A STUDY OF A CASE OF YAWS (FRAMBESIA
TROPICA) CONTRACTED BY AN AMER-
ICAN SOLDIER IN FRANCE *

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PHILADELPHIA

Yaws, or frambesia, is essentially a tropical infectious and contagious disease caused by *Spirochaeta pertenuis* and characterized by a frambesiform granulomatous eruption.

Our knowledge of yaws is due to the following investigators: Char-
louis,¹ who in 1881 proved by actual experiment that syphilis and yaws
are two distinct maladies. This investigator inoculated thirty-two
Chinese prisoners with crusts and scrapings from yaws lesions, and in
twenty-eight instances succeeded in producing characteristic yaws. He
also succeeded in inoculating a native suffering from yaws with syphilis,
thereby definitely disproving the assumption that the two conditions
were one and the same. It is a further matter of established fact that
a syphilitic patient may contract yaws in the usual manner, as well as
experimentally. For our clinical knowledge of yaws, we owe much
to Numa Rat² and more recently to Castellani.³ Rat's report, pub-
lished in 1891, has become classic. The most important contribution
to the history of the disease was the discovery of the causative agent
(*Spirochaeta pertenuis*) by Aldo Castellani³ in 1905. The organism
was cultivated in 1912 by Noguchi,⁴ and important immunologic studies
have since been made, notably by Neisser,⁵ Nichols⁶ and others.

Few, if any, genuine cases of yaws have been reported in which the
disease was contracted in regions other than the countries in which it is
endemic. However, cases of imported yaws occurring in nontropical

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1. Vierteljahrschr. f. Dermatol. u. Syph. **8**: 1881.

2. Rat, N.: Framboesia (Yaws): Its Nature and Treatment, London, 1891.

3. Castellani: J. Ceylon Branch Brit. Med. Assn., **6**:17, 1905.

4. Noguchi: München. med. Wchnschr. **58**:1550, 1911.

5. Neisser, Baermann and Halberstädter: München. med. Wchnschr. **53**:
1337, 1906.

6. Nichols: J. Exper. Med. **12**:616, 1910; **14**:196, 1911.

countries have been reported in the literature. French writers (Breton, Rocheford and Labat) state that yaws occurred along the Mississippi river among the Indians, especially among the tribe of Caribs. Wood⁷ reviews all the cases of yaws reported in the United States from the first authentic reference of the disease by Buckell, in 1737, to the year 1915. There were nine cases in all, including the case reported by Wood. Some of these were imported from tropical countries. In other cases the genuineness of the diagnosis may be questioned, particularly in view of the absence of laboratory evidence. In the case reported by White and Tyzzer⁸ the disease was observed in a West Indian. This case was probably an imported one.

In the case reported by us the disease was contracted in France, probably through contact with an infected man stationed there during the war.

In a personal communication to us concerning this case, Castellani writes:

From the description you give and the photographs, I would diagnose the case as one of yaws. I am not aware of the disease being previously recorded in France, but of course during the war a large number of native troops and workmen were imported into France from the tropical countries, and they may have imported the disease with them. As regards mode of infection, I am inclined to give more importance to direct contact than to insect carriers. Of course, in the tropics there is no doubt that in many cases the disease is carried by flies.

Dr. John A. Fordyce⁹ has personally communicated to us information concerning an American sailor who contracted yaws while on duty at Brest, France.

Cassar¹⁰ reports an observation on a patient with a tertiary case of yaws whom he had seen in France, September, 1918. This patient, an Annamite, was a soldier in the French army, who contracted yaws some years before in Ho-Keou. This is the only report of yaws occurring among soldiers recently mobilized in France that we have been able to find in the literature.

REPORT OF A CASE

The following is the history of an American soldier, in whom a clinical diagnosis of yaws was made. He contracted the disease while serving in France. He was admitted to the dermatologic service of Dr. Jay Frank Schamberg, at the Philadelphia General Hospital, Dec. 30, 1919.

7. Wood: *Am. J. Trop. Dis.* **2**:431, 1915.

8. White and Tyzzer: *Jour. Cutan Dis.* **29**:138, 1911.

9. Since this paper was written, C. S. Stephenson [*Military Surgeon* **47**:344 (Sept.) 1920] reports a case of yaws occurring in an American sailor who was infected in Brest, France. This case, we believe, is the same one mentioned above in a personal communication from Dr. John A. Fordyce.

10. Cassar: *Ann. de dermat. et syph.* **7**:12, 1919.

The family history had no bearing on the condition. The patient was born in Philadelphia. He denied having had any infectious disease, gonorrhea or syphilis. His occupation prior to army service was that of a plumber's helper.

He joined the Royal Canadian Army, enlisting in Canada, during the early part of 1917, and was sent to England a few months later. He arrived at Folkstone and remained there for three weeks; he was then sent to France. At this time he was a member of the Royal Canadian Dragoons (cavalry), and he remained with this branch of the service until he was discharged in 1919. The members of this organization were composed of Americans and Canadians. He arrived in France about July, 1917, departing about August,

Fig. 1.—Circumscribed, infiltrated raised patches on scalp.

1919; most of this time, at intervals of fifteen months, was spent at Etappes in the northern part of France. This place was a large base for cavalry and infantry troops. Thousands of soldiers were gathered here: Canadians, Australians, New Zealanders, South Africans (white men), New Foundlanders and Chinese—labor battalion. He said that there were no soldiers from Algeria or India, indeed no other men than white, except negroes from Canada and Australia. About the longest time that he was away from Etappes was for three months, which were spent at Cambrai and its environment. On this occasion the cavalry followed in the wake of the tank attack on the German lines. For a time he was stationed at Valency and Mont-Gardens. The only time he saw dark skinned soldiers of the Allies was when he would meet them along the streets or in such places as saloons and Y. M. C. A. huts. At no time was he in close contact with them, such as sleeping in the same barracks.

He left France during the early part of August, 1919, from the port of Boulogne. Prior to this time he was stationed at the base at Etappes for some months. On the boat crossing the channel there were only Canadian troops. He arrived at Folkstone, England, and then went directly to Aldershot, England, to the Duke of Connaught Hospital. He was sent to the hospital from France on account of illness. The first symptoms noticed (while at Etappes) were rheumatoid pains in the knees and shoulders. At times these pains were sufficiently severe to incapacitate him. He had no other complaint. He traveled from France to the hospital in England as an ambulatory case. On arrival at the hospital he was confined to bed; later he had fever, 104 to 105 F., for three or four days. He was in the hospital one month, the pain gradually disappearing; he had no skin manifestation at this time. In the

Fig. 2.—Lesions on nose and hands.

same hospital and in the same ward were British troops recently returned from India, suffering from malaria. He also came in contact with a white man from Africa, who, in the patient's opinion, had similar lesions to those the patient had when he came under our observation.

He left the hospital about the middle of September, en route to Whitly, England, awaiting debarkation. He remained there for one week and was then sent to Liverpool; he sailed from that port and landed at Halifax in the early part of October. He was sent to Toronto for discharge on October 15. From Toronto he came directly to his home in Philadelphia. He was feeling well at that time. About a week after his return he first noticed small "pimples" on his palms which gradually became larger until they reached the size of the present lesions. One week later lesions appeared on the scalp and soles of his feet, although he felt well.

Physical Examination.—The general physical examination was negative except for a generalized adenopathy. The lymph nodes, with the exception of the epitrochlears, were about the size of almonds.

Dermatologic Examination.—The eruption was distributed on the palms, soles, scalp, forearms, throat and penis.

On the scalp there were five distinct areas of circumscribed, infiltrated raised patches, exhibiting a distinct elevated border and central depression and covered with a firm, bright yellow crust. The patches in the main were roundish, except where the lesions had coalesced. They were approximately of the size of a five-cent piece. On the left side of the scalp, in the parieto-occipital

Fig. 3.—Lesions on palms of hands.

region, was a coalescent patch 8 by 4 cm. One of the patches was of crescentic shape with a raised border and a cicatricial base and center, where ulceration had previously been present (Fig. 1).

The lesions in general had a verrucoid and papillomatous surface and bore a general resemblance to the lesions of blastomycosis. For the greater part, the patches appeared to be devoid of hair. On the center of the dorsum of the nose, there was a conical, rounded lesion about 1 cm. in diameter, projecting about 5 mm. above the level of the skin and covered with a yellow and brown crust. The other lesions were situated as follows: a lesion the size of a five-cent piece on the posterior aspect of the arm, near the elbow; one, half that size on the flexor surface of the arm nearby (Fig. 2); one large lesion on the palm of each hand (Fig. 3); one lesion 1.5 cm. in diameter on the flexor aspect of the third phalanx of the ring finger of the left hand; three well developed lesions on the plantar surface of the right foot. There

was one lesion on the interdigital space (between the great and first toe). A lesion, the size of a quarter, was on the outer aspect of the right foot below the malleolus (Fig. 4). There were two large lesions, oval in shape and varying in a general way in size from that of one cent to that of a five-cent piece, on the inner side of the left leg, just above the malleolus. Another lesion the size of a five-cent piece was situated in the popliteal space. Nearly all of the latter lesions were elevated 5 mm. or so above the skin and had a distinct fungoid or papillomatous appearance. Many were covered with a crust, which on being detached, through violence, exposed an irregular, reddish, ulcerated surface. The palmar and plantar lesions projected well above the skin level, and showed an irregular, wartlike surface, covered with reddish and yellowish crusts. On the left forefinger, and scattered elsewhere on the palmar aspects of the fingers, were pinhead sized and large sized conical, papular reddish spots, with central horny plugs. As the central plugs fell out they left a depressed central pit.¹¹

On the prepuce were numerous wartlike excrescences which bore a rough resemblance to condylomata acuminata.

On the columna of the nose and on the left nostril were two, lentil-sized to pea-sized, obtuse, dull red elevations.

Stretching across the entire soft palate was a band, about 2 cm. in diameter, of a filmy whitish discoloration on a slightly inflammatory base. It had an appearance intermediate in character between a huge mucous patch and a leukoplakia. There was also a whitish noninflammatory patch on the right buccal membrane.

Dark Field Examination.—The serum obtained from the surface of some of the skin lesions showed spirochetes having the morphologic characteristics of *Spirochaeta pallida*. The secretion obtained from the throat lesion was negative.

Wassermann Reaction.—The Wassermann reaction was + + + + with cholesterolized, alcoholic, syphilitic liver and acetone, insoluble lipid antigens.

Blood culture was negative. Intratesticular injection into rabbits was made with an emulsion from one of the skin lesions. The results are given under the head "Experimental Studies."

Histopathology.—The microscopic changes in the skin in yaws have been carefully studied by Unna, MacLeod, Jeanselme, Plehn, and in more recent years, by Schüffner, Marshall, Shennan, Siebert, Ashburn, Craig, Löhe, and White.

Briefly stated, the changes found are: a marked thickening in the epidermis with elongation of the rete pegs; swelling, vacuolation and degeneration of the epithelial cells; not infrequently sharply circumscribed areas in the epidermis containing polymorphonuclear leukocytes and detritus (these in reality represent miliary abscesses, in which spirochetes are not infrequently found); marked edema of the corium and the presence of a diffuse cellular infiltration made of polymorphonuclear leukocytes, large and small mononuclear leukocytes, eosinophils, plasma and mast cells and connective tissue cells. In nodules that have existed for some time plasma cells are seen in large numbers.

11. These lesions bear some resemblance to "follicles." Castellani described lesions of a similar nature and referred to them as a "peculiar frambeside of the palms"; Castellani and Chalmers: *Manual of Tropical Diseases*, Ed. 3, p. 1550.

MacLeod has called attention to the fact that there is no perivascular cell infiltration nor endothelial proliferation, and that this contrast is of great importance in the differentiation from syphilis. In yaws, there are more changes in the epidermis and less in the corium than in syphilis. Furthermore, greater edema in the corium is encountered, and giant cells are as a rule absent.

In our own case, a nodule was removed from the right forearm and stained for histologic study; it was also stained with the Levaditi stain for spirochetes.

Fig. 4.—Lesions on right foot.

A well pronounced necrotic crust (Fig. 5) was seen covering a part of the epidermal surface. There was enormous hyperplasia of the epiderm, with great thickening and elongation of the papillary rete projections (Figs. 6 and 7). Parts of the epidermis appeared to be changed, but elsewhere the intercellular spaces were infiltrated with polymorphonuclear leukocytes. In one area a distinct miliary abscess was seen on a level with the summits of the papillae; in this abscess seven or eight spirochetes were seen in the Levaditi stained sections (Fig. 8).

Some of the epithelial cells exhibited a degenerative change. Throughout the corium edema was present, and a rich polymorphonuclear leukocyte infil-

tration was seen. Lymphocytes and plasma cells were present in moderate numbers.

The blood vessels exhibited no perivascular change, an observation corroborated by Prof. Allen J. Smith of the University of Pennsylvania and Prof. Randle C. Rosenberger of the Jefferson Medical College.

Treatment.—Neo-arsphenamin, 0.9 gm., was administered intravenously, resulting in the disappearance of many of the lesions and marked improvement in others in a fortnight. Fourteen days later a second injection of the same dose was given, which caused a complete resolution of the remaining lesions (Fig. 9). The Wassermann reaction at this time, performed with the three stated antigens, was + + + +. Frequent Wassermann tests were performed, and the reaction remained + + + + until the end of February, 1920, at which time the reaction was + + + with the syphilitic liver antigen, but remained at + + + + with the other two antigens. The table is a chronologic record of treatment and of the Wassermann reactions.

WASSERMANN REACTION

Date	Antigens		
	Cholesterolized	Alcoholic Syphilitic Liver	Acetone Insoluble Lipoids
Jan. 2, 1920.....	+ + + +	+ + + +	+ + + +
Jan. 9, 1920.....	+ + + +	+ + + +	+ + + +
Jan. 16, 1920.....	+ + + +	+ + + +	+ + + +
Jan. 22, 1920*.....	+ + + +	+ + + +	+ + + +
Feb. 1, 1920.....	+ + + +	+ + + +	+ + + +
Feb. 5, 1920*.....	Test not performed		
Feb. 13, 1920.....	+ + + +	+ + + +	+ + + +
Feb. 22, 1920.....	+ + + +	+ + + +	+ + + +
Feb. 26, 1920.....	+ + + +	+ + +	+ + + +
March 4, 1920.....	+ + +	+ +	+ + +
March 19, 1920.....	+ + +	+ +	+ +
April 2, 1920.....	+ + +	+ +	+ +
April 9, 1920.....	+ + +	+ +	+ +
April 14, 1920*.....	Test not performed		
April 19, 1920.....	+ + +	+ +	+ +
July 8, 1920.....	+	Neu.	Neu.

* 0.9 gm. neo-arsphenamin given intravenously.

A third intravenous injection of 0.9 gm. of neo-arsphenamin was given in April, 1920. No further Wassermann tests were made until July, 1920, at which time the tests showed a + reaction with the cholesterolized antigen and a negative reaction with the alcoholic liver and acetone insoluble lipoid antigens. The patient has remained subjectively well and has been free of any clinical occurrence.

PARASITOLOGY

Yaws, like syphilis, is a spirochetal disease. To the student of syphilis it is of particular interest since it is in many ways similar to this disease clinically and biologically. So closely clinically do the two diseases simulate each other that differential diagnosis is often difficult; indeed for a long time it was maintained by many that yaws was a tropical form of syphilis. No less an authority than Jonathan

Hutchinson concurred in this opinion. As we shall point out, the laboratory differentiation of the two diseases is likewise difficult. A knowledge of yaws is perhaps of aid to a better understanding of the immunologic problems of spirochetel diseases. A summarization of our knowledge of the differences in immunity tests, experimental lesions and in serum reactions between the two organisms is of interest.

Fig. 5.—Section of yaw stained with hematoxylin and eosin; necrotic crust overlies a part of the epidermal surface of the lesion with dense infiltration with polymorphonuclear leukocytes; $\times 70$.

Spirochaeta pertenuis is an extremely delicate spiral-shaped organism, varying in length from a few microns to 18 to 20 microns and even more. The organism belongs to the genus *Spirochaeta* (Schaudinn, 1905), the type organism of which is the *Spirochaeta pallida* (Schaudinn and Hoffman, 1905). The measurements of this genus, according to Noguchi are:

Length: 16 to 14 microns; pointed ends. Diameter: 0.25 to 0.3 microns, cylindrical. Spiral amplitude: 1 micron; regular, rigid; spiral depth: 0.8 to 1 micron; very constant. Waves: one or more slight undulating curves may be present. Axial filament: doubtful. The whole seems to consist of a spirally wound axial filament. Chambered structure: absent. Membrane: doubtful; if

there is one it must be flexible. Crista: absent. Terminal finely spiral filament: present; easily seen in cultures. Flagella: absent; highly motile end portion: absent. Division: transverse or possibly also longitudinal. Habitat of genus: two pathogenic and several harmless parasites. Other species: *pertenuis*, *microdentium*, *macrodentium*, *mucosum*, *calligyrum*, *minutum*. Staining properties of axial filament and cell membrane: membrane not recognizable.

Schaudinn and Castellani considered *Spirochaeta pallida* and *Spirochaeta pertenuis* practically morphologically identical, although Blanchard, Morton, Prowazek, Russell and others have pointed out some slight morphologic differences. This morphologic similarity exists among the entire species of the genus *Spirochaeta*, but notably among *Spirochaeta pallida*, *S. pertenuis mucosum* and *microdentium*. It is the consensus of opinion that the two organisms are morphologically indistinguishable. In this regard Castellani¹² states: "We believe that the differentiation of the two organisms . . . is to be based more on the biological results than on slight morphological differences."

We have observed *Spirochaeta pertenuis* in the dark field microscope with one portion of the organism straight and the remaining portion with the characteristic coils preserved. This has been observed only when the organism was in contact with obstacles. Castellani has also observed this phenomenon. The above morphologic changes can be contrasted with a similar change occurring in two organisms, *Leptospira icterohaemorrhagicae* (Inada and Ido) and *Leptospira icteroides* (Noguchi). The former is the causative agent of infectious jaundice and the latter of yellow fever. This change, as described by Noguchi, is as follows: *Leptospira icterohaemorrhagicae*, in the dark field picture in free space, is seen as a rapidly motile organism with a number of fine spirals with one or both ends semicircularly hooked. When motion ceases, many of them lose the typical hooks; when penetrating semifluid mediums, the organisms become serpentine, waved, and assume large wavy undulations, and the typical hooked ends disappear. When penetrating semisolid mediums, the organism again assumes a change in morphology. The change in the morphology of *Leptospira icteroides*, as given by Noguchi,¹³ is somewhat similar to *Leptospira icterohaemorrhagica*.

As we shall later point out, the morphologic deviation is more apparent in stained specimens of the organism. We have never observed a similar change in the morphology of the *Spirochaeta pallida* either in dark field or in stained specimens from human lesions.¹⁴ In speci-

12. Castellani: J. Trop. Med. **9**:3, 1916.

13. Noguchi: J. Exper. Med. **30**:1, 1919.

14. However, we find a reference by Noguchi in his Harvey lecture on "Spirochaetes," in which he states that organisms obtained from syphilomas of rabbits' testicles, immediately fixed and stained, exhibit striking irregularity of curves unlike the accustomed picture.

mens from human sources, the coils remain constant. Schaudinn states that under unusual conditions the coils are obliterated, and straight and artificial forms are seen. It is well known, and has been observed by us, that culture specimens of pallidum exhibit morphologic variations. Under such circumstances, irregular forms may be seen, the organism tending to become short and plump.

Staining Properties of Spirochaeta Pertenuis.—It is generally stated by writers that *Spirochaeta pertenuis* stains with difficulty. This has been our experience, and there is no doubt that this organism is more

Fig. 6.—Section of jaw stained with hematoxylin and eosin showing epidermal changes. The arrow points to a circumscribed collection of polymorphonuclear leukocytes in the epidermis: $\times 70$.

difficult to stain than *Spirochaeta pallida*.¹⁵ For staining the organism Castellani recommends Leishman's stain, the alcoholic solution to act for five minutes, and the subsequent admixture with distilled water

15. Indeed, in our opinion, the lesser affinity of *S. pertenuis* for the usual spirochetal stains is so striking as to constitute a point of important differential value. We have never had much difficulty in staining the *S. pallida*, but we have experienced the greatest difficulty in obtaining satisfactory stained specimens from our case of yaws, although scores of slides were stained.

for from one half hour to several hours. Other writers recommend one of the Romanowsky stains (Giemsa, Wright, Leishman), pointing out that it is necessary to have the stain act for from a few hours to many hours. With these stains we were unable to obtain satisfactory results; the organism was either faintly stained or not stained at all. With the Fontana stain we succeeded in staining what we considered to be the organism but with curves entirely obliterated. We obtained the best results with the anilin black stain of Rosenberger and Fanz. With this stain many of the organisms were well stained, but the organism did not appear so regularly curled as is shown in the dark field picture. Again, and this point we wish to emphasize, some appeared with one portion entirely straight and the remaining portion either with the curves intact or the curves were much more irregular and coarse (Figs. 10 and 11). Thus it was apparent to us that the stained organism presented a changed morphology. The curves in stained specimens of *Spirochaeta pallida* are perhaps less regular than in the dark field picture, but this change is considerably less apparent than with *Spirochaeta pertenuis* (Fig. 12). The truth of this becomes apparent when one contrasts published photomicrographic pictures of the pallidum and pertenuis. In this regard we may quote Bosanquet's¹⁶ statement: "In the illustrations given by Castellani, *Spirochaeta pertenuis* does not appear so regularly curled as is *Spirochaeta pallida*." In Ashburn and Craig's¹⁷ study of the *Spirochaeta pertenuis* they observed many variations in the shape of the stained organism, which they describe by dividing them into seventeen different types or classes. In the diagrammatic illustration of the types of stained specimens, these morphologic changes are well shown. They attributed the changed morphology to physical forces acting on the organism during the making and drying of stained specimens. They contrasted this change with similar changes that a spiral wire spring could be made to present when subjected to analogous forces when one or more of its coils are straightened out by traction and pressure. This explanation is doubtless correct; however, since all spiral organisms when stained do not present such marked morphologic changes, it must be regarded as a characteristic of *Spirochaeta pertenuis* and is valuable in the differentiation of stained specimens of *S. pallida* and *S. pertenuis*.

Leptospira icterohaemorrhagicae and *Leptospira icteroides* when stained may appear different than in the dark field. Noguchi¹⁸ has shown that the natural features of these organisms can be well pre-

16. Bosanquet: Spirochetes, Philadelphia, W. B. Saunders Company, 1911.

17. Ashburn and Craig: Philippine J. Sc. **2**:441, 1907.

18. Noguchi: J. Exper. Med. **25**:755, 1917; **27**:575, 1918; **30**:1, 1919.

served when they are fixed in osmic acid vapor and then stained over night with Giemsa's solution. Noguchi states that specimens of *Leptospira icteroides* fixed with methyl alcohol seldom retain the elementary spirals, and that the beauty of the organism as it appears by dark field illumination is never well retained in a stained preparation, even in the best specimens. In the latter, it appears almost as a totally different organism. This is apparently true also of *S. pertenuis*. For staining this organism Schüffner¹⁹ states that most satis-

Fig. 7.—Circumscribed islet of polymorphonuclear leukocytes in the epidermis indicated by the arrow in Figure 6; $\times 288$.

factory results are obtained by Romanowsky stain when preceded by osmic acid or formaldehyd vapor fixation. Further endeavors to obtain better stained specimens of *S. pertenuis* are being made by us.

Distribution of Spirochaeta Pertenuis in Tissues.—The organism is constantly found in the primary and secondary lesions, but rarely in the tertiary lesions. In men, they have been demonstrated in the splenic blood and in the blood of the general circulation and in the bone marrow of inoculated animals. They have never been found in

19. Schüffner: München. med. Wehnschr. **44**:1364, 1907.

the cerebrospinal fluid, nor has their presence been demonstrated in this fluid by animal inoculation. This observation is consistent with our clinical knowledge concerning the absence of neurol involvement.

Although there is a generalization of the parasite in yaws, pathologic visceral changes have not been demonstrated in man, and tertiary manifestations are relatively rare.

EXPERIMENTAL LESIONS IN THE RABBIT AND MONKEY

The susceptibility of the rabbit's testicle to syphilitic infection is duplicated with *Spirochaeta pertenuis*. Indeed, this susceptibility is successful in a greater percentage of cases than with *S. pallida*.

The species of animal used and the source of the virus and its concentration are factors that influence the percentage of positive inoculations with each organism.

Up to the present writing, six months since the initial inoculation of rabbits' testicles with a yaws lesion from the case herein reported, we have carried this strain of *S. pertenuis* through four transfers in rabbits.²⁰

Technic of Testicular Inoculation.—A yaws nodule removed from the patient's forearm was placed in a sterile mortar and finely minced with scissors. Sufficient sterile salt solution (0.85 per cent.) was added to make an emulsion containing from one to three spirochetes to the microscopic field. The fluid emulsion was aspirated into a small glass syringe fitted with a 20 gage needle, about three-quarters inch in length. The scrotum of the animal to be inoculated was painted with dilute tincture of iodine, and 0.5 c.c. to 1 c.c., depending on the size of the testicle, was injected into the center of each organ.

Rabbit transfers were made by removing aseptically an infected testicle. An infected node was removed and made into an emulsion as above described. Other rabbits were inoculated with this emulsion, the strength of which was approximately the same for each transfer.

Technic of Scrotal Inoculation.—The scrotum of the animal to be inoculated was painted with dilute tincture of iodine. A 16 gage needle was inserted just beneath the skin of the scrotum. A portion of a node from an infected rabbit's testicle was inserted through this needle by means of a wide trocar. In some animals the infected tissue was placed in the tunica vaginalis.

Technic of Inoculation of Anterior Chamber of the Eye.—The eye of the animal to be inoculated was cocainized with a 2 per cent. solution, an eye speculum was inserted and the eye fixed with a forceps. The anterior chamber was punctured with a 23 gage platinum needle inserted at the sclerocorneal junction. This procedure resulted in the evacuation of aqueous fluid and the collapse of the anterior chamber. To the needle was fitted a Fournier syringe, and three or four minims of an infected emulsion was injected.

Technic of Intravenous Injection.—Five c.c. of blood were withdrawn by venipuncture from the yaws patient. At the time of this withdrawal the

20. The organism is still under observation in rabbits and further studies are being conducted.

patient had not been treated and was in the acute stage of yaws. To this blood were added 5 c.c. of a 1 per cent. solution of sodium citrate in normal salt. This mixture was injected into the vein of the ear of each rabbit.

Technic of Inoculation of a Monkey.—On the eyebrow of a monkey a scarification was made, and on this area was rubbed a portion of a yaws lesion removed from the patient. A dark field examination of this yaws lesion disclosed many actively motile spirochetes. Another and similar attempt to inoculate a monkey's eyebrow was made with a node removed from an infected rabbit's testicle. In addition, an emulsion made from this node was injected subcutaneously in the region of the eyebrow.

Fig. 8.—Islet of polymorphonuclear leukocytes in the epidermis indicated by the arrow in Figure 6. This section was stained by the Levaditi method to show *S. pertenuis*; $\times 700$.

Testicular Lesions in the Rabbit.—We succeeded only in obtaining one variety of yaws lesion in the rabbit, namely, testicular. We failed to produce corneal and scrotal lesions and to infect the rabbit intravenously by the injection of the blood of the yaws patient while in the acute stage of the disease.

In the first series of rabbit inoculations, there were 50 per cent. positive results with an incubation period of about thirty-four days. In this series some died before the expiration of thirty-four days, and one was killed because of the development of a contagious infection. In the second transfer 75 per cent. gave a positive result with an incubation period of about thirty-nine days. In the fourth transfer 37 per cent. gave a positive result with an incubation period of about sixty-five days.²¹ In Nichols' ²² series, the incubation period with inoculation of fluid of lesions of the testicles, caused by *Spirochaeta pertenuis*, was forty-five days for the animal in the first transfer; for the last animals in the ninth to the fourth transfers it was twenty-nine days. With tissue inoculation the period averaged from twenty-three to twenty-five days. For the entire series of fifty-two animals, the incubation period was twenty-six days, or eight days shorter than the period required by his series of rabbits inoculated with *Spirochaeta pallida*.

There are essentially no differences in the experimental testicular lesions of syphilis and of yaws. From our examination of a testicle infected with yaws, this is apparently the case histologically. This examination disclosed similar changes to those resulting from syphilitic infection.

In the majority of our positive rabbits the inoculation first became apparent in an enlargement of the scrotum. This enlargement consisted of edema, and on puncturing the tunica vaginalis a gelatinous fluid was obtained, which contained *Spirochaeta pertenuis*. The appearance of edema usually forecast the development of one or several nodes, either in the epididymis, in the testicle or in both organs. The nodes (lesions), at first just appreciable to touch, developed to about the size of a pea. We did not observe lesions much larger than a pea; occasionally they did not progress to the size of a pea and these lesions rapidly disappeared. On puncturing the lesions numerous spirochetes were found. The organism was almost twice the length of the same organism studied from the original yaws lesion in the patient, and they were further characterized by the change of morphology already described. After removing the infected testicle, grossly the lesion was sharply margined and cartilaginous in consistency. Figure 13 is a photograph of the positive rabbits. The scrotum is enlarged and edematous. In each testicle a node was palpable.

In the infected lesions, numerous and freely motile *Spirochaetae pertenuis* could be demonstrated for only a short period, about ten days. After this period the organisms would suddenly disappear in

21. About ten rabbits were used in each transfer.

22. Nichols: J. Exper. Med. **14**:199, 1911.

the aspirated fluid. However, after a variable period they were again present in large numbers. In the interval between their disappearance and reappearance the gross appearance of the infected organ would remain unchanged and the infected nodules were palpably the same; no organism, either motile or nonmotile, could be demonstrated on puncture. At the time of reappearance of the organisms, the infected testicle was edematous. Our transfers were always made at the time the punctures showed numerous and freely motile organisms. How-

Fig. 9.—Disappearance of lesions after treatment.

ever, we made one transfer, during the time the organisms could not be demonstrated, by puncturing an infected node. The dark field examination of this infected node after removal was negative, yet, curiously the transfer made from this node gave a positive result with an incubation period of eighteen days. Further studies are being made concerning the infectivity of *S. pertenuis* in the different stages of experimental lesions.

Somewhat similar phenomena have been observed in experimental lesions in syphilis by Brown and Pearce,²³ who have described them in their excellent and comprehensive studies of experimental syphilis

23. Brown and Pearce: J. Exper. Med. **31**:4, 1920.

in the rabbit. We may divert here and dwell on this phenomenon, since it is of interest in the clinical visualization of syphilis and indeed of all spirochetal diseases. The course of syphilis and yaws in the rabbit is somewhat a replica of these diseases as observed clinically. Syphilis and yaws in the rabbit may be mild, transitory and spontaneously cured; again, the lesions may become quiescent or latent, and later active; in this way a cycle is developed. As stated by Brown and Pearce, the duration of this local infection, as in experimental syphilis determined by the presence of active lesions, was as variable as the course of the infection itself, and no fixed limits can be given, either for the several phases of the local reaction or for the infection as a whole. The period of active infection varies from one to more than twelve months. In some animals the entire process was represented by one intense cycle of acute reaction, which terminated within from four to six weeks after inoculation; in others, the infection continued through successive cycles of reaction, but the period of active infection was rarely longer than from two to four months. Brown and Pearce have also shown that *Spirochaeta pallida*, just before the height or relapse of the acute cycle, began to increase in number. This increase continued parallel with the development of the lesions, so that by the time the lesions had reacted to the acme of the first cycle of their development, actively motile organisms were present in large numbers. At this point the organisms suddenly began to lose their motility and to collect in tangled masses; following this phenomenon, they rapidly diminished in number so that within a few days organisms were difficult to find in fluid aspirated from the testicles, and those seen were either degenerated or showed slight motility; in many instances no organisms could be found. After passing through a crisis such as this, actively motile spirochetes again appeared in the testicular fluid and increased in numbers, thus presaging a renewed activity on the part of the lesions. These parallel changes continued throughout the existence of the local infection.

As noted, we have observed in a general way a similar cycle with *Spirochaeta pertenuis*, although our observations have not been sufficiently extensive to formulate an exact comparison. Brown and Pearce attribute the phenomena referred to above to a cyclic immunologic reaction. They have further shown that the infecting power of the organism at this stage is markedly diminished. In one of their experiments, a series of animals inoculated with approximately ten times the dose of immobilized and agglomerated organisms that was used in the controls, showed an incubation period of six weeks as contrasted with three weeks in the controls, while the lesions were as slow to develop and were less pronounced than in control animals.

Similar observations as to the inactivity of *S. pallida* at different periods of the infection were made, and there is no doubt in the minds of these workers as to the significance of the cyclic reactions they describe.

SCROTAL LESIONS IN THE RABBIT

As stated, we failed to produce lesions of the scrotum. Nichols,²² however, succeeded in producing such lesions. He inoculated seven animals under the skin of the scrotum with testicular tissue. In six days two animals had developed hard nodules which enlarged to typical chancres; the other five failed to show lesions. He observed eight chancres after inoculation of the testicle in other animals. The incubation period of these chancres averaged twenty-three to twenty-five days, a period less than half that in syphilis in Nichols' experience. He points out that in contrast with the difference seen in yaws and syphilitic lesions of the monkey's eyebrows, there is practically no difference in the lesions which are produced in the rabbit's scrotum by *S. pallida* and *S. pertenuis*, except as regards the incubation period.

INTRAVENOUS INOCULATION OF RABBITS

As already mentioned, we failed to inoculate rabbits by the intravenous injection of the patient's blood with yaws. Castellani²⁴ produced a generalized infection in rabbits by intravenous inoculation. He says that the character of the lesions produced, which occur mostly about the head, are distinctive of yaws to such an extent that this method may be used in differentiating *S. pertenuis* from *S. pallida*.

EXPERIMENTAL LESIONS IN MONKEYS

Neisser, Baermann⁵ and Halberstädter²⁵ and others—Prowazek, Castellani, Nichols, Levaditi, Ashburn and Craig—have shown that monkeys are susceptible to experimental infection with yaws. The character of the lesions resulting at the site of inoculation, usually the eyebrows, is distinctive; at first it is an infiltrated area which slowly increases in size; there is free secretion of serum that forms into a thick crust, which on removal exposes a granulating red surface. This lesion closely resembles the fungating yaws lesion seen in man.

In the low class of monkeys of the genus *Macacus* and the genus *Semopithecus*, the eruption is confined to the site of inoculation, although *Spirochaeta pertenuis* has been demonstrated by Castellani²⁶

24. Castellani: Biochim. e terap. sper. **8**:337, 1912.

25. Halberstädter: Arb. a. d. k. Gesndhts amte **26**:48, 1907.

26. Castellani: J. Hygiene **7**:558, 1907.

in the spleen and lymphatic glands, thus giving evidence of a generalization of the infection. However, Halberstädter succeeded in obtaining a general eruption in ourang-outangs.

We made several unsuccessful attempts to inoculate the eyebrow of a *Semopithecus* monkey. Nichols²⁷ gives the following differen-

Fig. 10.—*S. pertenuis* stained with anilin black (Rosenberger and Fanz).

Fig. 11.—*S. pertenuis* stained with anilin black. Note the irregular curves.

tiation between the experimental lesion of yaws and syphilis in the monkey: In yaws the incubation period is from two to three weeks; the lesion is elevated, slightly scaly and edematous. In syphilis the incubation period is about four weeks; the lesion is flat, dry and scaly.

27. Nichols: J. Exper. Med. **12**:621, 1910.

LABORATORY DIFFERENTIATION OF YAWS AND SYPHILIS

Neisser, Baermann and Halberstädter have shown that monkeys infected with yaws do not become immune to syphilis, and vice versa, monkeys infected with syphilis do not become immune to yaws. This experiment furnished further proof that yaws and syphilis are different diseases. In addition, it furnished a definite laboratory method of differentiating the two organisms. It becomes apparent from data herein presented that a laboratory diagnosis of yaws and syphilis is difficult. The diagnosis cannot be made by the Wassermann reaction or the dark field microscope. The rabbit's testicle is not suitable for the resistance experiment of Neisser, Baermann and Halberstädter for the following reasons: We have frequently observed, and it has also been observed by others, that there is a migration of

Fig. 12.—*S. pallida* stained with gentian violet.

spirochetes from an inoculated testicle to the noninoculated testicle. In addition, inoculation with *Spirochaeta pallida* or *S. pertenuis* does not give a positive result in 100 per cent. of cases. However, Nichols²⁸ succeeded in differentiating the two organisms by testicular inoculation and cross infections with syphilis and yaws after treatment with arsphenamin. He observed that rabbits infected with *Spirochaeta pertenuis* were permanently cured by a dose of 0.0045 gm. of arsphenamin per kilo, while animals infected with *S. pallida* and treated with a similar dose usually had a relapse; a smaller dose than 0.0045 gm. per kilo, however, failed to kill *S. pertenuis*.

Nichols treated syphilitic rabbits with 0.01 gm. of arsphenamin per kilo; fifteen days later he inoculated them with yaws. All the

28. Nichols: J. Exper. Med. **14**:209, 1911.

animals became infected with yaws, although the testicular lesions were smaller than normal and the incubation period longer. Other syphilitic animals were similarly treated and reinoculated with syphilis, thirteen to sixteen days after treatment. None of the animals became infected with syphilis. Hence, Nichols concludes that in rabbits, as well as in monkeys, a difference between the two diseases can be demonstrated by inoculation and curative experiments.

Although our observations regarding arsphenamin and neo-arsphenamin therapy in experimental yaws are not yet completed, we failed to cure rabbits infected with *S. pertenuis* with 0.005 gm. of arsphenamin per kilo, a slightly greater dose than that which, in Nichols' experience, cured permanently. Contrasted with the dose of arsphenamin, we observed the curative dose of neo-arsphenamin to be 0.008 gm. per kilo.

The most reliable and convincing method of differentiating between yaws and syphilis, by laboratory experiments, is the production of a chancre on one eyebrow of a monkey and the subsequent production of a frambeside on the other eyebrow or vice versa.

THE WASSERMANN REACTION IN HUMAN AND EXPERIMENTAL YAWS

Judging from the occasional reports in literature in which the Wassermann reaction in yaws was negative, it is evident that the test is not invariably positive. In Baermann and Wetter's²⁹ series of 125 cases of yaws studied in Java, the Wassermann reaction was positive in thirty-five of thirty-eight acute untreated cases. In ten treated cases the reaction was positive in six. In fourteen cases of latent yaws, in which the infection was of many years' duration and a long time had elapsed without symptoms or treatment, the reaction was positive in five.

According to Schüffner and Violle, the complement fixation reaction is frequently positive if an alcoholic extract of syphilitic liver is used as an antigen, while there is no fixation if an aqueous extract is used. It may be recalled that the original Wassermann technic provided for the use of an aqueous extract of syphilitic liver. When one contrasts the relative merits of these two antigens when used in the Wassermann reaction in syphilis, it becomes consistent with the experiment of Schüffner and Violle that an antigen of an alcoholic extract of syphilitic liver should give a greater percentage of fixation in yaws than an antigen of an aqueous extract of syphilitic liver.

The Wassermann reaction³⁰ of the serum of the patient with yaws was performed with the following three antigens: a 4 per cent. cholesterolized beef heart, alcoholic syphilitic liver and acetone insoluble

29. Baermann and Wetter: München. med. Wchnschr. **57**:2131, 1910.

30. The Wassermann tests were kindly performed for us by Prof. John A. Kolmer.

lipoids. In the acute untreated stage the reaction was ++++ with all antigens; however, after treatment the reaction with the cholesterolized antigen inhibited hemolysis to a greater degree; in other words, was stronger than the reaction performed with the remaining two antigens. The last reaction we observed was ++ with the cholesterolized beef heart antigen and negative with the other two antigens. It is interesting to note that the relative sensitiveness of these three antigens when used in the Wassermann reaction in yaws is the same as in our experience with syphilis.

The complement fixation test of the yaws serum was also performed with a salt solution extract of a testicular nodule from a rabbit infected with yaws.³¹ This extract contained about three *S. pertenuis* organisms to a microscopic field. The reaction with the

Fig. 13.—Rabbit's testicles successfully inoculated with *S. pertenuis* from cutaneous lesions in the case reported. The organs are enlarged and edematous; a palpable node is present in each organ. A dark field examination of the serum obtained on puncturing each node disclosed many spirochetes.

yaws serum yielded a slight, but definite, degree of fixation, whereas the reaction of the pooled serums of three syphilitic patients yielded separately a ++++ reaction with a cholesterolized, alcoholic, syphilitic liver and acetone insoluble lipoid antigens. From this observation it would appear that the Wassermann producing substance in yaws, as in syphilis, has a dual origin; on the one hand, it is a specific biologic substance caused by *S. pertenuis* and *S. pallida*, respectively,

31. It should be noted that salt solution was used in making this extract. Specific culture antigens employed in the complement fixation tests have been made by some investigators using alcohol as an extracting agent, but Dr. Kolmer believes that a salt solution extract gives better results.

and on the other hand, a nonspecific substance arising less directly from these organisms.

The complement fixation reaction obtained in human yaws serum stated above, using a specific yaws antigen, is in accordance with similar results obtained by Castellani³² and by Bowmann;³³ on the other hand, Baermann and Wetter³⁴ failed to obtain fixation in the serum of human yaws using a specific yaws antigen. Nichols³⁵ failed to obtain fixation with the serum of animals infected with yaws with a specific yaws antigen. He applied complement fixation tests to the serums of rabbits infected with *S. pallida* and *S. pertenuis*, in which he used culture antigens of these two organisms, as well as culture antigens of *Spirochaeta dentium* and a syphilitic liver antigen. He showed that rabbits infected with *S. pallida* and with *S. pertenuis* gave a ++ reaction with the syphilitic liver antigen, but no reaction with specific culture antigens either at the height of the lesions or after recovery.

The nature of the substance producing a positive Wassermann reaction in yaws is not definitely known; indeed, the underlying principle of this reaction in syphilis is not definitely known. We do know, however, that the Wassermann producing substance is of lipotropic nature, and that the character of the reaction is probably colloidal. That this substance is apparently not a specific biologic product of spirochetes is evidenced by the fact that the same, or at least a similar substance, is present at times in leprosy.

It will be recalled that weak complement fixation occurs with a small percentage of serums in human syphilis employing a specific antigen, that is, a culture of *S. pallida* or aqueous extracts of infected testicles. This observation, as already mentioned, points to a dual origin of the Wassermann producing substance in syphilis. However, this antigen is considerably less sensitive than the nonalcoholic extracts of syphilitic and nonsyphilitic tissue now in common use and therefore of no practical value in the conduct of the Wassermann test. Indeed, the more frequent and greater fixation obtained with nonspecific antigens is proof that the Wassermann test is not a specific antibody complement reaction. The complement fixation test with specific antigens, that is, aqueous (not alcoholic) extracts of pure cultures has not a sufficiently definite status to be of great value in the differentiation of yaws and syphilis; although our observations in this regard were positive, the observations of others were variable.

32. Castellani: J. Hygiene **7**:558, 1907.

33. Bowmann: Philippine J. Sc. **5**:485, 1910.

34. Baermann and Wetter: München. med Wchnschr. **57**:2131, 1910.

35. Nichols: J. Exper. Med. **14**:198, 1911; South. M. J. **5**:528 (Sept.) 1912.

There is a paucity of data in the literature concerning the persistency of the Wassermann reaction after the disappearance of yaws lesions following treatment. Many writers record the rapid disappearance of lesions following arsphenamin therapy, but make no mention of the behavior of the Wassermann reaction in these cases. For example, Rost³⁶ has reported that of 500 cases of yaws eighty-one, 8 per cent., were cured by the intramuscular injection of arsphenamin, 15 per cent. with two, and the remainder with three injections. In the light of the Wassermann studies in our case we can only regard such cases as a clinical cure. Indeed, it is a commonly accepted belief that Ehrlich's unfulfilled hope of accomplishing a therapeutic sterilisans magna with one injection of arsphenamin in syphilis is accomplished in the arsphenamin therapy of yaws. There is no doubt that yaws is more easily cured than syphilis, and that one injection of arsphenamin is considerably more potent than in syphilis.

Baermann and Wetter have observed that the Wassermann reaction may disappear in yaws after two or three injections of salicylate of mercury. After treatment there may be a clinical recurrence. This possibility, however, is considerably less than in syphilis. Both Strong³⁷ and Castellani³⁸ have reported recurrences after treatment with doses of 0.3 to 0.4 gm. of arsphenamin, although these recurrences were in a small percentage of the total number of cases treated. A therapia sterilisans magna may be accomplished in yaws with more certainty than in syphilis, but not in all cases, even though there is a disappearance of all lesions. In the light of modern knowledge it is erroneous to regard such cases as necessarily cured.

The persistency of the Wassermann reaction in our case suggests that yaws may continue for some time in an asymptomatic stage after complete disappearance of all the cutaneous lesions in a manner similar to that which occurs in syphilis. This receives confirmatory support from the experience of Castellani, who states that oral treatment should be prolonged for a long time after the complete disappearance of the eruption. As clinical experiments on inoculated monkeys prove that the specific spirochetes may and do persist in the lymphatic glands and internal organs long after the cutaneous manifestations have disappeared.

DISCUSSION

DR. FORDYCE stated that a case of yaws was brought to his clinic last winter from the Naval Hospital in Brooklyn. The patient was an American sailor who had been stationed at Brest, where he came in contact with sailors from all over the world. He had lesions similar to those mentioned by Dr.

36. Rost: München. med. Wchnschr. **59**:924, 1912.

37. Philippine J. Sc. **5**:433, 1910.

38. Castellani: Arch. f. Schiffs.-u. Tropen.-Hyg. **15**:11, 1911.

Schamberg. Professor Lindenberg of Sao Paulo, Brazil, who was visiting the clinic at that time, readily diagnosed the case as yaws. This was confirmed by the easy determination of the spirochetes under the dark field microscope. The Wassermann reaction was strongly positive. Dr. Fordyce suggested that as Professor Lindenberg was present at the meeting he be asked to tell the Association something regarding the distribution of yaws in Brazil.

PROFESSOR LINDENBERG said that he could not avail himself of the invitation to any great extent because he did not speak well in English, but the exposition of Professor Schamberg seemed very complete. He believed he had done all which should be done in the case, and he could only emphasize that in Brazil the most interesting thing was the comparison with syphilis. In Brazil they attached great importance to the difference in the location of the spirochete in the tissue in the two diseases. In yaws the spirochete was always found in the connective tissue; in syphilis, on the contrary, the spirochete is not found in the connective space. When the organisms were found in the miliary abscesses which formed, they were considered specific of yaws.

DR. HIGHMAN was particularly interested in the histologic picture thrown on the screen. He had seen the case Dr. Fordyce described and the histologic material from it. Unfortunately, the technician was ill during the time the Levaditi stain was being prepared, and it was not successful, but the general morphology was particularly interesting. The only striking difference between that specimen and this one was in the tremendous number of plasma cells in the infiltration. He understood from Professor Lindenberg and from the literature that there was a larger number of plasma cells in yaws than in syphilis, and there were much less marked vascular changes. It was the first case of yaws he had ever seen, but he gathered that it was a typical morphologic demonstration of the disease.

DR. RAVOGLI said that when visiting in Florence in the clinic of Prof. C. Pelliszori he saw a case of yaws in a man who had worked for many years in St. Paul of Brazil. He had a papular eruption all over the body, but the nose and palate were most seriously affected, the palate being nearly destroyed. Dr. Ravogli had read of several cases reported by Dr. Splendore, who was working with Castellani. It is a horrible disease, but arsphenamin treatment has diminished its destructiveness.

DR. POLLITZER stated that he was indebted to Dr. Schamberg for an account of his case and photographs, which he submitted to him after seeing the patient. The case had impressed Dr. Pollitzer as being one of yaws rather than syphilis. In addition to the many points brought up by the paper, he was struck with the location of the lesions. The fact that the man had for two months some systemic disorder of an indefinite type was important. If this had been syphilitic fever, the eruption would have appeared within two or three months after his infection. But the kind of eruption which the patient showed did not occur in syphilis so soon after infection and, above all, it did not present the distribution seen in this case. On the other hand, this was just the sort of eruption that one found in yaws. The preliminary period of incubation in which the patient had malaise and rise of temperature, followed by a spirochetal eruption of a character which was not like that of syphilis, spoke strongly in favor of yaws.

In the second place, the extremely rapid disappearance of the lesions after arsphenamin treatment was also characteristic of yaws. It was interesting to recall that in Batavia, where there formerly had been several large hospitals

devoted entirely to the treatment of yaws, these hospitals had been closed or devoted to some other purpose within a month after the introduction of arsphenamin treatment. The condition cleared up so rapidly under arsphenamin treatment that the treatment of yaws had become ambulatory.

DR. SCHAMBERG, closing, said he was particularly interested and pleased to learn from Professor Lindenberg that he regarded the finding of the spirochetes in miliary abscesses in the epidermis as indicative of yaws. Curiously, no such statement is made in Castellani's last book, in which there is a most excellent description of the disease from the clinical and pathologic side. No mention of the occurrence of miliary abscesses and the suggestive localization of the spirochetes in such abscesses is made.

A point of general interest is the fact that Ehrlich's hope of a *therapia sterilizans magna*, which has failed in syphilis, is apparently achieved in yaws. From the descriptions of various writers, the spirochetes of yaws differ as much from each other as from the spirochete of syphilis. Some contend that it is thicker than the *S. pallida* and others that it is thinner. Noguchi described several types of *Spirochaeta pallida*, one of which was thick and the other thin. Dr. Schamberg thought no one would attempt to differentiate the spirochete of yaws from that of syphilis on morphologic grounds alone. It was interesting that the spirochetes of yaws were largely exterminated by one dose of arsphenamin, while in syphilis this is not true.

DR. WILE asked whether the cultures under anaerobic conditions were negative.

DR. SCHAMBERG, replying to Dr. Wile, said that up to the present time the cultures under the strictest anaerobic conditions had been negative, but they were persisting in their efforts to cultivate the organism from the testicular material, and they hoped to achieve a successful result. He was under the impression that Noguchi had successfully cultivated the organism of yaws in culture. He thought it significant that this organism had failed to take stains in smears which *Spirochaeta pallida* took readily. Many writers had referred to the fact that the yaws' spirochetes were difficult to stain.

PROFESSOR LINDENBERG stated that during the time of slavery in Brazil, thirty or forty years ago, this disease was common among the slaves. After the slaves were made free and the hygienic conditions were improved it became a rather rare disease in Brazil. In the course of a year he would perhaps see only two or three cases. In his opinion improvement resulted not from the use of arsphenamin, but from the better hygienic conditions of the people and the fact that there was not so much chance for contagion as in the days of slavery when many of these people were crowded together in one room.