TREPONEMA PALLIDUM FOUND AT AUTOPSY, IN THE BLOOD-STREAM AND ELSEWHERE, IN A CASE OF CONGENITAL SYPHILIS

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It has been the experience that clinical histories, pathologic findings and the Wassermann test may indicate syphilis in many cases in which it is impossible to demonstrate the presence of *T. pallidum* in any of the tissues outside of the primary and secondary lesions accessible to external examination. This may in part be accounted for by the stage of the disease, the effects of treatment, and the difficulty encountered in getting the organisms present in a given preparation to reveal their presence when staining methods or silver impregnation are applied.

This disease, in both its acquired and its congenital forms, is perhaps as common on the Isthmus of Panama as elsewhere, yet it almost never happens that the demonstration of *T. pallidum*, either in smears or in sections, can be made from selected material taken at autopsy from the various tissues, such as liver, placenta, bone-marrow, spleen, heart, aorta, etc.

It is generally known that material from cases of congenital syphilis offers the best opportunities for such a demonstration; but how does the frequency of such findings compare with the incidence of this type of the disease or the frequency of positive responses to the Wassermann test?

We note that the *Journal of Pathology and Bacteriology*¹ publishes a list of rare materials wanted, and a request was made not long ago by a large institution for "congenital syphilitic liver, with spirochetes."

The results obtained in the case about to be described are so foreign to the usual results at Ancon in this respect that it is deemed worthy of some attention.

CASE REPORT

History No. 154570. The patient, a female child, 2 months old, of Panamanian parentage, was admitted to Ancon Hospital, Dec. 20, 1913. The father is a Spanish-Indian mixture, 32 years old, and is employed as a waiter. He had a chancre in June, 1910. Three months later a periostitis of the right tibia

1. Jour. Path. and Bacteriol., October, 1911.

was noted. The symptoms of this condition subsided and recurred frequently until November, 1912, when he presented himself for treatment. The Wassermann test was positive and he was given 0.6 gm. salvarsan intravenously. This was followed by a long-continued administration of mercury proto-iodid and potassium iodid. (It is not known how faithfully this treatment was taken). The Wassermann test was again positive in December, 1913.

The mother is of the same race as the father and is 21 years of age. She was admitted to the maternity wards of Ancon Hospital, Oct. 23, 1913. This visit occurred fifteen months after her marriage and was induced by the advanced stage of her first pregnancy and an associated eclampsia. Her delivery was accomplished by a cesarean section which was performed shortly after her admission. She and the child were both discharged at the end of twenty-three days, both apparently well.

The baby was readmitted at the age of 2 months. It had been nursing and in addition, feedings of a condensed milk mixture had been provided twice daily. The mother had noticed for a week prior to admission that the child had a fever, cold in the head, diarrhea and bloody discharge from the nose. During this time it had also refused to nurse.

Physical Examination.—There was a serosanguineous discharge from the nose and marked embarrassment to nasal respiration. Fissures had formed at the corners of the mouth, nose and eyes, and there was puffing of the hands, feet and face. The soles, palms and mucous membranes were quite pale and an exfoliative change in the skin over the dorsum of the feet and hands left denuded areas between the fingers and toes, from which oozed a thin pink serum. The gums were swollen and bleeding. The superficial sets of lymph-nodes were everywhere somewhat enlarged. Râles could be heard over any part of the chest. The size of the liver, spleen and kidneys could not be determined on account of the protuberant tympanitic abdomen. Blood-films failed to reveal malarial parasites.

The temperature ran an average course of about 100 degrees, the pulse averaging 132, and respirations 36. The child died twelve hours after its admission to the hospital. The clinical factors present and the father's known condition led to the diagnosis of congenital syphilis.

Anatomical Report.—Autopsy 3763. Performed three hours and twenty minutes after the death of the child. It was a plump brown baby showing no developmental variation on external examination. There was slight puffing of the face and the dorsum of the hands and feet. The pale conjunctiva and skin indicated a severe degree of anemia. The abdomen was protuberant and there was some pouting of the umbilical stump. A paper-like exfoliation of the skin was noted over each malar region, the dorsum of the hands and wrists, and over the feet and ankles. A thin pink serum exuded from such denuded areas. A maculopapular eruption similar to that observed in the secondary skin lesions of acquired syphilis was found over the anterior and external surface of the thighs. At the corners of the mouth and nose and eyes and about the vulva were oozing fissures and collections of dried serum scales. The nasal, buccal, vaginal and rectal mucosa revealed a congested fissured membrane but no "mucous patch" was observed. A copious serosanguineous nasal discharge was noted, and this was also present to a less degree from both eyes and the right ear. A gum-like exudate was found plugging the canal of the left ear.

Head Section: A firm chalk-white brain was present with no very noticeable increase in the cerebrospinal fluid. No gross focal lesion noted in brain or skull. The right middle ear contained a thick pink serum.

Neck and Mouth: The lymphatic glands were large, pale structures without evidence of focal necrosis or abscess formation.

Thorax: The costochondral junctions of the ribs presented no marked enlargement. The contour of the chest was normal. A small, pale thymus

gland was present, regular in outline and showing no gross lesion. The lungs were bluish-white in color and air-filled except for a few coin-shaped hemorrhagic areas in the visceral pleura about 12 mm. in diameter. The consistency of the pulmonary tissue beneath these areas suggested small consolidation. The heart was a pale-yellowish structure and the epicardium presented a gelatinous appearance. The muscle seemed friable when handled. Foramen ovale present. Slight increase in pericardial fluid. No focal lesions observed. Aorta: This vessel and its large branches were filled with an almost transparent thin watery blood without extensive clot formations. The intima revealed a few tiny points of degeneration in the thoracic portion of the vessel.

Abdomen: The peritoneum was moist and pale but otherwise normal. All glands were slightly enlarged and pink and showed no focal change.

The esophagus, stomach and duodenum revealed no gross lesion.

The pancreas was almost snow-white but it failed to present gross evidence of a lesion.

Intestine: Some reddening in the mucous membrane of the cecum, sigmoid and ileum (the dependent portions). No lesion and no parasite present.

Liver: Some enlargement. The dome of the right lobe was reddish-brown in color while the anterior margin was marble-white, and the consistency so increased that a uniform gummatous process was strongly suggested. This marginal zone extended backward into the right lobe for fully 2 cm., but showed none of the circumscribed peculiarities of the usual gumma. On section this process was found to extend in a lace-like pattern throughout the right lobe. The gall-bladder and ducts appeared normal.

Spleen: Somewhat enlarged and semisolid. Malpighian bodies quite prominent.

Kidneys: Enlarged and showed decided fetal lobulation. The yellowish color and friable tissue was similar to that found in the heart muscle.

Pelvic Organs: Normal.

External Genitalia: No additional note.

Smears were made from selected tissues which yielded the following results: Smears from blood of jugular vein were stained with a polychrome stain (Hastings). There was evidence of a severe degree of secondary anemia and a lymphocytosis of 56 per cent. was present. The lymphocytes were nearly all of the small type. Attention was arrested by the presence in almost every field of from one to three or more treponemas with the characteristic morphology of *T. pallidum*.

Similarly stained smears from the liver near the gummatous-like region revealed the same organisms in fair numbers. A more protracted search in smears from spleen and bone-marrow and lymph-nodes resulted in sparse findings of the same nature. A Wassermann test on the cadaver was obtained and found positive. Weights of the organs may be grouped as follows:

Brain	380 gm.	Combined kidneys.....	55 gm.
Liver	190 gm.	Spleen	55 gm.
Right lung	25 gm.	Heart	20 gm.
Left lung	25 gm.	Thymus gland	5 gm.

Microscopical Report.—Skin: This specimen was taken from the anterior surface of the right thigh and although no variation in its histology was noted in the sections stained with hematoxylin and eosin, yet in Levaditi preparations *T. pallidum*, in fair numbers, were found in focal manner in the superficial layers of the corium.

Brain: No lesion was found in any of the preparations. After a tedious search over many specimens of Levaditi preparations a few forms were found which faithfully represented *T. pallidum*.

Noguchi's² identification of this organism in the brain in cases of general paralysis made it seem quite likely that this case of congenital syphilis would easily reveal the presence of *T. pallidum* in fair numbers.

Lymph-Node: A specimen from a set near the liver was chosen for examination and the Levaditi preparations after an extended search revealed a few treponemas.

Heart: A more or less general and moderate fatty metamorphosis was present with no tendency anywhere to focal lesions of any character. Warthin's³ reports (on localization of *T. pallidum* in the heart muscle) stimulated our interest in the Levaditi preparations and many slides were carefully searched. It was disappointing to find these preparations of the heart among the most difficult in the body in our case in which to locate the organism. There was no relation between those found and a focal lesion or perivascular space.

Aorta: Levaditi preparations made from the regions containing tiny points of degeneration in the intima as well as sections from the arch of the vessel and elsewhere failed to reveal any of the organisms.

Liver: Sections from the dome of the right lobe were not far from normal. They simply presented the findings of a fatty change and a moderate round cell infiltration of the perilobular regions.

Sections from the gummatous-like margin showed almost complete destruction of the liver tissue. Columns of cells had been apparently obliterated except for little collections of one or more cells so distorted that the first impression was that of extensive giant cell formation. The new tissue, causing the compression and obliteration mentioned, appears to be a fibrogelatinous network filled with plasma cells. Here and there large areas of focal necrosis had occurred. Levaditi preparations from these regions would show at times a large network of treponemas covering several fields and then several fields might occur before any could be found. There was a more decided tendency in the liver for the coincident finding of a focal lesion and numerous organisms than in any other viscus. It is a noteworthy fact, however, that focal lesions (even in the liver) did occur without the organism being identified in or near the lesion, and on the other hand a rather plentiful finding of the organism was noted in other parts of the liver where no histologic change could be detected.

Kidneys: A general fatty change was noted and in addition many small areas of degeneration appeared which were not recognized grossly or in the hematoxylin and eosin preparations. Many times only a bare outline of a tubule remained. Very infrequently a degenerative glomerulitis was found. Here, also, the treponemas were to be found with or without the presence of a focal lesion. They seemed prone to live in the periphery of the tubules.

Pancreas: A marked interlobular change was found in the head of this organ showing the same type of fibrogelatinous material filled with plasma cells that was present in the margin of the liver. Infrequent focal degeneration was found throughout the organ. Treponemas were occasionally found in colonies but not with the frequency observed in the liver and kidneys.

Spleen: In a few instances central necrosis of malpighian bodies was apparent. Treponemas were found only in sparse numbers. The thymus gland and lungs revealed infrequent *T. pallida*. They appeared in the lung in the small consolidations noted beneath the visceral pleura. The pituitary gland, ovary,

2. Noguchi, H., and Moore, J. W.: A Demonstration of *Treponema Pallidum* in the Brain in Cases of General Paralysis, Jour. Exper. Med., 1913, xvii, 232.

3. Warthin, Aldred Scott, and Snyder, E. J.: Localization of *Spirochaeta Pallida* in the Heart Muscle in Congenital Syphilis in the Absence of Histologic Lesions or of *Spirochetes* Elsewhere in the Body, Jour. Am. Med. Assn., March 9, 1912, p. 689.

uterus, adrenal body, voluntary muscle and aorta failed to reveal any of the organisms after a prolonged search in Levaditi preparations. Some peripheral blood-smears that were made about twelve hours before the death of the child had been stained by Hastings' polychrome method; after these were overstained with Giemsa a tedious search was made for *T. pallidum* without finding any of them. This fact, in connection with their presence in the post-mortem peripheral blood less than four hours after death, is of interest.

It is pretty well established that these organisms prefer the lymph-stream or the sluggish channels of the blood-forming organs, yet at times they have been reported in the blood and in the peripheral blood of cases other than this type. Levaditi⁴ found one positive blood in six cases of general paralysis. It would seem that in cases in which it can be found in the blood-stream, it should be found in a uniform manner throughout all the viscera, yet the study of this case revealed the focal distribution already noted, the liver disclosing the greatest number, then the kidneys, blood from the jugular vein, pancreas, skin and lungs in the order named, while the other organs yielded sparse findings or none at all. Pearce⁵ states that of all the organs in the infected animal capable of transmitting the disease, infection follows most frequently after inoculation with the bone-marrow, the spleen, the lymph-nodes and the testicle, in the order named. It is interesting to note in connection with this statement that the treponema was found in stained smears made at autopsy from rib-marrow, splenic pulp, crushed lymph-node near the liver and from the peripheral blood, but the organisms were found with ease in these tissues only in the smears made from the peripheral blood.

Dr. Darling has suggested that, during the last few hours of life and the few hours intervening between death and the autopsy, the blood had lost to a great extent its normal amount of oxygen, and that this condition favored the presence and rapid development of *T. pallidum* in the venous blood-stream. This appears to be a logical explanation of the apparent absence of the treponemas in the smears of the peripheral blood twelve hours before death. The irregular manner in which they appeared in Levaditi preparations made from the various tissues is also thought by him to be due, in part at least, to the inability of the silver to impregnate the tissue in an even manner or to some characteristic of the parasite or the tissue about it which would not allow it to assume its proper relation to silver impregnation.

This case presents one instance in which, at present, all the conditions conform to Colles' law. The mother at the time of the death

4. Levaditi, C.: Presence of the Spirochaeta Pallida in the Blood of General Paralytics. (abstr. in Paris letter), Jour. Am. Med. Assn., Dec. 13, 1912, p. 2170.

5. Pearce, R. M.: The Wassermann Reaction in the Pathology, Diagnosis and Treatment of Syphilis, Arch. Int. Med., November, 1910, p. 480.

of the child and again six months later reacted in a negative manner to the Wassermann test performed by Dr. L. B. Bates according to Noguchi's modification of the test. Pearce⁶ claims that it has always been a question whether immunity is real or whether the mother is so lightly infected as to present none of the actual manifestations of the disease. At present, the mother has failed to present any symptoms of the disease while the father continues to respond in a positive manner to the test.

De Buys⁷ has found the mother so frequently positive to the Wassermann test that he recommends its application to the mother's blood when a suspected case of congenital syphilis is under discussion and it is found impossible to apply the test to the child.

6. Pearce, R. M.: The Wassermann Reaction in the Pathology, Diagnosis and Treatment of Syphilis, *Arch. Int. Med.*, November, 1910, p. 504.

7. De Buys, L. R.: A Study of the Wassermann Reaction in Connection with Hereditary Syphilis, *Am. Jour. Dis. Child.*, January, 1913, p. 65.