschichten. Man sieht, wie die Spirochäten in das Epithel eindringen und die aufquellenden Epithelien in spinnenförmigen Netzen umgeben. Dabei ist das Stratum corneum gelegentlich deutlich verdickt. Ich kann mich deshalb der geistvollen Theorie von *Juliusberg*, dass die Spirochäten in den Epithelien für die Pathogenese das Wesentliche sind, indem sie durch ihre erodierende Tätigkeit einen verminderten Gewebswiderstand bewirken und dadurch das Geschwulstwachstum hervorriefen, nicht anschliessen. Auch die therapeutischen Erfahrungen, die Recidive nach oberflächlichen Abkratzungen sprechen hiergegen und bestätigen die Anschauung, dass die Lagerung des Virus in den Gefässen und im Bindegewebe in der Hauptsache den Wachstumsreiz abgibt.

Aus den interepithelialen Lymphräumen gelangen, wie man gelegentlich direkt beobachten kann, die Spirochäten in die Lymphbahnen der Papillen und von hier aus in die erweiterten Gefässe, in denen ich dieselben in der Hälfte meiner Fälle nachweisen konnte. Im Gewebe verbreiten sie sich bis in die Subcutis hinein, wo sie im lockeren Bindegewebe zuweilen noch in grösseren Haufen sich vorfinden. Ohne

auf die Anatomie der Erkrankung näher einzugehen, möchte ich die gelegentliche stärkere Wucherung der adventitiellen Scheide der Venen hervorheben, da ich sie nirgendwo verzeichnet fand. In ungleichmässiger Weise umgibt eine Epithelwucherung wallartig eine Seite des Gefässes. Die beträchtliche Zahl meiner Spirochätenbefunde, ihre an anderem Orte ausgeführte Übereinstimmung mit klinischen Erfahrungen machen die Bedeutung der Refringens für die Ätiologie der Condylome immer wahrscheinlicher. *Juliusberg* (Archiv für Dermatologie, Band 84) hat übrigens mit *Schucht* in der *Neisser'schen* Klinik in Breslau ganz unabhängig von mir nach der Silbermethode von *Levaditi* eine Anzahl spitzer Condylome untersucht und in einem derselben im Schnittpräparat ebenfalls grössere Mengen von ganz gleichen Spirochäten dargestellt. Ebenso verdient ein Befund von *Walter Pick* bei einer framböesiformen (tuberculösen?) Hauterkrankung aus dem Archiv für Dermatologie und Syphilis. (Band 85) hier erwähnt zu werden. *Pick* beschreibt einen mit Wahrscheinlichkeit als Tuberculosis papillomatosa aufgefassten Krankheitsfall am Dorsum des Vorderarms einer 68 jährigen Frau, der sich durch seine Tendenz zur Narbenbildung und Abheilung im Centrum, durch chronischen Verlauf und Bildung neuer, in ihrem Ablauf acuter Efflorescenzen an der Peripherie auszeichnete. Im Gewebsausstrich und im Oberflächeneiter fanden sich mit Anilinfarben leicht färbbare, 3-4 flache Windungen besitzende, 5-10 μ lange, oft ein dichtes Netzwerk bildende Spirochäten, die mit Refringentes am meisten Ähnlichkeit zeigten. Auch im Gewebe fanden sich bei *Levaditi*färbung sowohl im Abscessinhalt wie innerhalb der Entzündungsherde im Corimm wenig gewundene und plumpe Spirochäten zusammen mit intensiv sich schwärzenden Bacillen. *Pick* sieht möglicherweise in der beschriebenen Infektion mit Spirochäten die Ursache der merkwürdigen papillomatösen Form, wofür ihm das glatte Abteilen der Affektion nach flacher Abtragung der Efflorescenzen spricht. Dass auch im Condyloma latum (zuerst von *Beer*, *Hoffmann* und *Sakurane*) in den oberflächlichen Schichten der Schnitte die Spirochäte refringens nachgewiesen ist, bestätigt meine vor Jahresfrist ausgesprochene Anschauung, dass das breite

Condylome durch eine Mischinfektion mit *Spirochäte pallida* und refringens entsteht. Rechtfertigt der anatomische Bau diese Ansicht, so wird ihre Wahrscheinlichkeit durch die Gewebssaftbefunde erhöht. Immerhin steht noch der Beweis aus, dass die Refringens beim breiten Condylom sich in der Gewebstiefe vorfindet.

Wenn dieser als Refringens bezeichnete Saprophyt nur so leicht und so oft zum facultativen Parasiten werden kann, so ist das Interesse an der völligen Sicherstellung dieser seiner Rolle kein geringes. Der experimentelle Weg ist bisher mit wenig Erfolg beschritten. Indes ist das Experiment noch keineswegs erschöpft. Auch die *Wassermann'sche* Reaktion der Complementbindung dürfte geeignet sein, die Refringensfrage aufzuhellen und ihre Bedeutung in das richtige Licht zu setzen. Antigene dürften aus den Filtraten der spitzen Condylome am leichtesten und meisten zu erhalten sein, und an der Bildung von Antikörpern darf a priori nicht gezweifelt werden, wenn man erwägt, wie häufig nach den vorliegenden Befunden die Refringens in die Blutbahnen gelangt.

Ganz dunkel erscheint noch die Antwort auf die Frage, welches Schicksal die Spirochäten im Blut erfahren. Ein Abschluss in einem lokalen Gefäßbezirk, der bei den obstruierenden Gefäßveränderungen der Syphilis wohl möglich erscheint, kann für die Refringens, die stets in stark erweiterten Gefäßen gefunden wird, nicht angenommen werden. Eine teilweise Vernichtung der Refringentes durch Aufnahme derselben in Leukocyten konnte ich mehrmals beobachten. Ob aber alle so und anders schadlos beseitigt werden, bleibt eine offene Frage. Dass wenigstens ein Teil der sogenannten parasyphilitischen Affektionen auf einer Refringensinfektion beruhen kann, muss mit in das Bereich der Möglichkeit gezogen werden. Die durchschnittliche Unheilbarkeit dieser Affektionen durch Quecksilber sowohl wie ihre gelegentliche Besserung durch dieses Mittel würden sich erklären, da Hydrargyrum eine zweifellose wenn auch geringe Wirkung auch bei spitzen Condylomen ausübt. Die Häufigkeit der Combination von Syphilis und vermehrtem Refringenswachstum, weiter aber auch des unabhängigen von Syphilis vorkommende parasitäre

wie saprophytische Wachstum der Refringens, namentlich im Mund und am Genitale einerseits und der Mangel aller Anhaltspunkte für Syphilis in einer Anzahl von parasymphilitischen Fällen andererseits würden harmonieren. Schliesslich möchte ich noch darauf hinweisen, wie häufig in der Anamnese der Parasyphilitiker einfache Genitalgeschwüre ohne spätere Erscheinungen von Syphilis vorkommen und meinen Zweifel daran ausdrücken, dass alle diese Fälle als Syphilisfälle in Anspruch genommen werden können. Jedenfalls steht nach den Untersuchungen von *Rona*, *Scherber*, *Müller* und anderen die Bedeutung der Spirochäte refringens für eine Anzahl von Genitalgeschwüren fest. Ich würde es unterlassen, von der angedeuteten Möglichkeit der Zusammenhänge zu sprechen, wenn nicht in klinischen Instituten von kundiger Hand eine eventuelle Lösung solcher Fragen mit der von *Wassermann*, *Bruck* und *Neisser* für die Syphilis inaugurierten Reaktion denkbar wäre.

Indem ich die Condylomfrage verlasse, füge ich einige Befunde von Spirochäten vom Typus der Refringens an, die ich an anderen Orten machen konnte, denen ich einen besonderen Wert nicht beilege. In zwei Fällen von akutem ersten Ausbruch einer Psoriasis vulgaris fand ich nach Abhebung der Schuppe äusserst spärliche Spirochäten, deren Abbildung ich herumreiche. Der Fundort war in einem Fall eine Papel der Brust, im anderen eine solche des Rückens. In vielen anderen Fällen konnte ich den Befund nicht bestätigen, und ich halte hier das gelegentliche Vorkommen für ein saprophytäres, um so mehr, als ich auch in zwei Fällen von Psoriasis vulgaris, deren Gewebstücke ich untersuchen konnte—ein Fall wurde in Serien untersucht—niemals Spirochäten fand. Derartige Untersuchungen bei Krankheiten mit unbekannter Ätiologie wurden zweifellos nach Bekanntwerden der Levaditimethode in zahllosen Fällen überall ausgeführt. Es dürfte aber nicht ganz müssig sein, wenn ich angebe wo ich selbst solche Silberschnitte resultatlos durchforschte. Ich untersuchte ausser den berichteten 2 Fälle von *Molluscum contagiosum*, 4 Fälle von *Lichen ruber planus*-formen, 2 papilläre Warzen, eine gewöhnliche Warze, ein *Ulcus rodens*, je eine *Vaccine Kaninchencornea* in Quer- und Flachschnitten

und einen Herpes genitalis. Bemerken will ich, dass bei Anwendung sehr starker Vergrößerungen (1500 fach) in den silberimprägnirten Präparaten bei Vaccine, Ulcus rodens und Molluscum contagiosum die bekannten Einschlüsse besonders gut erkennbar waren.

Indem ich nach dieser Abschweifung auf die Spirochäte refringens zurückkomme, so fand ich sie auch in auffallend grossen Mengen in dem abgekratzten Belage der Leukoplakia oris in drei Fällen. In einem derselben bestand gleichzeitig an anderer Stelle ein Zungencarcinom, in einem zweiten war Verdacht auf Syphilis vorhanden, in dem letzten bestand keine weitere Affektion. Obwohl ich an anderen Stellen des Mundes nur mehr oder weniger spärliche Refringentes fand, gebe ich auch diese Befunde mit aller Reserve und lediglich als Anregung für weitere Untersuchungen in gleicher Richtung wieder. Sind doch auch die Mengen der saprophytär, z. B. im Vorhautsack vorkommenden Spirochäten in gewissen Maassen schwankend. Dass die Ätiologie der Leukoplakie aber nicht mit dem Moment der Syphilis und des Rauchens erledigt ist, geht aus einer statistischen Aufnahme bei den Prostituirten der Stadt Köln hervor. Ich fand bei der polizeiärztlichen Untersuchung unter 412 Prostituirten 23 Fälle von Leukoplakie der Mundhöhle. Von diesen hatten 14=60,8% antisiphilitische Kuren durchgemacht, während 12=52% Cigaretten rauchten. Bei 7=30% der gesamten mit Leukoplakie Behafteten kommen beide schädlichen Momente (Syphilis und Rauchen) zusammen. In 4 Fällen dagegen=17,4% fehlte jeder Anhaltspunkt für die Ursache der Leukoplakie in der einen oder anderen Richtung. Diese unter allen Kauselen aufgenommenen Zahlen beweisen zwar, wie ich an anderem Ort in ausführlicherer Statistik belegen will, den längst bekannten Einfluss der Syphilis und des Rauchens auf das Entstehen der Leukoplakie, zeigen aber gleichzeitig, dass das eigentliche ursächliche Moment ein anderes sein muss.

Ich schliesse meine gesamten Betrachtungen über die Bedeutung der Spirochäten für die Pathologie, indem ich auf die trotz aller Verschiedenheit der Krankheitsbilder vielfach bestehenden Analogieen im Verhalten der Spirochäten

bei den einzelnen Affektionen hinweise, die auch weiteren Forschungen die Wege zu weisen geeignet sind.

SYPHILIS BEIM KANINCHEN, ERZEUGT MIT DER REINKULTUR DES SYPHILISBACILLUS VON NIESSEN

VON DR. MAX VON NIESSEN, WIESBADEN

Wie ich auf dem IX. Kongress der deutschen dermatologischen Gesellschaft in *Bern* 1906 bemerkte, ist es bei der nunmehr feststehenden experimentellen Tiersyphilis als erfreulicher Fortschritt zu begrüßen, dass die Dermatologie sich nicht auf Syphilisprodukte des Integuments als Impfmateriale beschränkt hat, sondern dass auch mit inneren Organen, ja selbst mit Tertiärprodukten und Blut bei Erbsyphilis die Übertragungen als gelungen anerkannt sind. Was indess immer noch als Mangel empfunden werden muss, ist einmal das Fehlen eines *reinen Impfmateriale* bei dieser Impfmethode. Mit Recht muss nämlich für die künstliche Erzeugung einer Infektionskrankheit das *Koch'sche* Postulat aufrecht erhalten bleiben: das Freisein des Impfmateriale von Verunreinigungen und Beimengungen von Bestandteilen des Tierkörpers. Der zweite Mangel der bisherigen experimentellen Syphilisforschung liegt darin, dass da, wo die Dermatologie versagt, also *äussere* Merkmale für die noch vorhandene Syphilis fehlen, die *Diagnose* meist mit völliger Sicherheit *nicht zu stellen* ist.

Von jeher habe ich daher mein Hauptaugenmerk auf die Erfüllung dieser beiden Forderungen gerichtet und mich bemüht, den Arzt instandzusetzen, dort, wo die dermatologische Kunst im Stich lässt, die Syphilis als Krankheitsursache zu erkennen. Nach wie vor kann ich nun für diesen Zweck nichts für geeigneter halten, als die bakteriologische Blutuntersuchung und nach wie vor muss ich an dem von mir für die Syphilisursache angesehenen *Bakterium* festhalten. Wenn ich mit diesem Befunde immer noch fast isoliert dastehe, so ist das neben Gründen mancher Art z. T. wohl dadurch bedingt, dass

ich, von Haus aus Neurologe, den Hauptnachdruck bei meinen Versuchen weniger auf eine chronologisch getreue Imitation des Syphilisverlaufes, als auf *Erzeugung von syphilitischen Erscheinungen im Inneren* und auf *kulturelle Reproduktion des Kontagiums bei Spätformen* legte. Immerhin haben meine früheren Versuche auch unzweideutige Syphiliserscheinungen der Haut ergeben.

Um nun diese Lücke mehr auszufüllen und angeregt durch die neue Spirochätenära, sowie die Misserfolge anderer bei Syphiliserzeugungsversuchen auf subkutanem Wege habe ich in den letzten 2 Jahren einige Versuche am Kaninchen gemacht und hier auf subkutane Beibringung der Reinkultur meines Syphilisbazillus ein so typisches Exanthem hervorbringen können, dass dasselbe den weitest gehenden Ansprüchen auch des *Dermatologen* genügen muss. Die Impfung erfolgte am Ohrflappen, ergab eine primäre Induration und nach 6 wöchiger Inkubation zeigten sich an mehreren Stellen sukzessive die Eruptionen, die mit der Zeit serpigginösen Charakter annahmen.—

Die letzten Jahre haben auf dem Gebiete der Syphilisforschung unverkennbar befruchtend gewirkt. Einen besonders nachhaltigen Anstoss gab die mehr und mehr argumentativ gestützte Erkenntnis *Schaudinns* von einem ursächlichen Zusammenhang einer Spirochätenform mit der Syphilis. Fehlt auch zur Zeit noch die Erfüllung des letzten der bekannten 3 *Koch'schen* Postulate für die spezifische Pathogenität der Spir. pall., die *Erzeugung der Syphilis mit ihrer Reinkultur*, so besteht bei der Mehrzahl der Dermatologen und Fachleute kaum mehr ein Zweifel an der ätiologischen Bedeutung dieser Spir. pall. Ein wirklich stichhaltiger Grund kann gegen den kausalen Zusammenhang der Syphilis mit der Spirochäte nicht mehr angeführt werden, sobald sie als das angesehen wird, was sie ist, als ein *Bakterium* u. z. *eine der vielen Wuchsformen des Syphiliserregers*. Danach ist sie also bereits reingezüchtet.—Angesichts der in letzter Zeit sich derart häufenden Befunde eines fast regelmässigen Zusammentreffens der Spir. pal. mit Syphilisprodukten kann man sich allerdings nur wundern, dass diese für viele so überraschende Erscheinung nicht schon eher erkannt worden

ist.—Von ganz besonderem Interesse mussten die Befunde für mich im Vergleich mit dem von mir für die Syphilisursache nach wie vor verantwortlich gemachten *Bakterium* sein. Der Vergleich lag um so näher, als eine möglicherweise zu erzielende Überbrückung der scheinbar so heterogenen Befunde mit einem Schlage den letzten Zweifel an der Echtheit sowohl des Bazillus wie der Spirochäte tilgen konnte, ja der Bazillus konnte als der ältere Bruder seiner jüngeren Schwester der Spirochäte zum Sieg verhelfen, sobald ihre gemeinsame Provenienz und einheitliche Genese erwiesen war. Diese Überbrückung musste vom *mykologischen* Standpunkte von vornherein nicht besonders schwierig erscheinen, denn Spirillen und Spirochäten sind in der Bakteriologie alltägliche Erscheinungen und speziell ich habe es vom bakteriologischen Standpunkt von vornherein als einen Hemmschuh für die Anerkennung der Spirochäte empfunden, dass man sie seitens der Zoologie, wenn auch nicht ohne Widerspruch mit Beschlag belegte. Eine Überbrückung der scheinbaren genetischen und morphologischen Kontraste war nun des weiteren um so eher ermöglicht, als der von mir für die Syphilisursache verantwortlich gemachte Bazillus nicht nur ein morphotisch überaus variabler Myzet ist, sondern auch gelegentlich und passager lange vor *Schaudinn* von mir in der Reinkultur wahrgenommene und abgebildete,¹ wenn auch weniger als besonders markant beachtete resp. weiter verfolgte Wuchsformen darbot, die nur für Spirochätenformen gehalten werden können. Es lag bei dem verdienstvollen Hinweis *Schaudinns* auf das konstante Prävalieren grade der Spirochätenform im syphilitischen Produkt, zumal der Erbsyphilis besonders nahe, das Augenmerk speziell dieser Wuchsform meines Syphilis bazillus auch kulturell mit mehr Nachdruck zu widmen.

Spirochäten sind als solche nicht präformiert, sie *werden* erst zu dem, als was sie uns imponieren, u. z. sind sie nichts anderes, als das mehr oder minder regelmässig gewundene *Fadenwachstumsstadium*, welches aus bazillären Einzelindividuen durch imperfekte Teilung hervorgeht. Auch im Gewebe, nicht nur in der Kultur, ist das entwicklungsge-

¹ Siehe *Beitr. z. Syphilisforschung*, viii., Taf. II., Fig. 13, 1904. Überreicht dem Berl. internat. derm. Kongress.

schichtlich zu verfolgen, ja hier ist die Spiralenform des Syphilerregers für ein bakteriologisch geübtes Auge besonders leicht auf ihre Metameren, den *Streptobacillus* zurückzuführen. Eine bis zu 20 und mehr Bögen bildende Wellenlinie, die im Gewebe nun und nimmer das Resultat erstarrter Eigenbewegung undulierender Art sein kann, entsteht selbstverständlich erst durch *sukzessives Wachstum*, denn die Spirochäte ist nicht wie eine Schlange im Ei vorgebildet, sie ist vielmehr als Kette und Summe mehrerer Einzelglieder kulturell und histologisch direkt nachweisbar. Es handelt sich also nicht um generatio spontanea, sondern um eine Entwicklungsphase innerhalb eines sehr mannigfachen und reichen Formenkreises, um einen vorübergehenden Generationswechsel. Wie diese Krümmungs-, Winden- und Schraubentendenz des Reihenwachstums in der Reinkultur des Syphilisbazillus unter bestimmten, ihr günstigen Züchtungsbedingungen eintreten kann, so scheint innerhalb des Gewebes ihr Zustandekommen durch besondere Phasen herabgesetzten Antagonismus begünstigt zu werden, sodass es zu üppiger Wucherung gerade dieses Stadiums kommt. Mir fällt dabei auf, dass dieses Stadium ein relativ kurzes ist, denn die Fortpflanzungstendenz im voll entwickelten Spirochätenstadium ist sehr gering, sie sistiert ziemlich schnell und für längere Zeit, bis sie von neuem in morphologisch veränderter Richtung erwacht. Hierauf beruhen einmal die Erscheinungen der Inkubation und Latenz und zum anderen der Erscheinungsreichtum der Syphilissymptome. *Syphilis gibt es auch ohne Spirochätenformen*, wenn letztere auch wohl im Verlauf jeder Syphilis mindestens einmal zur Entwicklung kommen mögen, und *nur etwa das* fortan für Syphilis zu erklären, was Spirochäten aufweist, wäre ein folgenschwerer Irrtum, eine kurzsichtige Ignorierung des überaus umfangreichen Universalbegriffs des Gesamtwesens der Syphilisursache. Nie ist die Spirochätenform zudem einzig vertreten, sondern stets finden sich in Kultur wie Gewebe die *bazillären Einzelgebilde*, Vorstufen und Zerfallsprodukte nicht nur involutiver, sondern auch *evolutiver* Art u. z. mit jeglichem Ausschluss etwaiger Verunreinigungen oder Mischinfektionen.—Ich habe mich von jeher bemüht, vom *phyletischen* und *vergleichend-*

mykologischen Standpunkt Analogien der Schizomyzeten mit den Fadenpilzen zu finden und den *ontogenetischen Pleomorphismus* phylogenetisch zu deuten gesucht, nun, wenn auch sinnverwirrend vielgestaltig für den Neuling, der Formenkreis im Generationswechsel des Syphilisbazillus incl. Spirochätenstadium, das nicht unerlässlich ist, ist nicht wunderbarer, als der des Schmetterlings.—Das Bemerkenswerteste aus dem von mir innerhalb 14 Jahren forgesetzten mykologischen Studiums insgemein vergleichend und speziell bei meinem Syphiliserreger ist nun die Beobachtung, dass *Kokken*, also das Prototyp der Schizomyzeten und der Monomorphie, *keimen* und so polymorph werden, nur eine Teilerscheinung in dem ontogenetischen Entwicklungsgang eines und desselben Myzetenlebens sind. Je nach den äusseren Bedingungen kann die ganze vielgliedrige Reihe der Einzelphasen durchlaufen, das eine oder andere Stadium länger festgehalten, eine Anzahl von Zwischenstufen übersprungen werden, rudimentär verlaufen, ja die Fortpflanzung kann einheitlich monomorph vor sich gehen, jede Tendenz zur höheren Entfaltung der immanenten, latenten Triebe kann ausbleiben, nicht zur Geltung kommen, schlummern. Man sieht, welch gewaltiger Spielraum zwischen üppigster Wucherung zu Gestaltungen schier unbegrenzter Möglichkeiten und scheinbar sterilem Vegetieren! Der *Syphilokokkus*, der *Hauptrepräsentant* des *Syphiliserregers*, seine *zweifelloos häufigste* und *weitest verbreitete Wuchsform* kann sonach bei entsprechender Kultivierung in beträchtlich lange Fäden auswachsen, so zwar, dass die Mutterzelle, wie beim Myzel der Hyphomyzeten spurlos verschwinden, resp. in dem Fadengebilde, z. B. der Gliederkette, einer Spirale aufgehen kann und statt des Kokkus resp. als dessen Produkt nunmehr ein mehr weniger langer Faden vorliegt.¹ Diese Kokkensprösslinge sind teils *gegliederte*, teils aber auch *homogen* erscheinende Fäden von je nach Züchtungsart recht verschiedenem Kaliber und ebenso schwankendem Längenmass. Diese Fäden und Gliederreihen haben

¹ Anm. Ein Mangel an Logic und mykologischen Kenntnissen ist es sonach, wenn die paternelle Syphilisheredität damit bestritten wird, dass die Spirochäte viel länger sei als der Kopf des Spermatozoons. In letzterem hat ein ganzes Dutzend Syphilismikrokokken Platz, aus denen erst die Aggregate u. weiteren Entwicklungsstufen des Syphiliserregers später hervorgehen.

nun die Fähigkeit, winklige Abknickungen, wellenförmige Bogenlinien und selbst Verzweigungen einzugehen, sie können am Triebende spitz auslaufen und auch an beiden Enden spitz erscheinen, wenn der Trieb nämlich von der ursprünglich in der Mitte des Fadens vorhandenen und abgestreiften oder in diesem aufgegangenen Mutterzelle aus nach zwei Richtungen des Wachstums erfolgte. Die ersten Kokkensprösslinge können auch isolierte resp. kohärente Bazillenindividuen sein, die Metameren können von Glied zu Glied die Form wechseln, an Volumen zunehmen und zu Endkolben von über Hefengrösse anschwellen. Einmal z. B. in Spirochätenform angelegt und präformiert scheint eine Art Tendenz zu bestehen, in der ursprünglich prävalierenden Keimart und Wuchsform auch die anderen primären Keimzellen quasi anzuregen, zu befruchten und sich in einer Reihe von Generationen derart fortzupflanzen, bis dieser oder jener innere oder äussere Anlass und Anstoss einen Rückschlag in andere Wuchsformen und Entwicklungsstufen bedingt. Die verschiedenen Stadien des Fadenpilzwachstums spielen sich also gleichsam in gedrängter Form en miniature und teils abortiv auch beim Schizomyzeten ab und werden kulturell und histologisch oft genug übersehen, können z. T. übersprungen werden, rudimentär bleiben. Hier konzentriert sich die Phylogenie des Myzeten gleichsam ontogenetisch und ich möchte behaupten, dass neben epidemiologischen, Faktoren derart daran schuld sind, wenn Zeiten kommen, wo die Spirochätenformen gegenüber anderen, regelmässigeren auch im Gewebe völlig in den Hintergrund treten. Im Blut sind sie so wie so selten genug. Es ist mir nun mehrfach gelungen, auf kulturellem Wege aus dem recht charakteristischen Kokkobazillenstadium meines Syphilisbazillus mit *Spirochätenformen völlig identische Entwicklungsstufen* nicht nur zu züchten, sondern auch in einigen Generationen der Kultur festzuhalten. Dies Stadium ist hier mutmasslich wegen der günstigeren Wachstumsbedingungen nach Ausschaltung der die mehr gewundene Spirochätenform anscheinend begünstigenden Widerstände des tierischen Zellgewebes,—zumal scheint der *moribunde Zustand* des letzteren, also der Nachlass des Tonus und des Antagonismus dem status nascendi des Spirochätenwachstums günstig zu sein—

ein meist ziemlich flüchtiges und wegen der Feinheit und geringen Pigmentaufnahme der ersten Keimschlauchanlagen leicht übersehbar.

Ich möchte sonach die *Spirochäte Schaudinns* als eine *Teilerscheinung* und *Entwicklungsphase* des an lebhafterem Formenspiel so reichen Generationswechsels *meines Syphilis-bazillus* ansehen und gleichzeitig hieran die Mahnung knüpfen, nicht einseitig fortab etwa nur das für Syphilis zu agnoszieren, was nur reine und ganz bestimmte Spirochätenformen aufweist, die ja auch niemals ganz ausschliesslich vorliegen.

Wie die Hautsyphilis nur ein Bruchteil der Syphilidologie ist, *so ist die Spirochäte nur ein Entwicklungsstadium der gewaltig umfang- und erscheinungsreichen Syphilisursache*. Es besteht zwischen den *Bazillen-Kokken und anderen Formen* nicht nur *kein prinzipieller Unterschied*, sondern ein *genetischer Zusammenhang*. Dadurch kann die Diagnose für den Nichtkenner erschwert werden. Hat man aber erst die *Eigenart der Kultur* erkannt, so sind die differenziell-diagnostischen Kriterien derselben den histologischen Merkmalen überlegen, wenn auch entsprechend den einzelnen Syphilisfällen die zugehörigen Bazillenstäme eine Art individuelles Gepräge darbieten können, was die Identifizierung bisweilen erschwert und verzögert. Die Kultur mit ihren vielseitigen Merkmalen ist sicher die *universellere* Methode, zudem gestattet sie weit sicherer die Konkurrenz zweifelhafter Elemente auszuschalten, was bei Anwesenheit mehrerer Spirochätenarten nur wenigen gegeben ist.—Ist sonach auch der einheitliche Charakter der Syphilis *ätiologisch*, d. h. vom mykologisch-phyletischen Standpunkt nicht so absolut feststehend, dass er keiner Revision bedürfte, sind auch die "Grenzgebiete" und "Übergangsformen" dieser an sich variablen Krankheit schwankend und mannigfach genug, grade die Bakteriologie ist hier als höchste Entscheidungsinstanz dafür berufen, was Syphilis ist, sobald sie exakt *vergleichend-mykologisch* vorgeht und *ontogenetisch* wenn auch noch so heterogen erscheinende Wuchsformen, nachdem sie ihren einheitlichen, entwicklungsgeschichtlichen Zusammenhang erkannt hat, gegenüber *phylogenetischen*, für praktisch-pathogenetische Gesichtspunkte zu weit abführenden Nachbargebieten abgrenzt. Dazu

wären schliesslich auch die neusten "Überbrückungsversuche des Mikrophytenreiches zu dem der Protozoen zu rechnen, wie sie z. B. *Dunbar* vertritt, wenn er soweit geht, zwischen Bakterien und Algen einen genetischen Zusammenhang nachweisen zu wollen. Zu welchem Reich die *Spir. pall.* zu zählen ist, darüber besteht zur Zeit selbst unter ihren Kennern keine Einigkeit. Dass sie von massgebender Seite der modernen Richtung tonangebender Grössen der Bakteriologie entsprechend zu den Protozoen gezählt wird, scheint mir mehr ein Akt der Pietät gegenüber ihrem Entdecker, dem Zoologen *Schaudinn* zu sein. Der bakteriologische Nachweis ihres kulturell-genealogischen Zusammenhanges mit veritablen Kokken bedarf dieser Hypothese nicht, muss sogar das unfruchtbare und unbegründete Festhalten daran für eine Erkenntnishaemmung ansehen und vor dem aussichtslosen Beharren dabei warnen.

Es spricht sonach bisher, so schwer das auch *sonst* definitiv zu entscheiden sein mag, rein *nichts* für die *Protozoënnatur* der *Spir. pall.*, wohl aber ist die Erkenntnis ihres kulturell zu erzeugenden genetischen Zusammenhanges mit einem *Bazillus* ein *unzweideutiger Beweis* für ihre *Protophytennatur*. Desgleichen ist der bakteriologische *Syphilisnachweis durch die Reinkultur aus dem Blut* bei sonst fehlenden Zeichen die bei weitem *zuverlässigste* und *universellste* Methode *in vivo ex vivo* u. das ist für den Praktiker die Hauptsache.

Zum Syphilisnachweis ist, wie gesagt, die Spirochätenwuchsform nicht unerlässlich und nur auf Vorhandensein von Spirochäten basierte Diagnosen würden zu den *folgeschwersten Irrtümern* Anlass geben,¹ da einmal ein grosser, wenn nicht der grösste Teil von Syphilis—ich erinnere nur an die langen Latenzstadien, die dubiösen Fälle, die Folgezustände, etc.—und damit andererseits der *Gesamtbegriff des Syphiliserregers* und des *Syphiliswesens* unerkant resp. verkannt bleiben würde.

Was bisher für "Körnung," "Fragmentierung," "Degenerations-" und "Involutionerscheinungen" der Spirochäte angesehen wird, sind meist verkannte Zeichen des gewaltigen

¹ Anm. Siehe hierzu: *Knauer*: "Negative Diagnose," in *München. med. Woch.*, 51, 1906.

Erscheinungsreichtums des Syphiliserregers, *evolutive* Formen, Mutabilitätsmerkmale, Generationswechselforgänge, die vom vergleichend- und phylogenetisch mykologischen Standpunkt von der grössten Bedeutung sind.¹

Die von mir zu den erfolgreichen Syphilisübertragungen auf Affen, Schweine, Pferd, Kaninchen, etc., verwendete, aus dem Blut der Eruptionsperiode stammende Reinkultur enthielt in mehrfachen Generationen zur Zeit der Impfung *keine Spur von Spirochätenformen*, sondern bestand lediglich aus reinen *Kokkobacillenformen*, in gleicher Weise wie die aus dem Blut der Versuchstiere kulturell reproduzierten Syphiliserreger, und doch kamen jene höchst markanten Syphiliserscheinungen damit zustande. Diese Tatsache wird durch meine neuesten, letztjährigen Versuche am Kaninchen bestätigt, von denen im folgenden 2 Fälle mit besonders bemerkenswertem Ergebnis auszugsweise wiedergegeben werden sollen, soweit sie bisher* gediehen sind.—Inwieweit bei der Syphilis, sei es der genuinen sei es der artifiziellen etwa intermediär Spirochäten mitwirken können, bleibe zunächst dahingestellt.—

Ich übergehe hier, um diesen Auszug nicht zu sehr auszudehnen, das, was bisher über die experimentelle *Kaninchensyphilis* von Vorarbeitern bekannt geworden ist. Nach *ƒ. K. Proksch's*,² des bedeutendsten lebenden Syphiligraphen, Zusammenstellung sind unzweifelhaft positive Syphilisübertragungen auf Kaninchen, *A. Fournier*, *Auzias-Turenne*, *Diday*, *Waller*, *Gailleton* und *Haensell* gelungen. Die 7 Kaninchenversuche des letzteren sind namentlich von ganz hervorragender Bedeutung, einmal weil sie z. T. mit tertiären Syphilisprodukten (Inhalt eines noch intakten Gummiknoten) gemacht wurden und zweitens weil dabei auch tertiäre Syphi.

¹ Anm. Es würde zu weit abführen und in einem kurzen Abstrakt nicht möglich zu schildern sein, wie sich die Kette des Generationswechsels vom Kokkus über Fadenform wieder zum Kokkus schliesst. Die Kokken zweiter Generation entstehen teils, wie bei den Hyphomyzeten, als Fruktifikationsprodukt, end- resp. wandständig aus Bazillen und Fäden, teils aus endogenen Sporen und schliesslich gleichsam konglobulativ als Zerfallsprodukte gequollener oder konfluierter Mutterzellen.

² Die venerischen Erkrankungen und deren Übertragbarkeit bei einigen warmblütigen Tieren. *Vierteljahrschr. f. Dermat. u. Syphilis*, Bd. x., pp. 309-353.

lissymptome erzielt werden konnten.—Bei den neueren Versuchen der Syphilisübertragung auf das Kaninchenauge fällt mir besonders das Fehlen konstitutioneller Erscheinungen auf, womit ich nicht bezweifeln will, dass die Keratitiden tatsächlich luetischer Natur sind.—Das Verdienst als erster *mittels der Reinkultur des Syphiliserregers* Syphilis auf Kaninchen übertragen zu haben, darf ich wohl für mich in Anspruch nehmen.—

Am 2. Juni 1906 injizierte ich einem ausgewachsenen weiblichen Kaninchen von gesundem, kräftigem Schlag $\frac{1}{2}$ ccm Bouillonaufschwemmung einer im Jahre 1899 aus dem Blut auf der Höhe der Syphiliseruptionsperiode beim Menschen gewonnenen Kultur des von mir für die Syphilisursache angesehenen Bazillus, den ich zuvor am Affen, Schwein und Pferd als spezifisch pathogen erprobt hatte. Die Kultur war also 7 Jahre alt und in etwa 25ter Generation fortgezüchtet. Sie war vor 14 Tagen frisch angelegt und enthielt keine Spirochätenformen. Ich bemerke, dass hier unter Generation nicht der Entwicklungskreislauf vom Kokkus über Bazillus-Faden- und andere Formen wieder zum Kokkus verstanden ist, sondern die Zahl Fortpflanzungen von einem Nährboden zum anderen. Wenn diese schnell und gleichmässig erfolgt, kann die Kokkobazillenform schier unbegrenzt lange weitergezüchtet und festgehalten werden, zumal wenn nur Gelatine verwendet wird und die Wachstumsbedingungen möglichst wenig variiert werden, soweit man es überhaupt in der Hand hat, diese von den Einflüssen der Jahreszeiten auf das Phytoplasma zu emanzipieren. Es scheint des weiteren für den Verlauf der Krankheit bei Mensch und Tier nicht gleichgültig zu sein, welchem Syphilisstadium beim Menschen der Syphilisbazillenstamm, deren ich bis jetzt 300 reinzüchten konnte, entnommen wurde und ferner in welcher Entwicklungsphase sich die jeweilige Reinkultur an sich befindet. Ich infizierte 3 Kaninchen in ganz verschiedener Weise, dieser Überlegung Rechnung tragend, derart, dass das eine, der oben genannte Fall 1, mit der reinen Kokkenform aus dem Blut der Eruptionsperiode während des Exanthems, das weite mit einer zur Polymorphie auch mit gewundenen Fadenformen nach Spirochätenart tendierenden Reinkultur aus dem Blut eines Falles

von multipler Periostitis gummosa, 14 Jahre nach der Infektion infiziert wurde. Die Blutgeber waren beide noch nicht behandelt, was für den Verlauf der Übertragung mir auch nicht irrelevant zu sein scheint. Das 3te Kaninchen erhielt eine Reinkultur aus dem Blut eines sehr schweren Falles von mehrfach behandeltem Aortenaneurisma auf syphilitischer Basis. Die Applikation war kombiniert subkutan und mittels Einstreichens in Haut-schnitte und Falten. Einen Primäraffekt und ein *typisches Exanthem* ergab nur der Fall 1, bei dem das Kontagium der *Eruptionsperiode* verwendet wurde. Fall 3 ergab neben tief greifenden ulzerativen Zerstörungen bei protrahiertem Verlauf innerhalb fünf-viertel Jahren *multiple* periostale, nicht entzündlich *erweichende Knoten* bis zu Kirschengrösse neben *typischer Lebercirrhose, starker Drüenschwellung* und ganz *merkwürdigem Haarschwund* bis zur *völligen Enthaarung* einzelner Partien. Das Tier magerte dabei sehr beträchtlich ab und zeigte Hyperonychie. Beim 2ten Kaninchen konnte bis jetzt ausser einer bemerkenswerten *Haarverfärbung* bislang pigmentierter Stellen an der Dorsalfläche der Pfoten zu *volligem Weiss* nichts besonderes bemerkt werden, doch ist der Versuch noch kürzeren Datums als die beiden anderen, immerhin über ein Jahr alt, was bei einer so kurzlebigen Tierart, wie dem Kaninchen schon immerhin eine geraume Zeit ist. Doch dies nur nebenbei. Später, wenn die Versuche beendet sind, mehr davon. Hier soll nur der erste, speziell den *Dermatologen* wegen seines markanten Verlaufes interessierende Versuch kurz geschildert werden, wemngleich auch er noch nicht abgeschlossen ist.—

Die Injektion fand bei dem erstgenannten Kaninchen an der Aussenseite des rechten Ohrlappens statt, sodass das Unterhautzellgewebe zwischen Knorpelschicht und Integument in Ausdehnung von mehreren Quadratcentimetern ausgefüllt, infiltriert war. Die Resorption erfolgte in kurzer Zeit reaktionslos, Störungen des Allgemeinbefindens wurden nicht wahrgenommen.

Am 7. Juni, nach 5 Tagen war ausser einem kleinerb-sengrossen Knötchen der Injektionsstelle nichts zu bemerken. Dieses schwand im Laufe von ca 2 Wochen.

Am 2. Juli, nach 4 Wochen zeigte sich an der linken

Ohrspitze ein hirsekorngrosses Knötchen und am 12. Juli, also nach 6 Wochen fanden sich an der rechten Rumpfseite in der Gegend des Rippenbogens die ersten Exanthemstellen im Umfang von ca 2 qcm. Diese glichen in *jeder* Beziehung einem schorfenden Syphilid der behaarten Kopfhaut des Menschen. Im Laufe von 14 Tagen etwa verschwand die flache, lachsfarbene, reaktionslose, verschorfende Exkoration *spontan* und die enthaarte, anfangs schuppene Stelle behaarte sich wieder im Laufe weiterer 2 Wochen allmählich mit neuem Pelz. Unmittelbar darauf zeigte sich am Rücken derselben Seite nach dem Schwanz zu eine gleiche Eruption mit demselben Verlauf, darauf eine 3te, nunmehr gegenüber, auf der linken Körperseite, und so fort im Verlauf des Juli, August und anfang September, also zwischen der 6ten und 14ten Woche 3 weitere solche, ziemlich konforme Stellen, im ganzen bis dahin 6. Ausserdem fand sich am linken Ohr, an dem die Injektion nicht stattfand, ein überaus derber, zentral tellerförmig eingezogener Knoten von über Erbsengrösse. Derselbe fühlte sich *knorpelig hart* an und persistierte hartnäckig von der 6ten Woche 8 Wochen lang kaum verändert ohne zu ulzerieren. Erst sehr allmählich im Laufe mehrerer Monate wurde dieser Knoten kleiner. Niemals fand sich irgend ein Zeichen entzündlicher Reaktion an und um denselben.

Der Verlauf der ersten Eruptionen war ein ganz gleicher, sie traten eruptiv und sukzessiv auf, nachdem die vorhergehenden abzuheilen begannen, in Rückbildung begriffen waren. Die letzte Stelle nahm indes *serpiginösen* u. z. *zirzinären* Charakter an, es bestand mehrere Wochen ein gradezu *frappant typisches Bild eines halbkreisförmigen, zirzinär-serpiginösen Syphilids*. Dasselbe breitete sich im Verlauf von 6 Wochen etwa später nach 2 Seiten hin ständig aus, indem marginal der sich rückbildenden, verschorfenden Stellen neue, gleichsam den Pelz unterminierend vorrückten. Die Restitution geschah *spontan* und relativ schnell, sie schien eine völlige zu sein, die Schorfe fielen ab, die betroffenen Stellen der enthaarten, feucht gelblich-rosa glänzenden, nicht eiternden Haut schuppten eine Weile, um sich schliesslich wieder langsam in der gleichen progressiven Richtung, in der die



FIG. 1.—Mit der Reinkultur des Syphilisbazillus von Niessen erzeugtes serpiginöses Hautsyphilid beim Kaninchen.

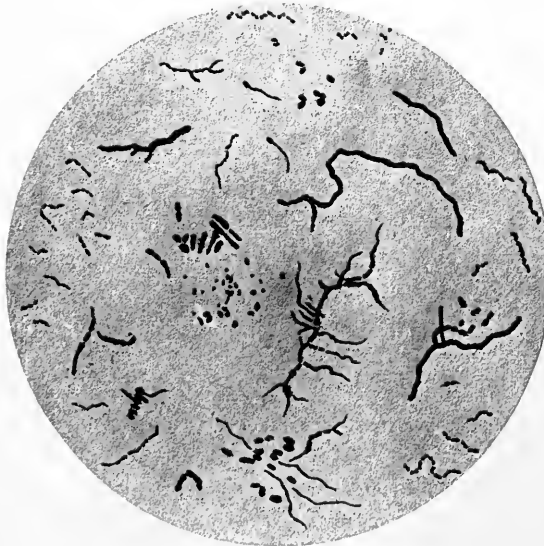
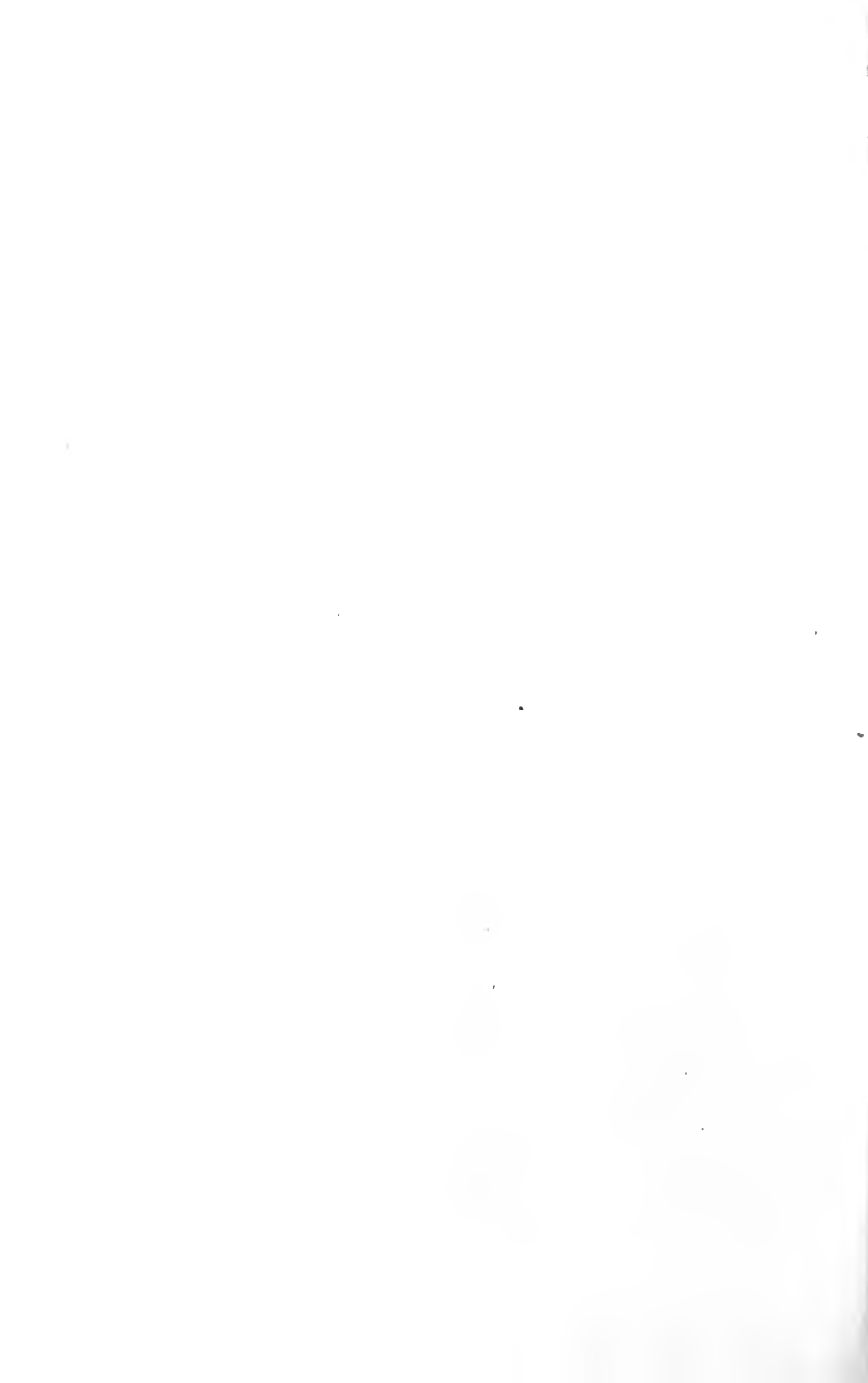


FIG. 2.—Eine Wuchsform des Syphilisbazillus von Niessen.



Eruption gewandert war zu behaaren. Das Allgemeinbefinden war in keiner Weise gestört, das Tier nahm nicht sichtlich ab, hatte einen vorzüglichen Appetit; nie bemerkte man, dass es sich an den erkrankten Hautstellen gekratzt hätte.—

Soweit ist der Versuch bisher gedingen. Ich habe ihn absichtlich nicht durch irgend welche Eingriffe gestört und werde s. Zt. weiter darüber berichten. Erneut sei nur hervorgehoben, dass die verwendete *Reinkultur zur Zeit der Impfung in 25ter Generation fortgezüchtet nur aus Kokkobazillenformen bestand und keinerlei Spirochätenwuchsformen enthielt*, auch nicht die Tendenz zeigte, in dieser Art auszukeimen. Wohl konnten aber aus demselben Stamm auch jene Kokkenkeimschläuche und spirochätenartigen Wuchsformen, wie auch ungemein pleomorphe andere Gebilde kulturell erzeugt werden.—

Die Inkubationszeit von 6 Wochen ist ja *relativ* kurz, da man aber die *subkutane Applikationsweise*, die *Kurzlebigkeit* und *vegetarische Lebensweise der Tiergattung* und die Tatsache zu berücksichtigen haben wird, dass auch beim Menschen die Inkubationstermine der Syphilis innerhalb beträchtlicher Grenzwerte schwanken können, so ergeben sich hieraus wohl keine Einwände. Der *Charakter* und *Verlauf* des *Exanthems* war trotz der Unterschiede zwischen Kaninchen- und Menschenhaut ein dem beim Menschen *durchaus analoger, für Syphilis gradezu typischer*. Die Gründe, welche die Inanspruchnahme dieses Falles für mit der Reinkultur aus menschlichem Syphilisblut erzeugte *Kaninchensyphilis* gestatten, sind also vollauf genügend gravierender Art. Ich würde mich hierzu auch bei weniger in die Augen springenden Merkmalen der Analogie für berechtigt halten, da es durchaus nicht gesagt ist, dass die Kaninchensyphilis, von der wir bisher noch sehr wenig wissen, in der menschlichen konformer Weise verlaufen *muss* und stets gleiche pathognomonische Kriterien aufweist. Hier steht der vergleichenden Pathologie und Mykologie noch ein weites Feld der Forschung offen. Das Syphilisbild ist auch beim Menschen nie schablonenmässig gleich, ja es kann selbst dem Spezialfachmann sehr grosse differenziell-diagnostische Schwierigkeiten machen. Diese nach Möglichkeit beseitigen zu helfen, ist der Zweck meiner

experimentellen Studien, wovon ich hiermit ein weiteres Ergebnis mitteilen wollte.

Ich fasse sonach zusammen:

Der Syphiliserreger ist ein *reiner Myzet* von überaus regem Formenwechsel. *Er ist in Reinkultur aus dem Blut bei Syphilis aller Stadien und Formen zu züchten.* Die Spirochätengestalt ist *nur eine* seiner ausserordentlich zahlreichen und verschiedenen Wuchformen und entsteht durch Keimung resp. Metamerenbildung aus der Kokken- und Kokkobazillengrundform. Diese Faden- resp. Filiform ist nichts anderes als das Analogon der Hyphenbildung der Schimmelpilze, ein *Streptobazillen-* resp. *Streptokokkenwachstumsstadium* mit mehr oder minder ausgesprochener und regelmässiger Krümmungstendenz in Schrauben oder Windenform, wobei die Septenbildungen bis zum völligen Homogenerscheinen der Fadengebilde, die niemals als solche präformiert sind, verschwinden können. *Diese Fadenformen* sind in jeder Kultur und in analoger Weise in jedem Syphilisfall *vorübergehende Entwicklungszustände*, die sich beliebig oft wieder holen können. Zwischen dem mykologischen Pleomorphismus und Generationswechsel des Syphiliserregers und der Pathogenese der erscheinungsreichen Syphilissemiotik und dem protrahierten, zwischen Latenz und Paroxysmus schwankenden, *repetierenden* Syphilisverlauf besteht ein kausaler Zusammenhang.—Mit der Reinkultur des Syphilisbazillus konnte bei *Tieren* nach Art und Verlauf der menschlichen konforme Syphilis erzeugt werden und aus dem Blut syphiliskranker Versuchstiere wurde der Syphiliserreger kulturell reproduziert.

Beim *Kaninchen* können auch auf subkutanem Wege mit der Reinkultur *typische Syphilisformen* der *Haut* erzeugt werden.

Adjournment at 1 P. M.

AFTERNOON SESSION—3 P.M.

PROF. THEODOR VEIEL, of Cannstatt (Württemberg), and
DR. ABNER POST, of Boston, Vice-Presidents, in the Chair.

EIN NEUES GEFÄSSYMPTOM DER SYPHILIS,
SEINE BEZIEHUNGEN ZUR CUTIS MAR-
MORATA, ZUM GROSSMAKULÖSEM SYPHILID
UND ZUR SPIROCHÆTA PALLIDA

VON PROF. S. EH RMANN, WIEN

Die Diskussion auf dem internationalen Dermatologen-
kongress zu Berlin brachte neue Beweise für die grosse ätiol-
ogische Bedeutung, welche die Syphilis für die Erkrankung
der grossen und zum Teil auch der peripheren Gefässe besitzt.
Mittlerweile erfolgte die Entdeckung der Spirochäte pallida
durch Schaudinn unter aktiver Mitarbeit Hoffmanns, es wurde
dann die Spirochäte in der Heller'schen Aortitis, sie wurde in
der Wand der Venen bei der Sklerose von verschiedenen
Autoren beschrieben.

In allen diesen Phasen, sowie auch früher vermisste ich
einen Hinweis auf eine Erkrankung der kleinen Hautarterien,
der ich seit Jahren, angeregt durch einen Fall meiner Beobach-
tung, die Aufmerksamkeit zuwende. Die Erscheinungen
derselben sind so klar, dass sie mir kaum in der Literatur ent-
gangen wären, wenn sie irgendein Autor beschrieben hätte.
Die Ursache, dass diese offenbar nicht gar zu seltene Erschei-
nung, der Aufmerksamkeit der Autoren entgangen ist, liegt
wohl darin, dass sie erst lange Zeit nach Ablauf der manifesten
bekanntesten Syphiliserscheinungen zu sehen ist, dass sie sich
offenbar auf dem Boden einer Cutis marmorata entwickelt
und den Kranken deshalb vollständig entgeht, weil sie sich
erst allmählich aus der Cutis marmorata entwickelt und
ihnen keine Beschwerden verursacht. Von den neun Fällen,

die ich bisher beobachtet hatte, waren nur zwei den gebildetsten Ständen angehörige, die wegen dieser Erscheinung meinen ärztlichen Rat verlangten. Bei allen anderen habe ich sie zufällig bei der Inspektion des Körpers, geleitet durch die zwei früher erwähnten Fälle, entdeckt.

Wenn ich die zwei ersten Fälle bereits fast vor einem Jahrzehnt gesehen habe, gehört die grössere Anzahl erst den letzten Jahren an. Dies kommt wohl daher, dass mein Beobachtungsmaterial sich in den letzten Jahren wesentlich vermehrte und dass ich früher zwar über ein zahlreiches aber nur ambulatorisches Material verfügte. Die oben erwähnten Fälle betrafen zufälligerweise beide *doctores juris*.

Fall 1. Herr Dr. G. Rechtsanwalt, 1897, von dem bekannten Neurologen Doc. Dr. Holländer in Wien behufs Konsultation mir zugesendet. Er kam mit der Diagnose Endarteritis Aortæ und Arteriosklerose der peripheren Arterien. Die Anamnese ergab 20 Jahre früher zweifellose Lues. Seine Herzdämpfung war verbreitet, er hatte einen Lungenkatarrh, die peripheren Arterien rigid, Erscheinungen von Angina pectoris vorhanden. Schmerzen im linken Arm. Auf der Streckfläche beider Oberschenkel ein grobmaschiges unvollständig geschlossenes Netzwerk von $\frac{1}{2}$ –1 cm. breiten lividen Hautstreifen, in deren Achse die livide Färbung eine stärkere war und die Haut auch mehr eleviert. Nach der peripherie waren diese Streifen verschwommen und endigten in stumpfen, verwaschenen Zacken. Durch die Mitte zog sich, beiläufig von der Spina des Darmbeins bis gegen das Knie ein intensiv gefärbter, starker elevierter unregelmässig zickzackförmiger Streifen, von dem das übrige Netzwerk wie ein Geäste ausging.

Patient war in so einen deploralen Zustande, dass er sich für eine energische Merkurielbehandlung nicht eignete. Jodkali brachte zeitweise Erleichterung seines Leidens, die Hautveränderungen gingen aber selbst nach einer leichten Einreibungskur nicht zurück.

Zwei Jahre später erfolgte Exitus letalis, 6 Jahre nachher kam die Witwe des Patienten in meine Behandlung mit einem serpiginoßen Spätsyphilid des Nackens, das durch Merkurieltherapie vollständig heilte.

Fall 2. Noch im selben Jahre konsultierte mich Dr. H.,

der zwei Jahre zuvor an Lues durch Collegen Professor R. Winternitz in Prag behandelt wurde und bei seiner Übersiedlung nach Wien mir zur Behandlung zugewiesen worden war. Er zeigte am rechten Oberschenkel eine über handgrosse Stelle in welcher unregelmässige livide, in der Achse gesättigt gefärbte Hautstreifen zu einen grösseren centralen Streifen zusammenliefen. Auf der anderen Seite waren nur auf einer etwa kinderflachhandgrossen Stelle Andeutungen dieser Hautveränderung. Eine neuerlich verordnete antisyphilitische Kur, mit Auflegen von grauem Pflastermull an die betreffenden Stellen brachte zuerst einen vollständigen Schwund der schwächeren Erscheinungen links und eine Herabsetzung rechts. Erst nachdem die Schmierkur (35 Einreibungen) durch eine Injektionskur ergänzt worden war und ein halbes Jahr fast kontinuierlich grauer Pflastermull getragen worden war, erfolgte vollständige Heilung.

Dies ist bisher der einzige Fall, bei welchem antiluetische Therapie von günstigem Erfolge begleitet war, es war aber auch der einzige, bei welchem die Erkrankung in einer recenten Epoche der Syphilis zur Beobachtung gelangt war, und der sich auch konsequenter Behandlung unterzog, während ein später anzuführender Fall in einem früheren Stadium noch mit makulösem Syphilde in Beobachtung kam, da er aber ein vagierendes Leben führte und sich keiner gründlichen Behandlung unterzog, mir aus den Augen verschwand und ich auch über den weiteren Verlauf nichts berichten kann.

Fall 3. Vorgestellt in der Sitzung der k.k. Gesellschaft der Ärzte vom 19. Oktober 1906.

Der Fall betrifft einen Mann von 52 Jahren, der von einer Infektion nichts anzugeben weiss, zweifellos ein Potator ist, und seit einer Reihe von Jahren über Schmerzen in verschiedenen Körperstellen klagt, welche als Neuritis ex abusu alcoholi gedeutet wurden. Auch die Hauterscheinungen wurden von Seite eines bedeutenden Internisten beobachtet, aber nicht weiter gedeutet.

Der Patient hat einen deutlich akzentuierten Aortenton. Die Herzspitze ist etwas nach aussen und unten gerückt. Er hat Stauungserscheinungen in der Lunge und anderwärts, insgesamt also Erscheinungen, welche auf Endarteritis aortae

hinweisen. Auf der Haut finden wir besonders in der Kreuzbein- und Glutäalgegend, auf den Oberarmen, besonders links, auf dem linken Unterarm, dann auf der hinteren Fläche des linken Oberschenkels typische, zu einzelnstehenden Linien angeordnete bis linsengrosse, schuppene, braune Tubercula cutanea syphilitica. Ausserdem findet man an den Seitenteilen von Brust und Bauch in der Lenden- und Glutäalgegend, auf den Armen in der Deltoideusgegend, ferner auf den unteren Extremitäten, besonders auf den Streckflächen baumförmige, seltener netzförmige Figuren, die eine gewisse Ähnlichkeit in der Zeichnung mit Blitzfiguren haben und in der Farbe, an die Leichenhypostasen erinnern. Sie sind von dunkellivider Farbe, 1-2 cm. breit, an den freien Endenspitzen zulaufend, und sowohl an diesen als auch an den Rändern verschwommen. In der Achse ist die Färbung besonders tief gesättigt, am tiefsten dort, wo mehrere Zweige zusammentreffen. Dass es sich um Hyperämie und nicht um eine Blutung handelt, zeigt ein einfaches Bestreichen der Haut, durch welches man in der Lage ist, die Hyperämie für einen kleinen Moment zum Schwinden zu bringen. Beim Anfühlen ist die Haut kühl, es handelt sich also um eine passive und Stauungshyperämie, weshalb die Färbung bei der Cutis marmorata eine hellere, hier eine leichenhafte ist.

Fall 4. H. S., 23 Jahre alt, Komiker (poliklinischer Patient). Infektion August 1906, mit Sklerose und grossmakulösem Exanthem, behandelt mit 8 Injektionen Hydr. salicyl. Stellt sich wegen Gelenksschmerzen am 15. III. wieder vor, nachdem er mittlerweile anderwärts wegen Rheumatismus mit Natr. salicyl. behandelt worden war. Er zeigt grossmakulöse Recidiv-roseola auf dem Stamm. In der Glutäal-, Kreuzbein-, Schulter-, und Oberschenkelgegend zerissene, nicht so wie bei anderen Fällen zusammenhängende, baumförmige, verzweigte, livide, ebenfalls an cadaveröse Flecken erinnernde Zeichnungen, die beim mechanischen Reiben nicht vollständig vergehen. Auf den Streckflächen der Ellbogen sieht man, dass sie zum Teil plötzlich, in noch vorhandene regelmässige Cutis marmorata übergehen. Patient klagt über Gelenkschmerzen. Bei genauer Untersuchung findet man die Sehnen des Biceps, des Semitendinosus und Semimembranosus beiderseits schmerzhaft

Nach einer Injektion mit Hydrargyrum salicylicum erklärt Patient Berufs wegen verreisen zu müssen und sich dann in stationäre Pflege zu begeben, ist aber leider nicht wieder erschienen, so dass ich über den Erfolg der Behandlung und den weiteren Verlauf der Erscheinungen nichts berichten kann.

Fall 5. Sch. A., 41 Jahre alt, Fiakerkutscher. Patient wird aufgenommen wegen eines Ekzems des Gesichts und der Hände. Ausserdem findet man an den Seitenteilen des Bauchs und der Brust an annähernd symmetrischen Stellen dendritisch verästelte Hautzeichnungen, bestehend aus einen etwa fingerlangen Stamm, von dem dünnere fingerbreite Äste abgehen. Die Farbe dieser Zeichnungen ist blau cyanotisch, jedoch sind weder Farbe noch Zeichnung so deutlich ausgeprägt wie in den anderen Fällen. Cirrhosis hepatis besteht nicht. Ausser diesen Zeichnungen finden sich kleinste erweiterte Hautvenen unter der linken und rechten Mamilla. Solche Hautveränderungen finden sich auch in beiden Inguinalgegenden, den zuerst geschilderten ähnlich in der Steissbein- und Glutäalgegend. In ersteren stellen sie ungleichmässig dicke transversale Streifchen dar, an Stellen der grössten Breite $\frac{1}{2}$ cm. breit. Bei genauem Zusehen sieht man deutlich ein Abgehen kleinster Äste nach oben und unten. In der Glutäalgegend links sind die Streifchen die kleinsten circa 3-2 cm. lang, auch hier deutlich ein wenn auch schmaler Hauptstamm mit kleinen Ästchen zu sehen. Bezüglich der Zeichnungen auf der Vorderseite des Stammes ist zu bemerken, dass sie einen blitzfigurenähnlichen Verlauf zeigen, auf Verstreichen vollständig verschwinden und erst nach längerer Zeit wieder sichtbar werden. Die auf der linken Seite verlaufen annähernd gerade, während der Mittelstamm rechts scharf zackig verläuft. Für Lues kein Anhaltspunkt. Potus zugegeben in starkem Grade.

Fall 6. S. W., 42 Jahre alt, Apothekerlaborant.

Wegen eines Jodoformekzems in Behandlung gekommen, bei der Inspektion des Körpers findet sich ausserdem: Am Rücken in den unteren Portionen finden sich mehrere weissliche, von etwas pigmentierten Säumen umgebene seidenweiche, leicht gerunzelte Narben, die keine besonders scharfe Begrenzung zeigen, möglicherweise von impetiginos herrührend.

Dagegen finden sich auf der Streckseite beider Unterschenkel narbige Veränderungen, welche rostfarbige Peripherie und ein mehr weissliches Zentrum zeigen. Diese Narben sind scharf begrenzt und unter das Hautniveau eingezogen. Die Form ist teils rund, teils serpiginös, nierenförmig. Am linken Unterschenkel befinden sich 4 derartige Narben in einem regelmässigen, nach aussen konvexen Bogen gestellt. Alle vier zeigen einen schmälere oder breitere peripher pigmentierten Saum und ein eingesunkenes, atrophisches, von braunen Pünktchen durchsetztes Centrum. Eine ganz gleich beschaffene Narbe lateral von der Tibie, eine ähnliche, jedoch kleinere, im oberen Drittel des Unterschenkels. Die bogenförmig gestellten Narben sind durchschnittlich hellergross.

Auf der Haut des Stammes beginnend von der vorderen Axillarfalte bis herab in die Unterbauchgegend, rückwärts von der vertebra prominens bis über die Glutäalgegend hinab, ferner auf der Beuge- und lateralen Seite des Oberschenkels, zum geringen Teil auch auf ihrer Streck und inneren Fläche, sowie auf den Patellae finden sich eigentümliche Hautzeichnungen von cyanotischer livider Farbe, die sich schon durch ihr Umschriebensein von einer Cutis marmorata unterscheiden, da stets grössere und kleinere vollständig normale Hautpartien zwischen ihnen zu finden sind. Sie bestehen aus im maximum fingerbreiten Streifen und Streifchen verschiedenster Länge die ganz verschiedene Anordnungen zeigen.

Fall 7 war die Patientin meiner Abteilung, M. L., Hilfsarbeiterin, 45 Jahre alt, aufgenommen 2. Januar 1906; hat einmal im Jahre 1880 normal geboren. Das Kind starb nach drei Jahren angeblich an Lungenentzündung. Fast durch zwanzig Jahre soll sie an starken "Gebärmutterblutungen" gelitten haben. Vor vier Jahren "Gebärmutterentzündung," seit sechs Jahren Kopfschmerzen, Kurzatmigkeit, blaue Flecken auf Stamm und Extremitäten.

Status praesens. Ueber den ganzen Körper verbreitet, besonders aber auf den Streckflächen der Extremitäten, eine unregelmässige marmorierte Zeichnung von lividbraun-roten, stellenweise etwas eleviert scheinenden Hautstreifen. Bei leichtem Reiben der Haut verschwindet die Zeichnung nicht wie bei Cutis marmorata, sondern nur einzelne blässere

Streifen derselben schwinden, um viel rascher wieder zurückzukehren als bei der *Cutis marmorata*. Die Hände zeigen ebenfalls livide Verfärbungen, fühlen sich ungemein kalt an, die livide Färbung wechselt mit kreideweisser und zinnoberroter ab, so zwar, dass, wenn man die lividen Stellen reibt, diese zunächst weiss werden, dann aber sehr langsam, viel langsamer als bei *Livedo coloriea ins Zinnoberrot* gefärbte übergehen, das aber nie so intensiv ist, wie bei *Livedo coloriea*.

Die Endphalangen sind gewöhnlich livid, zeitweise aber die ganzen Finger, am häufigsten die Zeigefinger weiss. Patient hat das Gefühl des Taubseins, die Muskelkraft ist so schwach, dass man den Druck der Haut kaum spürt. Die Fingernägel sind verbogen, in ihrer Substanz grünlich verfärbt, deren Farbe mit dem lividen Grundton ein eigentümliches Farbengemisch liefert. Im kleinen Finger links stechende Schmerzen.

Auf den Unterschenkeln teils zerstreut stehende, teils zu marmorartigen Streifen angeordnete rostbraune Pünktchen und Flecke (offenbar von Hämorrhagien).

Dieselben Erscheinungen, die an den Fingern bestehen, sind an den Zehen in geringerem Grade. Gefühl von Kribbeln und Ameisenlaufen. Bei der Inspektion sieht man die *Arteria brachialis* rechts pulsieren; dieselbe ist geschlängelt und fühlt sich wie ein knorpeliger Strang an, links weniger. Alle anderen tastbaren Arterien knorpelig hart, zum Teil knotig verdickt.

Herzbefund: Relative Dämpfung oben an der dritten Rippe, absolute Dämpfung an der vierten Rippe beginnend, links absolute Dämpfung bis zur Mammillarlinie, rechts bis zum linken Rand des Stammes. Spitzenstoss in der Mammillarlinie nicht verbreitet. Auskultatorisch erste Töne etwas unrein. Akzentuation des zweiten Aortentons.

Der Harnbefund zeigt keine auffallende Veränderung.

12. Februar. Plötzlich aufgetretene Parese der rechten oberen und unteren Extremität, rechtsseitige Facialisparesie. Babinsky und Patellarreflex rechts deutlicher als links.

10. März. Die Endphalange des linken Daumens cyanotisch, unempfindlich. Im weiteren Verlaufe wird diese Phalange lederartig gangränös.

14. Juni. Exitus letalis ziemlich rasch an einer Pneumonie.

Die Obduktionsdiagnose (Prosektor Dr. Zemann) lautete: Pneumonia crouposa lobi inferioris pulmonis utriusque in hepatisatione rubro-grisea. Endarteriitis chronica deformans aortae incipiens et gradus gravis arteriarum periphericarum praecipue arter. Carotidis utriusque, arteriarum fossae Sylvii; partim arteriarum ad convexitatem cerebri, ramorum singularium arteriae mesenteriae superioris et arteriae renalis utriusque. Encephalomalaciae in centro semiovali, hemisphaerae dextrae, in nucleo lenticulari laterali, in putamine et in globo pallido dispersae usque ad magnitudinem lentis, Oedema meningum acutum.

Bronchitis catarrhal. diffusa, Dilatio activa cordis totius. Emphysema pulmonum chronicum, Atrophia hepatis, lienis et renum, Catarrh ventriculi. Catarrh intestini tenuis. Pigmentationes multiplices subserosae intestini totius. (Haemosiderin.)

Fall 8. Johanna H. 57 Jahre, kath. verheiratet, Arbeitersgattin, Aufnahme: 2. IX. 1907.

Im Frühjahr dieses Jahres Hernienoperation im Franz-Josefs-Spital. Vor 14 Tagen wegen Iritis an hiesiger Augenabteilung behandelt. Das Fussgeschwür, wegen dessen Patientin das Spital aufsucht, besteht ang.—seit ca. 18 Jahren. Blaue Nase und Hände will Patientin seit ihrer Jugend nach Erfrierung haben. Von den Zeichnungen am Stamm weiss sie nichts.

Früher stets gesund.

Vor 35 Jahren Abortus, 1 Jahr später Geburt eines ausge tragenen Kindes, das im Alter von 4 Monaten stirbt. Ein Jahr später neuerlich Abortus. Patientin heiratet dann einen anderen Mann, mit dem sie keine Kinder hat. Patientin gibt Potus nicht zu doch zeigt es sich im Verlaufe ihres Spitalsaufenthaltes, dass sie heimlich öfters Weine und stärkere Alkoholika zu sich nimmt.

Status praesens. An der Aussenseite des linken Unterschenkels, der ziemliche Varicositäten zeigt, ein fast kindsfachhandgrosses seichtes unregelmässig begrenztes, schmutzig belegtes variköses Geschwür mit ziemlich starren, callösen Rändern, die weitere Umgebung bräunlich pigmentiert. Unterhalb des Malleolus internus ein zweites kleineres Ulcus varicosum. Auf der Oberfläche der oberen Extremitäten,

sowie an verschiedenen Stellen des Rückens finden sich Hautzeichnungen, die entfernt an "Blitzfiguren" erinnern.

Sie sind von bläulich durchscheinender Farbe und stellen baumförmig verzweigte Streifen dar, indem von einem längeren, durchschnittlich ca. $\frac{1}{2}$ cm. breiten axialen Anteil verschiedene, von maximum Fingerlänge kürzere oder längere, schmalere Seitenästchen in annähernd querer Richtung abgehen. An den Abgangsstellen sind sie manchmal etwas angeschwollen und verzüngen sich peripher zu. Dadurch entsteht daselbst eine verwaschene diffus bläuliche Färbung, die allmählich in die normale Hautfärbung übergeht, wodurch an diesen Punkten die sonst ziemlich scharfen Conturen der Zeichnungen unscharf werden.

Zum Unterschied von der *Cutis marmorata* verschwindet auch bei starkem Druck oder Reibung die Verfärbung nicht ganz, sondern wird nur um eine Nüance blässer, um kurz nach Aufhören der Reibung wieder deutlich hervorzutreten.

Die Brust mit Ausnahme der Seitenteile frei.

Auf Oberschenkeln und Glutäalregion die gleichen Zeichnungen, nur ist hier das axiale Stämmchen durchwegs breiter, und zieht sich von der *Spina ossis ilei* bis zum *Epicondylus externus*. Eine einzelne derartige Zeichnung, aus Stamm und Ästen bestehend, nimmt meist ein unregelmässig begrenztes oft flachhandgrosses Gebiet ein. Nur an einzelnen Stellen sind grössere Partien sozusagen kontinuierlich (d. h., abgesehen von den stets die Seitenäste trennenden normalen Hautgebieten,) von ihnen bedeckt. Hier treten nämlich (besonders in der unteren Rückenpartie und Glutäalregion zwei Centralstämmchen miteinander in Kommunikation, indem Queräste, die von ihren einander zugekehrten Seiten abgehen, zusammensetzen. An anderen Stellen wiederum (obere Rückenanteile), entstehen mehr ring- oder netzförmige Zeichnungen. Dies ist dort der Fall, wo der axiale Stamm nicht annähernd gerade von oben nach unten oder schief verläuft, sondern eine Bogenlinie beschreibt, welche durch die Seitenäste, die ebenfalls bogenförmig sich nach auf- bzw. abwärts krümmen, zum Kreis ergänzt wird (schematisch). Diese Stellen besitzen verhältnismässig die grösste Ähnlichkeit mit *Cutis marmorata*. Bemerk-

enswert ist ferner eine diffuse bläuliche Verfärbung der Arme, Ellbogen und der Nasenspitze, die sich ebenfalls als bedeutend feinere- netzförmige oder maschenartige gleichförmige Zeichnungen differenzieren lässt, aus welchen spärliche grobe Figuren, ähnlich denen am Stamm, hervorstechen. Die Haut der Hände diffus und cyanotisch, fühlt sich kühl an, ebenso die Nasenspitze.

Iritis chronica. *Radialis* deutlich sclerosirt, am Herzen keine stärkeren Veränderungen ausser dumpfen Tönen. Innerer Befund auch sonst negativ. Urinbefund negativ.

Am 19. X. 07. wird Patientin entlassen, im Dezember wegen Bronchitis neuerlich aufgenommen.

Hautzeichnungen unverändert, treten besonders, wenn Patientin nackt in der kühlen Luft steht, allmählich deutlich heraus, während sie bei Inspektion der im Bett liegenden Patientin nur verschwommen markiert sind.

Fall 9. Luise S., 21 J., ledig, Wirtshausdienstmagd.

Aufgenommen den 12. VI. 07.

Anamnese: Patientin früher niemals krank. I. Spitalsbehandlung. Bemerkt seit 14 Tagen offene Stellen auf den Genitalien. Früher nicht antiluetisch behandelt. Potus zugegeben. Kein Parties, kein Abortus.

Status praesens. Am freien Rande der grossen und kleinen Labien rundliche, knopfförmig aufsitzende und grösstenteils schon überhäutete durchschnittlich erbsenquerschnittsgrosse Papeln mit steil abfallenden Rändern. Ausserdem finden sich auf der bräunlich pigmentierten Genital- und Analgegend, sowie den Genitalfalten, von wo sich die Pigmentierung flügel förmig auf das Innere der Oberschenkel fortsetzt, flache, unregelmässige oder serpiginoöse, dabei scharf begrenzte plattenartige Erhebungen. Sie bestehen aus fleischfarbigen, verschieden grossen und geformten, steil geränderten, derb resistenten Elementarefflorescenzen, die derart miteinander confluiert sind, dass durch ein System vielfach sich kreuzender Furchen von einander getrennt sind. Links ad anum findet sich eine fast kindsflachhandgrosse Plaque, die anderen sind kleiner. Die Oberfläche der Plaques ist trocken und nahezu glatt, die Beweglichkeit infolge des breitbasigen Aufsitzens nur gering. Excision einer Plaque, die mehrere durch gyrusar-

tige Furchen voneinander getrennte Einzelefflorescenzen enthält. (Organisierte Papeln.)

Auf beiden unteren Extremitäten fallen folgende Hautveränderungen auf: Von der Mitte des Ober- bis zur Mitte des Unterschenkels finden sich livid-blaue, z. Teil noch unvollständige netzförmige Zeichnungen mit sehr groben Maschen in denen bereits längere grobästige Streifen durch ihre intensivere blaurote Färbung hervorstechen. Beim Reiben verschwinden nur die kleineren, feineren Netze, die gröberen bleiben zurück. Von den feineren bleibt nur eine leicht bräunlich-rote Färbung zurück.—Auf Hals und Nacken grosse, unregelmässige Leucodermaflecke.

21. VI. 2 halbe Spritzen Hy. salic. Die Papeln bedeutend abgeflacht.

28. VI. 4 halbe Spritzen Hy. salic. Involution der Papeln unter Pigmentierung fortschreitend. Graues Pflaster local.

20. VII. 07. 14 halbe Spritzen Hy. salic. Ad anum noch Reste der organisierten Papeln, sonst sind sie überall geschwunden.

2. VIII. 07. Mit XVIII $\frac{1}{2}$ Hy. Inj. geheilt entlassen und zur ambulatorischen Behandlung bestellt. Die Hautzeichnungen unverändert.

Zweite Spitalsaufnahme am 31. VIII. 07. wegen Blenorrhoea vaginæ. Ad anum et genitale hellbräunliche, ziemlich scharf begrenzte Pigmentationen nach den organisierten Papeln Hautzeichnungen unverändert.

1. X. 07. Patientin geheilt entlassen.

Innere Untersuchung ergibt nichts Abnormes. An der *Radialis* keine Zeichen von Sklerosierung.

Fassen wir zusammen, was allen den Kranken gemeinsam ist, so finden wir zunächst die Form der Hauptsymptome. Überall handelt es sich um livide baumförmige Hautfärbungen mit stärker elevierten axialen Anteilen, die immer flacher werdend, verwaschen in die umgebende Haut übergehen. In der überwiegenden Anzahl der Fälle ist ein stärker ausgeprägter Ast zu finden, an den sich die schwächer ausgebildeten Zweigen anschliessen, die spitz aber doch verwaschene endigen. Nur in einem Falle ist ein vollständiges, den ganzen Körper

überziehendes Netz vorhanden gewesen, in jenem nämlich, wo die Gefässveränderungen alle Körperarterien betraf, zur Gehirnhamorrhagie, zur Asphyxie der peripheren Körperteile und zur Gangrän eines Daumens führte.

Eine grosse Übereinstimmung zeigte auch die Lokalisation. Die Hautveränderungen betrafen hauptsächlich die Streckflächen der oberen und unteren Extremitäten, in zwei Fällen mit Einschluss Handrückens, die Glutäalgegend, die Schultergegenden und die seitlichen Rumpfpforten, also die Stellen, wo gemeinlich die *Cutis marmorata* zu sehen ist. Bis auf zwei Fälle hatten alle entweder unzweifelhafte Erscheinungen der Lues oder für Lues sprechende sichere Anamnese. Bei einzelnen war allerdings auch ausgesprochener Alkoholismus vorhanden. Bei allen älteren Individuen waren zugleich andere Erscheinungen der Arteriosklerose.

Und doch hängt die Erscheinung genetisch unzweifelhaft mit der *Cutis marmorata* zusammen.

In dem ausgedehntesten Falle, der zugleich eine allgemeine Arteriosklerose und Raynaud'sche Gangrän eines Fingers zeigte, ahmte der Prozess die Form der *Cutis marmorata universalis* nach, nur mit dem klinischen Unterschiede, dass das livide Hautnetz bedeutend eleviert war und nicht die vasomotorischen Erscheinungen der echten *Cutis marmorata* darbot.

In den Fällen, wo die Lues noch verhältnismässig recent war, zeigte sich ein deutlicher Zusammenhang.

Im Fall 2 war auf den Armen eine typische *Cutis marmorata*, während an den Unterschenkeln bereits das hier geschilderte Gefässphänomen ausgebildet erschien, ein Phänomen, das ich der Kürze halber, da die *Cutis marmorata* auch *Livedo marmorata* heisst, wegen der Baum- oder Astform als *Livedo racemosa syphilitica* bezeichnen möchte.

Noch viel deutlicher war der Zusammenhang mit der *Cutis marmorata* im Falle 4.

Nur in den zwei Fällen, wo erst seit der Infektion mehr als zwei Jahre verflossen waren, wurden diese vermisst. Funktionell zeigten alle älteren gegenüber der *Cutis marmorata* ein verändertes Verhalten. Während bei der *Cutis marmorata* auf Reibung zunächst durch eine Blässe der geriebenen Stelle antwortet um dann langsam sich von der Peripherie wieder

herzustellen, trat die Blässe hier nur solange auf, als der mechanische Druck anhielt, wiewer aufhörte, war auch sofort wieder die alte Zeichnung hergestellt.

Nebennierenpräparate wirkten in derselben Weise auf die Cutis marmorata wie auf diese Hautaffektion. Nach Abstreifen der Hornschicht zeigte sich Kontraktionsblässe. Der direkte Zusammenhang dieser Erscheinung mit einem grossmakulösen Syphilid war in den zwei Fällen möglich, wo Recidive der Syphilid noch bestanden. Dieser Umstand führt mich zu der Annahme, dass recidivierende grossmakulöse Syphilid den Ausgangspunkt dieser Erscheinungen darstellen.

Anatomisch wurde das Phänomen in drei Fällen untersucht, indem eine Partie aus einem größeren Ast exudiert und Serienschnitte auch senkrecht zur Achse des Astes angelegt wurden. Es ergab sich, dass erstens die Arterien des an der Grenze von Cutis und Subcutis liegenden Netzes Wucherungen hatten, die an verschiedenen Punkten ihres Verlaufes bald rings herum, bald einseitig, am Querschnitt halbmondförmig, bald in Form von Septen, stellenweise sogar das obliterierend angeordnet waren, stellenweise ganz fehlten. Die Veränderungen erstreckten sich auch auf die Arteriolen im Niveau der Schweissdrüsenkörper und reichten selbst weiter hinauf bis in die Arteriolen, welche in das subpapillare Gefässnetz und die Schlingen der Papillen um etwas erweitert, das Gewebe selbst kaum merklich ödematös; an den venösen Netzen konnte ich keine auffallenden Veränderungen finden. Der Mechanismus dieser Gefässerscheinungen, wie man sich ihn aus dem anatomischen Befunde vorstellen kann, wäre etwa folgender: Aus dem klinischen Befunde geht hervor, dass es sich um eine passive Hyperämie und Stauung im papillaren und subpapillaren Gefässnetz handelt. Diese kann unter den gegebenen anatomischen Verhältnissen nur dadurch erklärt werden, dass die Muskelenergie des Herzens in der Systole gerade nur hinreicht um durch die verengerten Arterien das Blut in das subpapillare Gefässnetz und in die Papillen zu treiben, dass aber im Moment der Erschlaffung des Herzmuskels in der Diastole die Elastizität der Arterien nicht mehr hinreicht um in ihrer Umgebung die Blutsäule vollständig durch die Capillaren in die Venen fortzubewegen. Es handelt sich nicht

um das gesamte Capillarnetz der betreffenden Hautpartien, sondern nur um die unmittelbar aus den in der Achse der lividen Hautstreifen verlaufenden Arterienäste des an der Grenze der Subcutis befindlichen Arteriennetzes.

Wie verhält sich nun diese Erscheinung zur *Cutis marmorata* einerseits und zum grossmakulösen Syphilid andererseits? Die Beobachtungen, welche wir gemacht haben, bei jenen Fällen, wo auf dem Boden einer *Cutis marmorata* sich ein grossmakulöses Syphilid entwickelt und dann in jenem Falle (siehe Krankengeschichte Nr. 2), bei welchem auf dem Boden einer *Cutis marmorata* ein grossmakulöses confluierendes Syphilid zugleich mit den ersten Anfängen der *Livedo racemosa* zusammenfiel, ergeben Folgendes: Das grossmakulöse Syphilid entsteht in der überwiegenden Mehrzahl der Fälle, wenn nicht absolut in allem, was mir sehr wahrscheinlich ist, und ich seinerzeit schon beschrieben habe, auf dem Boden der *Cutis marmorata* in folgender Weise. In den Knotenpunkten des gleichförmig ausgebreiteten Netzes entstehen tiefer gesättigte syphilitische Makulæ, die zugleich durch ihr bräunliches kupferfarbenes Aussehen sich von dem rosigen Netzwerk, an dessen Knotenpunkten sie sitzen, abheben.

Das einmal hier etablierte Syphilid modifiziert nun den vasomotorischen Tonus der Gefässe seiner Umgebung, ähnlich wie ein urticarielles Erythem, welches nicht selten von einem weissen Hof umgeben ist, während die übrige Zwischenhaut bei leichter Abkühlung bläulich wird. Die in den Gefässen und dem perivascularären Gewebe der Makula befindlichen Spirochäten, die von mir und anderen dargestellt wurden, bewirken durch ihre Anwesenheit oder ihre Toxine, eine Änderung im Tonus jener Blutgefässe deren Erweiterung bezw. Verengung das Bild der *Cutis marmorata* verursacht, in dem Sinne, dass das passiv hyperämische Netz zwischen den Effloreszenzen zerreist, und nun die Effloreszenzen ganz isoliert dastehen. Durch periphere Vergrösserung der Makulæ wird die normale Haut eingeengt auf schmale netzförmige weisse Hautstreifen zwischen dem Fleckensyphilid, so dass jetzt ein umgekehrtes Bild vorhanden ist, vor dem Ausbruch des Exanthems ein gleichmässiges livides Netz mit hellen Inseln, nach dem voll-



FIG. 1.—Verzweigte Livedo racemosa mit tüberösem Syphilid.
Fall 3.

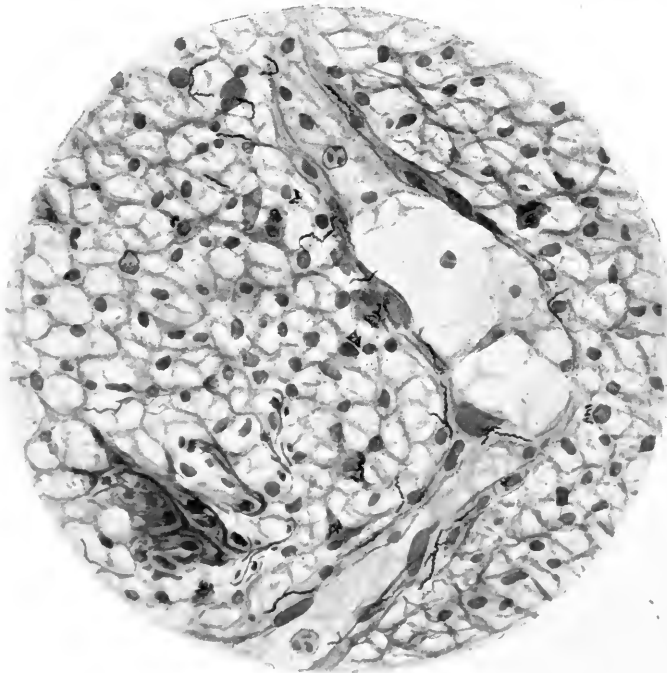


FIG. 2.—Spirochäta pallida im grossmaculösem Syphilid.

ständigen Ausbruch ein weissliches Netz zwischen kupferroten Flecken.

Die Verbreitungswege des Syphilids sind aber von den Blutgefässen gegeben. Es ist bekannt, dass das grossmakulöse Syphilid zu den hartnäckigst recidivierenden Hauterkrankungen gehört. Ich selbst kannte einen unglücklichen Kollegen, der trotz energischer Behandlung immer grossmakulöse Syphilide bekam, bis er an einem Gehirngumma starb. Einen ähnlichen, aber nicht so bösartigen Fall, der nur mit Demenz endigte, habe ich bei einem Diabetiker beobachtet.

Dies alles spricht für eine Persistenz der Spirochätenwirkung selbst oder einer uns unbekanntten Dauer- bzw. Wuchsform, an den Stellen der erkrankten tiefen Gefässnetze der Haut.

NACHTRAG! Nach Abschluss des Manuskriptes beobachtete ich noch einen Fall von Lues, dessen erste Erscheinungen ich selbst vor $1\frac{1}{2}$ Jahren gesehen hatte, mit makulösem Syphilid, das sich zu einer Livedo racemosa umwandelte und noch einen mit gumma des Rachens.

L'HÉRÉDO-SYPHILIS QUATERNAIRE¹ DU TISSU RÉTICULÉ (APPENDICITE. VÉGÉTATIONS ADÉNOÏDES ET SCROFULE)

PAR M. LE PROFESSEUR GAUCHER, PARIS

C'est seulement le tissu réticulé ou adénoïde de *l'arrière-gorge* et celui de *l'appendice cæcal* que j'ai en vue ici, car c'est particulièrement sur ces deux régions que l'hérédo-syphilis quaternaire porte son action.

Ces deux régions n'ont, d'ailleurs, pas seulement une constitution histologique semblable, leurs altérations sont souvent associées. Le Dr. Delacour a montré, dans un travail très important, la coexistence fréquente, soit chez le même

¹ Ce que j'appelle syphilis quaternaire, qu'il s'agisse de syphilis acquise ou de syphilis héréditaire, correspond à la *para-syphilis* de M. FOURNIER.

enfant, soit dans la même famille, des végétations adénoïdes et de l'appendicite.¹

La cause originelle des lésions du carum et de celles de l'appendice cæcal est également la même, comme je vais essayer de le démontrer. Cette cause commune est le plus souvent l'hérédité syphilitique.

L'origine syphilitique ou hérédosyphilitique de l'appendicite, que je soutiens depuis 1904,² a soulevé bien des contestations et n'est pas près d'être admise; il y a trop de médecins intéressés à ce qu'elle ne le soit pas. L'appendicite sévit avec une grande fréquence chez les médecins et dans leurs familles, parce que, de toutes les professions, après les officiers de marine, ce sont les médecins qui comptent le plus de syphilitiques. D'une façon générale, il y a environ un tiers de syphilitiques dans la population masculine; il y en a une moitié parmi les médecins.

C'est pour cette raison que jamais on ne publiera une statistique exacte. Il est d'autant plus licite de nier la syphilis dans les cas d'appendicite, en gardant le repos de sa conscience, que le traitement spécifique ne peut vraisemblablement avoir aucune action sur cette manifestation quaternaire de la syphilis; au moins, je n'ai jamais vu jusqu'ici qu'il pût faire éviter l'opération.

C'est presque émettre une banalité que de dire que *les dénégations, en matière de syphilis, n'ont absolument aucune valeur*. Dans les cas d'appendicite, on avouera maintenant moins que jamais. Qu'on me permette, à ce propos, de raconter une anecdote qui se rapporte à un cas d'appendicite dû à la syphilis acquise.

Un médecin, que j'ai eu comme élève autrefois, m'envoie un jour une de ses clientes à examiner, en s'excusant de ne pouvoir l'accompagner, parce que, m'écrit-il, il doit être opéré d'appendicite dans quelques jours par le chirurgien X . . . Ce chirurgien étant également un de mes anciens élèves, je lui écris :

¹ E. GAUCHER.—Diathèse et Dermatoses diathésiques. (*Gazette des hôpitaux*, 9 nov. 1905.)

² *Bull. de la Soc. de Dermatologie*, 11 mars 1904, et *Presse médicale*, mars 1904.

“Vous devez opérer prochainement notre confrère Y. . . d'appendicite; je vous serais reconnaissant de vouloir bien lui demander s'il a eu la syphilis.”—Le lendemain je reçois cette réponse: “Pour vous être agréable (souligné ironiquement), j'ai interrogé notre confrère Y . . . ; avec l'accent de la plus grande sincérité, il m'a répondu, en souriant, qu'il n'avait jamais eu la vérole.”—Or c'est moi qui ai soigné le Dr. Y . . . de son chancre syphilitique, de sa roséole et de ses plaques muqueuses, quinze ans auparavant!

Ce médecin, qui niait sa syphilis quand il ne s'agissait que de lui-même, l'aurait niée encore bien davantage s'il s'était agi de son enfant et il aurait pu la nier en toute conscience, car son aveu n'aurait eu qu'un intérêt scientifique et n'aurait pu servir au traitement.

Quoi qu'il en soit, dans mon mémoire de 1904, j'ai avancé que, dans les antécédents des malades atteints d'appendicite, j'avais trouvé presque toujours (29 fois sur 32 cas) soit la syphilis acquise, soit surtout la syphilis héréditaire. D'une façon précise, sur ces 29 malades, il y avait 8 anciens syphilitiques et 21 enfants de syphilitiques.

Depuis 1904, je n'ai vu que cinq cas d'appendicite, dont un cas chez une fille de syphilitique, âgée de 18 ans, dont j'avais autrefois soigné le père.

Le second cas est celui d'un homme de 30 ans, que j'ai traité dans son adolescence pour une ostéite de l'omoplate, guérie par l'iodure de potassium. Cet homme a un frère idiot, sa femme a eu une fausse couche, quelques mois avant son attaque d'*appendicite*, dont il a été opéré. Je n'ai jamais pu interroger son père, parce que je ne l'ai jamais vu seul, mais l'hérédité syphilitique ne me paraît pas douteuse.

Ma troisième observation concerne une femme de 26 ans, traitée dans mon service en mai 1906, et dont voici les antécédents:

Il y avait 11 frères et sœurs, dont 8 sont morts en bas âge. Elle eut à l'âge de 10 ans une kératite interstitielle double; elle présente encore des altérations pigmentaires de la rétine, constatées par M. Terrien; elle est très myope. Sa voûte palatine est ogivale.

Cette femme a été opérée d' *appendicite*, il y a 3 ans, par M. Pozzi.

Les deux autres cas étaient imputables à la syphilis acquise.

Après cet exposé général, je dois me borner à l'étude de l'appendicite chez les hérédo-syphilitiques.

Il y a un fait frappant dans l'histoire des appendicites; c'est l'existence fréquente de l'appendicite familiale. Tantôt c'est le père ou la mère et un ou plusieurs enfants, tantôt plusieurs frères et sœurs, tantôt même le père, la mère et les enfants qui sont atteints, parfois à peu de temps les uns des autres, et on met alors ces appendicites presque contemporaines sur le compte de la grippe; mais, dans d'autres cas, successivement, à plusieurs mois ou plusieurs années de distance, et il est alors plus difficile d'invoquer la grippe.

En réalité, toutes ces appendicites sont, en effet, dues à la même cause; mais cette cause n'est pas la grippe, c'est la syphilis. C'est la syphilis du père qu'il faut incriminer non seulement pour lui-même, mais pour la mère, infectée par la conception, et pour les enfants, infectés héréditairement.

La syphilis, qui est si fréquente, explique beaucoup mieux ces appendicites familiales que toute autre cause infectieuse.

J'ai observé deux cas qui, de prime abord, paraissaient contraires à la théorie que je soutiens.

L'un est celui d'une petite fille, opérée d'appendicite, dont le père avait contracté la syphilis après sa naissance; mais, dans ce cas, la syphilis remontait au grand-père maternel, dont je connaissais la maladie de jeunesse. Cet homme avait trois filles: l'aînée atteinte de strabisme convergent et de débilité intellectuelle; la seconde, en apparence saine, qui était la mère de la petite fille atteinte d'appendicite; la troisième qui présentait une dystrophie linguale, connue sous le nom de "langue fissurique" ou de "langue scrotale," affection qu'on doit également rattacher, comme je l'ai montré ailleurs, à la syphilis héréditaire, dont elle est une manifestation quinaire.

J'ajoute que la petite fille, qui fut atteinte d'appendicite, avait une sœur aînée, qui dût être opérée de *végétations adénoïdes*.

Dans le second cas, la mère et les deux enfants furent tous les trois opérés d'appendicite dans l'espace de trois années. Le père paraissait n'avoir jamais eu la syphilis, mais le grand-père maternel, que j'ai soigné, était également un ancien syphilitique.

De ces deux faits je conclus que *l'appendicite peut être le résultat d'une hérédité syphilitique à la seconde génération.*

L'existence d'une manifestation quaternaire, c'est-à-dire atténuée, de la syphilis à la 2^e génération, n'est pas plus invraisemblable que les accidents tertiaires dus à cette même syphilis de 2^e génération, accidents tertiaires qui ne sont plus contestés par personne. *A priori*, l'hérédo-syphilis quaternaire est encore plus admissible à la seconde génération que l'hérédo-syphilis tertiaire; car, par sa définition même, elle est le produit d'une infection plus ancienne, d'une virulence très affaiblie.

La cause de l'appendicite peut donc être non seulement la syphilis du père, mais aussi celle du grand-père.

Je n'ai d'ailleurs pas l'intention de soutenir et je n'ai jamais soutenu que la syphilis héréditaire, pas plus que la syphilis acquise, était la seule cause de l'appendicite. Je n'en sais rien et l'expérience d'un seul homme ne peut suffire pour établir cette affirmation. J'ai seulement constaté et j'essaie de prouver que l'appendicite familiale est une conséquence très fréquente de la syphilis.

L'influence de la syphilis sur le développement de l'appendicite a besoin d'être expliquée, car on m'a fait souvent dire ce que je n'ai jamais dit ni pensé.

Ce que produit la syphilis—héréditaire ou acquise—ce n'est pas à proprement parler l'appendicite, ce n'est pas la suppuration ou la gangrène de l'appendice vermiculaire, ni la péritonite qui peut en résulter. La syphilis n'a qu'une *influence prédisposante ou provocatrice; elle provoque l'hypertrophie et l'inflammation chronique du tissu réticulé de l'appendice*, qui prépare et favorise l'action des causes irritatives, infectieuses ou suppuratives quelconques.

En d'autres termes, on peut avoir à la rigueur une appendicite sans syphilis; mais, en pratique, la lésion du tissu réticulé qui, dans la majorité des cas, constitue la période

prémonitoire, la période pré-suppurative de l'appendicite, est presque toujours—j'allais dire toujours—une manifestation de la syphilis quaternaire.

L'hérédité syphilitique, soit directe, soit de seconde génération, est également la cause de l'hypertrophie du tissu réticulé du carum, qui aboutit aux végétations adénoïdes.

J'ai recherché avec soin, depuis plusieurs années, les antécédents de tous les enfants atteints de végétations adénoïdes, qui ont été soumis à mon observation et, le plus souvent, j'ai trouvé la syphilis héréditaire, prouvée par les aveux des parents ou par la constatation de tares syphilitiques concomitantes ou par l'existence de lésions syphilitiques chez les collatéraux.

Voici quelques observations que je choisis parmi les plus démonstratives:

1.—Petite fille de 7 ans au 6 avril 1904. Père syphilitique, mère contagionnée par son mari.

Enfant née avant terme à 8 mois, pesait à sa naissance 2 k. 250 gr.

N'a marché qu'à 2 ans.

Les dents n'ont commencé à pousser qu'à 18 mois. Elles sont écartées les unes des autres, striées, quelques-unes échan-crées sur leur bord libre.

Voûte palatine ogivale.

Urine au lit et dans ses robes.

Végétations adénoïdes.

2.—16 juillet 1906. Garçon de 4 ans, opéré de *végétations adénoïdes* il y a 1 mois.

Collatéraux: un frère aîné mort de méningite à trois mois. Une petite sœur de 14 mois, très peu développée, ayant l'aspect de *petit vieux*, ne peut se tenir debout, est atteinte de rachitisme des membres inférieurs; porte une hyperostose du pariétal droit; est apathique, d'une intelligence rudimentaire; très améliorée par le traitement spécifique, sort de l'hôpital éveillée comme un enfant de son âge.

3.—Fille de 12 ans, le 4 juillet 1906. *Végétations adénoïdes.*

Voûte palatine très ogivale et prognathisme.

La mère, 45 ans, entre à l'hôpital pour une syphilide ulcéreuse de l'épaule et une syphilide tuberculeuse de l'aile du nez, de la lèvre supérieure et de la joue, rapidement guéries d'ailleurs par le traitement spécifique.

4.—Fille de 10 ans. Le 9 juillet 1907. *Végétations adénoïdes* très volumineuses. Nez écrasé à la base par dystrophie, voûte palatine ogivale. *C'est la 3^e enfant.*

Antécédents héréditaires et collatéraux: née d'un père qui s'est marié en pleine infection syphilitique et a eu, au bout de 18 mois, un enfant né à terme et mort à 5 jours; un 2^e enfant, fille, née 18 mois après le premier, qui n'a marché qu'à 18 mois, a eu une kératite interstitielle à 13 ans; le nez est écrasé à la base, les dents sont atrophiées, érodées, les incisives supérieures échancrées à type d'Hutchinson, qui présente une voûte ogivale, un chapelet costal rachitique, un strabisme convergent.

5.—Garçon de 15 ans, le 11 juin 1906. *Végétations adénoïdes* constatées au toucher. Facies adénoïdien, dort la bouche ouverte. Dents crénelées, voûte palatine ogivale. Il a perdu un frère et une sœur en bas âge.

6.—Fille de 8 ans, le 28 juillet 1906. Née à 8 mois $\frac{1}{2}$. Rachitique, atteinte de débilité intellectuelle. Présente une parésie faciale gauche, reste d'une paralysie faciale qu'elle a eue à l'âge de 16 mois et qui a été traitée par le sirop de Gibert et les injections d'huile bi-iodurée. Quelque temps avant, avait eu une ulcération profonde de la langue, qui a laissé une cicatrice.

Voûte palatine ogivale; altérations dentaires; amygdales volumineuses et *végétations adénoïdes*; meurt de méningite, dans le service, en quelques jours.

7.—Une autre observation, qui m'a été communiquée par le Dr. Louste, montre un enfant opéré de *végétations adénoïdes*, en même temps atteint de scoliose et de rétrécissement mitral congénital, né d'un père syphilitique et d'une mère

vraisemblablement hérédo-syphilitique à cause des dystrophies multiples qu'elle présente.

Voici l'observation :

Famille D.—Le père est mort tabétique; la mère, grande nerveuse, hystérique, présente des stigmates dystrophiques; asymétrie de la voûte palatine, très ogivale, luvette bifide, dents malformées. Il reste actuellement 3 enfants; l'aîné, garçon bien portant de 35 ans, a des crises de migraine épouvantables avec scotomes, troubles visuels unilatéraux.

Deuxième enfant, fille de 24 ans, a un rétrécissement mitral congénital avec asphyxie locale des extrémités. Voûte du palais ogivale, front saillant.

Troisième enfant, fille de 19 ans, a été opérée pour végétations adénoïdes. Voile du palais asymétrique, voûte ogivale, dents malformées. Scoliose du côté gauche apparue à l'âge de 14 ans. Elle est atteinte aussi de rétrécissement mitral congénital. Ictère chronique depuis l'enfance.

8.—Comme dernière observation, je donne l'histoire d'une famille entière, dont l'un des enfants a été atteint de végétations adénoïdes, tandis que le père et la mère et les autres enfants, pour la plupart, ont présenté des accidents syphilitiques.

Le père, âgé de 43 ans, soigné par le Dr. Chabert, qui me l'a amené, est actuellement affecté de leucoplasie linguale. Il a eu la syphilis à l'âge de 20 ans.

Marié après trois ans et demi de maladie, il a eu : un premier enfant, âgé aujourd'hui de 19 ans, qui a échappé à l'infection héréditaire.

Un 2° enfant, mort en nourrice avec du coryza; un 3° enfant, mort à 7 ans de méningite, 10 ans après le mariage (à cette époque, sa femme a eu des plaques muqueuses de la vulve et de la gorge).

Un 4° enfant, âgé de 15 ans, sain; un 5° enfant, *opéré de végétations adénoïdes*, arriéré et sans intelligence.

Dans les cas où on ne trouve pas la syphilis des parents, il y a lieu, comme pour l'appendicite, de suspecter la syphilis des grands-parents.

J'ai déjà cité l'observation de deux petites filles dont

l'une dut être opérée de végétations adénoïdes et l'autre d'appendicite, et dont la syphilis remontait au grand-père maternel. Voici un nouvel exemple probant de *végétations adénoïdes dues à une syphilis de seconde génération*.

Un garçon de 11 ans $\frac{1}{2}$, que j'ai soigné antérieurement d'une ulcération gommeuse de la jambe gauche, est atteint de *végétations adénoïdes* constatées par le Dr. Bloch, qui l'ont même rendu un peu sourd. Il est le deuxième de 5 enfants vivants; sa mère a eu deux fausses couches et sa dernière grossesse a été une grossesse gémellaire. Or, on sait qu'habituellement les jumeaux sont des descendants de syphilitiques.

Le père de cet enfant paraît absolument indemne; mais son grand-père paternel est mort d'ataxie locomotrice et sa famille sait qu'il avait eu la syphilis.

Une observation analogue m'a été communiquée par le Dr. Louste et une autre par M. Van Huysen.

L'observation du Dr. Louste montre des végétations adénoïdes chez une hérédosyphilitique à la 2^e génération et, en même temps, une appendicite hérédosyphilitique de 1^e génération chez la mère.

Famille M.—Le grand-père maternel, mort de paralysie générale, a eu 4 enfants, 2 garçons, 2 filles, tous les quatre avec front olympien, dystrophies dentaires multiples.

L'aînée des filles, qui a 37 ans, présente un front olympien typique, un nez écrasé; les dents présentent presque toutes des malformations décrites comme dystrophies hérédosyphilitiques. Elle a été opérée d'appendicite. Elle a eu une fausse couche de 4 mois, puis un fils âgé de 11 ans, petit-fils du paralytique général, assez bien portant et très intelligent, mais ayant aussi un front saillant, une voûte palatine ogivale, des migraines et ayant été opéré l'an dernier de végétations adénoïdes. Une fille, âgée de 7 ans, bien portante, présente un nez écrasé à la base, aucune autre malformation.

L'observation de M. Van Huysen est encore plus intéressante, car elle montre à la fois, chez les mêmes enfants, hérédosyphilitiques à la seconde génération, l'appendicite, les végétations adénoïdes et le strabisme convergent.²

M. X., mort à 62 ans, *ataxique*, a laissé trois fils.

Premier fils. L'aîné, non marié, a aujourd'hui 45 ans. Assez bien constitué physiquement. Intelligence très médiocre. N'a jamais pu se livrer à un travail suivi. Restait quelques mois et souvent quelques jours seulement dans une place. Est devenu une sorte de courtier en prières. Se charge, moyennant une légère rétribution, d'aller prier dans les différents lieux de pèlerinage français.

Deuxième fils. Mort il y a deux ans de grippe compliquée de congestion pulmonaire, à 41 ans. Homme très intelligent; front olympien, *strabisme convergent*, luxation de la hanche vers 5 ou 6 ans, à la suite de grandes marches, dit-on dans sa famille. Marié, a eu six enfants.

Le premier n'a vécu que deux heures.

Le second, âgé aujourd'hui de 15 ans, très délicat, *végétations adénoïdes*, un peu de *strabisme convergent*; a eu à l'âge de 7 ans, de 9 ans et il y a deux mois de fortes crises d'*appendicite*. Une grande amélioration étant survenue, l'opération a été ajournée.

Le troisième (petite fille): *léger strabisme convergent*, *végétations adénoïdes*, morte à 7 ans d'*appendicite*.

Le quatrième (petite fille) morte à 18 mois de méningite.

Le cinquième (petit garçon) âgé aujourd'hui de 4 ans: front olympien, *strabisme convergent*, teint olivâtre, très délicat.

Le sixième (petite fille) 2 ans, front olympien, nez écrasé à sa base, *strabisme convergent*, figure vieillotte. A eu des convulsions à deux reprises différentes.

Troisième fils. Très bien constitué, très intelligent, mort à 30 ans d'une maladie de foie. Pas marié.

Dans la famille, on affirme que, chez les ascendants du côté du mari et de la femme, il n'y eut aucun cas d'*appendicite*.

Cette hérédité syphilitique de deuxième génération, si on la cherchait plus souvent et s'il était plus facile de la connaître, donnerait certainement l'explication étiologique de bien des cas de végétations adénoïdes et de bien des cas d'*appendicite*, qu'on ne rattache pas à leur véritable cause, faute de renseignements suffisants.

L'origine hérédo-syphilitique des végétations adénoïdes

est d'autant plus importante à connaître, que c'est dans l'existence de ces végétations et dans la suppuration du cavum qui en dépend qu'il faut placer, ainsi que l'a montré M. Gallois, le *substratum anatomique de la scrofule*.¹

En effet, la scrofule dont on ne parlait plus que pour mémoire, qui avait été presque entièrement absorbée par la tuberculose locale, renaît aujourd'hui de ses cendres; elle a été ressuscitée, si je puis dire, par la découverte des végétations adénoïdes.

Meyer, qui est l'auteur de cette découverte, montra que c'était dans ces végétations qu'il fallait chercher la cause des rhino-pharyngites chroniques et l'on ne tarda pas à constater que l'ablation de ces végétations faisait disparaître, en même temps, d'autres affections qui faisaient partie de l'ancien complexe scrofuleux, telles, par exemple, que les otorrhées et les adénites cervicales chroniques.

Ces affections dépendent, en effet, comme l'a montré M. Gallois, de l'infection chronique du rhino-pharynx. C'est dans le cavum et dans les anfractuosités des végétations adénoïdes que germent et que s'accumulent d'abord les microbes de la suppuration. Toutes les anciennes affections scrofuleuses ont une origine suppurative: l'impétigo, l'otite suppurée, la kérato-conjonctivite ont la même origine pyogène que la rhino-pharyngite; ils lui sont souvent associés et, quelquefois même, ils sont secondaires à l'écoulement nasal de cette rhino-pharyngite et provoqués par lui.

En dehors des affections locales, que détermine directement et par propagation la suppuration du cavum, les toxines microbiennes qu'elle engendre sont inévitablement résorbées par la muqueuse du rhino-pharynx, absorbées par les lymphatiques, et se répandent dans la circulation et dans tout l'organisme. Il en résulte une sorte d'*imprégnation toxinique* de l'économie, qui constitue la scrofule. Celle-ci est une *intoxication chronique d'origine microbienne*, dont le point de départ est dans le cavum.

La scrofule dérive donc de l'infection chronique du rhi-

¹ P. GALLOIS.—La scrofule et les infections adénoïdiennes, 2^e édit. avec préface de E. Gaucher.

GAUCHER.—Leçon sur la diathèse et les dermatoses diathésiques. *Gaz. des hôp.*, 9 nov., 1905, p. 2-3-4-5.

no-pharynx végétant. Or, les végétations adénoïdes, comme j'ai essayé de le montrer, ont une origine syphilitique plus ou moins lointaine, de sorte qu'en définitive, *la scrofule est une dépendance de l'héredo-syphilis quaternaire: la condition essentielle et primordiale de la scrofule est une syphilisation héréditaire.*

En fait, la plupart des scrofuleux sont des héredo-syphilitiques. J'insiste notamment sur la *fréquence des adénopathies cervicales*, même suppurées, chez les enfants qui présentent, d'autre part, des lésions de syphilis héréditaire indiscutable. Mes observations sur ce point sont si nombreuses que je crois inutile de les rapporter.¹ Chez presque tous les enfants atteints d'héredo-syphilis, j'ai trouvé des engorgements ganglionnaires. Or, l'adénopathie cervicale est, en quelque sorte, la signature de la scrofule et c'est sans preuve qu'elle est rapportée toujours à la tuberculose. Il y a, certes, un grand nombre d'engorgements et de suppurations ganglionnaires qui relèvent de la tuberculose; mais il y en a aussi quelques-uns qui dépendent de la syphilis héréditaire.

Discussion

DR. JOSEPH GRINDON, of St. Louis, said that great Congresses gave birth to great ideas, and, personally, nothing he had heard during the course of the meeting seemed so startling as the observations made by Prof. Gaucher. The progress of science seemed to be sometimes in a circle: our fathers believed in the syphilitic origin of scrofula. We smiled at their seeming ignorance, but if Prof. Gaucher was right, we were almost back where we started from. Some one long ago said that scrofula was the expression of syphilis in the third generation, and now we were told that the chronic inflammatory condition of lymphoid tissue due to an old syphilis might present a soil well disposed to the development of tuberculosis. In order to establish a causative relation, as claimed, between syphilis on the one hand and appendicitis and adenoid vegetations on the other, it would be necessary not only to show that a large number of cases of the latter conditions exhibited syphilitic antecedents, but that they did so in greater proportion than would be accounted for by the incidence of syphilis in the entire community.

¹ V. A. FOURNIER.—Syph. hérédit. tardive, p. 438.

DR. DE KEYSER, de Bruxelles, a dit qu'il avait écouté avec grand intérêt la communication de M. le Prof. Gaucher, mais il a avoué qu'il lui était difficile de se ranger à son opinion. La syphilis étant extrêmement répandue, surtout dans les grandes villes, il n'était pas surprenant, a-t-il dit, de la trouver dans les ascendants plus ou moins éloignés de malades fort divers. Pour établir une relation de cause à effet, il faudrait mettre en regard le nombre d'appendicites avec antécédents syphilitiques et le nombre de cas dans lesquels il n'y avait pas de syphilis. M. le Prof. Gaucher a trouvé dans presque toutes ses observations d'appendicite des antécédents de syphilis. Cela lui a paru surtout démontrer que les malades qui ont consulté le Dr. Gaucher étaient, avant tout, des personnes dont le passé était plus ou moins entaché de syphilis, et c'était tout naturel, M. le Prof. Gaucher étant syphiligraphe. Il était bien évident que la grande majorité des malades qui ont souffert d'affections du tissu réticule, d'appendicite, de végétations adénoïdes, ont consulté des médecins qui ne pratiquaient pas cette spécialité et les statistiques de ces derniers paraîtraient, pour cette raison, plus probantes.

DR. FREDERIC R. STURGIS, of New York, said that he was a little skeptical in regard to the transmission of these parasymphilitic lesions, and he doubted if syphilis was conveyed to the fourth generation. The speaker said that if a little levity on his part could be pardoned, he would like to refer to the views of Voltaire in regard to the transmission of syphilis by a young wife, almost from her marriage bed. The story was best told in the original French as follows:

"Il y a longtemps que j'exerce la chirurgie, dit Sidrac, et j'avoue que je dois à la vérole la plus grand partie de ma fortune; mais je la déteste pas moins; Madame Sidrac me la communiqua dès la première nuit de ses noces; et, comme c'est une femme excessivement délicate sur ce qui peut entamer son honneur, elle publia dans tous les papiers de Londres qu'elle était à la vérité attaquée du mal immonde; mais qu'elle l'avait apporté du ventre de madame sa mère, et que c'était une ancienne habitude de famille."

Dr. Sturgis said that while the plea of hereditary syphilis might at times be brought forward in order to save an awkward confession, he did not believe that appendicitis or adenoid vegetations could be traced to a previous syphilis, either in the grandparents or the great-grandparents. If that doctrine were true, few if any of us would not show some evidence of syphilis, for there were

perhaps none who could not claim the honor of having had a syphilitic ancestor. He wished to emphasize this fact, because he thought the doctrine promulgated by Prof. Gaucher was a dangerous one, backed as it was by one so well known as the reader of the paper. We all knew of many cases of appendicitis in persons who showed no evidence of hereditary syphilis. Of course, it was claimed that the word of a syphilitic was worth nothing, but in spite of the fact that syphilis was responsible for many remote lesions, the speaker said he frankly confessed his disbelief in the theory that an old syphilis was the usual causative factor of appendicitis, nor was he willing to concede the fact that because A, B, and C had been unfortunate enough to contract syphilis, therefore they were syphilitic for all time.

A CONTRIBUTION TO HEREDO-SYPHILOLOGY

BY DR. ROBERT W. TAYLOR, OF NEW YORK

Such has been the advance due to recent investigations that it is evident our early concepts concerning hereditary syphilis were largely erroneous and inadequate.

The following postulates summarize the accepted canons of belief on this subject:

1. Hereditary syphilis is peculiar to and generally limited to the period of first infancy. In bad cases the child is killed outright quite early.
2. The absence of general manifestations at birth or in the first years of life warrants the assumption that the child has not been infected.
3. Early treatment in default of symptoms is not contra-indicated, but is not urgently essential.
4. In many unexplained cases spontaneous involution of the diathesis may occur quite early.
5. Seeming immunity and absence of lesions in very early and infantile life warrant the belief that the child has escaped infection.
6. The disease may be cured by active treatment, and thereafter nothing is to be feared.
7. In the majority of cases the disease is exanthematic and only attacks the superficies of the body.

8. Visceral, osseous, and cerebrospinal manifestations are indicative of malignant development.

9. Late lesions are very exceptional, and their appearance (without the primordial outbreak) at later periods is rarely seen.

The ideas contained in the foregoing postulates are largely visionary and dangerously misleading. Such doctrines should no longer hold sway. It is time to fully appreciate the gravity of hereditary syphilis in all instances and only to accept established facts concerning it.

The following summary of conclusions is warranted by up-to-date observations, studies, and results:

1. The absence of very early manifestations in heredo-syphilis is no criterion that the infant is not infected. Spontaneous involution of the diathesis is most rare, and can never be asserted. It is not a haphazard accident.

2. In many cases the early exanthematic manifestations may be wanting, but later on specific or dystrophic lesions may show themselves.

3. Treatment of the infected infant should always be promptly begun and persisted in as sedulously as in the adult acquired disease.

4. Age and treatment tend to cure the child.

5. The view that inherited syphilis is at first superficial and later becomes deep and visceral is false, since the whole organism is involved from very early life.

6. Syphilis hereditaria tarda is not exceptional; it may occur at about the eighth and twelfth years, and even earlier, and frequently is encountered at all periods up to the thirtieth year of life, and perhaps later.

7. The opinion that the birth of one or several heredo-syphilitic infants is invariably followed by the procreation of other and later infected children or by constant miscarriages, and that such a mother may become permanently sterile, is not warranted by facts,—since luetic mothers may give issue to several infected children and by means of active prolonged treatment and by the lapse of time may be so relieved or cured as to enable them to give birth to seemingly untainted offspring. Such a result is obtainable in most cases if proper care is exercised.

The developments in heredo-syphilology concerning the *Spirochæta pallida* (or as Schaudinn preferred to call it, *Treponema pallidum*) have been very illuminating. If it is not the true causal agent in syphilitic infection this micro-organism is certainly in some way concerned in its inception and course. The fact of its hereditary transmission is startling and seemingly convincing. It appears that in hereditary syphilis it attains its most extensive generalization; it literally invades the whole organism.

Frohwein¹ found it in several placentæ; in the blood of the umbilical vein, by which it is carried to the liver and there produces its most severe manifestations, and hence throughout the whole economy, to the skin, to all ganglia, to the suprarenal capsules (to which it seems to have a special predilection), to the lungs, spleen, and to all viscera. Many other scientists have confirmed these findings.

Buschke² and Fischer found it on cartilaginous surfaces and near the osseous medulla; Bertarelli³ in the periosteum and medulla of bone, and Frohwein in the cartilage in cases of osteochondritis. The report of Queyrat, Levaditi, and Feuillié⁴ on a case carefully studied in all its aspects is most illuminating and convincing. It was that of a woman, twenty-three years old and five years syphilitic, who became pregnant in March or April, 1905, and on November 20th gave birth to a well formed, macerated foetus, whose foetal movements had ceased eight days previously. At the autopsy, eighteen hours later, myriads of *Spirochæta pallida* were found in the liver and spleen, around the vessels, and in other tissues generally. In this case the child being dead before birth, there was no possibility of microbial invasion through the lungs or the alimentary tube.

It will be noted that this virulent foetal infection of the child occurred in the fifth year of the syphilis of the insufficiently treated mother.

¹ *Münchener medizinische Wochenschrift*, April 3, 1906, No. 14, p. 696.

² *Deutsche medizinische Wochenschrift*, 1905, No. 20, pp. 791 *et seq.* *Ibid.*, 1906, May 10, pp. 752 *et seq.*, and *Archiv für Dermatologie und Syphilis*, lxxxii., H. 1, 1906, pp. 63 to 110, to which is appended a fine bibliography.

³ *Centralblatt für Bacteriologie*, xli., July 7, 1807.

⁴ *Annales de dermatologie et de syphilographie*, December, 1905.

We are as yet only on the threshold of scientific knowledge of this important branch of medicine. On this whole subject we need long-continued, painstaking observation and investigation. More attention should be paid to the chronology and late evolution of the hereditary taint.

The following chronicle extending over a period of thirty-seven years and involving twelve individuals may be accepted as a personal recital based on careful study and observation.

The father became syphilitic in December, 1869, presenting a typical chancre and papular and roseolous syphilides. He was a robust man, twenty-four years old, temperate and reasonably careful of his health. He took little treatment, had mild lesions for several years, and ceased all medication after four years. He lived to be fifty-two years old, indulged actively in athletics, and died of aortitis and nephritis, perhaps of specific origin. How much this, the first genitor, contributed to the pathological synthesis embodied in the fecundation of his progeny is an inscrutable problem.

His wife is now alive and fifty-seven years old. In February, 1866, when eighteen years old, she was married and in the same year had a miscarriage due to trauma. In 1867 she gave birth to a healthy girl, *A*. She came under my observation in November, 1870, and was then in the seventh month of her third pregnancy. In her third month she had been infected with syphilis by her husband. I found her body covered with a papular syphilide, interspersed with pigmented spots of a faded roseola. About the vulva were large masses of hypertrophied condylomata lata. She had cranial alopecia, pharyngeal angina, and laryngitis, was weak, thin, and anæmic. She proved always a careless and dilatory patient, hence the activity of the poison was persistent. During eight years she had many relapses, so that her body became covered with gummatous ulcers and scars.

This woman, the second genitor, was certainly the active source of infection in the gloomy cyclorama herein unfolded.

In January, 1871, she gave birth to a female child (she being syphilitic six months), which seemed well developed and healthy. In four months this infant (*B*) presented roseola, mucous patches, and coryza, was emaciated, cross, and peevish.

At its sixth month this infant presented many specific osseous and articular lesions on the extremities. Under treatment the osteochondritic swellings subsided and the health improved.

This child being the third, died of croup when three years old. Her sister *A* (the second child) was healthy until her fourth year, when she was infected, presumably by *B* or the mother. She had typical secondary manifestations of the skin and mucous membranes following an initial lesion on the lower lip.

This child suffered severely from so-called rheumatism, chiefly nocturnal. Very soon osseous lesions developed on the radius, ulna, and the metacarpal bones, and the phalanges of the right hand. Under active specific treatment the bone lesions disappeared, and the child became seemingly well.

This child was the victim of acquired syphilis, while its sister, her infector, inherited the disease. It is interesting to note the close similarity of the lesions in each child and the extended involvement of the osseous system in both. *A* lived to be five years old and died of dysentery.

The mother became pregnant again in 1872, and gave birth to a dead child. The same condition occurred in 1873, and resulted in a macerated foetus. We may class these children *C* and *D*.

In a year the mother gave birth to a seemingly healthy girl (*E*), which without perceptible syphilitic manifestations lived two and a half years, and died of gastro-enteritis.

During these pregnancies the mother had taken treatment sparingly and intermittently, but had occasional gummatous infiltration.

It is probable that the seeming immunity of *E* was due to the medication of the mother. At any rate she became more tractable at this period and spasmodically persisted in taking medicine (mixed treatment).

The fecundity of the mother was certainly phenomenal. Two years after the birth of *E* a male child (*F*) was born, which for a long period seemed entirely healthy and strong. This child is now a man thirty-two years old, who has been always a hard worker and never presented syphilitic manifestations or dystrophies until his thirtieth year. Then he

developed a gummatous osteomyelitis of the proximal phalanges of the left index finger and gummatous infiltration (histologically verified) into the investing connective tissue. Incision was necessary; local and general antisyphilitic treatment produced a cure in four months, with atrophy of the bones. The *Spirochæta pallida* was not found in the blood or the tissues. (It would scarcely be found at that late day and hardly in large numbers and an active state.) This man was not infected with acquired syphilis at any time. He now has a five-year-old child which seems perfectly healthy. His wife has been well and strong.

The mother after the birth of *F* remained anæmic and pale, and presented for several years sparse crops of small gummatous nodules. She took treatment sporadically, chiefly when she realized that she was pregnant. She then gave birth to four boys in succession, who are now respectively twenty-eight, twenty-five, twenty-three, and eighteen years old. We will designate them as *G*, *H*, *I*, and *J*. These men seem perfectly healthy. They have presented no evidence of inherited taint; certainly no dystrophic manifestations. They have been entirely free from rheumatism. Two are married and have healthy wives and children.

The tenth child, *K* (there being eleven in all, the first having appeared before the luetic era), is to all appearances a healthy and comely girl eighteen years old. She always seemed well developed, without any blemishes, active and alert. At her eighth year she had slight swellings and pain in both ulnæ, which lasted several months, and disappeared, it is said, as a result of simple remedies. When sixteen years old she began to suffer from nocturnal rheumatism, headache, pain in the back, and dyspepsia. She was treated in many ways by many doctors and got no relief. Her mother then suspected that her own old infection was the cause of the daughter's illness and she sought my aid. I found extensive nodular hyperplasia of both tibiæ (subcutaneous surfaces) and an elevated, deeply seated mass over the sacrum. These osteoperiostitic lesions, probably gummatous, were the seat of tenderness by day and pain by night. Systematic inunctions of mercurial ointment were ordered locally, together

with 10- to 20-grain doses of potassium iodide t. i. d. internally. The result was simply magical; the hyperplasiæ melted away; the pains ceased; the dyspepsia was cured, and the general health and morale of the girl became seemingly normal. She was relieved of all her sufferings and cured in less than three months. She had never been infected with acquired syphilis.

As in the case of *F*, this patient was ordered to take goodly doses of mercury and potassium iodide, with periods of remission, for at least six months and thereafter as the occasion might require.

The salient points in the foregoing cases are:

1. The seeming benignancy of syphilis in the father and its malignancy and inveteracy in the mother.

2. The synchronous development of similar specific osseous lesions in two sisters, one a heredo-syphilitic, the other a hitherto healthy child.

3. The evident effect of treatment of the mother upon gestation; death ensuing in two children when it was neglected, and seeming immunity being conferred when it was persisted in.

4. The development at the age of thirty of classical hereditary lesions without antecedent manifestations in one subject (*F*), in whom there was no infection by the acquired disease.

5. The apparent escape of four successive children while the mother presented mild, sparse gummatous lesions which were moderately well treated.

6. The evolution of specific manifestations at the eighth and the sixteenth year in the last and tenth child *K*, who otherwise had been without a blemish during life, and had never had the acquired disease.

In the light of the histories herein unfolded, a serious question presents itself, namely, What will be the fate of the survivors who seem to be in robust health and have never shown a blemish, and what will be the ultimate condition of their progeny? Time and scientific observation alone will answer these queries.

The foregoing considerations show the importance and the

necessity of study of the life history of all heredo-syphilitics for very long periods; they also impressively emphasize the urgent need for active, prolonged medication of the syphilitic mother and father. These sources of disease and race deterioration should be more generally and thoroughly investigated and treated than they have been in the past.

SYPHILIS AND MASSAGE

BY DR. ROBERT W. TAYLOR, OF NEW YORK

Among the curiosities of the literature of syphilis are those cases in which operators of various grades and kinds have been the medium by which this far-reaching infection was communicated, sometimes sporadically and again in epidemic form. Many articles on this subject relate to vaccinal syphilis in which the victims were reported by the hundreds. To-day this mode of infection is practically unknown.

A singular mode of transmission of syphilis is said to occur in Roumania and Russia. It is the custom in these countries to attribute all affections of the eyes (and trachoma is very frequent) to foreign bodies, for the relief of which there is a class of women called leeching oculists who cleanse the eyelids with the tips of their tongues. One of these women having mucous patches in her mouth conveyed syphilis to many persons; in some instances to whole families. Large numbers of cases have been reported in which lues was transmitted in the operation of tattooing. According to one recital, a tattooer who practised his calling for years over a large area of territory was arrested in Philadelphia, where, and in the vicinity, fifteen syphilitic infections were proved to have been caused by his ministrations, he having moistened with his saliva the tattooing instruments. In his mouth were discovered mucous patches, from which he had suffered for a year.

We no longer hear of luetic infection from the introduction of soiled catheters into the Eustachian tubes, a not uncommon accident many years ago.

A few old-time instances of syphilitic infection resulting from skin-grafting were reported in the past. They are hardly to be feared in these aseptic days.

Infection by means of dry and wet cups and by breast drawing is to-day, as of old, probable, but no recent record of such accidents has been published.

Though operations in dentistry have been cited as the starting-point of syphilis in many cases, there is not as yet a thoroughly authenticated case of this mode of infection.

While in many instances the good offices of the barber seem to have been the prelude to luetic infection, there is not on record a perfectly satisfactory history of a case of this accidental infection.

The culpability of both dentists and barbers as operators, should be established on clearly cut, salient, clinical evidence. Hazy, ill-reported cases should be rejected.

I desire to call attention to a mode of syphilitic infection by an operator which is as yet unmentioned. The unadorned history of the case is as follows:

On February 8, 1907, a gentleman, thirty-eight years old, undergoing treatment for chronic posterior urethritis, casually called my attention to a group of lichenoid lesions seated over the prominence of the right gastrocnemius muscle. He is of stout build, shows a tendency to obesity, and complains of mild, fugitive rheumatoid pains of uncertain seat and duration. He is a spare drinker of alcoholics, but much given to the pleasures of the table. He is of hirsute development and has had mild intermittent attacks of scattered lichenoid eruptions seated around hair follicles. He had severe gonorrhoea in 1897, and a relapse in June, 1903. From the latter date to this time he has had gleet, for which he sought treatment when he saw fit. He never had syphilis, as shown by his statements and several exhaustive examinations by me. The skin lesions, nine in number and sparsely scattered over an area of three inches, were conical in structure, of the size of two lines, distinctly elevated, lichenoid in character, and of a dull red hue. They were non-pruritic, whereas in the past itching had been a concomitant of his hair follicle hyperplasia. I attached little significance to the present crop and

concluded that cold and heavy flannels were the exciting causes. A camphorated zinc ointment (Lassar's formula) was ordered for inunctions and as a plaster. No internal medicine was given.

On February 20th the patient complained that his leg lesions were worse. I found the papules much increased in size, rather more elevated and scaly, resembling flat papular syphilides. The central lesions were redder than the rest, decidedly excoriated, resembling typical chancrous erosions. There was brawny induration over the morbid area; no heat nor tenderness. My suspicions were aroused. Further examination showed thickened, goose-quill-like vessels and lymphatics curving behind the inner condyle of the femur, and moderate hyperplasia of the ganglia at the saphenous opening and in the groin. The accessible ganglia of the body were very perceptible. The local treatment was continued and a placebo was ordered. There was no systemic reaction and no *Spirochætæ pallidæ* were found in the blood at any time.

Matters went on uneventfully until March 7th, when a group of eight scattered papules was exhibited to me, seated over the prominence of the left deltoid muscle. These lesions were similar, but less developed than those over the right leg. All the lesions at this time had the characteristic raw ham-like appearance of syphilis. In a previous interview the patient had asked inquiringly whether these exanthems had probably been caused by massage, which he took twice a week; at this time he stoutly expressed the conviction that they were thus produced.

On March 18th a typical erythematous syphilide was seen over the whole body, the lesions being markedly papular in the neighborhood of the leg and shoulder initial lesions. The usual symptoms of active secondary syphilis were present: mild fever, rheumatoid pains in joints and muscles, early incipient alopecia, and pharyngeal hyperemia. The patient was at once placed on active treatment; hypodermic injections of the bicyanide of mercury, and blue ointment was rubbed into the initial lesions. The patient responded promptly and well to treatment, and to-day, September 30th, has no

general eruption. The initial lesions, having faded, left coppery spots; the adenopathies are slowly subsiding.

Here, then, is a case of syphilitic infection seemingly caused by the manipulations of the massage-operator. The patient had not had coitus for months nor had he dallied with any woman. His habits were correct and the only person who had access to his legs and arms was the masseur.

He convinced himself that he had suffered from blood poisoning.

My interest in the case prompted me to run down the operator and ascertain his physical condition. This search took much time and demanded tact, prudence, and patience. After several weeks' inquiry I luckily found a companion of the operator, a male nurse. Through him I learned beyond a doubt that my patient's masseur was affected with recent active syphilis, and that he had had severe sore mouth and a swollen neck. The information was forthcoming that the buccal and pharyngeal lesions, thought to be diphtheritic, caused the patient much discomfort and to copiously secrete saliva; that he constantly slobbered and dried his mouth with his fingers and the backs of his hands. This action he performed very frequently. The mystery of my patient's syphilis was thus fully cleared up.

Here, then, is the case of a healthy man having simple efflorescences over the legs and arms who was infected by a luetic masseur in his vigorous ministrations, his hands becoming soiled with the secretion of mucous patches. The teachings of the case are evident.

The course of syphilitic infection here presented is clear; its salient features are as follows:

1. The development of multiple syphilitic chancres, seventeen in all.
2. The evolution of successive chancres in the intra-primary stage, a not uncommon instance of superinfection. The first lesions appeared presumably about thirty-eight days before the secondary climax and their successors eleven days before that event.¹

¹ R. W. Taylor: "The Development of Multiple and Successive Initial Syphilitic Lesions and the Pathology of Syphilis," *The Journal of Cutaneous*

3. The development of preponderating papular lesions just beyond and near the sites of the hard chancres,¹ whereas elsewhere the eruption was erythematous.

LES OSTÉOPATHIES DE L'HÉRÉDO-SYPHILIS QUATERNAIRE

PAR MM. GAUCHER ET LEVY-BING, PARIS

Dans un travail antérieur² l'un de nous a montré que l'hérédo-syphilis tertiaire pouvait produire des lésions osseuses suppurées absolument semblables cliniquement à des ostéites tuberculeuses et dont le diagnostic ne pouvait se faire que par l'action curative du traitement spécifique dont l'effet est, d'ailleurs, assez rapide. Le but de ce travail est de montrer que l'hérédo-syphilis quaternaire ou *para-hérédo-syphilis* est capable également de produire des lésions osseuses ou articulaires habituellement confondues avec des lésions tuberculeuses de même aspect, ou, au moins, que ces lésions osseuses ou articulaires existent, avec une fréquence incomparable chez les sujets qui présentent des dystrophies incontestables d'hérédo-syphilis.

Les enfants atteints de tumeurs blanches, de coxalgies, de maux de Pott sont très souvent, nous dirons même le plus souvent, des descendants de syphilitiques à la 1^{ère} ou à la 2^{ème} génération. Pour confirmer cette opinion, nous avons examiné systématiquement les enfants atteints de lésions osseuses suppurées, soignés dans les hôpitaux de Berck-sur-mer et nous avons été surpris de la proportion véritablement imposante d'hérédo-syphilitiques que nous avons rencontrée.

Nous avons d'abord parcouru, grâce à l'obligeance du Dr. Ménard, que nous tenons à remercier ici, quelques salles de l'hôpital maritime de Berck, où sont traités des enfants,

Diseases, September, 1906, and "The Evolution of Intra-Primary Lesions of Syphilis," etc., *British Medical Journal*, October 6, 1906.

¹ Hallopeau: "Proliférations locales *in situ* et à distance de l'agent infecteur de la Syphilis," etc., Clermont (Oise), 1905.

² Les ostéites suppurées et les ostéo-arthrites de l'hérédo-syphilis tertiaire par M. le Professeur Gaucher (*Annales des maladies vénériennes*, T. I., No. 1, Août 1907).

garçons et filles, atteints de lésions osseuses tuberculeuses (coxalgie, mal de Pott, tumeur blanche, etc.). Nous avons été frappés dès l'abord par le nombre considérable d'hérédosyphilitiques, dont le facies typique attire et force même l'attention: nez en pied de marmite, front olympien, veines du front et des régions temporales à réseau très développé et très saillant, crâne natiforme, malformations du pavillon de l'oreille, etc., etc. En examinant ces mêmes enfants de plus près, nous avons constaté d'autres dystrophies portant sur le crâne, la dentition, la voûte palatine, les yeux et le système osseux.

Toutes ces dystrophies sont extrêmement fréquentes, tantôt réunies toutes au grand complet sur un même sujet, chez lequel elles abondent et surabondent, au point de ne laisser subsister aucun doute sur l'hérédité spécifique certaine, tantôt plus discrètes, groupées au nombre de deux ou trois seulement, mais suffisantes encore pour permettre d'affirmer l'origine syphilitique de ceux qui les portent. Il n'est pas rare que la tare hérédosyphilitique ne s'accuse que par un seul stigmaté, mais nous n'avons pas considéré comme héréditaires les enfants ne présentant qu'une seule dystrophie, même typique, comme par exemple l'effondrement de la racine du nez, pour nous mettre à l'abri du reproche facile de compter comme spécifiques des sujets qui n'en offrent par les caractères certains. Et pourtant tout le monde sait que l'examen le plus attentif et le plus minutieux peut souvent ne pas révéler le moindre stigmaté chez un sujet dûment hérédosyphilitique. Aussi nous n'avons fait entrer dans notre statistique d'hérédos que les malades porteurs d'au moins trois stigmates, comme par exemple des altérations dentaires, un nez effondré à sa base et des ectasies veineuses fronto-temporales. Nous avons, de parti près, laissé de côté les enfants n'offrant qu'un ou deux stigmates, que nous considérons cependant comme suffisants pour porter habituellement le diagnostic d'hérédosyphilis; mais nous ne voulons pas encourir le reproche de voir partout de la syphilis ou de l'hérédité syphilitique, et il s'en suit que nos chiffres sont bien au dessous de la réalité.

A l'hôpital maritime de Berck, nous avons examiné 153 enfants pris au hasard, soit 71 garçons et 82 filles. Sur

ce nombre nous avons trouvé 30 enfants (dont 10 garçons et 20 filles) présentant tous les caractères de l'hérédo-syphilis. 10 de ces enfants étaient soignés pour des maux de Pott, 15 pour des coxalgies, soit droites soit gauches, 1 pour une coxalgie double, 3 pour des tumeurs blanches, dont une du coude et deux du poignet, 2 pour des adénites cervicales suppurées. L'âge des garçons variait de 28 mois à 7 ans et les filles étaient âgées de 3 à 12 ans.

Nous sommes redevables au Docteur Calot d'avoir pu visiter en détail l'hôpital de l'Oise,¹ où nous avons examiné tous les malades, au nombre de 94, qui se répartissent en petits, âgés de 3 ans à 12 ans $\frac{1}{2}$ et en grands, âgés de 15 à 18 ans. Les petits comprennent 70 enfants, dont 32 filles et 38 garçons; les grands ne sont qu'au nombre de 24, dont 12 garçons et 12 filles. Parmi ces 94 malades, nous avons relevé exactement 38 enfants présentant tous de très nombreux stigmates d'hérédo-syphilis, stigmates parfois si complets et si multiples qu'ils en faisaient pour ainsi dire de véritables types d'hérédité spécifique.

Parmi les 70 petits, nous avons noté 13 filles et 22 garçons hérédo-syphilitiques; parmi les 24 grands, nous n'avons trouvé que 3 hérédo-syphilitiques et tous trois des garçons; aucune des 12 filles ne présentait de dystrophies suffisamment caractéristiques et nombreuses pour être considérée par nous comme une héréditaire. Les lésions, pour lesquelles ces malades étaient en traitement à l'hôpital de l'Oise, peuvent être groupées dans les quelques catégories suivantes: coxalgies, dont deux suppurées, maux de Pott, dont 1 fistuleux, tumeurs blanches, arthrite du cou de pied, ostéite du tibia et gomme suppurée de la fesse droite.

Nous avons parcouru également l'Institut orthopédique du Dr. Calot et l'hôpital Cazin-Perrschaud. Là aussi nous avons été frappés par le grand nombre d'hérédo-syphilitiques qui séjournent dans les salles, mais nous n'avons pas étudié en détail tous les malades. D'ailleurs les chiffres que nous avons relevés dans les deux hôpitaux de Berck que nous venons

¹ Nous remercions vivement ses assistants, les Docteurs Michel et Privat, de leur grande amabilité et de l'empressement qu'ils ont mis à nous faciliter notre travail.

de citer (hôpital maritime et hôpital de l'Oise) nous suffisent pour le moment à la démonstration de ce que nous voulons prouver, c'est-à-dire la grande, l'extrême fréquence de lésions osseuses soi-disant tuberculeuses chez des hérédosyphilitiques quaternaires.

Les éléments qui peuvent servir au diagnostic de l'hérédosyphilis sont les uns empruntés à la famille du malade (ascendants et collatéraux); ces éléments, dans notre enquête, nous ont fait complètement défaut, de même qu'ils manquent dans les cas de beaucoup les plus usuels, surtout à l'hôpital. Les autres sont fournis par le malade même et ce sont les seuls dont nous ayons pu nous servir. Et encore dans ces éléments fournis par le malade, nous n'avons pu tenir compte des antécédents, car pour la plupart ces enfants étaient trop jeunes pour pouvoir répondre d'une façon utile à nos questions et nous donner des renseignements sur les accidents ou les particularités morbides de leur première enfance. L'examen seul du malade nous a permis et nous a suffi—bien mieux et bien plus sûrement que ces renseignements d'anamnèse—à établir le diagnostic d'hérédosyphilis.

En effet, tous les malades que nous avons classés dans notre statistique comme hérédosyphilitiques portaient en même temps, mais très variables comme nombre et comme combinaison, un très grand nombre des dystrophies que nous allons énumérer séparément et que nous avons groupées, pour mettre un peu d'ordre et faciliter leur lecture.

Nous avons rencontré parmi les dystrophies:

1° Du crâne et de la face:

le front olympien;

l'asymétrie crânienne;

le nez en pied de marmite;

la voûte palatine, soit ogivale soit très profonde en plein cintre;

dystrophies extrêmement fréquentes; et plus rarement, par ordre décroissant;

le crâne dolicocephale;

les malformations du pavillon de l'oreille;

le prognathisme inférieur;

l'élargissement transverse du crâne;

le crâne natiforme ;
 l'hydrocéphalie (2 cas) ;
 le bec de lièvre (1 cas) ;
 2° De la dentition ;
 l'asymétrie, la désorientation, l'amorphisme dentaire ;
 le microdontisme dentaire ;
 l'espacement anormal des dents ;
 la dent en tournevis ;
 les dystrophies cuspidiennes multiples et systématisées, dents
 crénelées et striées, toutes lésions des plus fréquentes ;
 l'absence des canines ou des incisives supérieures (2 cas) ;
 l'atrophie cuspidienne de la 1^{ère} grosse molaire (2 cas) ;
 la dent d'Hutchinson typique (2 cas).

3° Du système veineux :

les ectasies veineuses du front, des tempes et de la racine
 du nez, où elles forment des réseaux très développés et saillants.
 Nous avons rencontré ces hypertrophies veineuses chez un
 très grand nombre de nos petits malades.

4° Des articulations et des os :

des exostoses et des hyperostoses ;
 des déformations thoraciques (chapelet costal et thorax en
 carène) ;
 des déformations des membres (genu valgum, nodosités
 épiphysaires) ;
 des déformations rachidiennes, toutes très communes. Quel-
 quefois nous avons noté :
 des hyarthroses chroniques ;
 des arthropathies déformantes (4 cas) ;
 des luxations congénitales de la hanche (3 cas) ;
 des dactylites (2 cas) ;
 des spina ventosa multiples des doigts des deux mains (1 cas) ;
 des pieds bots (1 cas) et une main botte (1 cas).

5° Des yeux :

une kératite interstitielle en activité (1 cas).

Et le strabisme double convergent, sur lequel le Pr. Gaucher
 insiste tout particulièrement en tant que symptôme très
 fréquent de l'hérédité syphilitique.

Or, nous avons rencontré ce strabisme double convergent,
 plus ou moins marqué, *quarante-quatre fois* sur ces 68 hérédos

(21 fois chez les 30 hérédos de l'hôpital maritime et 23 fois chez les 38 hérédos de l'hôpital de l'Oise). Nous n'insisterons pas davantage sur ce stigmaté si fréquent et peu connu, que le Dr. Antonelli vient d'étudier dans un mémoire qui a paru au mois de Février 1907, dans le N° 2 des *Annales des maladies vénériennes*.

Il eut été aussi intéressant de faire l'examen ophtalmoscopique du fond de l'œil de tous les enfants examinés, et nous sommes persuadés qu'en examinant systématiquement tous les yeux, même ceux des enfants en apparence les plus dépourvus de dystrophies, nous aurions encore découvert un certain nombre d'hérédos que nous ne soupçonnions même pas et qui seraient venus augmenter les cas d'hérédité que nous avons signalés; d'abord parce que les stigmatés oculaires existent souvent seuls et en dehors de toute autre dystrophie héréditaire et ensuite parce que ces stigmatés oculaires sont les plus fréquemment observés. D'après le Pr. Fournier, ils donnent un pourcentage de 43 et Edmond Fournier indique même le chiffre de 48%. Or ce sont précisément ces lésions que nous avons pu le moins observer, car nous n'avons fait aucun examen ophtalmoscopique et à part les cas de strabisme que nous avons tous relevés et quelques cicatrices de kératite que nous avons notées, nous ne nous sommes pas occupés des stigmatés oculaires. Notre statistique pêche donc plutôt par insuffisance que par excès!

Ainsi donc sur 247 malades examinés, nous avons trouvé 68 enfants hérédo-syphilitiques. De là tirer la conclusion que les lésions osseuses ou articulaires présentées par ces enfants sont toujours d'origine syphilitique il y a un grand pas à franchir; mais cette coïncidence si fréquente de lésions tuberculeuses chez des enfants présentant par ailleurs tous les stigmatés d'hérédité spécifique est à noter et nous ne pouvons pas ne pas être frappés de ces rapprochements.

Bien entendu, ce qui manque encore à notre travail, c'est la preuve thérapeutique; il aurait fallu pouvoir soumettre ces enfants, surtout ceux qui étaient atteints de lésions osseuses suppurées, au traitement spécifique par les injections mercurielles solubles et par l'iodure de potassium. Nous pouvons cependant citer un cas personnel, où un enfant, ne présentant

aucun stigmate de syphilis héréditaire et porteur d'un mal de Pott fistuleux, a vu ses lésions très heureusement modifiées par le traitement hydrargyrique. Voici l'observation :

Enfant de 3 ans, toujours bien portante, sans aucune tare héréditaire, née d'une mère saine et d'un père, ancien syphilitique soigné pendant trois à quatre ans par des pilules et des injections d'huile grise. Elle est prise subitement, au mois de Janvier 1906, d'un torticolis du côté droit, très douloureux et ne permettant plus, au bout de 15 jours, le moindre mouvement de rotation ou de flexion de la tête. Ce torticolis est considéré d'abord comme d'origine rhumatismale et soigné comme tel par des liniments et des frictions. Les douleurs augmentant au point de rendre le sommeil impossible et la gêne des mouvements devenant de plus en plus considérable, les parents consultent un chirurgien qui porte le diagnostic d'arthrite cervicale, d'origine tuberculeuse. La petite malade est soumise à un traitement antituberculeux (suralimentation, huile de foie de morue, sirop iodo-tannique, etc.), et à l'immobilisation dans une gouttière de Bonnet. Mais l'arthrite, loin de s'améliorer, augmente et vient bientôt s'ouvrir dans la région cervicale par un long trajet fistuleux qui suppure abondamment. On cautérise, on curette, on panse cette fistule pendant un certain temps et à ce moment, devant l'inutilité des différentes médications tour à tour prescrites et essayées, nous ordonnons le traitement mercuriel sous forme de frictions, à raison de 4 grammes d'onguent napolitain par jour, auxquelles nous ajoutons de l'iodure de potassium. On fait d'abord une première série de 15 frictions, puis le mois suivant une seconde série de 15 frictions, et pendant la période de repos, l'enfant prend 1 gramme d'iodure par jour. Très rapidement, sous l'influence de cette médication énergique, la sécrétion se modifie très heureusement, peu à peu le trajet fistuleux s'oblitére et les douleurs disparaissent complètement, ainsi d'ailleurs que la gêne des mouvements; l'état général se relève et l'enfant reprend la mine superbe qu'elle avait auparavant. On continue cependant l'immobilisation.

Beaucoup de ces lésions, quoique d'origine certainement héredo-syphilitique, ne sont pas justifiables du traitement mercuriel, car ce sont justement des lésions d'héredo-

syphilis quaternaire; et c'est là précisément la différence entre les ostéites hérédo-syphilitiques tertiaires et les ostéopathies de l'hérédo-syphilis quaternaire: les premières guérissent rapidement et définitivement par le traitement spécifique, tandis que les secondes sont peu ou même pas modifiées par ce même traitement.

Mais, de toute façon, même quand il n'y a rien, même quand aucun renseignement ne peut être fourni par l'examen somatique du malade ni par l'interrogatoire, dans le cas de doute, si peu que l'anomalie de certains symptômes puisse faire soupçonner la syphilis héréditaire, il peut y avoir encore avantage et il n'y a, dans l'espèce, aucun inconvénient à administrer le traitement spécifique. Parfois on obtiendra par lui des guérisons inespérées ou tout au moins on modifiera heureusement le terrain sur lequel évolue une ostéopathie dont le diagnostic étiologique aura été éclairé par l'existence de dystrophies ou d'autres manifestations—hérédo-syphilitiques.

Comme conclusion, nous pensons que l'hérédo-syphilis directe ou de deuxième génération est un facteur important des lésions osseuses ou articulaires suppurées de l'enfance: tumeurs blanches, coxalgie et mal de Pott, soit que ces lésions dépendent directement de l'hérédo-syphilis quaternaire, soit que l'hérédité syphilitique ne doive être considérée que comme une cause prédisposante favorisant la production de lésions tuberculeuses.

RADIOGRAMS OF SYPHILIS OF THE LONG BONES

BY DR. MARTIN W. WARE, OF NEW YORK

Syphilitic affections of the bones have been the last of the bone diseases to be subjected to X-ray examinations. Whereas it cannot be claimed that a pathognomonic picture can be obtained in every instance, yet a succession of these radiograms shows a uniformity in the type of the findings which corresponds in a striking manner with the gross pathological findings of syphilis of the bones.

We are therefore justified in speaking of the "characteristic findings" which, taken in conjunction with the data of the anamnesis, materially add to the certainty of the diagnosis. Furthermore, a prognosis may be based on the radiograms and the efficacy of treatment estimated by the regressive changes visible in successive radiograms.

As exemplifying a typical finding, mark the circumferential thickening of the periosteum. It need not follow that the thickening should be circumferential and symmetrical. It may be localized, and this is apparent to a large extent in all the radiograms. In fact, this predominance of the thickened periosteum—aside from other bone changes—stands out conspicuously in favor of syphilis of the bones, as distinguished from the chronic infections of the bone. The interpretation of this shadow is that we have to deal with a gummatous deposit. In some instances this gummatous material encroaches upon the cortex of the bone. At some levels it becomes fused with the cortex, materially contributing to the thickening of the bone. At other levels, it remains quite distinct. In other instances again, the intensity of the shadow of the periosteum leads one to infer a deposit of lime salts in the periosteum. On the other hand, translucent areas

in the periphery of the bone speak for the destruction of the gumma and bone absorption. If the subperiosteal gummatous deposit be situated in the interosseous space, its diagnosis would escape detection, were it not for its exposition by a radiogram. Finally, the thickened periosteum may be lifted from the bone beneath.

In the bones we note an increase in their diameter, the distinctions in the shadows perceptible in a normal bone become obliterated, the corticalis appears as a denser shadow of wider extent and irregular in its outlines, often encroaching on the medulla to such an extent as to obliterate it. This is due to gummatous deposit in the bone. This may be irregularly deposited, giving rise to a striated appearance of the bone. If, as in the periostitis, this gummatous material breaks down, we have areas of more or less translucency, surrounded by areas of greater bone activity (osteosclerosis) which appear as dense shadows. The gummatous deposit of the periosteum in the bone is attended at times by a growth in the length of bones wherefore a bowing of these bones can be made out (Fournier).

Of great service is the use of the X-ray in aiding us to differentiate between a tuberculous and a syphilitic dactylitis. The distinctions are by no means always so easily made out.

These are, in substance, the findings in syphilitic affections of the long bones of acquired and late hereditary syphilis.

Note.—A number of lantern slides were shown illustrating the conditions described.

SEMPLICE E RAPIDO METODO DI RICERCA MICROCHIMICA DEL MERCURIO NELL' ORINA

DR. C. LOMBARDO, MODENA

Numerosi sono i metodi finora successivamente proposti da vari autori per la dimostrazione del mercurio nell'orina, ma nessuno, io credo, ha quei caratteri di praticità e rapidità per i quali possa essere impiegato correntemente nei laboratori delle cliniche, senza bisogno di delicati apparecchi e di particolari nozioni di chimica.

Questi requisiti credo abbia più di ogni altro il metodo che io propongo.

Esso è basato:

(a) Sul fatto che il mercurio si trova nell'orina, dei soggetti sottoposti a cura mercuriale, sotto forma di un composto non ancora bene definito, che però reagisce ancora al Cloruro stannoso, riducendosi sotto la sua azione in mercurio metallico, che opportunamente raccolto, anche in minime quantità, è riconoscibile al microscopio.

(b) Che la reazione del Cloruro stannoso sulle soluzioni dei sali mercuriali, e dei composti di questi colle albumine che è apprezzabile macroscopicamente solo per soluzioni al massimo all' $1 \times 50.000.$, a mezzo della aggiunta di tracie di albumina e della centrifugazione, si rende apprezzabile per soluzioni assai più diluite, ed al microscopio fino all'uno, al mezzo, al quarto, per un milione; come appunto si trova nell'orina.

Il metodo si pratica nel modo seguente:

“ In una provetta da centrifuga si versano, filtrando, 5. *cmc.* dell'orina da esaminare (preferibilmente subito dopo la minzione); messavi poi una piccola goccia di albume d'uovo, si agita e vi si aggiunge da due a tre *cmc.* di una soluzione al

12%, filtrata al momento di usarla, di Cloruro stannoso, iperacidificata con 25% di acido cloridrico.

“L'urina diventa dapprima torbida, poi chiara, ed infine opalescente, per il lento coagularsi dell' albumina; allora si centrifuga per qualche minuto, si decanta, e con una pipetta si raccoglie il precipitato. Questo messo su un vetro portaggetti, ricoperto con un vetrino, si esamina al microscopio con un ingrandimento di almeno seicento diametri.”

Se nell'urina vi è del mercurio, esso si trova nel precipitato sotto forma di minutissime goccioline nere di mercurio metallico.

E' bene contemporaneamente fare la reazione di controllo su orina normale.

Operando su maggiori quantità di orina si possono, sul precipitato raccolto, eseguire le reazioni chimiche proprie del mercurio.

Il metodo si eseguisce in pochi minuti, ed è sensibile quanto gli altri metodi più complessi e difficili.

PERIPHERAL SYPHILITIC ARTERITIS

BY DR. HERMANN G. KLOTZ, OF NEW YORK

Clinical and histological research of changes in the blood vessels and particularly in the arteries, directly due to syphilis, for a time was carried on almost exclusively on the arteries of the brain. Although much dissension has existed in regard to the histological detail, the fact that the syphilitic virus may directly produce an inflammatory process in the walls of the arteries, leading either to dilatation and the formation of aneurysma or to obliteration, has now been generally recognized, and the knowledge of syphilitic arteritis of the brain and its consequences is firmly established not only among syphilidologists and neurologists, but also among the general practitioners. The same can be asserted with regard to the syphilitic affections of the aorta and its larger branches; they are everywhere acknowledged as the principal and most frequent cause of aneurysma. Less well known even among

those who make a more special study of syphilis and skin diseases is the syphilitic arteritis of the extremities. It is true that quite a number of such cases have been reported and that several authors like Lang, Neumann, Mauriac, and others have duly recognized the importance of such an arteritis, but generally the text-books have not taken much notice of it. From its representation in literature the affection would certainly appear to be a rare one, but some authors, among them quite recently Merk, feel convinced that syphilitic arteritis of the extremities occurs frequently enough, but is either not recognized at all or reported under other names, especially under that of Raynaud's disease. In a Paris thesis of 1902, entitled "Contribution à l'Étude des Artérites Syphilitiques des Membres," Maurice Durandard has written an excellent monograph on the subject which deserves to be more widely known. Durandard reports one case of his own observation from the clinic of Dieulafoy, gives more or less fully the histories of sixteen cases mostly from the French literature, and refers more briefly or incidentally to other cases from literature. In the different chapters he treats the history, the pathological anatomy, the symptomatology, the clinical forms, diagnosis, prognosis, and treatment of this affection. He has given particular prominence to certain motor disturbances which heretofore had more or less escaped the attention of observers, especially to intermittent limping (claudication intermittente). The arteries most frequently affected were the subclavian, brachial, radial, ulnar, femoral, tibialis antica and postica, peroneal, and dorsalis pedis. Although Durandard cites a case of Leudet in which branches of the superficial temporal arteries were affected, and reports in full the very important case of D'Ornellas, he does not emphasize the arteritis of smaller peripheral branches. Still, as early as 1884 Hutchinson had insisted on the probability that such an arteritis might begin in the small peripheral blood vessels and ascend to the larger branches, in connection with the publication of a case under the title: "A Case of Syphilis in Which the Fingers of One Hand Became Cold and Livid; Suspected Arteritis." Lang, in a more theoretical manner, had considered the possibilities of such a peripheral

arteritis. Hutchinson's case and his claim of the existence of an ascending peripheral arteritis are generally mentioned wherever the subject has been considered at all, but that is about all that can be found in the literature as far as I have been able to ascertain, although the case of D'Ornellas, which was published in the *Annales de Derm. et de Syph.* for 1888 and has been widely quoted, demonstrates in the most perfect manner the correctness of Hutchinson's claim. The history of the case is as follows:

A man, forty-five years of age, married and the father of three healthy children, admitted to have had a chancre of the preputial fold twenty years previously, which had healed within three weeks without any treatment, and was not followed by any secondary or other symptoms. At the time he came under observation, however, he presented some lesions of the tongue of clearly tertiary syphilitic character. He stated that six weeks previously the four fingers of the left hand had constantly felt cold, greatly aggravated in cold weather, so that he had to wear woollen gloves whenever he went outside. Then the soft parts on the ulnar aspect of the diseased finger tip of the left middle finger became gangrenous. Along the course of the collateral arteries of the diseased finger hard cords could be distinctly felt, and the radial pulse was weaker than on the other hand, although perfectly perceptible. Later on gangrenous spots appeared on the radial aspect of the ring finger, accompanied by intense pain, particularly at night. Under specific treatment (iodide of potassium) the fingers as well as the ulcers of the tongue healed within several weeks. The patient then went into the country and against the advice of the physician discontinued all treatment. He remained well for seven or eight weeks; then the very same fingers again became affected, but much more extensively and in a more aggravated manner. The pain and the sensation of cold extended to the lower third of the forearm and within six days the middle finger became mummified as far as the proximal third of the first phalanx. D'Ornellas could now establish the entire absence of the arterial pulse in the left radial artery, in the palmar arch, the ulnar and the lower third of the brachial arteries, as well as the fact that the vessels were obliterated

and indurated, giving the sensation of a hard cord to the touch. In the middle third of the brachial artery the pulsations were weak, but in the axillary they were perfectly normal. Under renewed specific treatment, this time by inunctions of mercury and iodides, the fingers healed, of course with the loss of the gangrenous portions. Some time afterwards the patient was again examined; after continued treatment the arteritis and obliteration of the brachialis had not advanced farther upwards.

There can hardly be any doubt that during the first period of the patient's sickness, the syphilitic arteritis was restricted to peripheral branches of the vessels; the second period shows an affection of the larger branches similar to most of the cases reported by Durandard and those scattered through the literature. It seems by no means improbable that many of these cases did not come under observation until a later stage of the process had been reached; this is probably the reason why the peripheral arteritis is usually overlooked.

Almost unique is the case of Leudet, which was first published in 1874 in the *Clinique Médicale de l'Hôtel-Dieu de Rouen*, and again reported in 1884 to the *Congrès de l'Association Française pour l'Avancement des Sciences* at Blois. The arteritis became manifest in a circumscribed portion of the anterior frontal branch of the left superficial temporalis, and produced cessation of pulsation. The right side became similarly affected a few days later; then the arteritis developed symmetrically for a certain time, but healed later under the influence of general treatment with iodides and mercury. Leudet could follow on his patient all the phases of syphilitic arteritis: Induration, obliteration, diminution, and cessation of the arterial pulse. He could also follow the re-establishment of the circulation, the return of pulsation and definite restoration.

Cases resembling that of Hutchinson and published as examples of peripheral syphilitic arteritis seem to be extremely rare. Although I have been interested in the subject for over twenty years and have closely watched for such cases, I know only of very few. This is the more remarkable as I have personally observed three. The first one was seen in

1889 and was published in the August issue of the *American Journal of the Medical Sciences* under the title, adopted from Hutchinson: "A Case of Syphilis in Which Several Fingers of Both Hands Became Cold and Livid; Suspected Arteritis."

The patient was a man, twenty-five years of age. He had had a chance three years before and had been irregularly treated, but the disease seems to have been quite severe, since rather early he had large ulcers on the back, of which characteristic scars remained. At the time of the first examination ulcers had again broken out on the back, penis, nose, and scalp. About a month previous he had noticed that the tip of the right little finger was white and somewhat shrivelled in the morning. After three days the finger became blue and very painful at the tip. Soon after the ring finger of the same hand and a few days later the middle and the little finger of the left hand underwent similar changes. On examination all the affected fingers presented a decidedly bluish color and a somewhat mottled appearance, and were distinctly colder than the other fingers, which presented a perfectly natural appearance. On the affected fingers the free border of the nails is remarkably white, next to it a zone of fine reddish streaks surrounds the nail, which itself looks dark blue, like the entire distal phalanx. This discoloration extends over the whole finger, diminishing somewhat towards the knuckles. In the centre of the tip, close to the nail, on the left little finger, the epidermis over a well-defined spot is thickened, the surface being brittle and slightly scaling. On both wrists the radial as well as the ulnar pulse can be distinctly felt. The pain in the fingers, which had been quite intense and continuous, disappeared after a week of mixed treatment, and six weeks afterwards the affected fingers had resumed their normal appearance and temperature. In the morning they still felt cold for a while and in lower temperature they became more easily blue and cold than those which were not affected; the syphilitic ulcers were also healed. Thickened portions of the epidermis had previously become detached on some of the affected fingers. The further history of the patient is not known; he was addicted to irregular habits, and from a newspaper notice I believe that he died not very long afterwards.

The second case has been published by Dr. Geo. W. Jacoby in a paper entitled: "A Contribution to the Diagnosis of Raynaud's Disease," but not as a case properly assigned to that disease. (*N. Y. Med. Jour.*, Feb. 1891.)

The patient was a merchant, 37 years of age. He was infected with syphilis seventeen years previously, gave a clear history of several syphilitic manifestations during the three years following the infection and had undergone methodical treatment during this time. The symptoms in this case were almost identical with those of the one just described and with those of Hutchinson's patient. Both hands were affected; on the right one the three last fingers were most involved, being livid and cold at the ends and slightly swollen, extending upwards to the metacarpo-phalangeal articulations, but most marked at the distal ends. The difference in the temperature of the affected and of the healthy fingers was estimated to be at least 10° F. Pulsation was well marked in the radial and ulnar arteries of both hands. The pains were bearable during the day but so intense during the night that the patient was unable to sleep. After a long-continued treatment, partly in Hot Springs, Ark., the hands assumed a perfectly normal appearance, but still became cold very easily.

This patient was seen by me on several occasions during the active period of the affection and from time to time since, as late as July, 1907. The tips of the affected fingers are still slightly pale, somewhat attenuated: the epidermis over the tips is somewhat thickened and hard; in cold weather the finger tips become quite painful, but there has not been any decided change or relapse since 1890.

The third case has been briefly reported by me in the Transactions of the New York Dermatological Society for 1895 (*Journal of Cutaneous and Genito-Urinary Diseases*, xiii, p. 170). The patient, an agent, fifty years of age and personally known to me for years, had contracted syphilis twenty-eight years previously and at that time had been amply treated for several years, although mostly internally, and had not had any symptoms of the disease for twenty-five years. After occasional free indulgence in beer, much worry, and exacting work he had noticed for some time that his right arm was not as

vigorous as formerly and that certain movements became rather awkward. About a week before he had noticed that the right index finger became cold and blue, with impairment of its sensibility and quite severe pains, principally at night; the right thumb was similarly affected, but not nearly so severely. The index finger had a bluish, somewhat mottled color, felt decidedly cold to the touch, the nail appeared pale and livid, with longitudinal hemorrhagic lines near the lunula. The radial pulse was entirely normal. All these symptoms disappeared within a few weeks under the use of increasing doses of iodide of potassium. I have seen the patient on and off since. He has not had any similar symptoms again, but in very cold weather the affected fingers get cold and painful.

It must be noticed that in these three cases and in that of Hutchinson, gangrene was not in evidence except for the superficial necrosis and subsequent detachment of circumscribed patches of thickened epidermis; specific treatment had been commenced while the affection was in an early stage and while no damage had yet been done which was beyond repair. That gangrene would inevitably have followed, if the conditions had been allowed to go on, seems hardly doubtful in the face of the experience with other cases of syphilitic arteritis of the extremities. Most of these cases apparently have not come under observation until gangrene had actually taken place, but in some of them we have a history of several separate attacks following one another on different members, exhibiting the same early symptoms as in the cases described before.

Some such cases have been published as cases of Raynaud's disease, and syphilis is usually named among those affections which are considered as producing Raynaud's disease. M. Sée in Bésnier's *Pratique Dermatologique* takes exception to this view and is inclined to side with those who insist on the purely syphilitic character of the obliterating arteritis. Morgan designates his case as one of Raynaud's disease in an individual thoroughly tainted by syphilitic poison; others recognize a syphilitic arteritis with a superadded element of vasomotor spasm. Such interpretations can be explained only by the arbitrary and indiscriminate abuse of the term Raynaud's

disease, which has been unfavorably commented upon by several writers, among them particularly by G. W. Jacoby. But if you follow Raynaud more closely in his own writings, you will find that in reality he professes to describe a new disease which is characterized by paroxysmal attacks, separated by periods of apparently complete health. During these attacks, without any apparent anatomical changes of the blood vessels themselves, certain local changes (local syncope, local asphyxia, and eventually dry gangrene) are produced on symmetrical peripheral portions of the extremities (fingers and toes). These attacks own for their cause some error as to the innervation of the capillary vessels (vasomotor disturbance). Monro, in his monograph on Raynaud's disease, insists on the essential character of the paroxysm; bilateral symmetry he considers as very important but not as essential; if this feature be lacking, the other evidence must be very strong. Instead of restricting the use of the term Raynaud's disease to cases which really present such a clinical picture, the name has been applied without any further investigation to almost all kinds of instances of symmetrical and non-symmetrical peripheral dry gangrene, or to cases in which some of the local symptoms were present without any of the other important clinical features. Raynaud's explanation of this new disease by a vasomotor disturbance, as far as I understand, has by no means been universally accepted, although any other definite explanation, applying to all cases, has not been established. Therefore the question, whether syphilis itself could produce such paroxysmal attacks, cannot be positively answered at the present time.

It certainly cannot be denied that the local symptoms of peripheral syphilitic arteritis are indeed similar to or almost identical with those of Raynaud's disease. This appears quite natural, because in both instances we have to do with a more or less complete interruption of the flow of arterial blood into certain portions of the extremities (local syncope), and the subsequent stagnation of insufficiently oxidized blood in the widened capillaries (local asphyxia). If these conditions persist for some time, nutrition will cease and mortification of tissue must necessarily follow; gangrene, however, is not

an inevitable result in every instance either of Raynaud's disease or of peripheral syphilitic arteritis. The cause of the obstruction of the arterial flow (the spasm in Raynaud's disease) may cease before gangrene is accomplished, or in arteritis the occlusion of the lumen of the vessel may take place very gradually, or the conditions for the establishment of collateral circulation may be particularly favorable. However, in arteritis occasionally, the local process may run through all the stages to gangrene in a very abrupt manner, probably in consequence of thrombosis in the vessel which is undergoing obliteration. In Raynaud's disease the cause evidently is not a permanent or continuous one, but accompanies the paroxysm and ceases with it; the local changes may entirely disappear and perfect restitution may take place if no other attacks follow. But if the attacks repeat themselves even in more or less protracted intervals, the local syncope and local asphyxia will become permanent and in due time the final stage of gangrene will be established. In both instances symmetrical portions of the body, usually the extreme ends of the extremities or the ears or the tip of the nose, may become the seat of the local changes, but as a rule we must expect the simultaneous affection of symmetrical portions in Raynaud's disease where we have to assume that some general cause produces the paroxysmal occlusion. In peripheral arteritis symmetrical parts are not affected.

In nearly all cases, on close scrutiny, it will be found that the trouble began in one, or perhaps two, fingers or toes of one hand or of one foot, that only after a few days other fingers or toes of the same extremity become similarly affected. The corresponding hand or foot may show the first signs only after the lapse of some days or weeks, or there may be intervals of months and even years between the attacks of the different members. In this way the gradual spreading of the process may simulate in a way the repeated attacks of Raynaud's disease—however, without the appearance of a true paroxysm. Pain and the sensation of cold usually do not furnish any means for differentiation of the two affections.

In cases where the larger branches of the arteries of the members have become the seat of the inflammation, the con-

dition of the pulse, particularly its cessation on localities where it usually can be felt, and the demonstration of the obliterated vessel itself in the shape of an indurated cord may indeed greatly facilitate the diagnosis and allow at once the exclusion of Raynaud's disease, since the absence of occlusion of the blood vessels by organic alterations of their walls has been declared an important criterion by Raynaud himself. But if we have to do with peripheral arteries of small calibre, such as digital arteries, it seems doubtful whether we can always expect to find them accessible to the touch, to feel them as thickened, hard cords, or to demonstrate with absolute certainty the presence, diminution, or absence of pulsation. Therefore this symptom cannot be considered absolutely as a distinguishing feature between Raynaud's disease and peripheral syphilitic arteritis. However, in addition to the characteristic features of the local symptoms in the differentiation between the two affections, the clinical character and the development have to be considered: in Raynaud's disease, the paroxysmal attacks separated by free intervals; in arteritis, the continued insidious and chronic advance of the process, and in most instances the beneficial influence of specific treatment. In regard to the effect of mercury and iodides, Durandard has rightfully emphasized that in some cases of absolutely undoubted syphilitic origin of the arteritis, principally in the fulminant cases which rapidly lead to gangrene, specific treatment has been without the slightest beneficial effect. That in case of accomplished mortification of tissue treatment cannot have any influence on the portions already destroyed, but at best can only bring the process to a stop, is almost unnecessary to mention. Nevertheless, the influence which energetic specific treatment has been demonstrated to exert in the peripheral cases, as well as in affections of the larger branches of the arteries of the extremities, renders the whole question one of great practical importance, the more so as any reliable treatment of Raynaud's disease can hardly be claimed to exist. Therefore, if the diagnosis of this affection is sustained in cases of syphilitic arteritis, valuable time is liable to be lost in the application of the galvanic current and other methods of treatment which have been recommended

in large numbers. Durandard states that in comparison with other forms of arteritis, the prognosis of syphilitic arteritis is comparatively benign. Indeed there is hope in the beginning to successfully treat and to cure it. But to do this it is necessary to think of the possibility of an arteritis of specific origin. However, how can we expect the general practitioner or even the specialist to think of such an affection until it becomes more generally acknowledged, emphasized, and taught in clinics and in text-books, that a syphilitic affection of the peripheral and superficial arteries does occur as a distinct affection, that it can produce certain local symptoms which, resembling to a certain extent the local symptoms of Raynaud's disease, sooner or later may lead to peripheral gangrene. Then it will become the duty of the physician, whenever he finds cold, livid, and painful fingers or toes, not to rush to the diagnosis of Raynaud's disease, which at best is a somewhat mysterious entity, but to consider the possibility of syphilitic arteritis. The establishment of a clear history of previous infection with syphilis, or the demonstration of the actual presence of other undoubted symptoms of syphilis as in D'Ornellas's and in my first case, will strongly support the diagnosis of syphilitic arteritis. The absence of either, however, must not exclude such a diagnosis. It is only too well known how little reliance can be placed on the assurance of the patients; in a case published by Nash (*Journal of Cutaneous and Genito-Urinary Diseases*, xiii, 1895, p. 297), the patient, after repeated denials, finally admitted that he had had a chancre four years before and had been treated for three months. The absence of concomitant syphilitic symptoms is of even less significance and must be rather expected in cases where the infection has preceded the arteritis by many years, as twenty in D'Ornellas's, seventeen in Jacoby's, and twenty-eight in my third case. In D'Ornellas's case, the presence of a typical tertiary lesion of the tongue largely suggested the administration of specific treatment. In doubtful cases, therefore, the physician will be justified in the immediate commencement of antisiphilitic treatment. In the face of the gravity of the affection it seems advisable to apply energetic measures at once; Durandard states that Dieulafoy insists on mercurial

injections of the biniodide, and that it is useless to give iodides at the same time.

How important it is that the possibilities of the existence of peripheral syphilitic arteritis should be more widely known, may be judged from the fact that Hutchinson's case had been under his observation twenty years before he published it. Although in his experience almost unique, he had felt unable to offer any satisfactory conjecture as regards diagnosis, until on reading over the notes it occurred to him that the cause of the symptoms must have been inflammatory occlusion of the arteries of the hand. D'Ornellas, who evidently had not been cognizant of Hutchinson's case, says that he never heard anybody speak of such localized arteritis in the extremities, and that Verneuil, Fournier, Duplay, and other eminent physicians assured him that they had never seen a similar case, concurring at the same time in his diagnosis.

When I met with my first case I, fortunately, was acquainted with Hutchinson's publication, and Jacoby again recognized in his case the exact counterpart of my first one, which had been published only a short time before. I myself happened to come across Hutchinson's article while in search of information in regard to a similar form of circumscribed gangrene, for which I had not been able to find any other explanation but the sudden suppression of the blood supply through occlusion of small branches of arteries, probably due to an obliterating inflammation of their walls. In several instances, during close observation of the patients, I had been surprised by the sudden appearance, within areas of perfectly healthy skin, of round or oval patches of superficial gangrene of the skin. They were restricted to the malleolar region and depending parts of the extremity in general. In time the eschar became detached, leaving an ulcer which in shape and particularly in the configuration of the exposed surface bore great resemblance to the round ulcer of the stomach. I was absolutely sure that the skin on these spots had been healthy and free of any discoloration, inflammatory or gummatous infiltration which we are used to see precede and give rise to syphilitic ulcers. Here the surrounding skin and the immediate borders were smooth, without any

infiltration or even redness; there was no undermining or tendency to progress in the periphery. The ulcers themselves were extremely painful, sluggish, without any tendency either to heal or to get worse; they were apparently not affected by specific general treatment. At times a new epidermis would form over the surface, only to soon break down again. In later years I have not again had the opportunity of watching so closely the unheralded appearance of the gangrenous patches and their detachment before the appearance of the ulcers, but I have not infrequently seen ulcers of the character described before on portions of the lower extremities which evidently are supplied by terminal branches of the arteries. I submitted these observations exactly twenty years ago to the Section on Dermatology and Syphilography of the Ninth International Medical Congress, held at Washington, D. C., in September of 1887. Perhaps they are of more interest now in the light of recent discoveries and observations.

Discussion

DR. HOWARD FOX, of New York, said he was much interested in the subject of Dr. Klotz's paper on account of two cases of syphilitic endarteritis that he had reported. The speaker said he felt perfectly sure that symptoms of Raynaud's disease, including local asphyxia and gangrene, could be caused by syphilis. The subject of gangrene due to peripheral syphilitic endarteritis had recently been discussed by Maurice Druelle, a pupil of Prof. Gaucher, who had been able to collect only fourteen cases in the entire literature. Many cases had probably been unrecognized or had been wrongly called Raynaud's disease. It was important that cases of peripheral syphilitic endarteritis should be recognized as such so that proper treatment could be instituted.

DR. A. RAVOGLI, of Cincinnati, emphasized the fact that there should be a clear distinction between Raynaud's disease and peripheral syphilitic endarteritis, and he recalled two cases of so-called Raynaud's disease in both of which he could prove the existence of syphilis. The two conditions were entirely different, and personally he had had no difficulty in distinguishing between them. In Raynaud's disease we had to deal with an affection of the vasomotor nerves: there were redness and œdema, with

bluish discoloration followed by gangrene, but this had nothing in common with the gangrene that resulted from syphilitic endarteritis.

The speaker said he had recently seen five or six cases of peripheral syphilitic endarteritis, two involving the penis and the others the extremities. The gangrene in the cases was preceded by agonizing pains in the affected parts, together with severe inflammatory symptoms. In Raynaud's disease there are pains of neuralgic type, and no inflammatory symptoms; potassium iodide and mercury are of no avail, and Dr. Ravogli said he did not believe it was even a para-syphilitic condition, whereas in gangrene due to syphilitic endarteritis brilliant results from anti-syphilitic treatment were obtained. The two diseases were, in his opinion, entirely distinct.

CLINICAL REPORTS—(a) A CASE OF SYPHILITIC REINFECTION—(b) CASES OF SYPHILIS INSONTIUM

BY DR. G. K. SWINBURNE, OF NEW YORK

(a)—*A Case of Syphilitic Reinfection*

I feel impelled to report this case because of the comparative rarity of cases of this kind and because we are rather skeptical of these cases when reported.

A. M., about 28, was sent to me by Dr. W. L. Culbert in July, 1906, with an ulcer on the dorsum of the penis. It was a small circular ulcer with a ragged base, and there was nothing especially characteristic about it, but such uncharacteristic ulcers are frequently followed by syphilis. In common with many physicians, no matter how characteristic a lesion may be, I wait for other symptoms and always treat any kind of a lesion of the penis with suspicion, until it is proven *whether it is specific or not by its subsequent history*.

In the present case, which I am reporting, the patient had had syphilis seven years before, and had all the characteristic symptoms, chancre, general adenopathy, eruption, mucous patches; he was under treatment off and on for four

years under the care of Dr. Culbert. There can be no reason for imagining error here.

The ulcer I pronounced "an infected ulcer." There were reasons why the patient desired to be relieved of anxiety, not because he had a special fear about going through the disease again, but because at the time the lesion was a small pimply-like affair he had endangered a friend, a married woman, exposing her at a moment when the idea of syphilitic reinfection was unsuspected by him, so that, as it steadily increased in size, his fears were aroused. I told him I was not much of a believer in the possibility of syphilitic reinfection, that there was nothing especially characteristic at present, though a sore on the penis was always an object of suspicion. The period of incubation of this lesion could not accurately be determined, and it had none of the characteristics of a gumma. The lesion was then ten days to two weeks old.

I saw him again three or four weeks later when he had heard from his friend that she had a soreness of the vulva. She would not come to me, but was reassured by another physician whom she consulted that there was nothing the matter with her.

A short time after this, one or two weeks, the patient appeared again, showing a general glandular enlargement, especially marked in both groins. He said it had come on suddenly and that when he had his syphilis seven years before, the enlargement had come on suddenly in the same way. I told him that I did not believe there was any reason to suppose he had syphilis; he might expect such enlargement of the glands of the groin even after healing of such an ulcer as he had had. These glands in the groin, however, did have the characteristic enlargement and painlessness which we see in connection with syphilis. The epitrochlear glands could be felt at the time of his first visit and the gland in front of the inferior maxillary articulation could also be distinctly felt on one side. He said that that had always been there since his first attack of syphilis, that he had noticed it at that time and had often noted its presence since, and that it was unchanged.

A short time after this, seven weeks from the time he first

noticed his lesion, he came again with a macular eruption on the chest, loins, and front of arms. The situation was characteristic, but I did not think it had the look of a syphilitic macular, and pronounced it a pityriasis rosea. Dr. J. C. Johnston, whom I asked to look at the eruption, at once pronounced it pityriasis rosea. Nevertheless, as the eruption did not disappear, Dr. Culbert asked Dr. Elliot to see the case, and on his saying it resembled a syphilitic macular eruption, Dr. Culbert placed the patient on 1-60 gr. bi-chloride tablets and there was complete disappearance of the eruption in a few days. The mercury was not, I believe, continued for any length of time, and Dr. Culbert in November sent the patient to me again with characteristic mucous patches on the side of the tongue and on the fauces. In view of this I receded from my diagnosis of pityriasis rosea and accepted the diagnosis of syphilis, pronouncing it a case of syphilitic reinfection. The patient since that time has been under constant treatment, and during that time no other manifestations have appeared.

(b)—*Cases of Syphilis Insontium*

R. A. J., son of a physician, about 20 years old, a college student, a large, athletic, manly fellow, consulted me in the latter part of October, 1905. He had had a supposed attack of quinsy the previous August. All his life he had been subject to attacks of tonsillitis and had enlarged tonsils. The tonsil was removed early in September, but was not at the time subjected to pathological examination. Before the throat had entirely healed, he was training for the football team and noticed that he was receiving no benefit from it, but was affected with malaise, disinclination to work, and was obliged to give it up. He saw a throat man in the college town, who told him he had syphilis. He asked how that was possible, as there had been no exposure for two years. (I had treated him for a gonorrhoea acquired two years before in his freshman year, and he had since that time avoided the risk of contagion.) He was sent to a prominent dermatologist who gave the opinion that there were not enough

data to make a positive diagnosis. He came home and was then sent to me.

When he presented himself, he was distinctly anæmic, the submaxillary and cervical glands were markedly enlarged, so much so as to be very noticeable, but they were painless. There was no other glandular enlargement. The left tonsil, which had been removed, had healed. The right tonsil was enlarged. There were no lesions of any kind in the throat or mouth. I maintained that a diagnosis of syphilis could not be made and advised him to consult a prominent throat man of great experience, who agreed with me that the other tonsil be removed and that he be placed on tonics, avoiding any specific treatment whatever. This was done and he returned to college, but was kept under competent observation, while there.

He appeared again during his Christmas vacation, and I noted that he had recently had some falling of the hair. He had some seborrhoea of the scalp, and the falling of the hair was so slight that I thought it might be due to this. He had a very thick head of hair. The glands of the neck in the meantime had subsided somewhat. He was not nearly so anæmic. In February he had typical mucous patches in the throat and was then placed on inunctions. The glandular enlargement, then slight, subsided entirely, his ruddy color returned and he regained his strength completely and felt like a new man. The inunctions have been kept up until a month or so ago. No other manifestations have appeared since treatment was begun.

In looking for a possible source of infection, we made up our minds that the most likely source of infection came about in this way. Early in his summer vacation he made frequent trips to Coney Island. There he amused himself blowing up the lung testers which they have there. In this way he might readily have gotten the virus on his lips which from there was conveyed to his tonsil. The tonsils, always in a state of hypertrophy, might readily have served as a port of entry and the attack of tonsillitis in August was really the initial lesion which had become infected and was removed by tonsillotomy. The syphilitic infection must have occurred prior

to the tonsillotomy, as the typical glandular enlargement was noted at the time of the supposed tonsillitis.

I had had previous to this time two cases of syphilis insontium where the initial lesion was the tonsil.

The first case, P. R., about 25, consulted me in August, 1903, having a very peculiar looking ulceration covering the fauces, which proved to be due to an underlying syphilis. He denied chancre or any previous venereal disease; was married. He had chronically enlarged tonsils, was subject to tonsillitis and had had many attacks. The preceding February, while in Denver, Colorado, he had what was diagnosed as a quinsy, a painful and swollen tonsil, the glands of the neck became enormously swollen, but afterwards subsided. Early in April he had noted an eruption over his body which had passed away and he did not think much about it. In May began the peculiar ulceration in the throat which lasted up to the time he came to consult me. He had also at that time noticed some falling of the hair. The source of infection could not be made out and he absolutely denied unnatural practices. I had no doubt at the time that the supposed quinsy was really a chancre of the tonsil, and the source of infection was never known.

During the summer of 1902 I had under my care a young man with a chancroidal ulcer of the penis; the sore had healed and one day he appeared with a severe stomatitis which had come on suddenly and was the first manifestation of constitutional syphilis. I then learned for the first time that he was married but that he had had no relations with his wife since the appearance of his initial lesion. For the first time I warned him of the danger of kissing his wife. It was about a month later that he brought his wife to me complaining of a painful tonsillitis, which proved to be a chancre of one tonsil and was followed in due course by a syphilitic rash. At that time she was eight months pregnant, but was delivered at term of a healthy child, which remained healthy for three years, during which time I had followed all these cases. The child was brought up on artificial feeding.

The wife had always been subject to tonsillitis, and had had many attacks. The husband had refrained from kissing

her after he knew of the danger, but had kissed her after the syphilitic stomatitis had appeared and before he had consulted me about it. In this way undoubtedly the virus deposited on her lips had in some way reached the tonsil, and can be accounted for in no other way, it seems to me.

I wish to report three more cases:

1. A case of chancre of the tip of the tongue in a young man 23 years old; the source of infection could not be determined.
2. A young actress with a chancre of the lip; the only source of contagion admitted was due to the fact of a kissing scene between herself and the leading man on the stage, he kissing her on the lips nightly. He had told her that he had had syphilis one and one-half years, was under constant treatment and had no lesions of any kind: in spite of this knowledge the scene was made realistic. When the chancre of the lip appeared, the young woman left the company, came to New York, and placed herself under my care.
3. A young man this last year had graduated from college. He was a personal friend of the first case reported of tonsillar chancre. After leaving college, he went to work in a machine shop, for his own amusement. One day he noticed simultaneously that he had a painfully swollen gland under the jaw and a sore in the middle of the lower lip. Later he noted another similar sore on lower lip to one side of this. This was followed in due course by a very general macular eruption over the entire body, forehead and face as well. In this condition he consulted Dr. G. E. Brewer, who referred him to me for treatment. It was evident to me that he had a double chancre of the lower lip. The probable source of contagion was a ragged-edged tin can used by the working men as a drinking vessel at the machine shop, certainly a most favorable article to hold and convey syphilitic virus.

THE USE OF MINERAL WATERS IN THE TREATMENT OF SYPHILIS

BY DR. JEAN DARDEL, OF AIX-LES-BAINS

The complete treatment of syphilis comprises, in addition to the so-called specific treatment, auxiliary measures whose object is to reinforce the defence of the organism and to place it in a condition to support the specific medication. In other words we must: (1) combat the manifestations, (2) prevent their recurrence as far as possible, and (3) improve the general health.

Mercury is the drug which may truly be said to be specific in respect to syphilis; we may dismiss iodine and arsenic which are in no sense specifics but merely auxiliary remedies to be employed in response to special indications.

Mercury exerts a directly curative action on the lesions of syphilis, a statement that none will contravene.

Is mercury equally efficacious in averting the return of these lesions? The answer to this question is less affirmative, but most authorities, more particularly Professor Fournier, hold that mercury, given intensively and intermittently, appears to cure, or at any rate attenuate, the disease.

Although mercury effects the cure of syphilitic lesions, it behooves us to treat the soil on which the disease has grafted itself; in a word, to prevent the organism becoming debilitated, enfeebled, and incapable of resistance; in short, we must not lose sight of the subject while we are treating the disease.

Lastly, we must enable the organism to tolerate the remedy in adequate doses.

The syphilitic virus invades and permeates the organism as a whole, gravely interfering with general nutrition. The syphilitic infection no sooner gains a footing than the subject develops a tendency to anæmia, very aptly termed syp-

ilitic anæmia, which presents all the usual signs of ordinary anæmia *e.g.*, changes in the constitution of the blood, physical depression, pallor, dyspepsia, loss of flesh and general lassitude.

Pyrexial phenomena are often met with in the victims of syphilitic infection during the secondary period.

During this same period we not unfrequently witness a stage of intense exhaustion, known as syphilitic asthenia. The patient feels quite worn out, he complains of pain in the muscles and bones, and is a prey to attacks of suffocation, apprehension, and insomnia; he feels incapable of the slightest exertion. These symptoms, which are consequent upon nervous exhaustion and are most frequently met with in female patients render them anxious and do as much to destroy their peace of mind as the syphilitic lesions proper.

This brief sketch of the constitutional disturbances accompanying syphilis paves the way to the therapeutical principle that, while we look to mercury to get rid of specific manifestations, we are constrained to employ adjuvant measures to stimulate nutrition and sustain the organism.

In the present state of our knowledge, the virulence of the syphilitic poison can only be adequately fought by administering mercury to the point of saturation.

But this mercurial saturation which is indispensable to the therapeutical effects we have in view has a more or less depressing influence on the organism. Moreover the administration of the drug may give rise to disturbances of variable gravity, *viz.*: gastro-intestinal intolerance, mercurial stomatitis, renal and nervous intolerance and disturbances of nutrition, more particularly mercurial anæmia.

“We must therefore bolster up the organism to withstand the treatment and to tolerate the mercury so that a sufficient quantity may be given to obtain useful effects without detriment.”

It is with this object in view that we have recourse to the so-called adjuvant treatments: climatotherapy, hydrotherapy, the administration of preparations of iron and arsenic and, above all, the hydro-mineral treatment.

The hydro-mineral treatment, which is one of the most ancient auxiliary methods in the mercurial treatment of

syphilis, was originally purely empirical although now established on a more scientific basis.

In some instances we have recourse to the thermal treatment to combat cachexia, a state of physical depreciation induced by syphilitic intoxication. In other cases the treatment is intended to remedy certain organic defects existing prior to infection which are thereby aggravated and their course modified (scrofula, arthritism and nervous affections). Lastly, the thermal treatment very remarkably assists in rendering the organism tolerant of mercury.

Three classes of mineral waters are employed in the treatment of syphilis: sodium chloride springs, arsenical waters, and more particularly, sulphurous waters. The choice of a station will be decided in view of the physiological and therapeutical action of the waters.

Waters containing sodium chloride exert a powerful influence on nutrition and accelerate oxidation processes. They are specially indicated when syphilis is complicated by scrofula, as in syphilitic cachexia, when the general health claims our first attention.

Arsenical waters are recommended in the torpid forms of syphilis. Strictly speaking, they have no influence on syphilis but, according to Mauriac, are useful in dealing with certain affections that have supervened under the influence of the disease in which "the specific element is gradually eliminated and in the long run practically disappears."

Certain indifferent waters such as those of Nérès and Lamalou are recognized especially when the nervous system is attacked.

It is, however, by the aid of sulphurous waters that the most marked therapeutical effects are obtained. These facilitate the elimination of the mercurial compounds that have been stored up within the organism. They promote the absorption of mercury in large doses and in this way they enable us to carry out a truly intensive treatment.

With regard to the action of mineral waters in the treatment of syphilis, we may point out that the physiological action of the thermal treatment is exceedingly complex, being in fact the outcome of various factors. We have to take into

account not only the temperature but the chemical composition of the water. Then, too, apart from the factors inherent in the water itself, we have to consider those of equal importance, associated with balneotherapy, that is to say, the method of application; those dependent on the altitude, the station, the climate, the hygienic conditions and, lastly, the special conditions of the individual patient.

Each category of stations, indeed each station, has its special action and therefore its special indications.

We now come to the question whether the mercury should be administered to the patient before or during the hydrothermal treatment.

It is obvious that when a patient has just been through a course of *intensive* mercurial treatment it is unnecessary to repeat it during his thermal treatment. Except in this one eventuality it is as a rule desirable to administer the mercury coincidentally with the thermal course.

As to the particular mode of mercurialization to be adopted in each instance there is little doubt that the best, the most scientific, and in every respect the most active, is by the injection of soluble salts. The administration of mercury by the mouth cannot usefully be associated with the use of mineral waters. Inunction answers the purpose. Indeed, not long since it was, so to speak, the classical procedure; but at the present time we have no hesitation in preferring the injection of soluble salts.

It is impossible to lay down hard and fast lines concerning the dose, the number, and frequency of the injections. Each case must be judged on its merits. The practitioner's duty is to proceed cautiously but progressively and to be guided by the state of the patient.

We have referred to the physiological action of thermal waters in respect to the general health, and considerations of space preclude our dealing at length with their influence in promoting absorption and elimination of the mercurial compounds introduced into the economy.

Nor can we describe in detail the different balneotherapeutic procedures, plain and swimming baths, douches, vapour baths, inhalations, gargling and water drinking.

These are points that can only be discussed with advantage on the spot. The indications vary and must be elicited in each case and acted upon there and then.

I will now pass on to the classes of patients likely to benefit from the mineral water treatment. The question whether the patient will derive most benefit at this or that stage of the disease has ceased to be a matter for discussion. It is generally admitted that a course of mineral waters is beneficial at all periods. We may dismiss the so-called test treatment which, it was alleged, demonstrated the *reality, or otherwise*, of the cure. This method has been abandoned *in toto*: indeed, its application was a delusion and a snare.

We must bear in mind, however, that the subjects of arteriosclerosis, liver disease, and the grand neuroses cannot undergo active thermal treatment with impunity. With these reservations I will proceed to discuss the formal indications.

The mineral water treatment should be advised whenever mercury is badly borne or is only tolerated in inadequate doses and also when, in spite of its administration, we fail to obtain the desired therapeutical effects.

The grave forms of syphilis, especially those in which the grave symptoms come on early, cases in which syphilis is grafted on a bad soil, on used-up cachectic soils, and old standing cases that have proved refractory to treatment, all these are amenable to the mineral water treatment.

Lastly, certain cases imperatively demand an intensive treatment with effects rapidly induced by the injection of large doses of soluble salts, as carried out at mineral water resorts, as for instance in the presence of nervous symptoms due to syphilis, in syphilitic ulceration threatening the integrity of an organ or region, in fact all cases in which we must precipitate our intervention in order to cut short destructive lesions, cases in which lost time cannot be regained.

To sum up: it is not claimed that mineral waters cure syphilis; what they do is to assist and reinforce the specific treatment by promoting the absorption, the action, and the elimination of mercury and by improving the patient's general health.

LIST OF THE PRINCIPAL STATIONS TO WHICH SYPHILITIC PATIENTS CAN BE SENT

In order of importance we must distinguish—

1. Sodium sulphide waters.
2. Arsenical waters.
3. Sodium chloride waters.

1. *Sulphurous*

LUCHON.—In the midst of the Pyrenees at an altitude of 625 metres. Numerous springs, thermal, hyperthermal, sulphurous, and hydrosulphide. Natural sulphurous vapour baths at 40° to 42° C. The special feature of Luchon is the emanation of sulphurated hydrogen which is unconsciously inhaled by the patient in whatever part of the establishment his treatment takes him. In this way, although the treatment is to all appearance purely external, it is in reality also, internal.

AIX-LES-THERMES.—In the Pyrenees, at an altitude of 716 m. Sodic sulphide thermal and hyperthermal. Upwards of sixty springs at a temperature of from 22° to 77° C; mono-sulphide and hydrosulphide of sodium; sulphite and hyposulphite of sodium; precipitated sulphur. Used internally and for baths and douches.

BARÈGES in the Pyrenees.—Altitude 1332 m. Numerous thermal sodic sulphide springs containing an average of 4 cg. of sulphide per litre. Temperature 19° to 44° C. Is reputed for syphilis in scrofulo-tuberculous subjects.

CAUTERETS in the Pyrenees.—Altitude 932 m. Sodic sulphide waters. Twelve copious springs. Temperature 36° to 58° C. Variable richness in sodic sulphide, sulphites, and hyposulphites. This station is much frequented by debilitated syphilitics.

AMELIE LES BAINS.—Altitude 276 m.

AULUS and EAUX BONNES.—Altitude 748 m., also in the Pyrenees, are likewise worthy of mention.

URIAGE (in the Alps near Grenoble).—Altitude 400 m. Sulpho-chloride springs. Temperature 27° C. The salient feature of the Uriage waters is their richness in chemical

constituents: Chloride of sodium 1.5; sulphide of calcium 1.05; sulphate of magnesia 0.48. These waters possess very valuable qualities uniting as they do the action of chlorides with that of the sulphides.

CHALLES (Savoie) in the Alps near Chambéry.—Altitude 270 m. Temperature 13° C. Monosulphide 0.513. This water is the richest in sulphide, bromide and iodide.

AIX-LES-BAINS (Savoie) in the Alps.—Altitude 270 m. Thermal calcic sulphide. Temperature 45° C. The douche massage and the Berthollets or vapor baths of Aix are known world wide. The Aix treatment exerts a powerful influence on nutrition and circulation. It has an essentially tonic action.

MARLIOZ (a spring near Aix).—Sulphurous, alkaline, and contains iodine. Temperature 14° C. Very highly mineralized. Sulphide alkaline salts and iodine. Is well adapted for the internal sulphur treatment.

AIX-LA-CHAPELLE (Aachen) in Germany.—Is a chloro-sulphide water. Temperature 55° C. These waters enjoy a long standing reputation in the cure of syphilis. The treatment is carried out with the greatest care.

HARKANY (Hungary).—Calcic sulphide waters. Temperature 58° C.

FURDO (Hungary).—Calcic sulphide waters. Temperature 40° to 60° C.

TEPLITZ (Bohemia).—Calcic sulphide.

PRATIGORSK (Russian Caucasus).—Altitude 519 m. Temperature 25° to 45° C. Is the best known of the Caucasus watering places. The district is remarkably rich in mineral waters which are not as well known as their merits deserve.

SCHINZNACH (Switzerland).—Altitude 350 m. Temperature 34° C. Calcic sulphide.

VINADIO (Italy).—Altitude 1349 m. Temperature 33° to 63° C. Sulphurous and sodic chloride. Treatment by vapor baths, well applied.

RIOLO (Italy).—Altitude 160 m. Springs rich in sulphuretted hydrogen.

PORRETTA (Italy).—Altitude 370 m. Temperature 27° to 39° C. Chloro-sulphurous springs.

VIZELLA (Portugal, province of Minho).—Temperature 17° to 64° C. Copious sulphurous springs.

ARCHENA (Spain, province of Murcia).—Altitude 130 m. Cold springs chloro-sulphurous. Highly mineralized. Have a certain reputation.

II. Arsenical Waters

LA BOURBOULE (France, department of Auvergne).—Altitude 846 m. Temperature 19° to 60° C. Chloride, bicarbonate arseniated. Very useful for restoring strength in anæmic syphilitic subjects. There are many other arsenical waters but none of them lends itself as well to the treatment of syphilis.

III. Sodium Chloride Waters

SALIES DE BERN (France).—Altitude 30 m. Temperature 23° C. Very rich in mineral constituents.

SALINE (Jura).—Altitude 330 m. Cold. Sodic chloride, containing 22 of sodium chloride.

LA MOULIÈRE-BESANÇON (Jura). Altitude 354 m. Cold. Sodic chloride and iodo-bromide.

BOURBONNE LES BAINS (Haute Marne).—Altitude 304 m. Temperature 55° to 65° C. Chloride of sodium. Well organized establishment.

BEX (Switzerland, Canton of Vaud).—Altitude 400 m. Cold. Calcic sulphate and sodic chloride.

LAVEY (Switzerland, Canton of Vaud).—Altitude 375 m. Temperature 46° C.

ACQUI (Italy).—Altitude 149 m. Temperature 20° to 50° C. Sulphurous sodic chloride.

ALBENO (Italy).—Altitude 13 m. Very hot waters. Temperature 81° C. to 86° C.

BATTAGLIA (Italy).—Altitude 15 m. Temperature 58° to 70° C.

SALSO MAGGIORE (Italy).—Waters very rich in mineral constituents. Well organised balneotherapeutical establishment.

ISCHYL (Austria).—Altitude 480 m. Cold. Carefully applied treatment.

NAUHEIM (Germany).—Altitude 110 m. Temperature 21° to 39° C. Chloride of sodium, chloride of magnesium, large proportion of free CO .

KREUZNACH (Germany).—Altitude 110 m. Temperature 12° to 30° C. Sodid chloride and bromide.

KISSINGEN (Germany).—Altitude 190 m. Cold.

HOMBURG (Germany).—Altitude 200 m. Cold. Sodid chloride and ferruginous.

WIESBADEN (Germany).—Altitude 100 m. Temperature 67° C.

We may also mention in Roumania, Bughea and Lacul-Serat. These waters are excellent but little known.

In addition to the waters just mentioned certain others have been employed with success, *viz.*, the mineral mud of St. Amand and Barbotan.

Lastly a spring which has rendered great service is that of LAMALOU (France).—Altitude 190 m. Temperature 17° to 46° C. Chalybeate bicarbonated waters. The Lamalou waters are especially employed in the treatment of the nervous complications of syphilis more particularly in tabes for the purpose of calming the pains.

Lamalou is provided with a well-devised installation for the treatment of tabes and the treatment is very conscientiously carried out.

The foregoing is a list of the principal mineral waters of Europe available for the treatment of syphilis but the list is assuredly incomplete and there must be many other stations that might be resorted to with advantage.

One point should be borne in mind in selecting a station. Too much attention must not be attached merely to the richness of the spring in mineral constituents. This is an important but not the sole factor, for comparatively weak mineral waters also yield excellent results.

We must bear in mind the altitude, the climate, and especially the medical superintendence and mode of treatment which play at least as important a part in bringing about the result as the composition of the water.

It would hardly be practicable in an article like the present to describe in detail the methods of treatment in vogue at the various thermal stations. We may take as a model the treatment carried out at Aix-les-Bains which is the prototype of the thermal treatment applied to the treatment of syphilis.

The Aix treatment is essentially external. The Aix douche, a combination of douching and massage, constitutes a special feature. The operation consists of the kneading of muscles under a copious current to hot sulphurous water. The douche can be modified in respect to duration, pressure, and temperature in such wise that the effects obtained can be varied ad infinitum.

The so-called "bouillon" is a vapor bath given off by a column of hot water at a temperature of from 104° to 108° F. The patient is left in the bath for five or ten minutes which suffices to set up copious perspiration.

The "Berthollet" is a variety of vapor bath peculiar to Aix. The natural sulphurous vapor can be applied to the body as a whole or to any limb or joint.

The external treatment is supplemented by the internal administration of the Marlioz cold sulphur water which is very easy of digestion. A cold indifferent water—Deux Reines—is utilized as a diuretic and for depurative purposes. It may be added that Aix possesses a Zander Institute well provided with various physical and mechano-therapeutical appliances. carbo-gaseous baths, electrical baths, Dowsing baths, etc.

It will readily be understood that these complex treatments exert a powerful physiological influence and constitute a therapeutical instrument which the physician can manipulate at will. By selecting appropriate conditions of temperature, duration, and application we are enabled to obtain a stimulating or a sedative or a tonic action, in short, properly handled, the Aix thermal treatment renders very great service in the various forms of syphilis as well as in the multiple pathological states associated with or following the disease.

VERRUCÆ PLANTARES: THEIR PREVALENCE IN BOYS AND IN YOUNG MEN, AND THEIR PATHOLOGY

BY DR. JOHN T. BOWEN, OF BOSTON

The first to call attention to these plantar warts was W. Dubreuilh.¹ Up to that time the affection had not been referred to in the treatises on surgery or dermatology, although, as he states, it is far from uncommon. His description is so good that it may very properly be quoted.

“When the plantar wart is of recent date, it shows itself in the form of a slightly reddened elevation covered with a thin epidermis. When this covering is removed, bleeding appears from a number of orifices.

“Most often, however, the lesion presents at first sight the aspect of a large and extremely tender callus. The horny layer is thickened and elevated; sometimes the central part of this horny plaque is perforated by a sort of well, more or less deep, especially if there has been an attempt to scrape it off. If, however, the lesion has not been molested for some time, the superficial horny layer forms a complete covering.

“When the surface of the lesion is cut with a knife, the periphery of the lesion is found to have a hard, semi-transparent, horny layer, much like normal horny epidermis, or that which constitutes calluses and corns. Instead, however, of penetrating deeply into the corium with a horny mass as does the corn, this lesion possesses a soft and depressible central portion. It takes the form of a ring perforated by an orifice which becomes larger as one goes more deeply. This central part possesses a tissue of a very different appearance, a horny tissue, to be sure, but white, opaque, and milky; it is soft and resistant to the knife like wet tow.

¹ *Annales de dermat. et de syph.*, tome 6, 1895.

“While the horny ring at the periphery is homogeneous or stratified, the central part appears to be fasciculated and formed of columns which penetrate vertically downwards. Frequently a dark, hemorrhagic point is seen, and most often if one continues to cut successive layers of the lesion, drops of blood are poured out from a large number of capillary openings which dot the surface.

“It is at first difficult to make a curette penetrate into this soft and tenacious tissue. When once, however, the curette has reached its base, a soft, white, milky tissue is removed, which is divided into columns that run perpendicularly from the surface to the base.”

Such is Dubreuilh's description of this affection upon the soles of the feet. With regard to its frequency, I have been much struck by the large number of cases seen and heard of by me in and about Boston. Almost all of the cases are in young people, and the affection is especially prevalent in preparatory schools and colleges. Doctor Bailey, the medical visitor of Harvard University, writes me that he sees a large number of these cases every year, and that they average about twenty operations a year for plantar warts at the Stillman Infirmary, the hospital of the University. A great many cases occur, also, in the preparatory schools at Groton and Southborough. I have been unable to collect exact statistics on this point, as they were treated by different people, and sometimes I heard of cases which had not been treated; as, for instance, a boy who was my patient told me that perhaps half a dozen other boys of his acquaintance had similar lesions.

I have been able, however, to study thirty-four cases which I have seen and treated in my private practice, and of which I have preserved notes. In hospital practice the affection is far less common. We see it so rarely that statistics from this source would be of little value. Of these thirty-four cases, twenty-eight were males and six were females. The youngest was ten and the oldest sixty. Seven were under sixteen, fifteen were between sixteen and twenty, seven between twenty and twenty-five, and five between twenty-five and sixty. It is seen, therefore, that youths and boys under

twenty years of age are the ones by far most frequently affected.

Twenty of these thirty-four cases were in boys who were attending either a preparatory boarding-school or Harvard College. In almost all instances the boys would speak of some other boy or boys of their acquaintance who had the same affection, so that the conclusion is justified that in this vicinity, at least, the affection is far more common among boys and youths who are collected in schools and colleges than among other people. Its prevalence in this class is further corroborated by the local physicians in the neighborhood of these institutions.

Dubreuilh considers that local traumatism plays an important part in the development of these lesions. In the cases that I have studied it was impossible to decide that in any of the cases there had been a local injury. He also thinks that the localization of these lesions is in favor of the traumatic theory, in that they are especially common over the head of the third metatarsal bone. In my cases this localization was not so apparent, although it did occur in a number of instances. Contrary to Dubreuilh's experience, I have seen a number of times the coincidence of plantar warts with a like affection of the palms of the hands, and I have had two cases where they appeared on the palms alone. In one or two cases there had been a palmar wart preceding the attack of plantar warts.

As to the number of these warts, they may be few or many. In one of my cases there were as many as thirty. In two of my cases two members of the same family were affected either at the same time or at a short interval from one another. In one case it was two brothers aged respectively fifteen and twenty-one, and in the other, two sisters of whom the oldest was twenty. It must be admitted that the evidence here stated does not warrant the conclusion that these lesions are contagious, and yet there is enough to make such a theory probable. It is quite true that people most subject to these plantar warts are those who are most accustomed to exercise, such as running and tennis playing, and that in these sports an opportunity for irritation of the plantar surfaces is plainly

offered. On the other hand, this traumatism can be invoked as offering an opportunity for infection in such cases, and the well-known contagiousness of *verruca vulgaris* would be a point in support of this theory.

CASE 1. Boy of 19. *Verruca* of the sole of the foot, just below the third metatarsal.

CASE 2. Boy of 16, who lived at home and attended a day school. He had a *verruca* of the sole of the foot which had lasted several months. He said that two years previously he had had a similar lesion on the palm.

CASE 3. A boy of 14, at a day school. Lesion is situated upon the heel.

CASE 4. A lad of 18, who presented three large lesions on each sole, opposite the end of the third metatarsals.

CASE 5. Girl of 16, who presented a lesion on the ball of the foot.

CASE 6. A youth of 19, in college, who presented several lesions on the soles of each foot, the exact number not stated in the record.

CASE 7. A man of 26, one large extensive lesion of the flexor aspect of the thumb.

CASE 8. Boy of 10, a lesion on the sole of each foot over the metatarsal ending, of six months' duration.

CASE 9. A youth of 20, who had had multiple *verruca* of the soles of the feet for six months.

CASE 10. Youth of 18, who had two *verruca* of the soles, besides a large callus.

CASE 11. Young man of 21, who had several lesions at the base of the toes.

CASE 12. Girl of 15, with a lesion of the palm of the hand.

CASE 13. Boy of 14, at a boarding-school, a *verruca* of the sole.

CASE 14. Youth of 20, a *verruca* of the heel.

CASE 15. Young man of 21, in college, who had had *verruca* of the ball of the foot for two years, beginning while he was at boarding-school, while he was exercising in the fives court. He also had had one of the palm of the hand which had disappeared.

CASE 16. Boy under 16, at boarding-school, who presented *verruca* of the heel.

CASE 17. Young man of 21, at college, who presented six or eight lesions of the ball of the left foot, which first appeared two years ago when he was not exercising very much.

CASE 18. Young man of 19, at college, a verruca of the sole, which had lasted for six or eight months.

CASE 19. This was a boy of 15, at boarding-school, a brother of Case No. 15, who had a wart of the palm of the hand of three months' duration. This lesion had once been excised by a local physician and had recurred in the cicatrix.

CASE 20. Young man of 21, who had had verrucæ of the sole of the foot for a month.

CASE 21. Young woman of 20, who had had for nearly a year a plantar wart on the left foot over the third metatarsal. This appeared at the time that she was visited by her sister who had a similar one. She slept in the same room with this sister, but not in the same bed. Both played tennis, but, so far as could be remembered, had never worn each other's shoes.

CASE 22. A man of 53, a merchant, who presented a plantar wart over the first metatarsal bone.

CASE 23. A young man of 22, in Cambridge, an oarsman, who rowed in the University boat, presented quite extensive lesions of the palms and also of the sides and backs of the hands. Those of the palms were typical palmar warts. Those of the backs of the hands presented the aspect of ordinary seed warts. There may have been twenty of these lesions altogether. The affection had lasted for three years.

CASE 24. Young man of 16, living at home, who showed eight or ten plantar warts, chiefly over the metatarsal bones.

CASE 25. Young man, over 20. A palmar wart, of identical histological appearance with the plantar wart. Also a wart under the nail.

CASE 26. Man of 50, who had had a plantar wart on the sole of the right foot for nine months. It had appeared immediately after a trip to Mexico.

CASE 27. Woman of 60, who presented a half dozen plantar warts over the metatarsal region.

CASE 28. Young man of 21, who had had a verruca of the sole of the foot, in the metatarsal region, for six months.

CASE 29. Young woman of 18, who had a palmar wart on the middle finger of the right hand.

CASE 30. Boy of 16, at boarding-school. This was the most extensive case I have seen. Thirty plantar warts, scattered over the whole surface of the sole of the left foot, were counted at one time. There were also some on the plantar surface of the toes. They had first made their appearance six months before. Besides these there were two typical lesions of the palms which had appeared after those on the soles.

CASE 31. Woman of 30, who had a palmar wart, associated with an ordinary *verruca vulgaris* of the back of the finger.

CASE 32. Boy of 14, at boarding-school, who had had for six months several plantar warts, in a clump on the plantar side of the great toe.

CASE 33. Young man of 21, who had four or five plantar warts in the metatarsal region, of eight months' duration.

CASE 34. Boy of 14, at boarding-school, plantar wart of the heel.

Melchior-Robert, in the *Annales de dermat. et de syph.*, 1897, describes four cases, two palmar and two plantar, but without histological examination. He gives the name *verruë en puits* to that form that projects from the surface, but in which the papillary prolongations are deeply seated, and this is the type of both the plantar and palmar warts that I have examined.

D. W. Montgomery read a paper at the 54th annual session of the American Medical Association on "Papilloma of the Sole," in which he relates seven cases which he has seen and treated. Four of these cases were in people under 20. He refers to the well-like aperture that is uncovered when the outer horny layer is wanting or is removed by cutting.

At the meeting of the Dermatological Society of Great Britain and Ireland, on March 25, 1896,¹ Doctor Eddowes read a paper entitled "Warts on the Feet." Having previously been interested in this subject, he agrees entirely with Dubreuilh as to the clinical appearance of these growths, but had made no microscopical examinations. He considers

¹ *British Journal of Dermatology*, May, 1896.

that traumatism plays a prominent part in the production of these lesions.

The pathology of these lesions has been very thoroughly worked out by Dubreuilh, and with almost everything he says I can concur. I have examined microscopically more than twenty different cases of plantar and palmar warts, and in some instances several lesions from the same case were studied. In connection with these investigations a number of specimens of verrucæ of different histological appearance were also examined.

In the following description of the histological appearances, I am to a great extent in accord with the very excellent description of Dubreuilh. In verrucous growths which are not subject to habitual pressure, as on the back of the hand, the tumor is developed as a projection above the surface of the skin. In places, however, where there is a long-continued and strong pressure, the wart does not project to any extent, but burrows, as it were, into the cutis, while the adjacent epidermis becomes hypertrophied. A section through the centre of one of these palmar or plantar warts explains the characteristics obtained by curetting, for the wart is, as it were, subcutaneous and the similarity to a well is very striking.

There are no important changes in the cutis. The papillæ contain a certain number of cellular elements. I have not found the elastic fibres in the upper portion of the papillæ wanting as has Dubreuilh. In most of the lesions that I have examined the papillary projections and interpapillary prolongations were much flattened out at the centre, whereas I have in all cases noticed the lengthening out of these structures at the periphery of the lesions. In some instances they run almost horizontally to the surface at the periphery.

As regards the epidermis, an interesting feature, peculiar in my experience to these plantar and palmar warts, has been described by Dubreuilh. I have found it constantly in verrucæ of the palm and sole, never in other situations, while Dubreuilh describes it as occurring in a wart on the back of the hand. This change gives rise, in the centre of a large and well developed palmar or plantar wart, to a most extraordinary peculiarity.

Serial sections through an entire lesion show at the periphery the appearances in general of an ordinary verruca, a pronounced acanthosis, papillary enlargement, and down-growth of the rete pegs, together with a very pronounced hyperkeratosis. The granular layer is much increased in thickness. Very soon, advancing toward the centre of the lesion, the peculiar change described by Dubreuilh is encountered. This consists in a vacuolation of some of the rete cells, which cause them to assume a rounded form and a larger size than the neighboring cells. The lower basal cells I have never seen thus affected, but the appearances may often be seen in the layers near the basal cells. Oftentimes small clumps of rete cells are thus affected while the cells above them still retain their normal characteristics. Usually, in connection with this vacuolation, there is a precocious development of kerato-hyaline, which often is heaped up at the periphery of the cell around the central cavity. These cells retain their nucleus, which, as a rule, is very much swollen. Advancing toward the centre of the lesion, this vacuolation affects more and more cells, which fuse together until, at the centre of a well developed lesion, the portion corresponding to the rete is composed of a reticulated tissue heaped up with masses and blocks of kerato-hyaline.

The largest portion of the lesion is composed of the horny layer, which lies, much hypertrophied, over the reticulated rete as just described. That this layer is imperfectly keratinized is shown by the presence in places of the cellular elements which take the stain of the ordinary reagents.

In one of the first of these lesions that I examined, peculiar bodies were found in many of the nuclei of the rete cells. The appearances at first sight were so striking that the suspicion that they might be some form of protozoa was aroused, and it was on this account that I examined histologically so many cases. These bodies were found in a majority of all the cases, not, however, in all. They are small, usually round bodies, highly refracting, occasionally appearing as if concave in the centre, and in a few instances crescent-shaped. As a rule they are all of equal size. They are first seen in the third or fourth row of rete cells and seem to go hand in hand with

the vacuolation, as they disappear when what corresponds to the granular layer is reached. They are not seen in all the nuclei, but are most prominent in the enlarged and swollen nuclei which accompany the vacuolation. They are stained by the acid reagents, and are sharply differentiated in this way from the rest of the nucleus. No further data as to the significance and origin of these nuclear bodies could be obtained, and, so far as I know, such appearances have never been described in epithelial structures. It was, as I say natural at first to think of the possibility of their being some form of protozoa, and it is difficult to rule out such a possibility. On the other hand, their appearance in connection with the vacuolation, and their disappearance in the upper layers, would make it more probable that they represent some form of nuclear degeneration or alteration.

TREATMENT

I have had experience with quite a number of different modes of treatment in this affection. In many instances it was not possible, on account of the prejudice of the patients or their parents, to institute as radical methods of treatment as seemed advisable. In a considerable number of cases salicylic acid in collodion in ten per cent. strength was sufficient, after some time, to remove the lesions. It was painted on daily and the foot soaked every other day for twenty minutes in hot water, and then pumice soap used to remove as much of the lesion as possible, and then the painting renewed—much the same treatment that is used in the case of corns.

Many cases, however, will not respond to this treatment, and I have had some success with chrysarobin, which was added, in ten per cent. strength, to the salicylated collodion. In other cases success was attained by covering the lesions constantly with a sixty per cent. salicylated guttapercha plaster. It is my impression that almost all of these lesions will yield to this treatment, if it is persisted in long enough, but it may take many weeks, and the necessary patience has not been found in all persons.

Dubreuilh considers curetting the most radical and rapid treatment, which he performs under cocaine anæsthesia. The late Doctor Warren, of Groton, who had treated a large number of these cases in the boys of Groton School, wrote to me that he had formerly excised these lesions, but had given it up; that he had tried salicylic acid, corrosive sublimate, chromic acid, nitric and lactic acids; he had also used electrolysis, but had come to the conclusion that the Paquelin cautery was the best, surest, and quickest method. He first cocainized the wart, and with the round point of the Paquelin cautery thoroughly cauterized, beginning at the centre and sweeping around the whole periphery of the wart. This method he considered almost painless, produced the smallest possible scar, and needed but one sitting, if carefully done. With regard to excision, it has to be thoroughly done, and is practised with success at the Stillman Infirmary in Cambridge, where, as I have said, they average twenty operations a year for this affection. Even, however, when apparently thoroughly done, the lesion may reappear in the cicatrix, as I have myself seen.

Electrolysis has been effective in my hands, but without thorough local anæsthesia it is very painful, and the same may be said of the strong caustics, which I have repeatedly tried. By the advice of other practitioners, a number of the patients whom I have seen have been wearing plates in order to remove the weight from the part affected by the wart. I have rarely seen a cure produced by this mode of treatment alone.

End of Fifth Day

SIXTH DAY, SATURDAY, SEPTEMBER 14TH

DR. HENRY W. STELWAGON, of Philadelphia, Vice-President, in the Chair.

ZOSTER ARSENICALIS

BY DR. JOSEPH ZEISLER, OF CHICAGO

To judge from the number of publications devoted to it, and the frequency with which it recurs in the discussions of dermatological societies, the question of arsenical zoster does not seem to have lost in interest; nor is there perfect unanimity among observers concerning the causal relationship between the administration or ingestion of the drug and the subsequent cutaneous reaction. While some entertain no doubt as to their direct connection, a few still consider zoster arsenicalis merely as a coincidence—a *post hoc* and not a *propter hoc*. The majority of text-books barely mention it, disposing of it with a few words under the head of etiology. To me, the matter seems to involve a double interest: firstly, from the view-point of medicinal reaction, zoster being but one of a great number of cutaneous manifestations following the use of a drug which is still considerably—not to say too often—used in the treatment of many skin diseases; in the second place, as furnishing a valuable aid towards the understanding of the pathogenesis of zoster. A fair number of personal observations have long ago convinced me of the existence of true arsenical zoster, and have prompted me to once more bring the matter forward, in the hope of convincing some of the opposition.

To that careful clinical observer, J. Hutchinson (1), belongs the credit of first having pointed out, as early as 1868, the intimate relationship of zoster to the use of arsenic. In 1878 his statements were corroborated by Dyce Duckworth (2), while

J. C. White (3) considered the eruption as a mere coincidence. The next important communication was by O. Juliusberger (4) in 1884, who recorded three cases of zoster following the long-continued administration of arsenic. He, however, also looked upon it as a mere coincidence. In another report again from the same clinic, Neisser's assistant, Epstein (5), takes the opposite view, based upon two observations of arsenical zoster. In 1889, Bokai (6, 7) published a statistical study of the question. In one hundred and thirteen cases of chorea, treated mainly by arsenic, he observed herpes zoster three times, *i.e.*, in almost three per cent. of the whole number, and always after the administration of the drug for a long period—from thirty to fifty-four days—at a time when the original nervous trouble was sufficiently improved to allow its exclusion as an etiological factor. The most valuable statistical investigation on the subject has been made by Nielsen (8), whose observations, made during a period of twenty-five years, referred to three hundred and ninety psoriasis patients treated by arsenic. Ten of these developed zoster while still in the hospital. In two hundred and twenty other cases of psoriasis treated without the use of arsenic, there never occurred a case of zoster. In the year 1898 there appeared an important contribution by L. Geyer (9), with a careful record of the literature on arsenicism. His study is based largely upon observations in a district where the natural water contains comparatively large amounts of arsenic. After discussing arsenical melanosis, he says: "In Reichenstein also zoster is a very frequent occurrence, affecting the trunk and the extremities, unilaterally as well as bilaterally. The arsenical origin of zoster is still unexplained. It is very probable, though not sufficiently proven, that herpes zoster may be a consequence of the morbid effect of arsenic upon certain nerve trunks."

In a very careful monograph, Bettmann (10) discusses the whole subject very fully, and gives the details of a case of multiple lymphomata treated by subcutaneous injections of sodium arsenate besides the internal use of Fowler's solution. After about four weeks there developed a typical herpes zoster ophthalmicus, and in addition a generalized pustular eruption, plantar and palmar keratosis, and, finally, trophic

disturbances of all the nails. He considers his case as a weighty argument in favor of genuine arsenical zoster, on account of its symbiosis with other unquestionable arsenical effects upon the skin.

In his inaugural dissertation, Berthold Stein (11) comes to the conclusion that there is no doubt about the existence of true arsenical zoster, but that further observations are desirable.

In more recent literature, reference to the subject is frequently made by Haslund (12), Bury (13), Blaschko (14), Jadassohn (15), and others.

In the following I shall submit, very briefly, notes of my own observations, comprising eleven cases of arsenical zoster recorded in a period of twelve years.

CASE 1. Mrs. W. T., age 44 years, presented herself on June 26, 1889, with a typical case of pseudo-leukemia (Hodgkin's disease). There were enormous swellings of the lymphatic glands in the region of the neck and axilla and the inguinal spaces. Besides iron and quinine, the chief treatment consisted in the administration of Fowler's solution in gradually increasing doses. Ten weeks later, on the 4th of September, the patient, who lived out of town, visited me again, and with tears of gratitude reported what she considered a wonderful improvement. The glands in the cervical region had shrunk to one-fourth their former size, and a similar retrogression had taken place in all other localities. Quite incidentally, she now called my attention to an eruption which had appeared about ten days before and had since spread. Upon examination, I found a classical, fully developed zoster sacro-femoralis dexter, extending from the sacral region to the outside of the thigh and down to the popliteal space. To my mind, the causal connection of the eruption with the arsenical medication was clearly established.

Once more, on September 15, 1891, I saw the patient again. She had had two relapses of the glandular swellings in the meantime, but always improved under arsenical treatment. Now there was again a slight recurrence. There never had been any further cutaneous reaction since the first outbreak.

CASE 2. C. F. P., 24 years; diagnosis: psoriasis. Besides the usual local treatment, arsenic was prescribed internally in

gradually increasing doses. Treatment began on September 5, 1889. On January 2, 1890, the patient presented himself with a well-developed herpes zoster brachialis.

CASE 3. H. F. T., 42 years, November 29, 1889. Lichen planus since about two years, a typical case, particularly well developed on the wrists; on the glans penis—an annular lichen planus. Treatment by arsenic internally. On February 12, 1890, herpes zoster acromialis.

CASE 4. F. E. L., 30 years of age. Psoriasis since twenty years. Treatment began on February 28, 1890, by Asiatic pills. On March 24, herpes zoster pectoralis.

CASE 5. R. J., 28 years old, psoriasis patient. Treatment with arsenic internally began June 10, 1890. Six weeks later development of zoster dorsalis on the left side.

CASE 6. F. K. D., 34 years old, came under my care on June 27, 1890, on account of an alopecia areata of the beard. Besides other measures, arsenic was prescribed internally. On August 21, the appearance of a zoster pectoralis.

CASE 7. Miss K. W., 22 years old, psoriasis. September 10, 1892, treatment by arsenic. Five weeks later there developed an ophthalmic zoster.

CASE 8. D. K., 46 years of age, lichen planus. Treatment started April 17, 1895. On July 5, zoster pectoralis.

CASE 9. M. A., 42 years old, recurrent toxic erythema of the supra-orbicular regions. Among other measures, arsenic was prescribed on January 1, 1897. On February 2, there had developed a full-fledged zoster acromio-pectoralis sinister.

CASE 10. B. L., 55 years, lichen planus. April 17, 1900, treatment began by Asiatic pills. On June 21, zoster pectoralis.

CASE 11. W. H., 20 years, a medical student, had been treated by another colleague for psoriasis by arsenic, besides other medication. On the 8th of June, 1902, he visited me on account of zoster of the chest.

It does not seem necessary to me to give detailed accounts of these cases. The main point is that in all of them arsenic was the chief internal medication, and in all of them there developed, after a variable period, and usually when a

maximum dosage had been reached, a clinically unmistakable zoster.

In addition to these eleven cases, I have repeatedly observed, in patients treated for various disorders by arsenic, what might be termed an abortive zoster or so-called zosteroid eruption. By this I mean a localized, grouped vesicular outbreak, which ran a cyclical course without producing pronounced subjective or objective features, very much like a simple herpetic eruption. These miniature zosteres, as I might call them, are well known to dermatologists. Hutchinson, for instance, considered them as a particularly characteristic arsenical effect. Gerhardt (16), in referring to grouped vesicular eruptions after arsenical poisoning, had evidently the same lesions in mind. Their relation to real zoster may be explained in this way, that they are due to an irritative effect of arsenic upon the skin itself, while in true arsenical zoster the eruption is secondary to an irritation of a corresponding nerve ganglion, or even a central nervous organ.

It will be noted that in my eleven observations the underlying original trouble was psoriasis in five, lichen planus in three, pseudo-leukemia, alopecia areata, and erythema, each one case. The time interval required for the development of zoster was approximately: nine weeks, three months, ten weeks, four weeks, six weeks, eight weeks, five weeks, eleven weeks, four and one-half weeks, ten weeks, and unrecorded in the last case. It varied, therefore, from four and one-half weeks as the shortest period to three months as the longest. It always occurred while the patient was still taking his arsenic, and usually when a high dosage had been reached. It seems to me that the direct connection between the medication and the subsequent eruption of zoster in all these cases is easily established. To consider the appearance of zoster in all of them as a casual occurrence, would mean to wilfully ignore the chronological development of clinical phenomena. After all, zoster is not a very common affection, nor is lichen planus, which, in my own and the observations of others, frequently forms the underlying disease, a very ordinary trouble. To believe that two such cutaneous disorders should so often happen together as a mere coincidence would be strange logic.

Admitting the causal relationship, the question now occurs, if the vesicular eruption following the use of arsenic is a true zoster or a medicinal rash, as Lewin (17) would have it. To me the answer seems simple. Zoster is a clinical, not a pathological entity. A grouped vesicular eruption in a localized territory, following the course of one or more cutaneous nerves, usually unilateral and running a definite cycle, is always called a zoster, whether it is of traumatic, toxic, ganglionic, peripherally nervous, or any other origin. In the same way we call an ephemeral pomphous eruption always urticaria, no matter which of a dozen local or internal causes may have brought it on. We might further remark that were the eruption following arsenic a medicinal rash and as such due to a peculiar idiosyncrasy of some patients, it would recur after repeated medication. The fact remains, however, that after patients have once gone through an attack of arsenical zoster, they can safely continue with the use of arsenic without the risk of a second attack. They practically acquire immunity against it in the same way as other zoster patients.

In this connection I might mention Stark's (18) contribution, who reports a case of facial zoster in a patient treated by Fowler's solution for an ordinary acne. This patient showed, after three weeks, a slight relapsing vesicular eruption, which, however, lacked the classical features of a true zoster, and was probably one of those ephemeral rashes to which we have referred.

As to the time involved between the beginning of the medication and the appearance of the zoster, or rather the amount of arsenic necessary for its production, opinions differ somewhat. Blaschko (14), in a discussion of the subject before the Berlin Dermatological Society, states: "Not the maximal dose of arsenic, but the tolerance of the patient is of importance." He observed a patient, who, after minimal doses of arsenic, showed severe symptoms of intoxication, anidrosis, zoster, and general dermatitis. Jadassohn (15), in his contribution to the knowledge of lichen planus, says: "About arsenical zoster I have nothing new to report. I have observed it not at all rarely—three times out of my last thirty-three cases.

Once I could confirm the repeatedly made observation that it appears after relatively small doses, but that later, even with much more energetic treatment, zoster did not recur."

My own material, on the other hand, would rather teach that zoster developed only after arsenic had been taken for several weeks or months, *i.e.*, that up to a certain point there existed a tolerance for the drug, but beyond that a reaction would follow. The element of idiosyncrasy cannot be entirely eliminated, but that is a matter which it is difficult to analyze. Why do only a few of the many patients treated by arsenic develop a keratosis? Why is epithelioma, after all, a rare consequence of the same cause? The structure of the skin and general constitutional conditions certainly must play an important rôle in this respect.

Another interesting question is why arsenic should attack one special territory for the production of zoster. Nobody can answer this in a positive manner. By way of analogy one might refer to the development of zoster after poisoning with carbon monoxide gas; also medicinal rashes after a great many different drugs, often showing localized effects. We might refer, for instance, to localized urticaria after antipyrine and other anti-febrile drugs, the localized bromide and iodide eruptions, etc.

That arsenic carries with it a certain affinity for the nervous system, especially the peripheral nerves, is based on several observations, as for instance by Barton (19). Such an affinity would offer the best explanation for the pathogenesis of arsenical zoster.

In regard to the relation of the underlying disease treated by arsenic to the consequent zoster, nothing definite can be stated. Psoriasis seems to furnish the majority of examples, naturally, on account of its frequency. With lichen planus it has often been noted. Lymphatic swellings have been mentioned by Epstein (5), Katzenstein (20), myself, and others. I have referred to chorea. Without giving an explanation for it, I might say that in a large number of cases of dermatitis herpetiformis, which I as a rule treat by arsenic, I have never observed a consequent zoster.

In regard to other effects of arsenic upon the skin, I might

quote Brouardel (21), who describes the various forms of arsenical eruptions and mentions eleven different manifestations: 1st, erythema; 2d, papular exanthema and urticaria; 3d, purpura; 4th, vesicular herpetic and zosteroid eruptions; 5th, bullous eruptions; 6th, pustular and ulcerative lesions; 7th, melanosis; 8th, keratosis; 9th, œdema and hyperidrosis; 10th, alopecia and trophic disturbances of the nails; and 11th, carcinoma.

In regard to two of these forms which have for some time been of considerable interest to dermatologists, I might say that keratosis and epithelioma are, in my experience, the result of long-continued medication, while zoster occurs after comparatively shorter periods. It has taken a long time and many observations to finally convince some obstinate clinicians of the existence of genuine arsenical keratosis and of arsenical epitheliomata. To-day there are probably few doubters on these points. In a similar way I trust that the existence of true arsenical zoster will soon be universally admitted.

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Discussion

DR. M. B. HARTZELL, of Philadelphia, called attention to the fact that, considering the large number of cases in which arsenic was administered, only a small proportion developed zoster. In the case of hemorrhagic sarcoma which he had reported a few days ago a very painful thoracic zoster developed. In that case the zoster developed about three months after the beginning of the arsenic treatment, the drug having been given in the usual doses. The development of this form of eruption, Dr. Hartzell said, was apparently dependent not so much on dosage as it was on the duration of the administration of the drug.

DR. JOSEPH GRINDON, of St. Louis, said that before we could answer Dr. Zeisler's question whether zoster arsenicalis was true zoster we first had to decide what true zoster was. That depended on how we tried to establish it, whether on a clinical, etiological, or pathological basis. Clinically, zoster arsenicalis was much the same as true zoster. Etiologically, we could recognize several forms of zoster, but the true zoster as taught by Erb was a zymotic and probably a contagious disease. Again, there was a class of zosteriform eruptions due to a variety of causes; we also had the toxic cases, such as those due to arsenic.

If we chose to limit the term zoster to the true zymotic disease, then zoster arsenicalis was not true zoster. Clinically, again, we had different forms. We knew that the recurrent forms did not generally follow the perfect clinical type which we saw in true zoster, and they should be classed under an entirely different head. In other cases, intermediate between zoster and simple herpes, the lesions recurred on exactly the same spot; he should call them cases of repeating herpes rather than recurrent zoster. These cases resembled simple herpes in that the lesions recurred

on the same site, but they differed from simple herpes in avoiding the muco-cutaneous orifices, by oftentimes being followed by scarring and by being preceded by neuralgic pains. These cases corresponded closely with the *hépès génital névralgique* of Mauriac, but differed from it in that the lesions did not necessarily occur in the distribution of the genital or pudic nerves.

Dr. Grindon said that clinically the *zoster arsenicalis* he had seen had been quite the same in appearance as any other zoster—as true typical zoster—and yet it certainly would not be strange if it differed somewhat from true zoster, inasmuch as we recognized a variety of dermatoses after the administration of arsenic. The cases he had seen, however, had the typical appearance of true zoster, and he only regarded them as due to the arsenic because there was a history of the administration of that drug. Their presence could scarcely be regarded as a mere coincidence.

Inasmuch as Dr. Zeisler spoke of certain other arsenical dermatoses, Dr. Grindon said he wished to refer to a case which recently came under his observation. It was one of dermatitis herpetiformis in which large doses of arsenic had been administered for long periods of time. The patient took the drug on his own responsibility and finally got up an arsenical neuritis and a very pronounced arsenical pigmentation. The case was pronounced by very competent physicians as one of syphilis, they basing their opinion on the nerve symptoms, the pigmentation, and the lesions of dermatitis herpetiformis. As a matter of fact, it was not luetic. Instead of a keratosis of the palms and soles there was marked atrophy, like the idiopathic atrophy of the skin we sometimes saw affecting the palms and soles, especially the latter, so that the skin hung down in folds and wrinkles.

PROF. ERICH HOFFMANN, Berlin, bemerkte, er habe auch eine Reihe von Fällen von *Zoster arsenicalis* bei Patienten gehabt, die längere Zeit an Lichen ruber oder Psoriasis behandelt worden waren. Der *Zoster* trat, wenn er mit einiger Sicherheit mit der Arsenmedikation in Verbindung gebracht werden konnte, sowohl bezüglich der Extensität wie der Intensität der Erkrankung in seinen Fällen abortiv auf; die Bläschen zeigten nie makroskopisch bemerkbare Nekrose und hinterliessen auch keine Narben.

Über so intensive und ausgedehnte Fälle von "*Arsen zoster*," wie sie Dr. Zeisler beschreibt, habe er keine eigenen Erfahrungen.

Was die Pathogenese der *Arsen zoster*s betreffe, so glaube er, dass hier zweifellos eine direkte Einwirkung auf die Nerven an-

genommen werden müsse, und er habe diese Fälle gewöhnlich bei in Bezug auf ihr Allgemeinbefinden sehr gesunden, ja robusten Personen gesehen, die kein andres Symptom der Arsenintoxikation darboten. Es handele sich hier also um eine lokalisierte Erkrankung und um eine rein örtliche Empfindlichkeit gegen Arsen. Man könnte diese Frage für Arsen, Kohlenoxyd, bakterielle Toxine u. s. w. experimentell prüfen, wenn man diese Substanzen auf das freigelegte Ganglion intervertebrale z. B. von Schweinen oder Affen einige Zeit einwirken liesse und auf etwaige Folgeerscheinungen in dem zugehörigen Haut Gebiet beobachtete. Er habe vor Jahren diese Experimente in Aussicht genommen, jedoch noch keine Zeit gefunden sie auszuführen.

DR. LUDWIG GEYER, Zwickau, fand den Zoster arsenicalis nicht in dem Sinne auf, dass man unter ihm als pathologisch-anatomische Einheit verstehen müsse wie unter dem echten Herpes zoster, der eine vorübergehende Erkrankung der zum Hautbezirke gehörenden Ganglienzellen vorstellt. Die Arsenintoxikation äussere sich in ihren wesentlichsten Partien durch Veränderungen innerer Organe, die zu Ascites, Pleuritis, Pericarditis u. dergl. führen. Die Todesfälle an Arsenicismus träten meist aus diesen Ursachen auf. Hieraus könne man vielleicht den Schluss ziehen, dass auch die Hauteruptionen, welche ja selten in form typischer Herpes zosteren auftreten, meist abortiv seien und ebenso in bullöser und erythematöser Form vorkommen, nur als ein Ausdruck einer tiefergehenden Allgemeinwirkung des Arsens aufzufassen seien. Diese Anschauung von der Arsenikwirkung fordere uns auch zu grösserer Vorsicht in der Anwendung der Arsens bei durch andere Krankheiten Geschwächten auf.

DR. JAMES NEVINS HYDE, of Chicago, said that like many of his colleagues he had been on the lookout for many years for a case of symmetrical zoster. A few years ago, a patient was introduced to his clinic diagnosed by his assistant as one of symmetrical zoster. On the right side of the body there was a typical patch of zoster, the lesions being quite characteristic in size, contents, area, and distribution along the intercostal space. On the left side of the body, at the same time, there was an odd-looking vesicular eruption. Upon inquiry it was learned that the patient had been taking arsenic. On the right side were typical vesicles which had been described in the discussion as "true zoster"; on the left side, the lesions were distributed more irregularly, they were

less distended with serum than the vesicles on the opposite side, and the areola was less marked. The speaker said he therefore regarded it not as a case of symmetrical zoster, but as one in which there was a typical zoster on the right and an arsenical dermatitis on the left side.

DR. C. F. JAPPE, of Davenport, said he wished to refer to a few cases, in which the cart, so to speak, was turned around. These cases were in old people who developed an intercostal neuralgia following an eruption of zoster. Those patients were put on increasing doses of arsenic, and he was glad to report that they promptly got well.

DR. JOSEPH ZEISLER, in closing the discussion, said that the abortive zoster would never have given him an excuse for this communication; they were too well known. The eleven cases reported in his paper were full-fledged, clinically typical examples of true zoster.

STUDIES IN THE METABOLISM OF CERTAIN SKIN DISORDERS

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This work was undertaken in the hope of demonstrating, first, a connection between disordered metabolism and a number of inflammatory dermatoses by means of evidence deduced from urine examination and, second, of finding some rational means by which relapses in those inflammations could be controlled.

A preliminary communication ¹ relating to auto-intoxication in bullous eruptions alone was presented to the British Medical Association in 1906. Since then, a wider line of investigation with improved methods has been followed into other classes, erythemas and parakeratoses, the character of whose inflammatory exudate allies them to the bullous diseases. These three groups by no means exhaust the field where the method of research adopted affords promise, but suitable opportunity

for the study of such conditions as purpura, pemphigus, pompholyx, and dermatitis exfoliativa has not presented itself.

We have attached greatest importance to the results of the study of urinary nitrogenous compounds following numerous suggestions contained in recent literature. We shall present first, in order that there may be a standard for comparison with disease, a consideration of the nitrogen partition of normal metabolism and the significance of the compounds composing it.

THE NITROGEN PARTITION OF NORMAL METABOLISM

The table given below has been condensed from the one compiled by Ewing and Wolf² from Folin's figures based upon repeated examinations of the urine of healthy persons. Each of the percentages represents the results of urine examination of ten individuals for the space of three days—that is, of thirty twenty-four-hour specimens—and may be regarded as correct for all purposes of comparison.

Total N. Grams.	Urea N. % T. N.	Ammonia N. % T. N.	Uric Acid N. % T. N.	Kreatinin N. % T. N.	Rest N. % T. N.
3	63.6	12.1	3.0	15.5	8.7
7	78.6	5.5	2.3	8.4	6.6
11	83.0	3.3	1.3	4.6	7.7
15	87.0	3.3	1.2	4.1	4.7

The striking differences between the percentages in low and high total nitrogen output renders it necessary to keep the table in mind in order to interpret nitrogen ratios in disease. The divergence is probably due to the close approximation to constancy of total amount for the individual excreted in health of all the constituents except urea. The importance of these figures and of a thorough understanding of them is illustrated by this example: ten per cent. of rest nitrogen is high for a urine containing thirteen grams of nitrogen, while it would be hardly remarkable for three grams. Any wide variation from these standards may be regarded as evidence of disturbance worthy of attention. (For eliminations intermediate between the figures of the table the reader

is referred to Ewing and Wolf's² article, or he may take the mean of those given without fear of important error.)

SIGNIFICANCE OF CHANGES IN THE NITROGEN PARTITION AND
OF THE PRESENCE IN DISEASE OF CERTAIN COMPOUNDS
NOT CONSTITUENTS OF NORMAL URINE

Consideration of the origin of the urinary compounds which figure in our reports may seem a little trite at this late day, but it can do no harm to refresh the memory of the casual reader. Deviations from the normal while still under discussion are susceptible of fairly reasonable interpretation as a result of recent investigation.

Urea results from the synthesis in the liver of ammonia and the amino acids, basically, according to Hofmeister,⁸ an oxidative process. Failure in the urea-forming function, therefore, indicates a condition of suboxidation. Other investigators claim that proteid metabolism involves other processes such as hydrolysis and dehydration, and hold that the theory of deficient oxidation contains only a part of the truth. Ewing and Wolf¹⁰ prefer to call this failure to remove the amino group and convert it into urea and ammonia deficient desamidation. Low urea may result from a non-nitrogenous diet and in itself does not indicate deficient metabolic capacity. It must be associated with an increased percentage of ammonia or rest nitrogen or with both in order that no doubt of the failure of the synthetizing process may exist.

The rest or undetermined nitrogen fraction consists principally of amino acids, but contains also peptone, albumose, and the xanthin compounds. Under ordinary conditions, amino acids are largely removed by lytic or synthetic processes; their presence in increased ratio is an indication of a deficient desamidation. Kreatinin, according to Folin,⁶ is an index of endogenous metabolism, the result of the breaking down of the tissues. Uric acid is supposed to indicate in the same way the eliminable end product of purin metabolism.

Aside from the compounds constituting the nitrogen partition, there are others not present or present only in small quantity in normal urine which figure here. In the first

class are kreatin and the acetone compounds; in the second, indican. Their determination is an essential part of studies in metabolism. Indican is very well known as the product of oxidation of indol and a symptom in the urine of intestinal putrefaction. The acetone compounds, acetone, diacetic acid, and *B*-oxybutyric acid occur in the urine of diabetics, in starvation, and in conditions of enforced abstention from food as in persistent vomiting, and in anæsthesia, and are regarded as unoxidized by-products of the consumption of fat. Kreatin is a urinary abnormality whose origin and significance are still uncertain.

METHODS EMPLOYED, CONTROLS, AND SOURCES OF ERROR

The analyses were done in the Laboratories of Chemistry, Experimental Pathology, and Clinical Pathology, of Cornell University Medical College, chiefly in the last. We are especially indebted to Dr. T. W. Hastings, Prof. of Clinical Pathology, for extending to us the privileges of his laboratory. Kjeldahl's was the method used for the determination of total nitrogen; Folin's for urea,³ ammonia,⁴ uric acid,⁵ kreatinin and kreatin.⁶ Walter Hall's purinometer was used in the Clinical Laboratory. Control by examination of the urine of healthy persons is no longer necessary since Folin³ presented the results of his elaborate investigations. We have naturally selected the groups of dermatoses which promised results, but the individual cases were used as they occurred in dispensary or private practice, depending only on the patient's willingness to co-operate. Certain cases of pruritus, ichthyosis, and dermatitis hiemalis have served in a sense as controls, for they have given us no results although they might be expected to do so. We have omitted these reports except in one instance of pityriasis erythroderma to save space. Analyses done in the interval between attacks will be found in many of the tables.

The total urinary nitrogen varies with the weight of the individual, his habits, and the amount of proteid intake, but the error here is eliminated by comparison of the ratios with those of a normal person for the same total output. Since

reliance can be placed solely on variations in the relative proportions of nitrogen constituents for a given total, in deciding a question of disturbed metabolism we have not felt it necessary to weigh the food taken as a routine measure. It was done in three cases (XI, XII, and XXI). In case XI every particle of food and drink taken daily was weighed for a period of three months—in case XII for one month at beginning of treatment. In general, patients have been placed on a restricted purin diet and directed to consume as nearly as possible the same amounts of the same foods on the day preceding and on that in which the twenty-four-hour specimen was collected. Ammoniacal fermentation was excluded by adding chloroform to the first portion passed and shaking the bottle with each succeeding addition. The specimens consisted in almost every instance of the total urine passed in twenty-four hours. We have followed the cases through their phases whenever possible and desirable; single examinations were done to demonstrate a particular point.

Urinary changes are identical or nearly so in metabolism altered by bacterial invasion (pneumonia) and by changes originating within the body (toxemia of pregnancy). Our cases are sufficiently removed from the possibility of bacterial origin to relieve us of the necessity of blood-culture experiments. In the single case of erythema multiforme, the absence of leucocytosis precluded the likelihood of the presence of this causative factor. We have had no opportunity to study purpura or pemphigus in which blood culture would be imperative.

Error in the making of chemical tests is possible, to say nothing of the calculations involved. It is not likely to be very great, in view of the pains taken. Rest nitrogen ratios are liable to slight error, particularly in females from the presence of inflammation in the genito-urinary tract and consequent addition of albuminous compounds to its quota, but here again the percentage will not be markedly affected. In all cases where albumen was found in distinct quantity it was removed before the nitrogen partition was done.

REVIEW OF THE ANALYSES IN THESE CASES

The thesis we have undertaken is susceptible of proof most easily, perhaps only by the results of urine examination measured by the standards of normal metabolism. Variation in specific gravity or in the total weight of any solid constituent or constituents is too readily produced by many factors to be of any service in determining the presence of disordered metabolism. In order to stamp a urine analysis as showing such a state, it must exhibit one or all of three characteristics: (1) the presence of compounds not found in normal urine, such as albumen, the acetone compounds, and kreatin; (2) the occurrence in increased quantity of substances like indican which ordinarily appears in small amount, and (3) variations in the proportions of normal constituents wide enough to be recognized as departures from the standard.

A small amount of albumen, rarely more than a trace and generally of serum or nucleo-albumen, was found in eight of the twenty-one cases. It occurred in erythema multiforme as part of an acute nephritis; generally it appeared in connection with chronic diseases, in one case of chronic urticaria, in two of five examples of dermatitis herpetiformis, in one of three prurigos, in two acute (one nephritic) and one chronic eczema among seven. Its presence may be accounted for in certain cases by inflammatory exudate from the urogenital mucosa. When the cases were followed, it disappeared under treatment, although it persisted in one case for a year and a half through all the fluctuations. Acute relapse in the skin seemed not to affect the amount present. In two cases (I and XIV) where albuminuria reached the grade of nephritis, the renal change had no apparent effect on the nitrogen partition.

We do not attach the importance to indicanuria to which other observers seem inclined. It occurs in patients with bullous eruption quite constantly, particularly dermatitis herpetiformis, as Engman⁹ has pointed out. The quantity, too, is generally considerable, but it may be absent, as in Case VI, at the height of an attack. The irregularity of its behavior is illustrated in the prurigo patients. In two cases it was found in quantity. In one of them it had never disappeared

in spite of diet and medication; in the third it was absent in the beginning, to appear later coincidentally with the disappearance of the albumen. The urine of chronic urticaria and rosacea with gastro-intestinal disease and flatulence failed to show it. Acute attacks of urticaria and eczema are generally marked by indicanuria, but it is often absent in subacute and chronic cases. The amount rarely rises so high in eczema and urticaria as in the bullous group. Eruptions do not necessarily improve with its disappearance and may resolve partially or wholly while it continues. In Case XI, whose body was covered with prurigo, its appearance was delayed until six months after treatment was begun. No nephritis was discovered in the individuals in whom it continued longest and occurred in greatest amount.

In consideration of these facts, we are inclined to attribute slight, certainly not etiological, importance to indican, although there can be no reasonable doubt that circulating, unoxidized indol may contribute materially to a general intoxication. (Excessive amounts of indican are indicated in the reports by a single or double plus sign.)

The acetone compounds were not found in these examinations. Kreatin was discovered once in the urine of an old man with scrotal eczema; it disappeared before the next report although the disease had spread extensively.

The suggestion was offered in the preliminary report referred to that the most striking variations in the ratios of the nitrogen partition may be expected in the prodromal stage of an acute attack. That point has been demonstrated convincingly, we think, by these reports, not only in bullous disease but in erythematous and scaling disorders and in the first few days of eruption as well as in the prodromal period. In general, the economy soon accommodates itself to the disturbance and the evidences of it disappear from the urine. At times, however, particularly when the rules of diet are not rigidly observed, the derangement persists.

Relapse in the course of chronic disease shows exactly the same changes in the partition. In chronic disease without exacerbation, the urine may show no radical divergence from what obtains in healthy persons (Cases IV, VI, XVI, and XVII),

even when the eruption is at its height, covers large areas, and has existed for some time. This rule has notable exceptions in cases pursuing an uneventful course (XI and XVIII). Typically chronic inflammations, seborrhœic eczema, erythrodermie pityriasique, and psoriasis exhibit normal partitions in spite of violent attacks of indigestion.

The disorder of metabolism shown in our cases almost invariably is failure of urea synthesis or defective desamidation, consisting in a decided drop in the urea, with a corresponding rise in the rest nitrogen percentage, or in the latter alone. In the prodromal period of eczema rest N. reached 11.9%, in dermatitis herpetiformis 11.4%, in prurigo 16.6%, in urticaria 16.5%; corresponding figures for urea being 80%, 73.6%, 71.2%, and 71%. In Case V before relapse the urea percentage was 61.9, rest 25.6 for a total N. output of 9.46 grms. The figures correspond closely in the prodromal and onset stage of a first attack, after complete remission, and in relapse during the course of chronic disease. Case XIII (beginning eczema) showed high undetermined N. 11.9%, with normal urea 80.2%, total nitrogen 8.72 grms. The same condition occurred in prurigo. The greatest variation observed was in Case XI before active treatment was begun; urea 60.7%, rest 28.1%, total N. 8.44 grms. Besides this instance, moderately high rest N. was found in chronic dermatitis herpetiformis and eczema (Cases VII and XVIII). Very low rest N. ratios in prurigo and erythrodermie, 0.3% and 0.4%, may be the result of error in analysis. They have not, so far as we know, been seen before. The determinations were made in periods of remission in the prurigos when full doses of thyroid were being given.

An increase of ammonia N. was sometimes associated with low urea and high rest N. but its behavior is uncertain. It may remain low with accompanying evidence of deficient desamidation, or it may increase, as in Case XI, as relapse subsides and the partition is returning to normal.

Kreatinin was increased in amount and percentage in psoriasis associated with gastro-enteritis, in the prodromal period of eczema dependent on extensive visceral lesions (Case XIV) and at the onset of dermatitis herpetiformis. Its highest percentage, 9.7, occurred with suspiciously low rest N.

in prurigo. In the remainder of the cases, the change is too slight to be worthy of notice. Uric acid N. varies little either in acute or chronic disease.

If the changes in the nitrogen partition form a reliable indication of metabolic disturbance, the state of affairs met with in Case XV requires explanation. The patient was a robust girl of ten, subject to recurrences of eczema of a sub-acute type. During a period of seven days preceding and following operation under ether anæsthesia for adenoids her rest N. rose from 5.1% to 20.9%, while urea sank from 88.4% to 70.2%. She was in bed and on a fluid diet at the time. No eruption appeared and recovery was uninterrupted. The only reasonable explanation is that, although the disturbance of metabolism was present, the usual toxins failed of elaboration or, being elaborated, failed of their usual effect as in the exanthems and recurrent erythemas without skin lesion.

EFFECT OF TREATMENT ON THE NITROGEN RATIOS IN DISORDERED METABOLISM

Observations in this connection are vitiated by the gradual return to normal after the stage of onset which occurs in most cases—though not by any means in all—under natural conditions. We have found occasionally that derangement persisted during elimination treatment when diet rules were not observed (in Cases V and VII).

Two points developed during medication which if confirmed are the most important we have to record. Seeing the result in Case V of indulgence in excessive meat-eating, we induced Cases X and XII to increase their proteid food to rather large quantities twice a day. In both instances, after a lapse of ten and in the second of thirteen days, the experiment was followed by eruption which was preceded by a rapid increase in rest N. percentage. The conjunction of the two symptoms seems rather convincing. The urea percentage showed little change.

In the second place, under injections of extract of autolyzed whole sheep thyroid, in Cases XI and XII, the same phenomenon occurred, but to a greater degree. In Case XI the

high figures were total N. 13.77 grms, urea N. 71%, rest N. 16.5%. The urine change here was unaccompanied by eruption, but there can be scarcely any doubt of the connection since the same process was repeated when injections were renewed after a period of withdrawal of them. The partition always returned to normal while they were continued.

BLOOD CHANGES

Importance attaches to blood examination in bullous and scaling eruptions because it may give in relapse a fairly reliable indication of impending outbreak. Eosinophilia was exhibited to a marked degree among bullous eruptions. In one case of prurigo it receded under treatment from 21% to 2.6%. It begins at the time of the other prodromal symptoms, four or five days before eruption. We have not recorded the few estimations made, but lymphocytosis occurs in acute scaling disorders in much the same way. Both fall to normal when improvement becomes pronounced, often before eruption disappears.

SIGNIFICANCE OF THE DISORDERS IN URINE AND BLOOD AND THEIR RELATIONSHIP TO CUTANEOUS DISEASE

With the exception of indican and perhaps certain amino acids contained in the undetermined nitrogen, it can not be said that any of the urinary compounds figuring in these reports are themselves toxic, certainly not in any quantity in which they occur in the body. Still less are any of them, including the two exceptions, likely to be specific in the causation of any member of the three groups. For example, indicanuria or increase in rest nitrogen, occurring often unassociated with skin lesions and indifferently with all the types of inflammation included here, can hardly stand in direct etiological connection or in fact do no more than contribute to general depression.

Taking into consideration the facts that disturbance in the nitrogen partition is most common and conspicuous in the prodromal period, that it is associated with other symptoms

generally recognized as those of intoxication, and that the figures return to the individual normal as improvement goes on, the conclusion seems justified that this change and the skin lesions are related in being effects of the same cause. What the actual exciting agent or agents may be in the production of the primary error of metabolism or of their effect on the skin there is no way at present of finding out. When once a state of intoxication is established it is not unlikely that by-products eliminable through the kidneys ordinarily without injury may add to the poisoning of already altered tissues.

A suggestion may be offered as to the point of departure in these intoxications. We have been struck by the evidence of slight change in nitrogen ratios in cases of severe disease referable to failure in primary digestion (Cases IV and XXI) and the wide variations in those in whom no such disorder could be discovered. These observations and the marked effect of thyroid medication in bullous disease apparently point to the intermediary metabolism as the primary seat of disturbance.

Eosinophilia and lymphocytosis in their respective groups must be regarded with skin lesions and urine changes as part of the symptom-complex, additional evidence of systemic poisoning, their regression synchronizing with abatement of other symptoms.

The uniformity of the character of the change in nitrogen ratios in all three groups suggests that their pathogenesis is the same and that the lesional type of an outbreak is an expression of idiosyncrasy (*e.g.*, the multiformity of quinin rashes) or of a specificity in the toxic agent. The individual as a general rule shows the same eruptive type throughout his relapses; but it is a matter of common observation that types approximate closely and even merge into one another. Papular urticaria may become frank prurigo in time; prurigo in regression exhibit grouped vesiculation; an acute eczema subside into inveterate psoriasis. With successive relapses of bullous dermatitis herpetiformis, as severity lessens under treatment, the lesion reaches the grade of erythema only. These considerations, particularly the various eruptions produced by over-

feeding with proteids, seem to warrant the deduction that the differences between the members of the three groups are those of degree, cutaneous expression of the intoxication being determined by personal reaction and to some degree by local irritative factors. It may become possible in time to change the character of the eruption by therapeutic measures.

TREATMENT

Therapeutics suggested by this work do not differ essentially from the line followed for generations in handling most of the members of these groups. Regulation of diet, always of first importance, should take the form, except in cases dependent on gastric hyperacidity, of limitation of proteid intake, to the point of total prohibition for a time in acute cases. In practice, individuals accustomed to a full meat diet do not accommodate themselves for any considerable period to a regimen of fats and carbohydrates alone, but, as Chittenden has pointed out, they can do well on much less than appetite suggests to the average American. They should reconcile themselves to a permanent restriction in this regard. Green fruits and vegetables are pointedly indicated. Medication in the erythemas and scaling disorders takes the form of elimination alone by the intestine, kidneys, and skin. Diaphoresis is obviously contra-indicated in acute eczema; otherwise it seems universally applicable and is better secured by the hot air cabinet than by pilocarpin. Saline cathartics with occasional doses of mercurials give better results in intestinal putrefaction than antiseptics and are sufficient aids in excretion. (In Case XVIII an overdose of hydrarg. cum creta permanently removed an intertrigenous eczema of years' standing.) Elimination by the kidneys may need no further aid than quantities (three quarts daily) of non-aërated water, but saline diuretics were generally resorted to in addition.

These with appropriate local measures are generally sufficient in the scaling group and acute urticaria. Relapses, even of dermatitis herpetiformis, have been aborted in a few days by vigorous eliminative treatment along these lines. The chance is greatly improved by taking the attack in the

prodromal period, whose threatening onset the patient learns soon enough to recognize. It was found, however, in prurigo and the general run of dermatitis herpetiformis that treatment by diet and elimination carried the patient only to a certain point, no matter how energetically pursued. We began then with thyroid administration in prurigo in the hope of controlling to some extent the intermediary proteid reactions. These cases after the preliminary period of intoxication was over improved under tri-weekly or daily injections of 2 to 5 cc. of aqueous extract of the autolyzed whole sheep gland. We now use, except in emergency as in the beginning of a relapse in either disease or the exhibition of a tendency to stand still, the nucleo-proteids of the thyroid, gr. $\frac{1}{10}$ in milk sugar once, twice, or three times a day. Both the extract and the nucleo-proteids are prepared by Dr. S. P. Beebe of the Loomis Laboratory. The objections to the use of the extract are those of all hypodermatic medications—a local reaction at times pronounced and an occasional general intoxication lasting for a day or two and due to the presence in the injection of poisonous products of autolysis. Nucleo-proteids by the mouth, a little less efficacious, are non-toxic. (One patient on her own initiative took gr. $\frac{1}{10}$ daily without symptoms.) Indications for increasing or lowering the dose are obtained from the progress of the skin lesions and the condition of the pulse. When hard or high-tension pulses generally present in chronic cases become soft, the dose is sufficient.

Thyroid medication is not useful in the treatment of chronic urticaria. In general or local idiopathic pruritus in certain cases it does influence the disease favorably but only after a long period of administration. Arsenic in dermatitis herpetiformis exercises some control over both eruption and nitrogen metabolism.

GROUP I

ERYTHEMA URTICARIA

CASE I.—*Diagnosis:* Erythema multiforme gyratum.

History of Present Illness: Eruption appeared about Jan. 1, 1907, on legs and patches have appeared daily on trunk, neck,

and extremities. Face free. Had headache and feverish feelings at onset, no chill, bowels regular.

Present Condition: Well nourished, mucous membranes good color, tongue coated. General lymphadenitis. Heart, lungs, and liver negative. Temperature $100\frac{3}{8}^{\circ}$ F. Pulse 118, good volume and tension. Fauces red and congested, redness not gyrate, no ulceration. Spleen distinctly palpable below costal margin. Skin, extensive erythematous eruption on trunk, neck, and extremities. Eruption consists of separate rings; of lesions where different rings have joined and edges have disappeared so forming erythema gyratum. In other places erythema iris type is seen.

Blood Examination: Jan. 8, 1907, Hb. 100%. Red blood cells, 4,800,000. White blood cells, 10,000. Red cells, normal. Parasites, none found.

Differential count of 300 white cells:

Polynuclears	81.0%
Lymphocytes	10.0%
Large mononuclears	1.6%
Transitionals	7.0%
Eosinophiles	0.4%
Mast cells	0%
Myelocytes	0%

Referred to Bellevue Hospital for treatment.

We were kindly allowed to make the following notes from the history kept in Bellevue Hospital:

Jan. 8th. T. varied from 102° F. to 101° F. Pulse from 90-100. Treatment: calomel, sod. bicarb., at night. Sal. Rochelle in morning. Milk diet.

Jan. 9th. T. 101° - 103° . Pulse 92-120. Treatment: Acid salicyl., sod. bicarb., four times daily.

Jan. 10th. T. 101° - $102\frac{4}{8}^{\circ}$. Pulse 100-104. Patient feeling comfortable, sleeping well. Rash fading.

Jan. 11th. T. $102\frac{4}{8}^{\circ}$ in A.M. Pulse 96. $101\frac{8}{8}^{\circ}$ in P.M. Pulse 100. Doing well—treatment continued.

Jan. 12th. T. $102\frac{1}{8}^{\circ}$ in A.M. Pulse 90. T. 101° in P.M. Pulse 102. Treatment: sod. bicarb., salol, ol. ricini, four times daily.

Jan. 15th. Patient has steadily improved, but left hospital to-day before complete cure, against advice.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone bodies.	Indican.	T.N. Grms.	Urea N.	NH ₃ -N.	U.A.-N.	Kreatinin-N.	Rest-N.	Micros. Ex.
									Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	
1907 Jan. 20	860	1.025	acid	++	o	o	++	13.48	12.34 91.6	0.37 2.8	0.08 0.6	0.51 3.8	0.13 1.0	Hyaline and granular casts, Hyaline casts.
Jan. 22	1180	1.019	acid	+	o	o	o	16.5	14.5 88.0	0.77 4.7	0.14 0.9	0.69 4.2	0.31 1.9	

N. B. Albumen removed before N.-partition was done.

CASE II.—*Diagnosis*: Acute urticaria.

Duration: two days. Face and anal region especially affected. Appetite and digestion good. Bowels regular. Nothing particularly noteworthy in the eruption.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone bodies.	Indican.	T.N. Grms.	Urea N.	NH ₃ -N.	U.A.-N.	Kreatinin-N.	Rest-N.	Micros. Ex.
									Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	
1907 May 5	1840	1.008	acid	o	o	o	++	9.89	7.1 71.8	0.51 5.2	0.35 3.6	0.26 2.7	1.63 16.5	Squamous cells.

CASE III.—*Diagnosis*: Chronic urticaria.

Duration of Disease: three weeks. Male. Patient is great eater of salted food, pickles and meat, and drinks a great deal of beer. Appetite and digestion good. Bowels regular. Constantly recurring outbreaks. The urine examination, done before treatment was begun, shows only a slight increase in the rest-nitrogen percentage.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone bodies.	Indican.	T.N. Grms.	Urea N.	NH ₃ -N.	U.A.-N.	Kreatinin-N.	Rest-N.	Micros. Ex.
									Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	
1907 Mar. 28	1800	1.014	acid	o	o	o	++	16.02	12.92 80.7	0.8 5.0	0.3 1.9	0.64 4.0	1.29 8.1	Squamous cells.

CASE IV.—*Diagnosis*: Chronic urticaria. Remains of old lichen circinatus.

Man, aged fifty. Leads an active life; no bad habits. Present illness dates from May, 1906, when he had an attack of "ptomaine poisoning" from spoiled chicken. Has never been free of urticaria except for short intervals since. He is neurasthenic with poor peripheral circulation, high tension pulse and headaches. Small eater, but eats very irregularly. Digestion poor, sensation

of fullness coming on shortly after eating, bowels irregular, tongue coated, flatulence marked. Area of hepatic dulness extends from sixth interspace to below border of ribs. Skin very dry, never sweats even in Turkish bath.

The amount of eruption varied during the day and was commonly worse late in the afternoon and after eating. The face, shoulders, upper arms, flanks, and thighs were generally attacked. The lesions ranged in type from large areas of angioneurotic oedema to small papules and patches of erythema, but all of them itched furiously.

After a thorough trial of eliminative measures including pilocarpin and restriction of diet without success, daily injections of Beebe's extract of the whole thyroid were begun, an initial small dose increased to two ccm. per diem. Pulse became soft and there was for a time comparatively little itching, good sleep ensuing. The injections were continued for seventeen days and then abandoned because they seemed to exert no permanent beneficial influence. On one occasion an induration was left at the site of injection, there was pain in bones, joints, and head. These symptoms passed off in twenty hours. After an ineffectual trial of calcium lactate, intestinal antiseptics and astringents were given with good effect. The primary seat of the disturbance would seem to be in the intestinal tract, not in the intermediary metabolism as was at first supposed.

The urine, we regret to state, was not taken during the thyroid administration because the patient refused to collect it. The specimen examined shows no pathological variation in the nitrogen partition. Treatment by diet and intestinal antiseptics had been undertaken a month previous to the examination.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.		U.A.-N.		Kreatinin-N		Rest-N.		Remarks.	
								Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.		
1907 Feb. 13	645		acid	trace	o	o	trace	10.10	8.18	0.54	0.13	0.46	0.79				Taken before beginning thyroid injections.
									81.0	5.3	1.3	4.5	7.8				

GROUP II

BULLOUS DISEASES

CASE V.—*Diagnosis*: Dermatitis Herpetiformis.

Past History: Erysipelas twelve years ago. Gonorrhœa three

times. Alcohol, tobacco, tea, and coffee used moderately. Never any eruption on body before present illness started. No headaches, malaria, or rheumatism. Appetite and digestion good. Bowels regular.

History of Present Illness: In past year has been subject at irregular intervals to recurring attacks of water blisters seated on reddened base, preceded and accompanied by severe burning and itching. The patches have come out here and there over the body, so that he has never been entirely free from disease since it started.

Present Condition: Rather poorly nourished, mucous membranes a little pale, tongue clean. Pulse 78, regular, normal volume and tension. Heart, lungs, liver, spleen, and abdomen negative. Skin: Eruption is seen on dorsal surfaces of hands, front of neck, over shoulders and scapulæ, over sacrum, anterior surfaces of thighs and legs, and inner aspect of knees. The eruption is polymorphous, consisting in places of erythematous patches, in others of grouped vesicles on erythematous base, and here and there a few bean-sized bullæ, especially on the forearms. In some places where the eruption is older the vesicles have broken, leaving reddened and infiltrated patches and in still other places pigmentation.

Blood: Hb., 80%. Red blood cells, 7,376,000. Index, 0.54. White blood cells, 14,000. Red cells, normal. Parasites, none found. Blood plates, moderate number.

Differential count of 300 white cells:

Polynuclears	74.6%
Lymphocytes	13.4%
Large mononuclears	6.4%
Transitionals	0.4%
Eosinophiles	2.6%
Mast cells	2.6%
Myelocytes	0%

Patient consented to bring twenty-four hour specimen of urine for examination before any medication was given and without making any change in his mode of living, diet, etc. The results of the examinations of these specimens follow as given in table.

Sept. 13, 1906. Eruption practically unchanged.

Calamin and zinc locally. Restriction of proteid diet.

Sod. phosphat. 3 i. every morning.

℞ Sod. salicyl. gr. x.

Pulv. rhei. gr. ii.

Sod. bicarb. gr. v.

Aquæ 3 i. t. i. d.

Sept. 17, 1906. Old lesions drying up and disappearing, practically nothing new has appeared. Treatment continued.

Sept. 20, 1906. Improving. Treatment continued.

Sept. 24, 1906. Quite extensive acute erythematous-vesicular eruption on the scrotum—by a fortunate coincidence patient was collecting a twenty-four hour specimen of urine just at time this new eruption was developing (*v.* table). Attention may be called to the very marked rise in the Rest N. both relatively and absolutely. From this time on, patient steadily improved, having no new outbreaks and skin being clear when last seen, Nov. 26, 1906. Treatment as outlined above was continued throughout.

Two more analyses of urine were made in this period. It may be noted that both before and after the acute outbreak of Sept. 24th the Rest N. was persistently at or above the normal high limit for the total nitrogen excreted.

Aug. 21, 1907. Patient was not seen again till this date when he came in response to a note sent him. He reports that since his last visit he had recurring attacks in above localities almost every day. About two months ago he started taking arsenic and since that time he has had no new outbreaks. Appetite, digestion, and bowels normal. Skin is clear except for slight scaling, thickening, and pigmentation at site of previous eruptions. The urine was examined three times and it will be noted that the partition had returned to within the normal limits.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N. Grms. % T.N.	NH ₃ -N. Grms. % T.N.	U.A.-N. Grms. % T.N.	Kreatinin-N. Grms. % T.N.	Rest-N. Grms. % T.N.	Micros. Ex. & Remarks.
1906 Sept. 6	650	1.028	acid	o	o	o	++	7.91	6.15 77.9	0.28 3.6	0.11 1.5	0.47 6.0	0.84 10.7	Few squamous cells.
Sept. 10	1210	1.028	acid	o	o	o	++	12.36	9.62 77.9	0.69 5.6	0.30 2.5	0.59 4.8	1.10 8.9	
Sept. 13	1340	1.023	acid	o	o	o	++	12.27	9.59 78.2	0.55 4.5	0.25 2.1	0.69 5.7	1.11 9.1	Do.
Sept. 24	960	1.022	acid	o	o	o	++	9.46	5.85 61.9	0.17 5.7	1.9 1.9	0.50 5.30	2.4 25.6	Do. Cf. history
Oct. 1	950	1.020	acid	o	o	o	++	7.6	5.25 69.1	0.82 10.8	1.6 1.6	3.8 3.8	12.4 12.4	Do.
Oct. 24	1015	1.024	acid	o	o	o	++	9.9	7.29 73.7	0.55 5.6	0.19 1.95	0.52 5.3	1.29 13.1	Do.
1907 Aug. 23	1300	1.021	acid	o	o	o	+	10.48	7.97 76.1	0.52 5.0	0.33 2.2	0.73 7.0	0.97 9.3	
Aug. 26	1500	1.015	acid	o	o	o	+	10.75	8.44 76.6	0.81 7.6	0.22 2.1	0.62 5.8	0.61 5.6	
Sept. 5	1240	1.023	acid	o	o	o	+	11.00	9.0 81.9	0.28 2.6	0.22 2.0	0.64 5.9	0.81 7.4	

CASE VI.—*Diagnosis*: Dermatitis Herpetiformis. Syphilis.

A woman aged forty-five, occupation chambermaid. Had severe headaches and sore throat fifteen to sixteen years ago, otherwise has always been in fair health. Digestion always good till two years ago; she could eat anything without discomfort. Used always to eat sweet things and drank tea to excess. For past two years digestion has been very poor and her main diet has been bread, coffee, and tea. Alcohol used in moderation. Bowels costive. Menopause began June, 1907. Patient has been married, had one full term child who died at age of eight from scarlatina and had always been healthy previously. No miscarriages. Patient is a poorly nourished woman of neurotic type, subcutaneous tissue scanty, mucous membranes rather pale, tongue coated. Heart, lungs, spleen, liver, and abdomen negative.

On skin, an eruption is seen occupying the flexor surface of arms and elbows, in axillæ, over sternum. There is an extensive confluent area covering lower abdomen, sacrum, buttocks, and groins, extending down thighs as far as middle. The eruption is polymorphous consisting in part of grouped vesicles on an erythematous base, partly of papules and bean-sized tubercles with circinate outline. In many places the horny layer has been removed by scratching, showing the mucous layer which in places is exuding a clear serous fluid. In others the fluid has dried to a dark yellow crust. In older areas where the acute process has ceased a dark brown pigmentation is left.

This condition first began in Feb., 1907, and was characterized by the appearance of grouped papules and vesicles on an erythematous base which were intensely pruritic. The condition has persisted without remission since. Beside the above eruption there is also to be seen on the ulnar border of the left forearm a group of pea-sized depressed scars surrounded by light brown pigmentation and there is evident thickening of the bone beneath. The soft palate and fauces are also much scarred as a result of severe ulceration fifteen to sixteen years ago. The lesions on the forearm and throat were considered to be undoubtedly of syphilitic origin and at first there was some doubt as to whether the whole eruption was not of syphilitic character also.

Blood (Dec. 5, 1907): Hb., 70%. Red blood cells, 5,840,000. White blood cells, 6000. Red cells normal. Parasites—none found. Plates—moderate number.

Differential count of 300 white blood cells:

Polynuclears	70.0%
Lymphocytes	8.4%
Large mononuclears	7.6%
Transitionals	4.0%
Eosinophiles	9.6%
Mast cells	0.4%
Myelocytes	0%

Before being put on any treatment whatever patient was requested to bring two twenty-four hour specimens of urine at a few days' interval (*v. table*).

Dec. 12th. Specific treatment was instituted in form of inunctions of Ung. Hg., and Pot. Iod. was given internally in doses of gr. 20 t. i. d. The only result markedly was to increase the itching and cause a new outbreak of distinctly grouped vesicles on an erythematous base. This led to the opinion that the whole pruritic eruption was of metabolic origin, probably an aberrant form of dermatitis herpetiformis. On Dec. 21, 1907, specific treatment was stopped and the patient was given the Elix. of Fe, Strych., and Quin. of the National Formulary in drachm doses three times daily after meals, also Sol. Fowleri beginning with three drops t. i. d. and increasing by drop doses. The result was a distinct change for the better in the patient's condition—no new eruption appeared after Dec. 23, 1907—and by Jan. 7, 1908, she was greatly improved. No new eruption had appeared, the old lesions were drying up, the thighs and buttocks being almost clear of acute lesions. The itching had also much lessened.

In the urine examination it will be noted that the N. partition is within the normal limits which we have found to be usually the case at the height of an acute outbreak—at which time these specimens were collected.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T. N. Grms.	Urea-N. Grms. % T. N.	NH ₃ -N. Grms. % T. N.	U. A. -N. Grms. % T. N.	Kreatinin-N. Grms. % T. N.	Rest-N. Grms. % T. N.	Micros. Ex.
1907 Dec. 7	640	1.028	acid	o	o	o	o	5.7	4.45	0.29	0.14	0.31	0.48	Squam. epith. much cal. oxal.
								78.2	5.1	2.5	5.5	8.5		
Dec. 10	825	1.020	acid	faint trace	o	o	o	5.63	4.35 77.3	0.55 9.8	0.15 2.8	0.32 5.8	0.21 3.9	

CASE VII.—*Diagnosis*: Dermatitis Herpetiformis.

Past History: Male, aged forty. Scrofula at seven years,—otherwise healthy. Does not drink, has smoked ten cigars daily for many years. Drinks five or six cups of coffee daily. Married five years—history of marked sexual excess.

History of Present Illness: Present eruption has been present practically constantly for four years—he is never entirely free, but has periods of exacerbation and improvement. Eruption, comes out in crops as grouped vesicles on an erythematous base, and is accompanied by intense itching, lassitude, and headache, but no fever. As eruption fades away brown areas are left. Appetite and digestion good. Bowels regular. No urinary symptoms.

Present Condition (Jan. 20, 1906): Poorly nourished; mucous membranes rather pale, tongue clean; hands and feet rather clammy and cyanotic. Skin oily, relaxed, cheeks hollow. General lymphadenitis. Extensive eruption on whole extensor surfaces of arms and forearms, over sacrum, inside of thighs, and round knees. Eruption consists of grouped vesicles on an erythematous base—in other places vesicles have been destroyed by scratching and are capped with blood crusts. In still other places are brown pigmented areas which have been the site of former eruption. Pulse, 80, soft, rather collapsing in character. Arteries not palpable. Spleen, distinctly palpable two fingers' breadth below costal margin. Liver dulness begins in mammary line at sixth rib and extends to two fingers breadth below costal margin—not palpable.

Blood: Hb., 75%. Red blood cells, 4,960,000, pale, otherwise normal. No plasmodia. White blood cells, 12,000.

Differential count of 200 leucocytes:

Polynuclears	81.0%
Lymphocytes	8.0%
Large mononuclears	10.0%
Eosinophiles	1.0%
Mast cells	0%
Myelocytes	0%

Jan. 26, 1906. Condition same.

Treatment: Mag. sulph. 3 ii. every morning. Acetate, bicarb., and citrate of potassium, $\bar{a}\bar{a}$ gr. 15, four times daily. Lotion of Magnesium, Zinc, and Ichthyol locally. Pilocarpin gr. $\frac{1}{16}$ by mouth three times daily.

Feb. 27, 1906. Patient was kept on above treatment and considerable improvement resulted.

April 3, 1906. Patient has neglected treatment since last visit and is distinctly worse. There is quite an extensive new outbreak and severe itching. Treatment continued.

May 1, 1906. Constantly new outbreaks since last note. Patient has continual feeling of weariness.

Nov. 1, 1906. Has been in country all summer and has had no treatment. Eruption has been appearing in crops right along and the skin has never been entirely free. The thighs and legs are now most affected, the forearms only slightly. Trunk and arms are practically free from eruption. Bowels have been regular, digestion good. Has been eating meat once daily—drinking five to six cups of coffee. No alcohol. Tobacco to excess.

Aug. 15, 1907. Not seen since last note.

The urine at the height of the attack, contrary to the usual state, shows a distinct increase in the rest-nitrogen fraction which was very little modified by diet and purely eliminative treatment.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N.		NH ₃ -N.		U.A.-N.		Kreatinin-N.		Rest-N.		Micros.Ex. and Remarks.
									Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	
1906 Jan. 23	900	1.025	acid	o	o	o	++	9.63	7.33 76.2	0.46 4.8	0.14 1.5	0.39 4.1	1.29 13.4						No casts. Before diet and eliminative treatment. After treatment.
Feb. 15	870	1.026	acid	o	o	o	o	8.09	6.26 77.4	0.34 4.3	0.38 4.7	0.14 1.8	0.95 11.8						

CASE VIII.—*Diagnosis:* Dermatitis Herpetiformis of vesicular type.

Female nurse, aged twenty-three. Healthy up to time of entering training school five or six years ago. The attacks began or rather have been coincident with periods of overwork and mental stress. Within the last year they have come apparently without discoverable cause. The patient is otherwise normal with no personal or family history bearing on the eruption. The outbreaks have averaged three or four a year, occurring always in the form of grouped vesicles on knees, elbows, sacrum, and about axillæ. The areas burn furiously and deep pigmentation is left after subsidence. The prodromal symptoms are very marked and consist of lassitude, anorexia, headache, joint pains, and sometimes chills and fever. In one such period eosinophilia rose to 11 per cent.

Several attacks have been aborted by the use of vigorous eliminative measures.

With a practically vegetarian diet and constant attention to eliminative function, the attacks subsided during the fall of 1907, into abortive outbreaks with much less pigmentation, preceding occasionally the beginning of the menstrual period. She has recently begun to take thyroid nucleo-proteid at such times to break up the habit. Her urine taken in a marked prodromal period twelve hours previous to the appearance of any lesion shows a considerable increase of undetermined N. with correspondingly lowered urea percentages.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T. N. Grms.	Urea-N. Grms. % T. N.	NH ₃ -N. Grms. % T. N.	U. A. -N. Grms. % T. N.	Kreatinin-N. Grms. % T. N.	Rest-N. Grms. % T. N.
1907 Mar. 1	900	1.025	acid	trace	o	o	ob- scured by drug reaction	10.43	7.67 73.6	0.68 6.6	0.18 1.8	0.65 6.3	1.18 11.4

24-hour specimen taken 12 hours before eruption.

CASE IX.—*Diagnosis:* Dermatitis Herpetiformis.

Past History: Negative except that patient had been a very heavy meat eater for four years. No venereal history, no alcohol, tobacco used moderately.

History of Present Illness: For six months has been subject to crops of water blisters grouped together and occurring irregularly over body. Has not been entirely free since, new eruption appearing at intervals of one to two days and always accompanied by intense burning and itching.

Present Condition: Well nourished, muscles well developed, tongue clean. Appetite and digestion good, bowels regular. Skin, irregular areas of pigmentation are noticed on extensor surfaces of knees and elbows, on anterior axillary folds, over shoulders and scapulæ. Two large pigmented areas on each side over great trochanters. Pigmentation is evidently the remains of previous eruption, as patient says eruption has been almost entirely confined to above-mentioned localities. Only a few vesicles to be seen now, occurring two or three together on an erythematous base.

Treatment: Ung. menthol 2%. Urine March 24, 1907.

May 26th. About same. Treatment, restriction of proteid diet. Calamin and zinc locally.

B.—Acetate, bicarbonate, and citrate of potash gr. 15, three times daily.

April 2d. Has been almost entirely free from eruption since last visit. Both examinations show normal conditions in the urine, a state of affairs to be expected in a case of such long standing.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N. Grms. % T.N.	NH ₃ -N. Grms. % T.N.	U.A.-N. Grms. % T.N.	Kreatinin N. Grms. % T.N.	Rest-N Grms. % T.N.	Micros. Ex. and Remarks
1907 Mar. 24	2240	1.011	acid	o	o	o	++	15.20	12.32 81.1	1.12 7.4	0.59 3.9	0.62 4.1	0.48 3.2	Before diet restriction. Few squamous cells.
April 2	2200	1.010	acid	o	o	o	o	12.76	10.33 81.0	0.95 7.5	0.21 1.7	0.31 2.5	0.91 7.2	

CASE X.—Prurigo of Hebra.

Aug. 17, 1907. Girl aged twenty—occupation cigar maker. Apart from present illness she has always been in good health. Appetite always good, digestion good. Bowels constipated. Until the past two years she had always been a very heavy meat eater—a considerable amount two to three times daily. She gradually however learned that meat-eating increased the frequency and duration of the attacks and so for the past two years she has taken it only once a day. Her diet consists now mainly of vegetables and fruit—she drinks no milk and eats about five eggs weekly. Drinks one cup of coffee daily and only about two glasses of water. Does not use alcohol. The disease from which she is now suffering began seven years ago and she has been troubled with it every summer since. The eruption always appeared with the onset of warm weather and lasted until cool weather began when it would disappear spontaneously. The face and extensor surfaces of the arms, forearms, and hands have been the parts always affected. Only in the present attack has the eruption appeared on the extensor surfaces of the legs.

The disease is characterized by the constant recurrence of pin-head-sized papules deep in the skin, which gradually approach the surface till they can be distinctly seen and felt. They are accompanied by intense itching, are pale red in color, discrete, and never fuse into plaques. There has never been any surface exudation; after regression the papules leave white areas surrounded by brownish pigmentation. In the present outbreak the face, neck, extensor surfaces of arms, forearms, and hands, and extensor surfaces of thighs and legs are affected as above described. The

patient otherwise seems to be in good health, is well nourished, mucous membranes of good color.

Physical examination of heart, lungs, and abdomen negative, No treatment was given and no alteration of diet was made, but patient was told to collect a twenty-four-hour specimen of urine for examination. Urine examinations of Aug. 19th and 23d show condition before any treatment was inaugurated.

On Aug. 23d she had a new outbreak on her face; otherwise her condition was the same. She was told to eat meat twice daily as an experiment.

Aug. 28th. Condition about the same—urine examination of that day showed however a distinct increase in the percentage of rest-nitrogen, unaccompanied by increase in the eruption.

Sept. 7th. Distinct relapse began Sept. 2d—extensive new outbreak of papules accompanied by most intense itching (*v.* urine table). Treatment was now begun—she was given a saline cathartic every morning and alkaline diuretics during the day, her proteid diet was markedly restricted, and she was told to drink water freely. She was kept on this treatment without any distinct improvement in her condition until Oct. 22d, when she was given in addition one capsule (gr. $\frac{1}{10}$) of the nucleo-proteid of thyroid gland (Beebe's). Since then improvement has been taking place, though somewhat slowly.

Attention should be given to the fact that disturbance in the nitrogen partition, following five days of proteid feeding, preceded relapse in the eruption by the same length of time. The urine of Sept. 18th indicates the prodromal period of another attack.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N. Grms.	NH ₃ -N. Grms. % T.N.	U.A.-N. Grms. % T.N.	Kreatinin-N. Grms. % T.N.	Rest-N. Grms. % T.N.	Micros. Ex. and Remarks.
1907 Aug. 19	600	1.029	acid	o	o	o	++	8.63	6.72 77.9	0.5 5.9	0.08 0.1	0.62 7.3	0.61 7.1	Squam. epith.-mucus; much Cal. Oxal. Do. Slight new outbreak Rt. cheek. After eating meat b. i. d. for 5 days. Relapse since Sept. 2d.
Aug. 23	680	1.028	acid	o	o	o	+	9.0	7.2 80.4	0.38 4.3	0.13 1.5	0.52 5.8	0.69 7.7	
Aug. 28	1240	1.025	acid	o	o	o	++	12.15	9.54 78.6	0.49 4.1	0.24 2.0	0.54 4.5	1.28 10.6	
Sept. 7	840	1.021	acid	o	o	o	+	6.35	5.07 79.9	0.46 7.4	0.14 2.3	0.36 5.8	0.27 4.4	
Sept. 18	1280	1.021	acid	o	o	o	o	8.67	6.61 76.3	0.36 4.2	0.21 2.5	0.46 5.4	0.97 11.3	

CASE XI.—Prurigo.

Male, aged forty-six, janitor by occupation, born in the U. S.,

came under observation Dec. 23, 1904, suffering from a very itchy eruption all over the body.

Past History: Fever and ague as a youth; otherwise has always been healthy. Has used alcohol moderately, does not smoke. No venereal history. Has lived in Kansas, Michigan, and California. He went to Alaska in 1900, remained there till Oct., 1902, when he returned to N. Y. State where he has since lived.

History of Present Illness: In July, 1904, he first noticed an eruption of pin-head-sized, very itchy papules on the extensor surfaces of the right forearm. On scratching a clear watery fluid appeared. The eruption gradually spread up the arm to the trunk, neck, face, legs, and till the entire body was affected, even between the toes. From this time on he was never entirely free—he would have outbreaks at various intervals on different parts of the body. The first thing noticed was intense burning and tingling, then small, hard nodules could be felt deep in the skin. These would gradually approach the surface and there appear as pin-head, whitish or pale red papules. On scratching a profuse watery fluid appeared, so profuse at times that it could be scraped off with a knife. This fluid would later dry to a dark crust. The skin over the entire body gradually became very thick so that it could not be picked up. It also gradually became much darker in color.

He was treated at first for chronic eczema, then for premycotic stage of mycosis fungoides by X-ray without any material improvement in his condition. Attacks kept recurring, the skin did not lose any of its thickness or pigmentation. It was not till Feb., 1906, when the skin had begun to clear a little, that the true nature of the disease was recognized and another line of treatment instituted. At that time his condition was as follows:

Fairly nourished man, mucous membranes good color, tongue clean. Moderate general lymphadenitis. Heart, lungs, liver, spleen, and abdomen negative.

It is difficult to give a pen picture which will convey an adequate idea of the condition of the skin. The universal involvement, consequent absence of any distinguishing lesion, and the accidents of scratching made a diagnosis very difficult. Everywhere but on the palms and soles the skin shows a thickening so great that it can be picked up only with great difficulty. Its thickness was increased a dozen times and the surface marked with deepened lines to an extent sufficient to create the impression of elephantiasis.

In addition to lichenification, eczematization, excoriation,

pigmentation, and pustulation are generally prominent. Brows and cheeks were thickened and lined so as to give almost a leonine appearance. The scalp was covered with a diffuse infiltration. There was a deep brown pigmentation practically everywhere relieving small areas of leucoderma, depigmentation resulting from localized processes. Slight branny desquamation was universal but not prominent. As a result of the thickening and consequent immobility of the skin there was distinct fissuring in the neighborhood of the joints. The hair of the eyebrows, moustache, scalp, and pubic region was very scanty, dry, lustreless, and broken off.

Blood: Hb., 90%. Red blood cells, 3,808,000, normal in appearance, no malarial parasites found. White blood cells, 26,000.

Differential count of 300 white cells:

Polynuclears	64.0%
Lymphocytes	4.3%
Large mononuclears	9.6%
Transitionals	1.0%
Eosinophiles	21.0%
Mast cells	0%

Line of treatment instituted Feb. 8, 1906. Reduction of proteid diet, cereals and vegetables allowed, water ad lib. Sweat bath daily, also Scotch douche. Pilocarpin gr. $\frac{1}{10}$, increasing gradually to an amount sufficient to keep skin moist—reaching eventually a dose of gr. $\frac{1}{30}$ five times daily. Saline cathartic every morning and alkaline diuretics during the day. Locally, soothing applications.

This line of treatment was kept up till Oct. 11, 1906. During this time the patient improved very considerably. He had relapses at irregular intervals, but each relapse tended to be shorter in duration, less in extent, and less severe than the preceding one. The skin became progressively thinner and the pigmentation gradually faded. By October the only parts liable to be affected in a relapse were the forehead, neck, anterior axillary folds, flexor surfaces of the elbows, and the sides of the abdomen. These places still remained somewhat thickened and reddened and papules could always be felt in the skin. Over the rest of the body the skin had returned almost to its normal thickness, it could be picked up easily, and there was no longer any tendency to fissuring. The pigmentation had faded markedly all over the body. Hair beginning to grow again.

Blood (Aug. 14, 1906): Hb., 98%. Red blood cells, 6,112,000, normal in appearance. No malarial parasites found. White blood cells, 21,000.

Differential count of 300 white cells:

Polynuclears	70.7%
Lymphocytes	11.3%
Large mononuclears	3.3%
Transitionals	5.7%
Eosinophiles	9.0%
Mast cells	0%
Myelocytes	0%

Patient though much improved seemed to have reached a standstill; therefore on Oct. 11, 1906, in addition to the treatment outlined above he was given one capsule of nucleo-proteid of thyroid (gr. $\frac{1}{10}$) twice daily which was gradually increased till he was taking five daily. This was kept up till Nov. 13, 1906, when the capsules were discontinued. If anything, his condition had become worse and the capsules were thought not to agree with him. The other treatment was continued.

From Nov. 13th to Dec. 15th he remained in very good condition, having no new outbreaks. On Dec. 15th, however, a distinct relapse occurred affecting the face, flanks, and slightly the arms. This relapse persisted until Jan. 15, 1907, when he seemed distinctly easier and the eruption seemed to be lessening. From this time till Feb. 26th he kept in fairly good condition, though a few papules kept appearing every few days on forehead, neck, and flanks especially. The same treatment was followed throughout. On Feb. 26th in addition to his other treatment he was given an injection of one tube (2.5 c. c.) of S.T.E. (extract of autolyzed sheep's thyroid).

Blood (Feb. 27, 1907): Hb., 98%. Red blood cells, 6,520,000, normal in appearance. White blood cells, 12,000.

Differential count of 300 white cells

Polynuclears	67.0%
Lymphocytes	22.0%
Large mononuclears	4.0%
Transitionals	3.0%
Eosinophiles	2.6%
Mast cells	1.4%
Myelocytes	0%

Examination of fæces for ova negative.

This injection treatment was kept up until Nov. 20, 1907—the patient slowly but steadily improving. As indicated on the urine chart he received daily an injection of one to two tubes of S.T.E. (sheep's thyroid extract) or one to two tubes of S.T.N.P. (sheep's thyroid nucleo-proteid). The dose was regulated by the condition of the pulse as regards frequency and tension.

On Nov. 21, 1907, the injections were stopped and he was given one capsule daily of nucleo-proteid of the thyroid as prepared by Dr. Beebe. Improvement under this treatment has continued and at the present writing (April, 1908) he shows no lesions.

The urine chart is too elaborate for further analysis than the numerous references in the general discussion. We believe that it will repay the interested reader for some close reading and would like to direct particular attention to the changes preceding relapse and following injection of thyroid extract.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N. Grms. % T.N.	NH ₃ -N. Grms. % T.N.	U.A.-N. Grms. % T.N.	Kreatinin-N. Grms. % T.N.	Rest-N. Grms. % T.N.	Micros.Ex.
1906														
Feb. 6	1450	1.015	acid	+	o	o	o	8.44	5.12	0.34	0.23	0.34	2.36	Few squam. cells. No casts.
Feb. 14	2060	1.020	acid	+	o	o	o	10.09	60.7	3.9	2.9	4.1	28.1	Do.
Feb. 20	1350	1.012	acid	+	o	o	o	6.65	69.1	5.1	5.4	4.1	16.1	Do.
Feb. 26	2070	1.012	acid	+	o	o	o	9.15	43.6	0.23	0.33	0.27	1.42	Do.
Mar. 27	1325	1.017	acid	+	o	o	o	9.9	65.6	3.6	5.0	4.1	21.5	
Oct. 11	1620	1.018	acid	+	o	o	+	10.7	66.7	5.3	4.6	4.1	18.8	
Oct. 23	1400	1.017	acid	+	o	o	+	11.17	7.32	0.51	0.41	0.53	1.06	
Nov. 8	2070	1.010	acid	+	o	o	+	12.75	74.0	5.2	4.3	5.4	10.8	
Nov. 20	2300	1.013	acid	+	o	o	++	19.3	8.05	1.34	0.33	0.51	0.38	
1907														
Feb. 28	2300	1.010	acid	+	o	o	o	14.49	75.3	12.6	3.3	4.8	3.6	
Mar. 1	1780	1.013	acid	+	o	o	o	11.91	9.09	0.46	0.27	0.55	0.75	
Mar. 2	1840	1.020	acid	+	o	o	o	12.26	81.4	4.2	2.5	5.0	6.8	
Mar. 4	2825	1.015	acid	+	o	o	o	13.77	10.74	0.57	0.47	0.7	0.21	
Mar. 5	1850	1.018	acid	+	o	o	o	11.8	84.3	4.5	3.7	5.5	1.7	
Mar. 6	2070	1.018	acid	+	o	o	o	11.8	16.4	0.38	0.51	0.69	1.25	
Mar. 7	2680	1.012	acid	+	o	o	o	13.4	85.0	2.0	2.7	3.6	6.5	
Mar. 9	1620	1.015	acid	+	o	o	o	11.8	12.57	0.69	0.43	0.59	0.14	Injections begun Feb. 26,
Mar. 11	2860	1.008	acid	+	o	o	o	11.09	86.8	4.8	3.0	4.1	1.0	1-2 tubes S.T.E. daily.
Mar. 12	2170	1.010	acid	+	o	o	o	11.48	10.02	0.54	0.32	0.54	0.42	
									84.2	4.6	2.7	4.6	3.6	
									9.5	0.51	0.36	0.49	1.33	
									77.5	4.2	3.0	4.0	10.9	
									9.77	0.64	0.55	0.49	2.27	
									71.0	4.7	4.0	3.6	16.5	
									9.69	0.47	0.35	0.37	0.87	
									82.2	4.0	3.0	3.2	7.4	
									10.36	0.46	0.37	0.54	0.04	Injection stopped Mar. 6. (Rest?)
									87.8	3.9	3.2	4.6	0.4	
									11.61	0.58	0.45	0.4	0.29	
									86.7	4.4	3.4	3.0	2.2	
									9.88	0.48	0.31	0.48	0.59	
									83.8	4.1	2.7	4.1	5.0	
									8.65	0.37	0.52	0.52	0.96	Injections resumed
									78.0	3.4	4.7	4.7	9.0	Mar. 11, 1-2 tubes S.T.E. daily.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T. N. Grms.	Urea-N. Grms. % T. N.	NH ₃ -N Grms. % T. N.	U. A. -N. Grms. % T. N.	Kreatinin N. Grms. % T. N.	Rest-N. Grms. % T. N.	Micros. Ex
Mar. 13	2760	1.010	acid	+	o	o	o	12.26	84.9	4.3	3.6	3.3	4.8	
Mar. 15	2650	1.010	acid	+	o	o	o	11.42	10.44 85.2	0.66 5.4	0.47 3.9	0.5 4.1	0.82 6.7	
Mar. 18	2910	1.009	acid	+	o	o	o	15.56	8.49	0.61	0.45	0.44	1.38	1-2 tubes S.T.N.P. daily.
Mar. 20	1730	1.013	acid	+	o	o	o	13.66	74.4	5.4	4.0	3.9	12.1	
Mar. 22	1760	1.014	acid	+	o	o	o	12.8	11.77	0.73	0.52	0.51	1.97	
Mar. 26	1990	1.013	acid	+	o	o	o	12.6	75.7	4.7	3.4	3.3	12.7	
April 1	1750	1.014	acid	+	o	o	o	13.7	11.7	0.66	0.31	0.45	0.49	
April 5	2220	1.010	acid	+	o	o	o	10.25	85.7	4.9	2.3	3.3	3.6	
April 8	2580	1.009	acid	+	o	o	o	12.9	10.26	0.38	0.33	0.61	1.12	
April 12	1870	1.010	acid	+	o	o	o	12.4	80.2	3.0	2.6	4.8	8.8	
April 16	1725	1.011	acid	+	o	o	o	11.85	10.48	0.51	0.45	0.64	0.46	1-2 tubes S.T.E. daily.
April 19	1460	1.016	acid	+	o	o	o	13.1	83.2	4.1	3.6	5.1	3.7	
April 23	2050	1.010	acid	+	o	o	o	12.68	11.5	0.69	0.31	0.64	0.47	
April 26	2240	1.015	acid	+	o	o	o	13.67	84.1	5.1	2.3	4.7	3.5	
May 7	2850	1.010	acid	+	o	o	o	12.68	8.59	0.55	0.41	0.46	0.2	
May 10	1850	1.016	acid	+	o	o	o	12.8	83.9	5.4	4.0	4.5	2.0	
May 17	1630	1.010	acid	+	o	o	o	7.9	10.56	0.81	0.46	0.56	0.46	
May 21	1960	1.011	acid	+	o	o	o	12.15	81.9	6.3	3.6	4.4	3.6	
May 24	1200	1.017	acid	+	o	o	o	12.24	10.52	0.9	0.4	0.48	0.03	Rest?
May 28	2100	1.012	acid	+	o	o	o	11.5	84.9	7.3	3.3	3.9	0.3	
May 31	1930	1.010	acid	+	o	o	o	11.0	9.78	0.69	0.29	0.55	0.48	
June 4	1710	1.015	acid	+	o	o	o	11.8	82.6	5.9	2.5	4.7	4.1	
June 7	1710	1.020	acid	+	o	o	o	20.4	10.16	0.89	0.32	0.37	1.33	1-2 tubes S.T.N.P. daily.
June 11	1530	1.013	acid	+	o	o	o	11.66	77.6	6.8	2.5	2.9	10.2	
June 13	1350	1.018	acid	+	o	o	o	12.47	8.93	1.07	0.35	0.50	1.76	
June 18	760	1.023	acid	+	o	o	o	10.73	70.5	8.5	2.8	4.0	13.9	
June 21	1240	1.016	acid	+	o	o	o	10.83	9.45	1.5	0.42	0.62	1.61	Recrudescence began April 25; change to S.T.E., 2 daily.
June 26	1500	1.020	acid	+	o	o	o	15.54	69.2	11.0	3.1	4.6	11.8	Recrudescence over and pat. comfortable.
June 28	1770	1.014	acid	+	o	o	o	10.9	8.95	1.42	0.51	1.47	0.31	Recrudescence over and pat. comfortable.
July 5	1710	1.010	acid	+	o	o	o	11.86	70.6	11.2	4.1	11.6	2.5	
July 9	1130	1.017	acid	+	o	o	o	12.14	9.85	1.35	0.39	0.56	0.6	
July 11	1210	1.017	acid	o	o	o	+	10.6	77.0	10.6	3.1	4.4	4.7	
July 16	1350	1.012	acid	o	o	o	+	8.3	5.6	1.0	0.36	0.35	0.54	
July 19	1050	1.019	acid	o	o	o	+	9.67	71.1	12.7	4.6	4.5	6.9	
									9.56	0.59	0.38	0.54	1.0	
									78.7	4.9	3.2	4.5	8.3	
									10.44	0.36	0.25	0.55	0.57	
									85.3	3.0	2.1	4.5	4.8	
									8.85	0.81	0.42	0.55	0.82	
									77.0	7.1	3.7	4.8	7.2	
									7.99	0.2	0.43	0.58	1.72	Recrudescence.
									72.7	1.9	4.0	5.3	15.7	1-2 tubes S.T.N.P. daily.
									10.04	0.25	0.35	0.57	0.5	Well again.
									85.1	2.2	3.1	4.9	4.3	
									17.62	0.42	0.36	0.89	1.0	
									86.4	2.1	1.8	4.4	5.0	
									10.45	0.16	0.49	0.6	0.1	
									89.7	1.4	4.3	5.2	0.9	
									10.72	0.22	0.34	0.53	0.61	
									86.0	1.8	2.8	4.3	4.9	
									8.88	0.57	0.16	0.66	0.4	
									82.8	5.4	1.5	6.2	3.8	
									9.14	0.21	0.26	0.54	0.61	
									84.4	2.0	2.5	5.0	5.7	
									13.27	0.57	0.27	0.77	0.57	
									85.4	3.7	1.8	5.0	3.7	
									8.58	0.49	0.45	1.0	0.5	
									78.8	4.5	4.2	9.2	4.6	
									10.16	0.59	0.26	0.6	0.2	
									85.7	5.0	2.2	5.1	1.7	
									9.77	0.24	0.19	0.74	1.16	
									80.5	2.0	1.5	6.1	9.6	
									9.07	0.23	0.19	0.64	0.44	Slight recrudescence.
									85.6	2.2	1.8	6.1	4.2	
									6.64	0.22	0.17	0.63	0.63	
									80.0	2.7	2.1	7.7	7.6	
									8.24	0.24	0.2	0.55	0.41	
									85.3	2.5	2.2	5.7	4.3	

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T. N. Grms.	Urea-N.		NH ₃ -N.		U. A. -N.		Kreatinin-N.		Rest-N.		Micros. Ex.
									Grms.	% T. N.	Grms.	% T. N.	Grms.	% T. N.	Grms.	% T. N.	Grms.	% T. N.	
July 23	1100	1.016	acid	o	o	o	+	10.07	8.27	0.25	0.16	0.57	0.78						
July 26	1770	10.10	acid	o	o	o	+	9.56	82.2	2.5	1.6	5.7	7.8						
July 30	850	10.20	acid	o	o	o	+	10.37	7.87	0.27	0.23	0.73	0.4						
Aug. 1	2225	1.010	acid	o	o	o	+	11.29	82.4	2.9	2.5	7.7	4.2						
Aug. 6	1325	1.016	acid	o	o	o	+	10.5	8.82	0.2	0.3	0.59	0.42						
									85.1	2.0	2.9	5.7	4.1						
									9.72	0.21	0.28	0.79	0.22						
									86.2	1.9	2.6	7.0	2.0						
									9.04	0.23	0.21	0.65	0.32						
									86.1	2.2	2.1	6.2	3.1						

CASE XII.—Male; prurigo.

History of Present Illness: Disease began sixteen years ago, since when patient has never been entirely free. It appeared first on genitals with intense burning and itching, then small pin-head-sized lumps could be felt deep in the skin. These gradually approached the surface and formed small papules—always itching intensely. Never any exudation. For all these sixteen years he has been subject to similar frequently recurring attacks. At times the whole body has been affected but the parts most frequently attacked have been the face, especially the forehead and nose, all round the neck, flexor surfaces of elbow, flanks, and genital folds. In the localities most frequently affected the skin gradually became and remained considerably thickened and pigmented and the small lumps aforementioned could always be felt in it. The itching has been so intense that the patient could not sleep for nights at a time. It is less in cold weather but is relieved if patient gets into a profuse perspiration.

Past History: No skin eruption except present disease. No malaria or rheumatism, no headaches—always in good health except for present illness. Appetite good, digestion good, bowels always very constipated. No alcohol, tobacco moderately. Has always been a very heavy meat eater—taking regularly about 1½ lbs. twice daily. He has a predilection also for pastry.

Present Condition: Well nourished, mucous membranes good color, tongue clean. General lymphadenitis. Pulse 80, regular, good volume, tension increased. Heart, lungs, liver, spleen, and abdomen negative.

Skin: Pin-head to small-pea-sized pale papules are to be seen on face, especially forehead, on anterior surfaces of elbows and forearms, internal surfaces of thighs, on scrotum and penis, and on sides of abdomen. In some places papules have fused to make variously sized plaques markedly indurated, reddened, and slightly scaly and pigmented.

The initial lesion is seen especially on the flanks as a pale vesico-papule, pin-head in size.

Blood (May 6, 1907): Hb., 105%. Red blood cells, 5,936,000, normal in appearance. White blood cells, 14,000. Parasites, none found. Plates, increased.

Differential count of 300 white cells:

Polynuclears	74.0%
Lymphocytes	13.0%
Large mononuclears	2.0%
Transitionals	8.0%
Eosinophiles	3.0%
Mast cells	0%
Myelocytes	0%

Treatment: Ung. carbol. 5% externally. Given no internal treatment and no change made in diet. Told to bring twenty-four hour specimen of urine.

May 10, 1907. Condition same as before, itching so intense as to prevent sleep. Continue treatment.

May 13, 1907. Condition same as before—encouraged to eat more meat as an experiment.

May 17, 1907. Distinctly worse since last visit; considerable new outbreak of papules on forehead, neck, and flanks especially. Itching most intense. (See urine table.)

Treatment: Meat and eggs cut off entirely. Allowed one quart of milk daily, vegetables and fruit. Encouraged to drink much water. Acetate, bicarbonate, and citrate of Potassium gr. 15, four times daily. Mag. sulph. $\frac{3}{4}$ ss. every morning. Sweat baths.

May 24, 1907. Says itching is considerably less, seems easier.

May 28, 1907. Distinct recrudescence, face, neck, and head, for two days. Treatment continued.

May 31, 1907. Relapse continues, many papules felt and seen in skin. Itching intense, so that sleep is impossible.

June 4, 1907. Admitted to Bellevue Hospital—suffering intensely. Considerable new outbreak of papules especially on face, neck, head, anterior surface elbows, and flanks. Face, nose, and cheeks red and angry-looking, skin infiltrated. Itching excruciating, so that patient spends most of day applying various lotions without however gaining any material relief. Same treatment was continued, but the milk was cut down to one pint daily. He was also ordered sweat bath, needle and Scotch douche daily for two hours.

June 9, 1907. Itching somewhat less, slept better last night. Beginning to-day gets daily injection of two tubes of extract of entire sheep thyroid as prepared by Dr. Beebe (see Case XI). Other treatment continued.

From June 9th to June 23d the same treatment was kept up and patient improved very markedly. No new papules appeared, skin became less red and angry-looking and became more soft and pliable, and itching lessened very much. After June 12th patient slept practically without any discomfort all night.

June 23, 1907. Patient very much better. Treatment continued. Beginning to-day, gets daily injection of three tubes of extract of nucleo-proteid of thyroid.

June 28th. Complains of slightly more itching, especially about forehead. Otherwise keeps in very good condition. Treatment continued.

July 3d. Left hospital in very good condition—itching quite bearable and sleeps well. Resumed treatment at the Cornell Dispensary and same treatment was continued except that he could take the sweat baths only three to four times weekly.

July 5th to 10th. Keeps in good condition.

July 11th. To-day has distinct new outbreak of papules on face accompanied by severe itching (*v. urine table*).

July 15th. Relapse of July 11th continues, new outbreak on forehead, itching severe.

July 16th. Condition same. Treatment continued, except that he was given daily injections of extract of whole thyroid.

July 18th. Itching continues. New papules on face. Continue treatment and injection daily, but told to cut off milk entirely for some time and also to stop oatmeal, of which he had been eating considerably.

Sept. 20, 1907. Patient has been on same treatment as regards diet, cathartics, diuretics, etc. The application of oleum cadini before taking his sweat bath has added materially to his comfort. The injections have been varied as indicated on the chart. On the whole the condition has tended to improve but not altogether satisfactorily. We have become doubtful as to whether the patient adheres to the diet ordered him, though he maintains that he does.

From Sept. 20 to Nov. 12, 1907, same treatment was kept up with a certain amount of steady improvement. On Nov. 12th the injections were stopped and capsules of nucleo-proteid of thyroid were substituted, gr. 1-200, once daily. This dose has been

increased gradually till at the present writing (Jan. 11, 1908) he is tending steadily towards improvement. It may be stated that while under injections patient at times seemed to get an overdose as he would complain shortly afterwards of having chilly sensations, violent headache, and pains all over body and general malaise. This condition would gradually subside in the course of two to three days. The symptoms were probably due to toxic by-products of the process of autolysis, employed in the preparation of the gland extract.

The interesting relationship of urine change to relapse is clearly brought out by the figures of the accompanying chart, also the marked effect of injections of thyroid extract on the ratios of urea and rest-nitrogen. The latter is particularly noticeable in the relapse beginning July 11, 1907. Rest-nitrogen figures never reached during treatment those taken before its institution.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N. Grms. % T.N.	NH ₃ -N. Grms. % T.N.	U.A.-N. Grms. % T.N.	Kreatinin. N. Grms. % T.N.	Rest-N. Grms. % T.N.	Micros. Ex. and Remarks.
1907														
May 10	2800	1.014	acid	o	o	o	+	17.32	12.33 71.2	1.21 7.0	0.31 1.8	0.55 3.2	2.87 16.6	Few squamous cells.
May 13	2090	1.021	acid	o	o	o	+	21.0	15.26 72.7	1.21 5.8	1.87 8.3	0.69 3.3	3.23 15.4	Do.
May 17	1530	1.024	acid	o	o	o	++	16.79	14.0 83.4	1.02 6.1	0.3 1.8	0.67 4.0	0.75 4.5	Do. After eating more meat. New outbreak.
May 28	2025	1.018	acid	o	o	o	++	18.91	15.67 82.9	0.69 3.7	0.37 2.0	0.49 2.6	1.58 8.4	Do. Relapse beginning May 26.
May 31	920	1.021	acid	o	o	o	++	12.12	9.64 79.6	0.47 3.9	0.22 1.9	0.27 2.3	1.56 12.9	Relapse continues.
June 7	880	1.025	acid	o	o	o	++	12.5	11.27 90.2	0.25 2.0	0.16 1.3	0.58 5.1	0.13 1.1	Relapse continues. June 9, 2 tubes S.T.E. daily. Much easier.
June 11	1350	1.022	acid	o	o	o	+	13.8	11.32 82.1	0.52 3.8	0.57 4.2	0.34 2.5	1.25 9.1	
June 14	1530	1.023	acid	o	o	o	+	14.13	12.05 85.3	0.22 1.6	0.35 2.6	0.80 5.7	0.65 4.6	
June 18	1080	1.021	acid	o	o	o	+	11.99	10.15 84.7	0.33 2.8	0.17 1.5	0.56 4.7	0.71 6.0	
June 21	1170	1.023	acid	o	o	o	+	10.28	8.62 83.9	0.2 2.0	0.19 1.9	0.6 5.9	0.61 6.0	June 23, 3 tubes S.T. N.P. daily
June 25	1300	1.024	acid	o	o	o	+	11.64	10.21 87.8	0.32 2.8	0.22 2.0	0.54 4.7	0.30 2.6	
June 28	1500	1.019	acid	o	o	o	+	14.7	12.49 85.0	0.07 0.5	0.27 1.9	0.66 4.5	1.13 7.7	
July 2	1190	1.027	acid	o	o	o	++	13.72	10.89 79.4	0.57 4.2	0.13 1.0	0.58 4.3	1.49 10.9	
July 8	1160	1.015	acid	o	o	o	++	9.19	7.03 76.6	0.47 5.2	0.18 2.0	0.54 5.9	0.92 10.1	
July 12	2100	1.019	acid	o	o	o	++	13.8	12.18 88.3	0.16 1.2	0.24 1.8	0.82 6.0	2.4	Relapse beginning July 11.
July 16	1720	1.022	acid	o	o	o	+	11.89	9.45 79.5	0.23 2.0	0.26 2.2	0.76 6.4	1.15 9.7	3 tubes S.T.E. daily.
July 19	1120	1.021	acid	o	o	o	++	9.28	7.53 81.2	0.13 1.5	0.19 2.2	0.58 6.3	0.78 8.5	
July 23	1340	1.024	acid	o	o	o	++	10.3	8.49 82.5	0.29 2.9	0.27 2.4	0.70 6.8	0.51 5.0	

Date.	F	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N.		NH ₃ -N.		U.A.-N.		Kreatinin-N.		Rest-N.		Micros. Ex. and Remarks.	
										Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.		
July 27		1260	1.018	acid	o	o	o	+	10.37	8.49	0.42	0.18	0.62	0.62							Distinctly better.
July 30		1460	1.018	acid	o	o	o	++	11.44	81.9 8.84 77.3	4.1 0.5 4.4	1.8 0.26 2.3	6.0 0.76 6.7	6.0 1.04 9.1							
Aug. 2		950	1.020	acid	o	o	o	++	8.56	7.18	0.3	0.19	0.83	0.01							July 31, 3 tubes S.T. N.P. daily. Rest N.!
Aug. 6		1000	1.010	acid	o	o	o	+	5.99	83.9 4.41	3.6 0.21	2.3 0.11	9.7 0.35	0.2 0.84							
Aug. 9		1450	1.018	acid	o	o	o	+	10.96	73.7 8.93	3.6 0.51	2.0 0.16	5.9 0.56	14.1 0.74							Relapse.
Aug. 15		1990	1.016	acid	o	o	o	+	10.4	81.5 7.49	4.7 0.55	1.5 0.26	5.2 1.44	6.8 8.8							
Aug. 20		1800	1.018	acid	o	o	o	+	11.5	72.1 8.62	5.3 0.4	2.5 0.27	5.8 0.71	13.9 1.27							Aug. 13, 2 tubes S.T.E. Improving.
Aug. 28		1850	1.016	acid	o	o	o	+	8.18	75.0 6.15	3.5 0.51	2.4 0.28	6.2 0.48	11.1 8.8							
Sept. 5		1120	1.013	acid	o	o	o	+	6.55	75.3 4.94	6.3 0.43	3.5 0.12	5.9 0.46	8.8 0.55							Slight recurrence.
Sept. 20		870	1.025	acid	o	o	o	+	9.8	75.5 7.97 81.4	6.6 0.57 5.9	1.9 0.14 1.5	7.1 0.49 5.0	8.5 0.57 5.9							

GROUP III.

SCALING DISEASES.

CASE XIII.—*Diagnosis*: Acute Erythematous Eczema.

Woman, aged twenty-four. Duration four days. Face, neck, chest, and arms markedly swollen, red, and itchy. Has had similar eruption twice before.

Urine shows a considerable quantity of indican and as usual at the beginning of an attack rather high Rest N. The percentage of urea is normal and of ammonia slightly reduced for the total N eliminated. The eruption having been in existence four days, the urine undoubtedly shows less change than it did twenty-four hours previous to the outbreak. The case pursued the usual course of vesiculation, weeping, and final scaling.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N.		NH ₃ -N.	U.A.-N.		Kreatinin-N.		Rest-N.		Micros. Ex. and Remarks.
									Grms.	% T.N.		Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	
1907 April 24	700	1.022	acid	+	o	o	++	8.72	6.99	80.2	0.18	0.12	0.36	1.03				Few squamous cells. Albumen removed in N partition.

CASE XIV.—Acute Vesicular Eczema.

Woman aged sixty-nine. Deeply alcoholic. Suffered from a variety of ailments, chiefly bronchitis, gastro-enteritis, arterio-

sclerosis, nephritis, and cystitis. Legs edematous, fluid in peritoneal and pleural cavities. Had been on a reduced diet for weeks owing to anorexia and lost both flesh and strength. The first urine examination, which marked the time of admission to hospital, shows nothing beyond the evidences of nephritis. The N partition for the total excreted shows no marked deviation from normal. Indican occurred in very small amount. The second taken four weeks later antedated the eruption of a diffuse vesicular eczema of the trunk by four days. The patient had improved as a result of rest and feeding and withholding liquor. The amount of urine tripled but on account of a restricted, almost exclusively milk diet the total nitrogen had risen very little. The uric acid and Rest N percentages are rather high; ammonia and kreatinin, low, while the nephritis remained unchanged. The low kreatinin was probably due to diminished endogenous metabolism following complete rest and restricted diet. The urea percentage is above the normal for the total nitrogen excreted. The figures are not indicative of a failure of urea synthesis, although there is defective desamidation.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N. Grms. % T.N.	NH ₃ -N. Grms. % T.N.	U.A.-N. Grms. % T.N.	Kreatinin-N. Grms. % T.N.	Rest-N. Grms. % T.N.	Micros. Ex. and Remarks.
1907 Sept. 18	530	1.017	acid	trace	o	o	+	2.99	2.07 69.3	0.14 4.9	0.13 4.6	0.31 10.5	0.31 10.5	Casts.
Oct. 10	1680	1.015	acid	trace	o	o	+	4.04	2.9 72.5	0.11 2.9	0.29 7.2	0.21 5.2	0.47 11.8	Casts.

CASE XV.—*Diagnosis*: Subacute Scaling Eczema; type continued through many successive outbreaks.

Girl aged eight, robust in appearance, but subject to sharp attacks of illness. Disease has continued for several years, rarely showing any lesional variety other than scaling. Spots occur exclusively on neck and extensor surfaces, appearance clean, border shading into the surrounding skin. In one attack a patch covered the vulva but there was no suspicion of a seborrhœic element. Outdoor life, diet, and general measures failed entirely to prevent relapse. It was decided to operate for adenoids in April, because of pronounced mouth breathing and in hope of increasing oxygenation. A twenty-four hour specimen of urine was taken several days previously but part of it was lost. As the patient had had several slight attacks of pyelitis, the findings were regarded as suspicious of an impending attack because the total amount

was undoubtedly small and the specific gravity high; consequently ether was used instead of chloroform. A few days after the operation, May 6, 1907, a second specimen was taken in which the percentage of urea was considerably lessened and that of rest-nitrogen enormously increased. The low specific gravity was due to an almost fluid diet which was also in exhibition at the time the specific gravity rose before operation to 1.030, a fact only explainable on the ground of an acute suppression in the latter instance. An outbreak of eczema was confidently expected but no new lesions appeared and the child was practically well on May 20th. The reason is difficult to assign but these explanations occur to us: First, the excess of Rest N may have been stored in the body during the period of suppression, being poured out when it ended; second, the failure of urea synthesis may have been the result of the anæsthetic and the specific poison may not have been elaborated; third, it may resemble those cases which Osler calls erythema multiforme without exanthem, meaning that the constitutional disturbance fails to produce its cutaneous effect.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone bodies.	Indican.	T.N. Grms.	Urea-N.	NH ₃ -N.	U.A.-N.	Kreatinin-N.	Rest-N.	Rema'ks.
									Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	
1907 April 29	260	1.030	acid	o	o	o	+	5.42	4.79 88.4	0.18 3.5	0.04 0.9	0.1 1.9	0.27 5.1	Taken before operation. Part lost. Taken after operation.
May 6	900	1.012	acid	o	o	o	+	7.96	5.58 70.2	0.32 4.1	0.19 2.4	0.17 2.2	1.66 20.9	

CASE XVI.—*Diagnosis*: Erythemato-squamous eczema.

A subacute type involving extensor surfaces which had had no very acute stage. Such a condition is accompanied by no demonstrable urine changes. The case is introduced for comparison.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N.	NH ₃ -N.	U.A.-N.	Kreatinin-N.	Rest-N.	Micros. Ex.
									Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	
1907 April 16	1.930	1.010	acid	o	o	o	o	7.83	6.5 83.1	0.5 6.4	0.18 2.3	0.24 3.1	0.37 4.8	Squamous cells.

CASE XVII.—*Diagnosis*: Chronic eczema of scrotum, perineum, and thighs.

Man aged seventy-six. Health fairly good for age. Little

arterial tension, no sclerosis. Habits always moderate, with regard to alcohol, tea, and tobacco. Bowels irregular. Considerable flatulence fairly constant. Occasional mild attacks of indigestion.

Skin of penis, scrotum, perineum, and thighs extremely thick, fissured, and excoriated. Paroxysms of itching intense, particularly at night. Recovered entirely from attack which had continued a year after six weeks.

Acute vesicular outbreak occurred in August, 1907, and continued to October 21st, brought on and kept up by dietary indiscretions. Patient was held strictly to milk diet after Sept. 19th. The second specimen was taken a week later, eight weeks from beginning of attack. It is practically normal with an increased volume and diminished urea output, both results of diet. In November of same year, there remained only occasional attacks of pruritus scroti. This is the only one of our series of cases in which kreatin was found. The normal state of the nitrogen partition while the body of a man aged seventy-six was covered with weeping eczema forcibly indicates how little likely the urine is to show evidence of disturbed metabolism after the state is thoroughly established.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.		Urea-N. Grms.		NH ₃ -N. Grms.		U.A.-N. Grms.		Kreatinin-N. Grms.		Rest-N. Grms.		Micros. Ex. Remarks.
								% T.N.	% T.N.	% T.N.	% T.N.	% T.N.	% T.N.	% T.N.	% T.N.					
1907 June 1	1180	1.027	acid	trace (nucleo)	o	o	+	13.33	11.05 82.9	0.3 2.3	0.23 1.8	0.46 3.5	1.21 9.1							Kreatin found. Cylindroids. Oxalate cal. crystals. Squamous epithelium. No kreatin. Milk diet. Acute attack.
Sept. 26	1895	1.009	acid	o	o	o	+	7.75	6.31 81.4	0.27 3.5	0.12 1.5	0.38 4.9	0.67 8.7							

CASE XVIII.—*Diagnosis*: Chronic eczema of vulva, perineum, and thighs. Woman aged seventy. At time of birth of last child thirty years ago sustained severe laceration of cervix and perineum which was never repaired. As a result there has been profuse leucorrhœa which caused no local irritation until recent years. Three years ago, itching became annoying and continued until time of urine examination. Bowels were regular but flatulence was common. Moderate eater, something of a tea drinker but not sufferer from indigestion. Skin red, thickened, fissured, and

lichenified in eczematous area. Under treatment, the leucorrhœa lessened. Misunderstanding directions she took nine grains of hydrargyrum cum creta and had eight to ten movements next day. The eczema absolutely disappeared within the following ten days and has not recurred after a year. It was not possible to obtain another specimen of urine because she was leaving town. The failure of urea synthesis is remarkable in degree in view of the long continuance of the eczematous process.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N.		NH ₃ -N.		U.A.-N.		Kreatinin-N.		Rest-N.		Remarks.
									Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	
April 19 1907	860	1.023	acid	o	o	o	o	7.6	5.78 76.1	0.25 3.3	0.21 2.8	0.31 4.2	1.02 13.5	Exception to rule of normal N - partition in chronic cases.					

Trace of urobilin.

CASE XIX.—*Diagnosis*: Seborrhœic eczema and rosacea.

Male, age fifty-two. Weight, one hundred and twenty-seven pounds. Teacher.

Had an attack of acute indigestion years ago from which recovery has never been complete. Subject to neuralgia and fits of depression. Distress comes on immediately or an hour after eating. Flatulence constant. Tongue coated. Bowels constipated. Liver tender on deep palpation.

Eruption limited to face and head. Erythematous areas of rosacea overlaid with greasy crust-scale of seborrhœic eczema which extends also over bald scalp. There are on face small scattered areas showing red, denuded mucous body, quite distinct from the papules of rosacea, possibly seborrhœic also. The case was selected as a control, showing a normal urine with no indican and a serious disturbance of digestion.

Date.	Vol. c. c.	Sp. Gr.	Reaction	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N.		NH ₃ -N.		U.A.-N.		Kreatinin-N.		Rest-N.		Remarks.
									Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	Grms.	% T.N.	
1907 May 27	1700	1.015	acid	trace	o	o	o	6.50	5.14 79.1	0.4 6.2	0.29 4.5	0.35 5.4	0.3 4.7	Few cells.					

CASE XX.—*Diagnosis*: Erythrodermie pityriasique en plaques disseminées.

Past History: Usual children's diseases. Acute rheumatism ten years ago. No venereal history. Uses alcohol and tobacco to excess. Operated on for piles ten years ago. Appetite good, digestion good but has occasional morning nausea. No headaches. Bowels regular.

History of Present Illness: Eruption first appeared Dec. 4, 1906, on arms, two or three days later it came out on legs and trunk. It first started as scattered pea-sized pinkish areas with scanty dry silvery scaling. The patches gradually increased and joined with neighboring ones, forming on trunk and thighs extensive areas. Disease is itchy especially at night.

Present Condition: Fairly well nourished, mucous membranes good color. Has Riggs's disease in marked degree. Conjunctivæ have icteroid tint. Heart and lungs negative. Liver dulness begins at sixth rib in mammary line and extends downwards for eight inches, the edge being distinctly palpable, smooth, and rounded. Spleen dulness begins in ninth intercostal space in mid-axillary line, edge is felt $1\frac{1}{2}$ inches below costal margin. Skin, a diffuse pinkish eruption is scattered practically all over the body but seen most abundantly on extensor surfaces of arms, sides of trunk, anterior and external surfaces of thighs, and on penis. The early lesion seems to be a pinkish pea-sized spot with rather indefinite margin, very superficial and covered with scanty dry powdery scales. On trunk and thighs are seen large confluent areas evidently formed by the coalescing of small patches. None of patches show any tendency to central involution.

Treatment: Sod. phosphate $\frac{3}{4}$ ss morning and evening in hot water. Ung. resorcin 3% locally. Milk diet.

Blood (Dec. 15, 1906): Hb., 97%. Red blood cells, 6,160,000, normal, no plasmodia found. White blood cells, 18,000.

Differential count of 300 cells:

Polynuclears	69.0%
Lymphocytes	22.6%
Large mononuclears	0.8%
Transitionals	7.6%
Eosinophiles	0%
Mast cells	0%
Myelocytes	0%

Patient improved very slightly under treatment and disappeared from view Dec. 20, 1906.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N. Grms. % T.N.	NH ₃ -N. Grms. % T.N.	U.A.-N. Grms. % T.N.	Kreatinin-N. Grms. % T.N.	Rest-N. Grms. % T.N.	Micros. Ex.
1906 Dec. 18	880	1.022	acid	o	o	o	++	14.4	12.97 90.1	0.66 4.6	0.2 1.4	0.56 3.2	0.08 0.6	Mucus-squamous cells. Rest-N doubtful.

CASE XXI.—*Diagnosis*: Inveterate Psoriasis.

Man aged forty. Sedentary life, but has no habits calculated to injure health. Has "violent indigestion" for months at a time in spite of diet and outdoor life. During these periods nothing seems to be digested. Distress comes on immediately after eating. Not infrequently diarrhoea is set up within an hour after meals. Diet has never been properly regulated. Stools quite foul. No hepatic enlargement can be made out. This condition resulted in considerable emaciation after a lapse of several years, the patient not being able to set an exact date.

Psoriasis appeared some times after the digestive disturbance began. It has run its usual course of remission and exacerbation, but the body has never been entirely free in the last five years. It exists in the form of large patches on the extensor surfaces, back, and scalp, which are very thick, lichenified, and resistant to treatment. They have yielded practically only to X-rays, although a lotion of eugallol and acetone has benefited the scalp recently.

The first specimen of urine taken was before treatment was begun, the others afterward. None of them show any material change, including the last which was taken after severe X-ray burns on both elbows and exposure of a large part of the body to their influence. Kreatinin percentages, an indication of tissue change according to Folin, remained about the same, increasing slightly after limitation of proteid intake. For thirty-six hours preceding the collection of the last three samples the patient consumed by weight the same amounts of the same foods in order to eliminate error in this direction as far as possible. It was very difficult to increase the amount of urine even when large quantities of water were taken. A curious feature is the comparatively small amount of indican occurring with unmistakable intestinal fermentation, and increasing for a time after a marked change for the better took place.

The X-ray burns referred to occurred early in May, 1907, on elbows alone, following usual exposure but with a new tube.

They had almost healed by June 10th and the psoriasis was gone, a depigmented area being left in its place in each instance. On Sept. 6th there appeared on the burned areas coinciding exactly with the previous distribution of the psoriasis determined by the lighter color, an acute vesiculation and weeping. No noticeable increase in gastro-intestinal symptoms occurred at the time. Spontaneous ulceration appeared over both elbows resembling exactly the original burns. The remainder of the eczematoid eruption disappeared under appropriate treatment but the ulcers show no tendency to heal at this writing (Dec. 1st) and are exquisitely painful. Inside the left elbow there is a persistent spot of psoriasis.

Although this is an extreme case and we are forced to grant that the gastro-intestinal disorder and the skin lesion may be coincident and not casually connected, a reasonable view would seem to be that the very slight urine changes indicate here as in other chronic disorders the accommodation of the detoxicating functions of the economy to conditions of stress. The intractability of the skin lesion would seem to indicate a persistence of causative disturbance.

Date.	Vol. c. c.	Sp. Gr.	Reaction.	Albumen.	Sugar.	Acetone Bodies.	Indican.	T.N. Grms.	Urea-N.	NH ₃ -N.	Purin-N.	Kreatinin-N.	Rest-N.	Micros. Ex.
									Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	Grms. % T.N.	
1907 April 16	1500	1.015	acid	o	o	o	+	12.75	10.27 80.6	0.59 4.7	0.25 2.0	0.54 4.3	1.03 8.1	Sq. epith.; few leuco- cytes; mucus.
April 26	1580	1.013	acid	o	o	o	++	9.18	7.45 81.2	0.54 5.9	0.21 2.3	0.53 5.8	0.41 4.5	Do.
April 30	1720	1.012	acid	o	o	o	++	8.18	6.78 83.0	0.41 5.1	0.22 2.8	0.48 5.9	0.23 2.9	Do.
May 10	1300	1.013	acid	o	o	o	++	8.73	6.87 84.7	0.47 5.4	0.22 2.6	0.51 5.9	0.6 6.9	Do.

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Discussion

DR. MARTIN F. ENGMAN, of St. Louis, said the paper of Drs.

Johnston and Schwartz appealed to him on account of the work he himself had been doing during the past year in connection with this subject. He considered this an extremely important paper. When we glanced back at the work of Osler on "The Erythema Group" we could more readily realize its value. Dr. Osler, in his list of eruptions, in this "Erythema Group" included a large number of so-called skin diseases which embraced purpura, recurrent urticaria, erythema multiforme, and some forms of bullous dermatoses. Among this group, Dr. Engman said, he had repeatedly found such evidences of intoxication as Dr. Johnston had shown. Several of the cases he had seen had gone on to a fatal termination in the course of a few years. He was particularly interested in that part of the paper which referred to the injections of the thyroid extract in order to increase the nitrogen metabolism. We were still ignorant in regard to the etiological factors that brought about this intoxication. The speaker said that, with others, he had thought it highly probable that the intestinal putrefaction was not the cause of the symptoms that Dr. Johnston had pointed out, and that back of it there was probably a failure in resistance which allowed the micro-organisms in the intestinal canal to produce putrefactive changes.

In dermatitis herpetiformis he had always found an increase in indican. These observations he had pointed out about two or three years ago, and taking that as a symptom and guide, he had obtained most excellent results by placing these patients on an absolutely vegetarian diet and giving intestinal stimulants, usually mercury in some form to keep the bowels open.

Another disease which responded well to this test was pompholyx. In these cases there was always indican in excess, and a vegetarian diet, together with catharsis and care, promptly eliminated the disease. When a recurrence took place, the patient invariably gave the history of having gone back to a proteid diet. The important element in the treatment of these cases, of which he had seen seventeen during the past summer, was the vegetable diet. The use of drugs was of secondary importance.

DR. T. CASPAR GILCHRIST, of Baltimore, said he joined with Dr. Engman in congratulating Dr. Johnston and Dr. Schwartz upon their valuable paper, as it opened up a line of work which had been too much neglected by dermatologists. The sweat apparatus, taken collectively, was a gland which compared with the kidneys in its functions. The elimination of deleterious substances through the

sweat glands might be the cause of skin eruptions and these substances were probably eliminated by the kidneys also, and that fact had been emphasized by the authors in their paper. Some work along similar lines had been done at Johns Hopkins in connection with the careful estimation of food taken and the eliminative processes during the puerperal period. These same methods might be employed in connection with the toxemic eruptions of the skin. It was well known that toxic or bacterial substances might be eliminated by the kidneys as well as the sweat glands.

PROF. E. GAUCHER, de Paris, a dit qu'il ne croyait pas que la cause première de la dermatite herpétiforme fût une auto-intoxication, car il avait toujours trouvé dans cette maladie un rapport azoturique normal. La cause de la dermatite herpétiforme était un choc nerveux qu'on trouvait chez presque tous les malades. D'ailleurs la bulle est l'expression cutanée habituelle des altérations trophiques d'origine nerveuse.

SOME EXPERIMENTAL OBSERVATIONS ON THE HISTOPATHOLOGY OF URTICARIA FACTITIA

BY DR. T. CASPAR GILCHRIST, OF BALTIMORE

The author exhibited about sixty lantern slides demonstrating the histopathology of wheals which were produced artificially by drawing down the finger nail or a blunt instrument rather sharply over the skin of patients suffering from urticaria factitia, no other disease being present. Fifteen cases were examined, but the lantern slides represented photomicrographs of sections taken from only seven of the most pronounced cases of this disease. Usually the lesion was excised fifteen minutes after the wheal was produced, but in one case portions of wheals were excised after two minutes, five minutes, eight minutes, fifteen minutes, twenty-five minutes, forty minutes, and sixty minutes. In the section excised after three minutes there was present fragmentation of nuclei which seemed to show death of cells preceding the inflammatory changes which followed. Sections of the wheals from

severe cases showed marked emigration of polynuclear leucocytes, emigration of lymphocytes, pronounced fragmentation of polynuclear leucocytes, and fixed connective tissue cells, apparent increase in mast cells, swelling of the cells of the sweat glands, and fibrin scattered throughout the corium. In the sections excised one hour after, many polynuclear leucocytes were still present but very little fragmentation was noticed. Portions of normal skin were excised under similar conditions so that proper comparisons could be made.

In one very severe case the polynuclear leucocytes were nearly all fragmented almost directly after leaving the blood vessels. In all the cases the wheals usually disappeared clinically within an hour. The pathological picture is undoubtedly one of typical acute inflammation (Cohnheim), and the fragmentation of nuclei is as remarkable as that produced by diphtheria toxin (observation by Dr. William H. Welch, after carefully going over the specimens).

The only explanation which appears to be possible is that some toxin is circulating in the blood, and when a wheal is produced some of the toxin is set free and produces death of cells which is followed by acute inflammatory changes. Therefore a true wheal is an acute inflammatory oedematous swelling due either to local inoculation of irritating substances, as in insect bites, etc., or to drugs or to some toxin probably originating in the alimentary canal.

The author's observations have extended over the last thirteen years and references to his earlier experiments are to be found in Duhring's *Text-book on Cutaneous Medicine*, vol. i, p. 129 (1895); also vol. ii, p. 293, and in the *Johns Hopkins Bulletin*, vol. vii, No. 64, p. 141 (1896).

Discussion

DR. HERMAN LAWRENCE, of Melbourne, said that in 1905 he experimented with a considerable number of patients, children and adults, in connection with the subject of factitious urticaria, and the question arose as to the part this phenomenon played in the chronicity of some of our skin diseases. He recalled the case of a man who was employed in a factory where he was obliged to handle

blackwood and inhale considerable dust; he suffered from dermatitis with well-marked factitious urticaria, the attacks recurring every time he returned to his work, but they finally ceased when he gave up his occupation. X-ray treatment was resorted to in this case with very satisfactory results.

NOTE ON A CASE OF SARCOID

BY DR. S. POLLITZER, OF NEW YORK

Since the first publication by Professor Boeck, of Christiania, describing a new disease under the title of multiple benign sarcoid of the skin, the observations of that disease have multiplied to a sufficient extent to show that the condition is not one of such rare occurrence as its late discovery would seem to indicate. So, for instance, in his latest publication on the subject, Boeck is able to record ten personal cases, while in France, counting in the subcutaneous variety of the same disease described by Darier, nearly as many cases have been noted. Publications on this subject, however, from other countries—Germany, Austria, Italy, America, etc.—have recorded very few cases, or have been wanting altogether. It would seem unlikely that the disease is so much more frequent in Norway and in France than in other parts of the world, and it is reasonable to attribute the paucity of the reports to a lack of acquaintance with the disease. From this point of view alone my case would be worth noting; it appears to me particularly to merit a record, because it presents some unusual features.

The patient, a married woman, 35 years old, is well nourished and healthy-looking; but when she first consulted me she had just returned to New York after a prolonged residence in a sanitarium in the Adirondack Mountains, where she had gone on account of a tuberculosis pulmonum, which had advanced to the formation of a large cavity in the right lung. The cutaneous affection began about five years ago with the sudden appearance of bright and dull red, round or oval, slightly elevated areas from 5 to 20 mm. in diameter, with flat normal surfaces and sharply defined border; no subjective

sensations. On palpation these plaques give the impression of moderately firm infiltrations in the cutis, which is freely movable over the subcutaneous tissues. From their first appearance to the present time they have remained practically unchanged, except that during the first weeks after their occurrence many of them increased slightly in area. New patches, however, have appeared from time to time up to six months ago, since when there has been no fresh eruption. The plaques are located in the face, forehead, cheeks, and nose, the neck, shoulders, the left arm, both forearms and wrists, the abdomen, and the right leg. In their distribution they show only an indifferent symmetry and no predilection for either the flexor or the extensor surface; so, for instance, at the right elbow there are two small patches on the flexor and two on the extensor side. There are in all about twenty-five lesions, and except one near the umbilicus and one on the right leg above the ankle, they are all located on the face and upper extremities. At the tip of the nose and on the *alæ* there is a group of five small lesions from 3 to 8 mm. in diameter which lately have shown a tendency to coalesce. The lesions in the face assume a bluish hue when the patient is exposed to the cold or has a spasm of coughing. Three of the larger plaques—one on the forehead, one on the left arm, one on the left wrist—show near their centre a hemispherical prominence about 4 mm. in diameter, in appearance and to touch suggesting a soft mole (*verruca mollis*). None of the lesions show any scaling, none have shown any sign of atrophy; the inguinal and axillary glands are not notably enlarged; a blood count yielded nothing of interest.

In the diagnosis of the case lupus erythematosus, sarcoma, and pernio were considered, but only to be rejected; and it was only after making histopathological studies and advising with Dr. Darier, of Paris (to whom I desire here to express my obligations), that it became clear that we were dealing with a variety of Boeck's sarcoid. From this disease, however, my case differs in the following particulars:

The color of the lesions is bluish or brownish red rather than yellowish brown; there is no scaling, no central depression, no network of the dilated capillaries, and the very irregular



FIG. 1.—SARCOID:—A sharply circumscribed "Tubercle" in middle cutis, showing giant, epithelioid, and lymphoid cells.

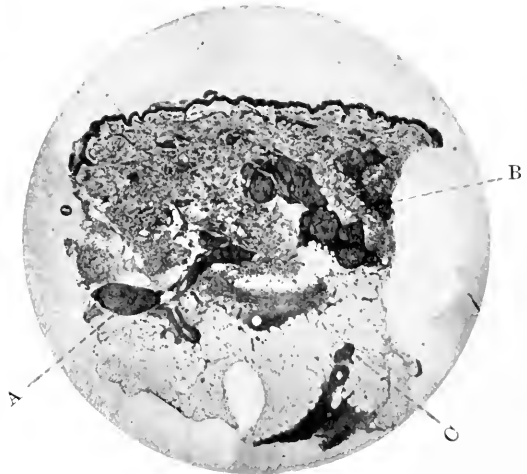


FIG. 2b.



FIG. 2a.

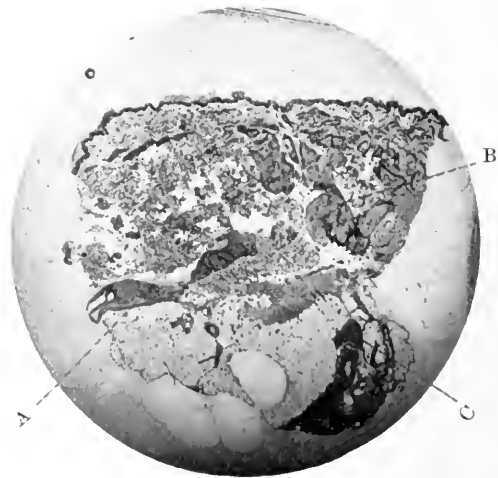


FIG. 2c.

outline with narrow raised yellowish border is absent; there are no yellowish pinhead lichenoid papules; there are no large packets of lymph nodes.

The study of an excised plaque shows the lesions, however, to be identical in structure with the sarcoid of Boeck. This has been described so well by Boeck, and especially by Darier, that I shall pass over it briefly. The sections show larger and smaller cell-masses, round or irregular in outline, lying in the cutis, which is characteristically free from any signs of reaction. These cell masses are scattered through the cutis from the border of the subcutaneous fat up to the subpapillary layer. In Boeck's cases much more massive cell aggregations are described than occur in my case, and they are located, as a rule, rather high in the upper layers of the cutis. I find these cell-masses in relation to the larger vessels occupying a peculiar position; they are usually located on one side of the vessel, seldom surrounding it. In detail these cell-masses consist of epithelioid and lymphoid cells, with a few giant cells. (Plate liii, Fig. 1.) Many of the smaller masses present a picture strikingly like that of tubercle, so that one can realize the force of Darier's statement, that if this be not tuberculous tissue, he would not know what to call it. And yet the most careful search for tubercle bacilli yielded no result, and injections of a suspension of a large part of the excised plaque into the peritoneal cavity of three guinea-pigs provoked no tuberculosis in them.¹

For the purpose of determining the mutual relations of the cell-masses in the cutis a portion of the excised plaque was cut in serial sections. I show you here three views (Plate liii, Fig. 2, *a*, *b*, *c*), approximately from the beginning, middle, and end of the series. The small oval infiltration at the subcutaneous border on the left of the first section may be traced obliquely across the field in the successive sections till it merges into the larger mass of cells in the upper cutis on the right. Similarly the small infiltration near a large vessel in the sub-cutis on the right of the second section gradually passes up to unite with the same mass above it. It seems to me likely, therefore,

¹ The histological work in this case was done in the Pathological Laboratory of the Mt. Sinai Hospital; the animal experiments in the Research Laboratory of the N. Y. Department of Health.

that all the various round, oval, or irregular masses of cells which constitute the new tissue, widely scattered as they appear throughout the cutis, are simply irregular ramifications of one extensive infiltration shaped like the twisted and gnarled root of an old tree with its fantastic tuberosities and outrunning branches.

We are in the habit of regarding a tubercle as an approximately spherical mass. I am in some doubt as to the bearing which the peculiar shape of the irregular infiltration I have described will have on the theory of the relation of the cutaneous process to a distant tuberculous focus. A large number of these cases of sarcoid present evidences of tuberculosis, or at least respond positively to the tuberculine test. You are aware that Boeck has accepted the identity of his sarcoid with the disease described by Darier as *lupoide en disques*, and has agreed with him in regarding it as a tuberculide.

To sum up the points of this brief communication, we have:

1. A case presenting clinically the essential features of Boeck's sarcoid, but differing in some notable respects, occurring in a woman highly tuberculous.

2. Histologically the case presents a picture almost identical with Boeck's sarcoid and Darier's subcutaneous sarcoid, but differing from the former in extending quite uniformly throughout the entire cutis, and from the latter in its virtual absence from the sub-cutis; in this respect it may be described as an intermediary form.

3. The cell-masses on section strikingly resemble tubercle, but the various sections appear to be different parts of a single, or, at most, a few widespread irregular infiltrations, for the most part following the blood vessels. Tuberculosis is excluded by the absence of bacilli and the result of experimental inoculations.

THE FINAL GENERAL MEETING

Following the completion of the official programme, the PRESIDENT, DR. WHITE, said that before the adjournment of the Congress he would call upon the Secretary-General, Dr. Fordyce, to make a supplementary report.

DR. FORDYCE said that since the opening of the Congress cable messages had been received from Prof. Ehrmann and Dr. Spiegler, of Vienna, expressing regret at their inability to be present and wishing the Congress every success.

Letters had also been received from Dr. Unna, of Hamburg, and Dr. Castellani, of Ceylon, expressing their best wishes for the success of the Congress. A letter had also been received from Surgeon-General P. M. Rixey, of the United States Navy, representing President Roosevelt, in which he expressed congratulations at the unusual success of the Congress and the interest that was taken in its work.

DR. M. B. HARTZELL, of Philadelphia, moved that a vote of thanks be extended to the Trustees of the New York Academy of Medicine for their generosity in permitting the use of their building for the meetings of the Congress.

Unanimously carried.

DR. STOPFORD TAYLOR, of Liverpool, said it was impossible for the Congress to adjourn without extending a hearty vote of thanks to the Organization Committee. He proposed a vote of thanks for the way in which they had managed the Congress. The Committee to-day stood in the position of having engineered the best International Dermatological Congress that had ever been held, both from a scientific and social point of view. He expressed regret that his own country had not sent a larger delegation; still, it was their loss, and those who had come would return to their own land well repaid for their time and trouble.

It was also moved and seconded that a vote of thanks be

extended to the President of the Congress, Dr. James C. White, to Dr. James Nevins Hyde, Dr. John A. Fordyce, and Dr. George Henry Fox.

Unanimously carried.

M. le PROF. GAUCHER, de Paris, a dit qu'avant la clôture du Congrès, le devoir de tous était d'adresser des remerciements et des félicitations au comité d'organisation; d'abord au President, le Dr. White, qui, par la dignité de son caractère et la droiture de sa vie, a fait l'admiration de tous; au Dr. Hyde qui l'avait secondé avec autant de dévouement que d'aménité, au Dr. Fordyce qui avait été la cheville ouvrière du Congrès, aux dames charmantes qui avaient embelli le séjour de tous à New York et aux membres du comité. À tous il a rendu grâce et il a été l'interprète de toutes les nations représentées à New York.

Et comme l'Amérique avait transmis à l'Italie le flambeau de la dermatologie internationale, il a souhaité au Congrès de Rome un succès égal à celui du Congrès de New York.

M. le PROF. BERTARELLI, de Milan, a dit qu'il désirait d'abord remercier le très estimé confrère, M. le Prof. Gaucher, des paroles aimables qu'il avait prononcées en faveur de Rome et de l'Italie ainsi que des vœux qu'il avait exprimés pour le succès du Congrès de Rome.

Il espérait que ces vœux émis par l'éminent confrère qui représentait la faculté de Paris si estimée partout, seraient un bon augure pour le prochain Congrès. Il avait confiance que l'accueil de l'Italie répondrait à celui que les Congrès précédents avaient trouvé à Paris, à Vienne, à Londres, à Berlin et à New York, tant au point de vue scientifique, qu'au point de vue de l'amabilité pour tous les confrères qui viendraient à Rome en 1911.

Puis le Prof. Bertarelli a adressé de nouveau les remerciements les plus sincères à M. le President, au Comité et aux confrères Américains pour l'aimable accueil que tous les membres avaient reçu à New York.

THE PRESIDENT, DR. WHITE, before the final adjournment of the Congress, delivered the following valedictory:

"And now, fellow members, we have reached the end of our programme. We may well claim that the interests of Derma-

tology have been advanced by this meeting, and that our mutual acquaintance and respect have been enlarged and strengthened. May we all find in its spirit and accomplishment inspiration for future labors and progress. I thank you all sincerely for the kind consideration you have shown me and for the happily expressed appreciation of our efforts. May you all reach your homes in safety.

“A spark from our embers has been transmitted to Rome, where vestal fires are well preserved, which shall burst forth in full effulgence in nineteen hundred and eleven.

“I now declare this Sixth International Dermatological Congress dissolved.”

End of Proceedings



OFFICIAL SOCIAL PROGRAMME

On Monday evening, September 9th, from eight until eleven o'clock, the President of the Congress officially received the visiting delegates, members of the Congress, and many members of the medical profession of the City of New York at the Hotel Waldorf-Astoria.

On Wednesday afternoon, September 11th, an excursion by boat up the Hudson River and down the bay to Coney Island was provided for the visiting members. In the evening a shore dinner was given at Coney Island and the excursionists participated in the various amusements offered by this unique summer resort.

On Friday evening, September 13th, a banquet was given at the Hotel Waldorf-Astoria by the American members to the foreign members of the Congress. The banquet-hall was appropriately decorated with the flags of the United States and of all the countries represented. Dr. James Nevins Hyde acted as toastmaster and introduced the following gentlemen, who spoke for their respective countries:

Prof. E. Gaucher, for France.

Dr. H. Radcliffe-Crocker, for Great Britain and Ireland.

Prof. Theodor Veiel, for Germany.

Dr. Ambrogio Bertarelli, for Italy.

Dr. Carl Rasch, for Denmark.

Dr. Francis J. Shepherd, for Canada.

Dr. L. de Keyser, for Belgium.

Dr. Tamaharu Tanaka, for Japan.

Dr. Henry W. Stelwagon, for the Sixth International Dermatological Congress.

In addition to these official entertainments, numerous private dinners, luncheons, and theatre parties were given.

A Ladies' Committee, with Mrs. George Henry Fox as Chairman, entertained the visiting ladies during the sessions

of the Congress. To this end one of the parlors of the Hotel Seymour was reserved for their exclusive use, a tea was given on Monday afternoon, September 9th, and during the week there were shopping parties and trips to various points of interest about the city.

LIST OF CASES DEMONSTRATED

TUESDAY, SEPTEMBER 10th

ACANTHOSIS NIGRICANS	Dr. L. Duncan Bulkley
ADDISON'S DISEASE	Dr. Edmund L. Cocks
ADENOMA SEBACEUM	Dr. Charles T. Dade
ANNULAR SYPHILIDE IN A NEGRO INFANT	Dr. Howard Fox
BLASTOMYCOSIS IN A NEGRO	Dr. George Henry Fox
CASE FOR DIAGNOSIS	Dr. E. P. McGavock
CASES FOR DIAGNOSIS (5)	Dr. John A. Fordyce
CONGENITAL ALOPECIA	Dr. George Henry Fox
DERMATITIS HERPETIFORMIS (2 cases)	Dr. John A. Fordyce
ELEPHANTIASIS	Dr. George Henry Fox
ENDARTERITIS LUETICA	Dr. Adelbert B. Berk
EPITHELIOMA (5 cases)	Dr. John A. Fordyce
EPITHELIOMA OF EYELID	Dr. Samuel Stern
EPITHELIOMATA (MULTIPLE) RECURRING FOR THIRTY YEARS	Dr. Samuel Stern
ERYTHEMA INDURATUM (2 cases)	Dr. John A. Fordyce
FOLLICULITIS DECALVANS CURED WITH X-RAY (2 cases)	Dr. S. Lustgarten
GENERAL ALOPECIA WITH NEUROTIC ECZEMA	Dr. L. Duncan Bulkley
IDIOPATHIC MULTIPLE HEMORRHAGIC SARCOMA (KAPOSI)	Dr. Adelbert B. Berk
LENTICULAR CARCINOMA AND CARCINOMATOUS LYMPHANGITIS	Dr. John A. Fordyce
LUETIC INFECTION WITH SYMMETRICAL CUTANEOUS ATROPHY	Dr. John A. Fordyce
LUPUS VULGARIS (4 cases)	Dr. John A. Fordyce
MELANODERMA	Dr. George Henry Fox
MULTIPLE TELANGIECTASES, WITH SPONTANEOUS HEMORRHAGE	Dr. William S. Gottheil
MYCOSIS FUNGOIDES	Dr. S. Lustgarten
PARAPSORIASIS	Dr. William B. Trimble
PITYRIASIS RUBRA (HEBRA) (2 cases)	Dr. George Henry Fox
PITYRIASIS RUBRA PILARIS	Dr. Adelbert B. Berk
PRURIGO (HEBRA)	Dr. John A. Fordyce

RHINOSCLEROMA	Dr. William S. Gottheil
RHINOSCLEROMA TREATED WITH X- RAYS	Dr. Samuel Stern
RHINOSCLEROMA TREATED WITH X- RAYS (2 cases)	Dr. S. Lustgarten
SCROFULODERMA (2 cases)	Dr. John A. Fordyce
SYPHILIS INSORTIA IN A BOY OF EIGHT YEARS	Dr. L. Duncan Bulkley
URTICARIA PIGMENTOSA OF THIRTY- THREE YEARS' DURATION	Dr. Prince A. Morrow
XANTHOMA TUBEROSUM MULTIPLEX	Dr. William S. Gottheil

WEDNESDAY, SEPTEMBER 11th

BLUISH DISCOLORATION OF THE SKIN, CASE FOR DIAGNOSIS	Dr. William T. Corlett
CASE FOR DIAGNOSIS	Dr. T. Caspar Gilchrist
CASE FOR DIAGNOSIS	Dr. James Nevins Hyde and Dr. Frank H. Montgomery
DARIER'S DISEASE	Dr. Jay F. Schamberg
EPIDERMOLYSIS BULLOSA WITH ATROPHY	Dr. Henry W. Stelwagon
ERYTHEMA FIGURATUM PERSTANS	Dr. William T. Corlett
ERYTHEMA PERSTANS	Dr. George Henry Fox
EXFOLIATIO AREATA LINGUÆ	Dr. M. B. Parounagian
EXTENSIVE FOLLICULITIS AND PERIFOL- LICULITIS	Dr. William B. Trimble
EXTENSIVE NÆVUS PILOSUS	Dr. George Henry Fox
IDIOPATHIC MULTIPLE HEMORRHAGIC SARCOMA (KAPOSI)	Dr. M. B. Hartzell
LENTIGO (an unusual case of)	Dr. George Henry Fox
LEPRA—MIXED FORM	Dr. Charles T. Dade
LEPRA—MIXED FORM	Dr. M. B. Parounagian
LEUKOPLAKIA BUCCALIS IN A NEGRO	Dr. Howard Fox
LUPOID SYCOSIS WITH BLEB FORMA- TION	Dr. Jay F. Schamberg
LUPUS ERYTHEMATOSUS DISSEMINATUS CURED BY HOLLÄNDER METHOD	Dr. Adelbert B. Berk
LUPUS ERYTHEMATOSUS IN A COLORED WOMAN	Dr. Jay F. Schamberg
LUPUS VULGARIS CURED WITH X-RAY, MORPHŒA ASSOCIATED WITH GOITRE,	Dr. Jay F. Schamberg Dr. George Henry Fox
PECULIAR ATROPHIC ERUPTION PRE- SENTING AN APPEARANCE ANAL- OGOUS TO LINEAR NÆVUS	Dr. William T. Corlett
RODENT ULCER (MULTIPLE)	Dr. T. Caspar Gilchrist

SCLERODERMA (2 cases)	Dr. George Henry Fox
TUBERCULIDE	Dr. George Henry Fox

THURSDAY, SEPTEMBER 12th

ACNE NECROTICA	Dr. George Henry Fox
ACNE VULGARIS AND ADENOMA SEBACEUM OF THE CHEST	Dr. John A. Fordyce
ADENOMA SEBACEUM	Dr. George Henry Fox
ARGYRIA	Dr. Daisy Orleman-Robinson
BROMODERMA TUBEROSUM (around the eyes)	Dr. Adelbert B. Berk
CARCINOMA OF THE CÆCUM CURED BY EXTRA-ABDOMINAL X-RAY EXPOSURES	Dr. Carl Beck
CASE FOR DIAGNOSIS	Dr. George Henry Fox
CASE FOR DIAGNOSIS	Dr. William B. Trimble
CHANCRE OF THE ELBOW	Dr. Adelbert B. Berk
CHANCRE OF THE PALM	Dr. Boleslaw Lapowski
CHANCRE OF THE PENIS IN A BOY OF NINE YEARS	Dr. William S. Gottheil
DERMATITIS HERPETIFORMIS	Dr. William B. Trimble
DERMATITIS MEDICAMENTOSA (potassium iodide)	Dr. George Henry Fox
DERMATITIS VEGETANS (2 cases)	Dr. John A. Fordyce
EPIDERMOLYSIS BULLOSA WITH PSEUDOMILIA	Dr. John A. Fordyce
FAVUS OF SCALP AND NAILS IN A WOMAN OF TWENTY-FOUR YEARS	Dr. Boleslaw Lapowski
GANGRENE OF THE TOES DUE TO SYPHILITIC ENDARTERITIS	Dr. Howard Fox
IDIOPATHIC MULTIPLE HEMORRHAGIC SARCOMA (KAPOSI)	Dr. Boleslaw Lapowski
LEPRA—MIXED FORM	Dr. Adelbert B. Berk
LEPRA TUBEROSA	Dr. L. Oulmann
LICHEN PLANUS	Dr. L. Duncan Bulkley
LICHEN PLANUS ANNULARIS	Dr. Jerome Kingsbury
LICHEN PLANUS HYPERTROPHICUS	Dr. John A. Fordyce
LICHEN PLANUS VERRUCOSUS OF SKIN AND MUCOUS MEMBRANES	Dr. Boleslaw Lapowski
LUPUS ERYTHEMATOSUS	Dr. John A. Fordyce
LUPUS ERYTHEMATOSUS (2 cases)	Dr. S. Pollitzer
LUPUS ERYTHEMATOSUS: RESULTS OF TREATMENT BY THE CURETTE (2 cases)	Dr. George Henry Fox

LUPUS VULGARIS INVOLVING THE GROINS, LOWER ABDOMEN, AND PENIS: CURED BY CURETTAGE AND THE THERMO-CAUTERY	Dr. Prince A. Morrow
MILIARY TUBERCULOSIS OF THE SKIN AND MUCOUS MEMBRANE	Dr. Boleslaw Lapowski
NÆVUS PIGMENTOSUS REMOVED WITH LIQUID AIR	Dr. William B. Trimble
NÆVUS UNIUS LATERIS	Dr. L. Oulmann
NEUROFIBROMATA (MULTIPLE)	Dr. L. Oulmann
ONYCHOSIS CHRONICA OF FINGERS AND TOES	Dr. Boleslaw Lapowski
PITYRIASIS RUBRA PILARIS (DEVERGIE)	Dr. S. Pollitzer
PRURIGO FEROX (2 cases)	Dr. James C. Johnston
SCLERODACTYLITIS ASSOCIATED WITH RAYNAUD'S DISEASE	Dr. Howard Fox
SCLERODERMA	Dr. Adelbert B. Berk
SCLERODERMA AND SCLERODACTYLITIS	Dr. John A. Fordyce
SLOWLY SPREADING PIGMENTATION OVER LEFT SCAPULA AND CLAVICLE,	Dr. A. R. Robinson
TINEA OF NAILS AND BODY IN A GIRL OF SIXTEEN YEARS	Dr. Boleslaw Lapowski
TRICHORRHEXIS NODOSA	Dr. L. Oulmann
TUBERCULIDE	Dr. George Henry Fox
TUBERCULIDE (2 cases)	Dr. Boleslaw Lapowski
XANTHOMA MULTIPLEX	Dr. James M. Winfield
XANTHOMA TUBEROSUM COMPLICATED BY DIABETES	Dr. Howard Fox

EXHIBITION OF PHOTOGRAPHS, MODELS, SPECIMENS, ETC.

DR. ALDO CASTELLANI

Elephantiasis.

Framboesia tropica—twenty-four illustrations showing primary, secondary, and tertiary eruptions; four photographs showing experimental framboesia in monkeys; two illustrations of *Spirochæte pertenuis*.

Pityriasis flava (face), *pityriasis nigra* (neck).

Pityriasis versicolor—tropical forms of.

Illustrations of fungi, cultures, and clinical features.

Tinea imbricata—clinical and microscopical.

Tinea intersecta—clinical and microscopical.

DR. EMILIO ECHEVERRIA

Elephantiasis arabum.

Lepra—twelve photographs showing various types and stages.

Papalomoyo.

DR. WILLIAM J. ELSER

Bouillon culture of blastomyces.

DR. MARTIN F. ENGMAN AND DR. WILLIAM H. MOOK

Acne rubra seborrhœica—face.

Actinomycosis—neck and face.

Blastomycosis—leg.

Chancre—chin.

Dermatitis gangrænosa infantum—general.

Dermatographism.

Epidermolysis bullosa—face and hands.

Feigned eruption—leg and thigh.

Fordyce's disease.

Herpes zoster (gangrenous)—chest.

Keratosi follicularis—general.

Keratosi palmaris et plantaris.

Lepra.

Lichen planus moniliformis—hand.

Lichen planus—mouth and hands.

Lupus erythematosus disseminatus—face.

Lupus hypertrophicus—face.

Megalosporon ectothrix infection—beard.

Multiple benign cystic epitheliomata—distributed over body.

Paget's disease—back.

Pigmentation following lichen planus—general.

Spirochaeta pallida—photomicrographs showing organisms in foetal liver and kidney.

Sycosis vulgaris.

Syphilis (framboesiform)—face.

Syphilis (tubercular)—back.

Telangiectases following X-Ray burn—neck.

Tinea circinata—hands.

Tinea favosa—scalp.

Tinea unguium.

Tuberculosis verrucosa cutis—knuckle.

Verruca plana—forehead.

Vitiligo—arm.

DR. JOHN A. FORDYCE

Acne varioliformis.

Alopecia (complete) in secondary syphilis.

Arsenical pigmentation.

Atrophy of skin.

Atrophy with syphilis of skin and nervous system.

Biskra button.

Bullous and erythematous eruption (recurring)—hand.

Cancer of both breasts, cancer en cuirasse and cancerous lymphangitis.

Chancre—(a) lower lip, (b) upper lip, (c) chin, (d) temple, (e) inner canthus of eye, (f) breast, (g) back of hand, (h) finger, (i) penis with beginning gangrene.

Cornu cutaneum—penis.

- Darier's disease.
- Dermatitis herpetiformis.
- Dermatitis medicamentosa—(a) iodide, (b) bromide, (c) iodoform.
- Dermatitis papillaris capillitii.
- Dermatitis vegetans.
- Ecthyma térébrant.
- Elephantiasis—(a) leg, (b) vulva.
- Epidermolysis bullosa.
- Epithelioma, primary, of mucous membrane simulating actinomycosis.
- Epithelioma—leg—following sprain.
- Epithelioma—(a) temple—34 years' duration, (b) after X-Ray.
- Epithelioma—(a) eyelid, (b) nose, (c) forehead, (d) cheek, (e) back of hand, (f) upper lip, (g) lower lip, (h) back of ear, (i) neck.
- Erythema induratum.
- Erythema perstans.
- Erythema multiforme following ulcerative gummata of soft palate and tonsil.
- Erythrodermie pityriasique en plaques disseminées.
- Favus—scalp.
- Feigned eruption—mineral acids.
- Folliculitis decalvans.
- Folliculitis—coccogenic.
- Fordyce's disease.
- Gangosa.
- Gangrene—arm—spontaneous.
- Ichthyosis.
- Idiopathic multiple hemorrhagic sarcoma (Kaposi).
- Keratosis plantæ.
- Keratosis pilaris with lichenification.
- Lepra—(a) tubercular, (b) contracture of fingers.
- Lichenification—universal.
- Lichen planus—universal.
- Lichen planus hypertrophicus.
- Lichen planus with pigmentation resembling syphilis.
- Lupus erythematosus—lower lids.
- Lupus erythematosus—face—telangiectic form.
- Lupus erythematosus discoides

- Lupus erythematosus disseminatus.
Lupus erythematosus—face and backs of hands.
Lupus vulgaris—20 years' duration—arms, legs, face.
Lupus vulgaris—early—face.
Mal perforans.
Marjolin's ulcer.
Morbilli.
Multiple benign cystic epithelioma—(a) mother, (b) daughter.
Multiple benign cystic epithelioma with malignant transformation.
Multiple sarcoma of skin.
Mycosis fungoides.
Nævus—eyelid.
Nævus papillaris.
Paget's disease—(a) nipple, (b) gluteal region.
Pemphigus vegetans.
Pemphigus vulgaris.
Pigmentation following—(a) pemphigus, (b) epidermolysis bullosa, (c) tuberculosis of the kidney, (d) dermatitis herpetiformis.
Pigmentation—(a) premycotic (b) in hyperthyroidea.
Pityriasis rubra pilaris.
Porokeratosis.
Psoriasis.
Purpura hemorrhagica.
Pustular dermatitis following demodex infection of sebaceous glands of the back.
Raynaud's disease—ears.
Rhinoscleroma.
Sclerodactylitis—radiograph showing deformity of phalanges.
Sclerodermia.
Seborrhœic dermatitis and secondary syphilis.
Symmetrical circinate and gyrate erythema.
Syphilis—A series of photographs illustrating unusual types of secondary and tertiary eruptions.
 Congenital.
 Hereditary—showing cicatrices about mouth.
 Hereditary—ulceration simulating an initial lesion.
 Syphilis en nappe.

Syphilis and facial paralysis.

Syphilitic dactylitis.

Syphilitic glossitis.

Syphilitic myositis (sterno-cleido-mastoid).

Syphilitic pigmentation in patient with chronic nephritis.

Saddle nose in acquired syphilis in a child.

Tinea barbæ.

Tinea circinata.

Tinea tonsurans simulating alopecia areata.

Tuberculosis of lip.

Vicious cicatrix following burn of neck.

Vitiligo—(a) white man, (b) negro.

Von Recklinghausen's disease.

Xanthoma.

Photomicrographs of

Adenoma sebaceum.

Angioma—(a) cavernous, (b) hypertrophic.

Blastomycosis.

Carcinomatous lymphangitis.

Comedones (single and double).

Dermatitis seborrhœicum.

Dermatitis vegetans.

Eczema.

Epidermolysis bullosa with pseudo-milia.

Epithelioma (various types of squamous and basal-celled).

Erythema induratum.

Folliclis.

Gangosa.

Herpes zoster.

Ichthyosis.

Idiopathic multiple hemorrhagic sarcoma (Kaposi).

Keloid.

Keratosis follicularis.

Lepra.

Leucoplakia.

Lichenification.

- Lichen hypertrophicus.
 Lichen planus.
 Lupus erythematosus.
 Molluscum contagiosum.
 Mycosis fungoides.
 Nævus papillaris.
 Nævus unius lateris.
 Paget's disease—(a) nipple, (b) buttock.
 Pemphigus.
 Pityriasis rosea.
 Pityriasis rubra pilaris.
 Psoriasis.
 Psoriasis and epithelioma.
 Sclerodermia.
 Syphilis, illustrations of typical and atypical primary, secondary, and tertiary lesions and a series showing thrombosis of vessels and giant cell formation in serpigenous lesions.
 Syphilis and epithelioma.
 Tuberculosis—various types of tuberculous infection of the skin.
 Verruca.
 Von Recklinghausen's disease.
 Xeroderma pigmentosa.
- Cultures of different varieties of microsporon and megalosporon and of achorion Schönleini on glucose agar.
- Gross pathological specimen of gangosa received from the Island of Guam.
- Microscopic specimens of the rarer as well as common cutaneous lesions.

DR. GEORGE HENRY FOX

- Alopecia areata—(a) male, (b) female.
 Chromophytosis—arm (2 cases).
 Chromophytosis diffusa—(a) back, (b) chest.
 Chromophytosis gutta—back.
 Dermatitis calorica—fingers.
 Dermatitis herpetiformis—erythematous form—chest.
 Dermatitis herpetiformis—pustular form.
 Dermatitis herpetiformis—vesicular form—back.
 Dermatitis medicamentosa—(a) bromide, (b) copaiba.

- Dermatitis traumatica (electric spark).
 Dermatitis venenata (Rhus)—(a) back of hand, (b) wrist (2 cases).
 Dermatophia diffusa.
 Dermatophia linearis.
 Dermatophia maculata.
 Eczema—(a) palm, (b) back of hand, (c) soles, (d) inguinal region, (e) breasts, (f) neck, (g) legs.
 Eczema impetiginosum.
 Eczema papulosum.
 Eczema psoriasiforme.
 Eczema pustulosum.
 Eczema seborrhœicum—(a) chest, (b) scalp.
 Eczema squamosum.
 Eczema squamosum (case of Dr. Robinson).
 Eczema unguium.
 Eczema verrucosum.
 Eczema—vitiligo—macroductylia.
 Erythema multiforme bullosum.
 Erythema multiforme—(a) face, (b) back, (c) back and thighs, (d) arm and chest.
 Erythema nodosum.
 Favus—legs (2 illustrations).
 Folliculitis decalvans (3 cases).
 Hypertrichosis—partial treatment.
 Ichthyosis—(a) face and trunk, (b) trunk (2 cases), (c) legs (2 cases).
 Impetigo contagiosa—(a) hand, (b) foot.
 Lepra maculata—(a) trunk (2 illustrations), (b) forearm and palm, (c) back and legs.
 Lepra—perforating ulcer!
 Lepra tuberculosa.
 Leuconychia.
 Lichen planus—(a) hand, (b) forearm (2 cases), (c) thighs and legs (6 cases), (d) sacral patch, (e) back and axilla, (f) back, (g) trunk and legs.
 Lichen ruber—acuminate and umbilicated lesions.
 Lichen ruber—(a) back of neck (2 cases), (b) arms and legs, (c) buttocks, (d) popliteal space, (e) buttocks and thighs, (f) buttocks and popliteal spaces, (g) backs of hands, (h) backs of hands and forearms, (i) palm (2 cases), (j) knees, (k) back, (l) buttocks and legs, (m) arm, (n) cubital space, (o) palm, (p) knees and ankles, (q) chest.

Lichen ruber moniliformis (2 illustrations).

Lichen ruber papulosus (2 illustrations).

Lichen ruber rugosus—(a) popliteal spaces, (b) back of hands, (c) knees.

Lichen ruber squamosus.

Lichen ruber squamosus (psoriasiform type).

Lupus vulgaris.

Lupus vulgaris. Treated with dental burr.

Mycosis fungoides—(a) premycotic stage, (b) axilla (2 illustrations), (c) shoulder (3 illustrations), (d) back (2 cases), (e) face and breasts, (f) legs (3 cases), (g) thighs (5 illustrations), (h) inguinal region (2 cases), (i) face (2 cases. Case of Dr. Lustgarten), (j) buttock and thigh (case of Dr. Trimble).

Myxœdema.

Nævus linearis—(a) neck, (b) palm.

Nævus pigmentosus—(a) before treatment, (b) after treatment.

Nævus vasculosus—(a) before treatment, (b) partially removed by electrolysis.

Onychauxis.

Osteoarthropathy (2 illustrations).

Pemphigus vegetans.

Pemphigus vulgaris.

Pernio.

Psorospermosis—(a) back, (b) chest.

Purpura—legs (3 cases).

Rare papular disease of the axilla.

Rosacea erythematosa.

Rosacea hypertrophica (2 cases).

Rosacea pustulosa (2 cases).

Sarcoma (4 cases).

Sclerodermia—generalized (2 illustrations).

Syphilis—chancre of lip (3 cases).

Syphilis—pustular.

Syphilis—squamous (2 cases).

Syphilis—tuberculo-squamous.

Syphilis—tuberculo-ulcerative.

Tuberculosis disseminata.

Tuberculosis verrucosa.

Verruca ulcerans.

Vitiligo and morphœa.

DR. HOWARD FOX

SKIN DISEASES OF THE NEGRO.

Acne vulgaris—face.

Acne indurata—face (2 cases).

Blastomycetic dermatitis—buttock.

Chromophytosis—(a) arm, (b) chest, (c) chest and abdomen.

Dermatitis papillaris capillitii (3 cases).

Eczema—breast and arms.

Fibromata—back.

Keloid—(a) neck, (b) chin (2 cases), (c) chest, (d) head and trunk (4 illustrations. Case of Dr. R. B. Carmichael.)

Leuconychia (2 illustrations).

Leucoplakia buccalis (2 illustrations).

Lichen planus—(a) leg, (b) wrist, (c) back of hand and wrist, (d) forearm (2 illustrations).

Lichen ruber acuminatus—(a) shoulders, (b) forearm and palm.

Lupus vulgaris—face (2 illustrations).

Pigmentation following syphilis (2 cases).

Pityriasis rubra (Hebra)—(a) face, chest, and arms (2 illustrations. Case of Dr. Martin Engman), (b) back, (c) hands.

Syphilis—annular (early)—(a) neck (2 cases), (b) face (3 cases), (c) upper lip, (d) lip and chin, (e) face (case of Dr. J. A. Fordyce), (f) face, trunk, and arms (4 illustrations. Case of Dr. R. B. Carmichael).

Syphilis—chancre of lip.

Syphilis—congenital—(a) chin, (b) legs.

Syphilis—papular—trunk.

Syphilis—papulo-pustular (3 illustrations. Case of Dr. R. J. Devlin).

Syphilis—serpigenous—back of hand.

Syphilis—tubercular circinate—(a) neck, (b) back.

Tinea capitis et corporis.

Vitiligo—(a) back of hand, (b) prepuce, (c) palm, (d) penis and scrotum, (e) face (2 illustrations), (f) back and legs, (g) anterior trunk and extremities, (h) legs, (i) elbows, (j) trunk (case of Dr. R. J. Devlin).

Zoster—(a) neck, (b) lumbar region.

T. CASPAR GILCHRIST

Acne vulgaris.

A series of photomicrographs illustrating the pathology and bacteriology; showing that nodular acne is a giant cell granuloma and due to the presence and growth of bacillus acnes (Gilchrist).

Urticaria factitia.

A series of photomicrographs illustrating the histopathology of experimental urticaria factitia. Photographs showed wheals, produced artificially, which were excised after 2, 5, 8, 10, 15, 30, and 60 minutes.

Numerous photographs of common skin diseases grouped for the purpose of teaching dermatology to students.

Two gross pathological specimens of dogs' lungs, showing nodules produced by intravenous inoculation of pure culture of blastomycetes dermatidides from the first case of blastomycetic dermatitis.

DR. WILLIAM S. GOTTHEIL

Wax Casts of

- Carcinoma (fungating)—penis.
- Chancre (eroded).
- Chancre—lip.
- Chancre—penis.
- Chancroids.
- Chancroids—penis—negro.
- Dactylitis syphilitica.
- Epithelioma—ear.
- Epithelioma—nose.
- Erythema multiforme.
- Gumma (exulcerated)—leg.
- Gumma (exulcerated)—penis.
- Gummata—arms.
- Keratosis syphilitica hereditaria.
- Onychia syphilitica.
- Onycholysis.
- Perifolliculitis—knee.
- Pompholyx.
- Pseudochancres (gumma of penis)
- Psoriasis—nails.
- Rhinophyma.
- Rhinoscleroma.

- Rupia syphilitica.
 Syphiloderm (healing)—leg—negress.
 Syphiloderm (papulo-squamous)—palm.
 Syphiloderm (tertiary)—ear.
 Syphiloderm (tertiary ulcerative)—knee.
 Syphiloderm (tubercular)—nose.
 Verruca subungualis.

DR. JOSEPH GRINDON

- Arsenical pigmentation.
 Epithelioma adenoides cysticum.
 Granuloma inguinale tropicum.
 Keratosis follicularis (White).
 Lepra (tubercular).
 Lupus vulgaris (56 years' standing).
 Lupus vulgaris showing epithelioma at site of X-ray burn.
 Pemphigus acutus (post mortem).
 Xanthoma diabeticorum.

DR. JAMES NEVINS HYDE, DR. FRANK H. MONTGOMERY,
AND DR. OLIVER S. ORMSBY

- Arsenical pigmentation and keratosis—generalized.
 Blastomycosis.—A large series of photographs of a number of reported and unreported cases of cutaneous and systemic blastomycosis, illustrating the clinical and histological features of the disease; cultures and microscopical preparations of blastomycetes and experimental blastomycosis in the guinea-pig.
 Carcinoma (?) Sarcoma (?)
 Dermatitis gangrænosa infantum.
 Dermatitis—local traumatic—face.
 Keratodermia.
 Lepra tuberosa.
 Lichen planus et atrophicum (Hallepeau).
 Lupus pernio.
 Morphœa—resembling "White Spot Disease of Westberg."
 Morphœa guttata (White Spot Disease) and sclerodermia in same patient.
 Nævus—extensive unilateral pigmented.
 Paraffine prosthesis—results of in the skin.

Persistent erythematous points and areas simulating purpura.
 Recurrent erythema.
 Tumor following paraffine injections.
 Urticaria pigmentosa with xanthoma-like lesions.
 Verruca plana.
 Verruca simplex.
 Xanthoma multiplex.
 Xanthoma multiplex et planum.
 Xeroderma pigmentosa—in three members of one family.

DR. A. D. MEWBORN

Fifty living cultures of different varieties of microsporons—(a) lanosum,
 (b) Audouinii, (c) felineum; three weeks old; grown on glucose-agar
 Six cultures of achorion Schönleini on glucose-agar.

DR. HOWARD MORROW

Fibroma.
 Lepa.
 Lichen planus.
 Culture tubes of blastomyces and coccidioides.

DR. MAX VON NIESSEN

Syphilis bacillus von Niessen.

A series of illustrations showing cultural characteristics and microscopical features of the bacillus von Niessen.

Photographs of experimental syphilis in rabbits produced by bacillus von Niessen.

DR. WILLIAM A. PUSEY

Atrophy, idiopathic, of skin (2 illustrations).
 Dermatitis vegetans.
 Epidemic scarlatiniforme erythema (Savill's disease).
 Epidermolysis bullosa (2 illustrations).
 Erythema bullosum.
 Erythema iris bullosum.
 Erythema iris (Zeisler's case).
 Erythema multiforme (2 illustrations).
 Erythema multiforme bullosum (2 illustrations).
 Erythema multiforme papulosum.

Erythema scarlatiniforme.

Granuloma pyogenicum.

Keloid.

Kraurosis vulvæ (2 illustrations).

Lupus erythematosus.

Nævus, (b) result with carbon dioxide.

Nævus vascularis, (b) result with carbon dioxide.

Osteomata of fingers, (b) skiagraphs of same hand.

Pemphigus foliaceus.

Urticaria from aspirin.

DR. M. L. RAVITCH

Lupus erythematosus.

DR. JAY F. SCHAMBERG

Bullous and ulcerative lichen planus (clinical and histological).

Chicken-pox, (a) average eruption; (b) unusually extensive eruption; (c) eruption in adult; (d) impetigo varicellosa.

Lupus erythematosus—extensive—negress.

Lupus vulgaris—extensive—cured by X-rays.

Measles, the different forms of the exanthem; cancrum oris.

Parakeratosis variegata (clinical and histological).

Rubella—(a) normal type; (b) morbilliform variety; (c) scarlatiniform variety.

Scarlet fever—(a) miliary vesicles as a part of the exanthem; (b) desquamation upon the face; (c) pronounced desquamation upon the trunk; (d) desquamation upon the dorsa of the hands; (e) of the palms; (f) exfoliation of the horny layer of hands en masse; (g) enlargement of lingual papillæ; (h) purpura hemorrhagica in scarlet fever.

Small-pox—(1) serial photographs illustrating the course and development of the eruption; (2) congenital small-pox; (3) photographs illustrating the protective influence of vaccination; (5) variola modificata (varioid); (6) hemorrhagic small-pox; (7) photographs illustrative of the mild type of small-pox; (8) cutaneous complications—(a) alopecia, (b) gangrene of the skin, (c) consecutive exfoliative dermatitis, (d) purpura, etc.; (9) photograph illustrating the effect of iodine upon the small-pox eruption.

Typhus fever eruption.

Vitiligo—negro; almost universal.

Vitiligo—(a) negress; (b) restoration of pigment in some areas.

Various dermatoses.

Ulerythema sycosiforme with bleb formation (clinical and histological).

Kaiserling specimens of small-pox skin.

A new comedo extractor.

DR. FRANCIS J. SHEPHERD

Blastomycosis.

Dermatolysis.

Lupus vulgaris.

Pityriasis rubra pilaris.

Sarcoma.

Tertiary syphilides.

DR. HENRY W. STELWAGON

Actinomycosis (2 cases).

Acne varioliformis (2 cases).

Blastomycosis (3 cases).

Dermatitis exfoliativa (3 cases).

Dermatitis herpetiformis (3 cases).

Epidermolysis bullosa.

Larva migricans.

Lichen variegata.

Linear nævus (3 cases).

Pityriasis rubra pilaris (4 cases).

Tuberculosis verrucosa cutis.

DR. STOPFORD TAYLOR AND DR. R. W. MACKENNA

Adenoma sebaceum—a family disease

Disseminated follicular lupus.

Epidermolysis bullosa hereditaria.

Epithelioma developing on lupus.

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