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THE PATHOLOGY OF CONGENITAL SYPHILIS *

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In dermatologic practice the opportunities for postmortem investigation are infrequent and clinical observations are limited largely to a consideration of the appearances presented by lesions occurring in a single organ, the skin.

In a field thus restricted, it is not surprising to find a natural tendency among those of us who confine our activities to the dermatologic branch of medical art to overlook the importance of studying disease from the point of view of its effects on the body as a whole, and to content ourselves with the mental picture of a pathologic process obtained from the visualization of its external manifestations in one organ only, while we neglect to take into consideration the equally important pathologic changes that may be taking place in those organs or tissues which are beyond the realm of external inspection.

The case that forms the basis for this presentation serves to illustrate the importance of studying disease from the broad point of view of the general pathologist, for in it we find not only characteristic lesions in the skin, but in practically every organ of the body. We have, in short, the opportunity of studying at first hand the majority of the anatomic changes that have been described as occurring in congenital syphilis, with the additional interest and satisfaction of having been able to demonstrate the infective organism in the tissues.

It is a widespread belief that *Spirochaeta pallida* can always be demonstrated in the material obtained at necropsy in cases of congenital syphilis, but such a belief does not find support from the observations of many pathologists who frequently find it impossible to demonstrate the infective organisms even when the clinical histories,

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pathologic findings and Wassermann test all point to the diagnosis of syphilis. Noguchi¹ has frequently found it difficult to demonstrate spirochetes in the tissues at necropsy, and he refers particularly to the few organisms found and the difficulty of their demonstration in cases of syphilitic infants who lived a few days after birth. Clark and Gates,² with a wide experience in the Canal Zone, were unable to find the organisms in the majority of their cases examined postmortem, and Norris³ states that frequently they are not found, and that this may be due in some cases to the effect of antisyphilitic treatment on the mother. It was the experience of Levaditi,⁴ who holds the distinction of being the first to demonstrate spirochetes in congenital syphilis, that the organisms could not be demonstrated in those cases in which there was advanced maceration—an observation which indicates their destruction by autolysis. The experience of others also lends support to the view that the organisms of syphilis do not survive long in the presence of autolytic ferments. Warthin⁵ does not attempt to demonstrate spirochetes in the tissues unless the necropsy is conducted within an hour or so after death. And in this connection it is significant that in the case under study, in which the necropsy was not performed until thirty-six hours after death, although anatomic lesions characteristic of syphilitic infection were found in the tissues of almost every organ, the most painstaking examination following the method of Levaditi failed to reveal the presence of spirochetes except in the membranes of the brain which, according to Dunlap,⁶ are often very resistant to the autolytic process.

REPORT OF A CASE

History.—A girl of 7 months' development was born of a mother who gave a history of perfect health. There was no history of abortion and no evidence of syphilis in five children previously born. During the summer of 1918 (about June) the husband had a genital sore and "red spots" on his arms. The mother denied emphatically ever having had any sore, rash or symptoms that might indicate syphilis. Her Wassermann reaction (tested in three different laboratories) was + + + + both with alcoholic extract and cholesterinized antigens. The syphilitic infant was born in August, 1919, and died after a few inspirations.

1. Noguchi, H.: Spirochaetes, Harvey Lectures, Series 11, 1915-1916, p. 174.
2. Clark, H. C., and Gates, I. N.: *Treponema pallidum* Found at Autopsy, in the Blood Stream and Elsewhere, in a Case of Congenital Syphilis, *Am. J. Dis. Child.* **9**:126 (Feb.) 1915.
3. Norris, Charles B.: Personal communication.
4. Levaditi, C.: *L'Histologie pathologique de la syphilis hereditaire dans ses rapports avec le spirochaete pallida*, *Ann. de mal. vener.* **1**:22, 1906.
5. Warthin, Aldred Scott: The Presence of Active Lesions and Spirochaetes in the Tissues of Clinically Inactive or "Cured" Syphilis, *Trans. Assn. of Am. Phys.* **29**:416, 1914; *Am. J. Med. Sc.* **152**:522, 1916.
6. Dunlap, Charles B.: Personal communication.

Examination.—On external inspection at the time of delivery a rose-colored macular eruption was observed on the skin of the limbs and trunk and bullous lesions and denuded areas (the remains of ruptured bullae) were present on the soles of the feet, palms, wrists and fingers. A few of these bullous lesions can still be seen on the preserved specimen, but the macular eruption disappeared, as most skin lesions do, shortly after death.

LITERATURE ON TYPE OF ERUPTION IN CONGENITAL SYPHILIS

In regard to the type of eruption usually present in congenital syphilis of the infantile type, various writers have reported different findings. In an observation of 100 cases, Veeder and Jeanns⁷ found an absence of bullous lesions in all their cases, and in 48 per cent. they report the presence of an eruption which was largely an exfoliative or desquamative dermatitis involving the soles of the feet and palms of the hands, the skin beneath the scaling epiderm being "red and glistening." These authors claim that this type of eruption, which in their series was far more frequent than the macular or maculopapular form, is the most characteristic form of skin lesions, and it is never seen in any other condition. Post⁸ has found the maculopapular lesion and a peculiar shiny redness of the palms and soles to be the most common type of skin change, while Sequeira⁹ states that the bullous eruption is the earliest type of cutaneous manifestation. Stelwagon¹⁰ records the observation that when the skin manifestations are present at birth they are of the bullous type, while in those cases in which the eruption does not appear until several weeks after birth, it usually assumes the maculopapular form, which does not differ in appearance from the same type of lesion encountered in the acquired form of the disease. Highman¹¹ believes that the type of skin lesion is an indication of the stage of development of the fetus at the time of its infection in utero; if the infection, for example, occurs about the fifth month of intra-uterine life, the eruption will consist of papular or bullous lesions on the palms and soles, but if it is delayed until a latter period, say the seventh or eighth month, the skin changes will be those of the early

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7. Veeder, Borden S., and Jeanns, Philip C.: Observations on One Hundred Cases of the Infantile Type of Hereditary Syphilis, *Am. J. Dis. Child.* **2**:177 (March) 1916.

8. Post, Abner: Clinical Course and Physical Signs in Hereditary Syphilis of Early Age, *Am. J. Dis. Child.* **12**:364, 1916.

9. Sequeira, James H.: *Diseases of the Skin*, Ed. 3. Philadelphia, P. Blakiston's Son & Co., 1919.

10. Stelwagon, H. W.: *Diseases of the Skin*, Ed. 6, 1916, Philadelphia, W. B. Saunders Company. The age of the patients observed by Veeder and Jeanns ranged from 1 month to 6 years. It is not stated whether any of the lesions were observed at birth.

11. Highman, Walter J.: Congenital Syphilis, Pathogenesis and Symptoms, *New York M. J.* **104**:592 (Sept. 23) 1916.

secondary stage. While this is a plausible assumption, and probably holds true in a large number of cases, the findings in many cases would indicate that there are probably other determining factors. The skin appearances in Veeder and Jeann's series, which are remarkable in that they were contrary to the teachings of modern textbooks, certainly do not meet the conditions imposed by Dr. Highman's theory.

Fig. 1.—Section of skin from a bullous lesion of the palm; low power. Showing separation of the corneum from the prickle layer by serum and some fibrin, edema and collections of round cells and polymorphonuclear leukocytes in the papillae; proliferation of fibroblasts in the corium.

EXAMINATION OF THE ORGAN

Two sections of skin were taken for microscopic study — one from the palm cut so as to include a bulla, and the other from the breast cut through the nipple. In the first section (Fig. 1) the principal feature

was edema of the malpighian layer and a cellular exudate in the papillae composed largely of polymorphonuclear leukocytes and a few lymphocytes. In the subcutis many of the arterioles showed marked proliferation of the intimal connective tissue, in some instances resulting in obstruction of their lumina (endarteritis obliterans). There was nothing in the histology of this section, excepting the changes in the vessel walls, characteristic of syphilis, but the specimen taken from the breast showed the presence of the usual round and plasma cell perivascular infiltration.

Fig. 2.—Section of subcutis showing obliterating endarteritis of the arterioles—below and to the right transverse sections of nerve fibers.

There was nothing abnormal in the gross appearance of the heart. The valves were free and there was no evidence of aortitis or change in the pulmonary artery. In this connection it is of interest to note that the heart and large vessels do not always escape infection. Flament¹² reports a case of right side hypertrophy and endocarditis of the mitral

12. Flament, R.: Pathology of the Heart in a Syphilitic Infant, *Nourrisson* 6:340 (Nov.) 1918.

and tricuspid valves, and Fordyce¹³ quotes Rach and Wiesner as having found changes in the aorta and pulmonary artery in 67.4 per cent. of cases of congenital syphilis.

The lungs were massive, heavy, firm and presented a gelatinous grayish-white appearance. The parenchyma was mottled throughout with solid patches of a deeper white color. Histologically, these patches consisted of cellular embryonic connective tissue diffusely infiltrated with plasma cells and endothelial leukocytes. The patches were usually

Fig. 3.—Lung: (1) Interstitial fibrosis especially round the bronchi and vessels; (2) desquamation of epithelium in alveoli and bronchi.

around the bronchi. The lumina of the bronchioles were filled with serum, fibrin and polymorphonuclear leukocytes. Here and there were solid patches of another type characterized by distention of the alveoli with desquamated epithelial cells, but these were few in number. Everywhere the alveolar walls were greatly thickened by cellular

13. Fordyce, John A.: Some Problems in the Pathology of Syphilis. *Am. J. Med. Sc.* **119**:781 (June) 1915.

fibrous tissue of the embryonic type. There was also marked thickening of the vessel walls and the lumina of some of the arterioles had been completely obliterated by proliferation of the connective tissue cells of the intima (Figs. 3 and 4). The visceral pleura was markedly thickened and presented a picture which, as far as I am aware, has not been described in syphilis before, namely, the presence in distended lymph vessels of numerous large phagocytic cells holding lymphocytes in their cytoplasm (Figs. 5 and 6). Occasionally, cells of the same nature were found in lymph vessels of the lung tissue. The picture was strikingly similar to that seen in typhoid fever. Levaditi⁴ has observed phagocytes filled with the parasites, but they were in the alveoli. Large mononuclear cells were present in the alveoli in this case, but they were of an entirely different type from that of those seen in the lymph vessels, and are undoubtedly alveolar epithelial cells.

The pancreas was slightly enlarged, of very firm consistency, and on section presented a grayish-white color. Microscopic study of the sections (Fig. 7) revealed the presence of similar interstitial changes to those described in the lungs. The picture was that of an intralobular pancreatitis, the marked hyperplasia of the interstitium causing a wide separation between the individual acini. It is interesting to note, however, that the acini, though small from compression, were perfectly formed and well preserved. The islands of Langerhans were apparently normal in structure and number. Such changes probably represent the most commonly found type of reaction to the toxin of the spirochetes in pancreatic tissue, but it must be remembered that this (intralobular pancreatitis) is not always the type of change found. Recently Dr. Ewing showed me a pancreas literally peppered with gummatous lesions. Another point of interest in connection with syphilis of the pancreas, and the same is true of the lungs, is that these organs, while they are frequently involved in congenital syphilis, are rarely attacked in the acquired form of the disease.

The liver was apparently very large, but it must be remembered that at birth the liver normally occupies the greater part of the abdominal cavity, and constitutes from one-twentieth to one-eighteenth of the body weight. Microscopic examination of the liver tissue showed the sinusoids packed with hemopoietic elements—myeloblasts, nucleated red cells, etc.—an appearance suggesting a retardation of development and continuation of fetal function. There was marked edema—in some areas giving the appearance of interstitial change—but compared with the lungs and pancreas the interstitial changes were very slight, the chief histologic feature here being the presence of a round and plasma cell infiltration in the connective tissue of the portal systems (Fig. 8).

Pathologists are for the most part of one mind in regard to the appearance of the spleen in congenital syphilis. Ewing,¹⁴ Councilman¹⁵ and others claim that enlargement of the organ is one of the most frequent findings, and Veeder and Jeanns⁷ assert that an enlarged spleen occurring in an infant under 6 months without symptoms of an "exudative diathesis" means always either tuberculosis or syphilis. In the case under study the organ was greatly enlarged and of a firm consistency. A study of the microscopic anatomy (Fig. 9) showed replacement of

Fig. 4.—High power showing thickened alveolar walls.

the pulp by numerous plasma cells and proliferated reticular cells, the latter acting as phagocytes and frequently showing many lymphocytes in their cytoplasm. Examination of the lymph nodes, especially those in the region of the pancreas, revealed a histologic picture very similar to that of the spleen. Histologic study of the kidneys showed a round and plasma cell infiltration in the interstitial tissue of the cortex, especially underneath the capsule.

14. Ewing, James A.: Personal communication.

15. Councilman, William T.: Pathology, Boston, W. M. Leonard, 1912, p. 274.

On opening the skull, the dura, bone and brain substance in the region of the orbital plates and frontal eminences were found to be involved in one gummatous mass (Fig. 10). In the right temporal fossa there was a circular yellowish-gray area of gummatous osteitis, which was not connected with the membranes, the dura over this area being perfectly smooth and glistening—an appearance which would indicate that this bone lesion did not originate as a result of extension

Fig. 5.—Section of lung showing thickened pleura with dilated lymph vessels containing phagocytes.

of the inflammatory process in the pia arachnoid. There were other necrotic lesions scattered over the internal surface of the base of the skull, and as many of these were especially prominent over centers for ossification, it would appear that the syphilitic organism has a selective affinity for the growing centers. The skin was dissected from the nasal bones, but no abnormal features were observed.

Sections of the meninges stained by Levaditi's method revealed the presence of numerous *Spirochaeta pallida* (Fig. 11). With the

hematoxylin and eosin stain the histologic picture presented an appearance which indicated the presence of two distinct types of reaction (Fig. 12). There was an inner layer of pia arachnoid where the predominating pathologic change was represented by the presence of proliferated fibroblasts and a slight exudate composed of a very small number of lymphocytes and plasma cells and a second or outer layer which presented the appearance of an acute meningitis of nonsyphilitic origin superimposed on the more chronic syphilitic process, a condition

Fig. 6.—High power of a dilated lymph vessel in interlobular septum of the lung. The red cells which are present have been carried there from the sinusoids of the inflamed lymph node.

which sometimes occurs in cases of adult syphilis, e. g., general paralysis (Dunlap⁹). As a further aid to our study of the histologic changes occurring in syphilis of the meninges, I am able, through the kindness of Dr. Dunlap,⁹ to show here (Fig. 13) a section from one of the first cases of adult syphilitic meningitis, in which *Spirochaetae pallidae* were demonstrated. It was a case of gummatous meningitis with the typical so-called endothelial leukocytes, an occasional phagocyte (rare

in syphilis, but common in tuberculosis of the meninges) and giant cells that might easily be mistaken, if one attempted a diagnosis on their anatomic appearance alone, for the giant cells of tuberculosis.

The line between the epiphyses and diaphyses of the long bones presented on section a perfectly even, smooth, pearly gray appearance, the histologic examination of which revealed nothing abnormal. This absence of epiphyseal involvement, according to the findings of many eminent pathologists, is exceedingly rare. Ewing¹⁴ has found it pres-

Fig. 7.—Pancreas. Intra-lobular fibrosis. Acini widely separated by young edematous fibrous tissue.

ent in all cases which he examined postmortem, and considers it of diagnostic value, even when other characteristic lesions are absent. Jorres¹⁶ has had a similar experience, and MacCallum¹⁷ states in his textbook on pathology, that osteochondritis is “a characteristic lesion

16. Jorres, Leonhard: *The Commoner Diseases, Their Causes and Effects*, trans. by William H. Woglam. Philadelphia, J. B. Lippincott Co., 1915.

17. MacCallum, W. G.: *A Textbook of Pathology*. Philadelphia, W. B. Saunders Co., 1916, p. 688.

found practically always in syphilis of the new-born." The placenta was thick and of firm consistency, the villi were well preserved. The maternal portion showed numerous areas of necroses, leukocytic infiltration and thrombosis in the blood vessels, but whether these changes can be attributed to a specific infection is uncertain. Examination of the remaining organs, suprarenal glands, etc., did not reveal any changes worthy of note.

Fig. 8.—Liver: (1) Periportal lymphocytic and plasma cell infiltration; (2) blood islands in sinusoids; (3) some young liver columns—cells with deeply chromatic nuclei and little cytoplasm.

TRANSMISSION FROM PARENT TO OFFSPRING

Formerly, practically all syphilographers believed that the father was able to convey the disease to the offspring without the mother becoming infected, and it must be admitted that before the days of the Wassermann reaction, the evidence in support of this view was abundant. Syphilitic children were born to mothers who were free from all clinical signs of the disease and apparently immune to infection. The suckling syphilitic child could infect its wetnurse, but could

not give the disease to its mother (Colles' law), and even when these mothers were injected with syphilitic material, which was done by Caspary¹⁸ in several instances, they failed to acquire the disease. But with the advent of the Wassermann test the chief argument in support of the theory of direct paternal transmission has fallen to the ground, for it has been shown that 95 per cent. of these mothers have a positive Wassermann reaction, and Baich, Trinchesse and Weber "constantly found spirochaetae in the maternal portion of the placenta and in the intervillous spaces even in negatively reacting women."¹³ With these revelations the pendulum has swung around so that the great majority of present day authorities believe that all mothers of syphilitic infants have the disease themselves and that transmission to the offspring is solely a question of placental infection.

There are those, however, who still maintain that the disease may be conveyed by direct germinal transmission from the father. Some of the advocates of this view are not willing to accept the Wassermann reaction as a deciding factor, and they even deny the diagnostic reliability of the test. As an illustration, take the following quotation from Wile,¹⁹ who claims that the majority of congenital syphilitic children receive their infection directly from the father:

It is an accepted fact that there is an interchange of immune substances between the maternal and fetal circulation. A Wassermann positive mother, therefore, may receive her complement binding substance by filtration of these substances through the placenta, from her infected product of conception.

This theory, first set forth by E. von Düring,²⁰ not only involves the erroneous assumption that the Wassermann reaction indicates the presence of immune bodies, but also is inconsistent with numerous well established facts.

The substance that gives the Wassermann reaction is not a specific immune body. The presence of the specific immune body of syphilis is elicited by the luetin reaction, and the Wassermann reaction is never regarded as an indication of immunity, but rather of the presence of active syphilis that needs further treatment. When the patient is in a state of cure his Wassermann reaction is negative, but the luetin reaction may be positive.

Furthermore, even if we should admit that the substance in the blood causing the Wassermann reaction is an immune body, the

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18. Caspary, quoted from Holt, L. Emmet: *The Diseases of Infancy and Childhood*, New York, D. Appleton & Co., 1906, p. 1108.

19. Wile, U. J.: *Some Observations on the Transmission of Syphilis with Particular Reference to a Paternal Source of Infection*, *J. Cutan Dis.* **34**:645 (Sept.) 1916.

20. Von Düring, E.: *Monatschr. f. prakt. Dermat.* **20**:245, 1895.

immunity conferred on the mother, according to this theory, would be a passive one and should disappear shortly after the supply from the fetal blood is removed, which, as is well known, does not happen. On the contrary, women who give birth to syphilitic children remain Wassermann positive indefinitely.

And here it may be interesting to recall those cases in which simultaneous examination of specimens of the mother's and children's blood reveals in the former positive and in the latter negative reactions.

Fig. 9.—Spleen: Pulp replaced by proliferated reticular cells, plasma cells and endothelial leukocytes, many of which are engulfing lymphocytes.

For example, it has been demonstrated repeatedly that syphilitic infants born of Wassermann positive mothers may give negative Wassermann and luetin reactions. DeBuys and Maud Loeber,²¹ in a study of foundling children with the view of determining the incidence of congenital syphilis, found negative Wassermann reactions in 106 children ranging

21. DeBuys, L. B., and Loeber, Maud: Study in a Foundling Institution to Determine the Incidence of Congenital Syphilis. *J. A. M. A.* **73**:1028 (Oct. 4) 1919.

Fig. 10.—Internal surfaces of frontal bones and internal surface of base of skull showing areas of gummatous osteitis (yellow areas).

in age from 1 month to 6 years, and these investigators claim to have proven that eighty-six of these children were syphilitic. The objection may be raised that the routine medical care of the new-born in this institution is the administration of gray powder, but in spite of this fact I feel that those who have had experience in the treatment of syphilis, especially the congenital type, will be inclined to share the opinion that a few doses of gray powder are not sufficient to change the Wassermann reaction. Kolmer²² reports negative reactions in fifty-seven of

Fig. 11.—Section of meninges showing spirochetes; silver impregnation, Levaditi's method.

eighty-eight children born of syphilitic mothers and examined at birth. Of those giving a negative reaction, forty-two showed no symptoms of syphilis during a period of three months of observation. Two died with evidence of syphilis in the internal organs and thirteen developed

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22. Kolmer, John A.: *Infection, Immunity and Specific Therapy*, Philadelphia, W. B. Saunders Co., 1917, p. 489.

Fig. 12.—Section of meninges showing outer layer of acute inflammatory exudate superimposed on the specific proliferative meningitis.

symptoms after birth and gave positive reactions. Weber²³ also found a large number, about 50 per cent., of syphilitic infants giving a negative Wassermann reaction, and Dr. Sweeny,²⁴ who has been kind enough to consult for me the records of the New York Foundling Hospital, frequently finds the coincidence of negatively reacting children and positive mothers. In these circumstances the mothers could not have received either immune bodies or the elements that produce the Wassermann reaction from their unborn children.

In opposing the view that the fetus receives the disease from the mother by way of the placenta, Wile¹⁹ states that "Clinical evidence shows bacterial infection through the placenta to be rare, that the fetal blood is not ordinarily infected in sepsis of mother, and this is true not only of ordinary infections, but also of typhoid, malaria, septicemias," etc., and therefore, by analogy he argues that spirochetes rarely pass from the maternal blood to the fetus unless there is a break in the placental circulation, such for instance as that which occurs at the time of birth. In answer to this it may be said that we should not carry reasoning by analogy too far. Congenital tuberculosis, for example, by whatever mode of transmission, is rare; congenital syphilis, on the other hand, is common. Consequently, we must draw our conclusions from observations made on cases of syphilis of which, unfortunately, we have an abundance. Fournier,²⁵ who admits the fact of germinal transmission through the father, in his extensive tables gives statistics which show that transmission by the mother alone is more than twice as frequent as is the so-called paternal transmission. Thus when the transmitter is the father alone the morbidity ("Nocivite") is 37 per cent.; when the transmitter is the mother alone, the morbidity is 80 per cent., and when both parents are syphilitic the morbidity is 92 per cent.

Wile's claim that syphilis of the maternal side of the placenta is practically unknown is not supported by the experience of other observers. Weber²³ states that not only are the lesions on the maternal side of the placenta, but also that spirochetes are invariably found in the maternal blood, and Trinchese and Weber²⁶ have demonstrated

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23. Weber, F.: *Die Syphilis im Lichte der modernen Forschung*, Berlin, S. Karger, 1911.

24. M. J. Sweeny is house physician of the New York Foundling Hospital.

25. Fournier, A.: *L'hérédité Syphilitique Lecons Cliniques recueillies et rédigées*, p. 421.

26. Schindler, quoted from *Die paterne Uebertragung der Syphilis auf die Nachkommenschaft, Eine kritische Untersuchung*, Arch. f. Dermat u. Syph. **113**: O. 935, 1912.

histologically the passage of the organisms from the maternal blood spaces through the syncytium, thus proving the migration of spirochetes from mother to child.

It would seem, therefore, that there is a convincing array of facts in support of the theory that at least in the great majority of cases of congenital syphilis the mode of transmission is through the mother. Nevertheless, we are still confronted with the difficulty of explaining the route of infection in a small percentage of cases of mothers (about 5 per cent.) bearing syphilitic offspring in whom there is not a par-

Fig. 13.—Section of adult syphilitic meninges showing gumma, typical Langhans' giant cells and perivascular round cell infiltration.

ticle of evidence of the presence of syphilis on the basis of either clinical or laboratory findings. Veeder²⁷ observed six such cases over a period of ten years, and Fordyce²⁸ refers to cases observed after thirty years, in some of which syphilitic children were born during the observation period.

27. Veeder, Borden S.: Hereditary Syphilis in the Light of Recent Clinical Studies, *Am. J. Med. Sc.* **152**:522, 1916.

28. Fordyce, John A.: The Diagnosis and General Treatment of Syphilis, *Am. J. Med. Sc.* **152**:469 (Oct.) 1916.

THEORETICAL POSSIBILITIES IN PATHOGENESIS OF CON-
GENITAL SYPHILIS

In seeking an explanation of this difficulty, it may be well to discuss briefly a number of theoretical possibilities in the pathogenesis of congenital syphilis.

1. The spirochetes may be introduced and commence to multiply in the germinal stage of development (roughly, up to the formation of the first rudiments of the embryo). In such a case there would be formed metabolic products from the life and multiplication of the organisms which would have some effect on the life of the embryo, and we must be guided by the results of experimental work in estimating what the nature of this effect would be. It is the consensus of opinion among embryologists whom I have consulted that any infection occurring in this stage would produce death of the embryo with subsequent abortion, or monstrosities. Trinchese²⁹ points to experiments of a number of authors (Samasa, Spemann, Driesch, Roux and Kopsch) who succeeded in demonstrating that even in the lower vertebrates destruction of even a single blastomere was sufficient to inhibit the development of the embryo, or to result in anomalous development. Stockard,³⁰ by treating the fertilized eggs of the common minnow (*Fundulus*) with solutions of magnesium chlorid produced as high as 50 per cent. of cyclopean monsters of various degrees of abnormality. Stockard³¹ says that any interference before the stage of gastrulation, which retards for a time the rate of development, results in the production of twins or other anomalies. Similar treatment of the spermatozoa with chemicals results in abnormal development of eggs subsequently fertilized.

There can be no doubt that if a spermatozoön is actually affected by a direct chemical treatment, the egg which it fertilized will develop more or less abnormally. The radium and roentgen-ray experiments of Bardeen and Hertwig, as well as fertilization by foreign spermatazoa, give conclusive evidence on this point (Stockard and Papanicolaou³²).

In the early part of this stage the ovum is uncovered by decidua, and this is the only period in which a spirochete from the father could reach the ovum without traversing maternal tissue. We can readily admit the possibility of such a mode of infection, but we must believe

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29. Trinchese, quoted from Weber.

30. Stockard, Charles R.: The Influence of External Factors, Chemical and Physical, on the Development of *Fundulus heteroclitus*, J. Exper. Zool. **4**: 165, 1907.

31. Stockard, Charles R.: Personal communication.

32. Stockard, Charles R., and Papanicolaou, George N.: Further Studies on the Modifications of the Germ Cell in Mammals. The Effect of Alcohol on Tested Guinea-Pigs and Their Descendants, J. Exper. Zool. **26**:119 (May) 1918.

that the result would be as above stated and not the production of what we mean by congenital syphilis. Indeed, early abortion, monstrosities and "dystrophies" have been traditionally ascribed to syphilitic parentage, both paternal and maternal, but these things are not "syphilis"—they are not even specific results as they are as readily produced by other causes.

Fig. 14.—Section of lung from normal fetus (see text).

As an illustration of the continuously accumulating clinical evidence against such early or germinal infection the following quotation from Williams³³ is worthy of note:

Syphilis is usually mentioned as one of the most frequent factors concerned in the production of abortion. In my experience it plays but little part during the first half of pregnancy, but, on the other hand, it constitutes the most important single factor in the etiology of premature labor. Additional probability is lent to this view by the fact that all observers agree that spirochetes are not present in the tissues of fetuses expelled by syphilitic mothers during the first half of pregnancy, but are found with increasing frequency in each successive month of the second half.

33. Williams, J. Whitridge: *Obstetrics*, New York, D. Appleton & Co., 1917, p. 662.

2. The spirochetes are introduced and begin to multiply in the embryonic stage, i. e., roughly the period before the completion of the development of the various organs. In this case the infective organism would have to pass through maternal tissue in order to reach the ovum, and if the mother escapes infection, we must assume a pure accident or a natural immunity on her part. But here, as in the germinal stage, established facts lead us to believe that the result of infection would not be congenital syphilis, but anomalies or malformations of the organs. This is well illustrated by the results of experimental injuries to the developing heart. Loeb³⁴ has demonstrated experimentally the effect of injury to the heart on development, and Knowler,³⁵ who worked with frog tadpoles, has confirmed Loeb's observations proving that mechanical or chemical injuries to the heart of embryos cause malformations. In answer to those who say that congenital heart lesions are cases of purely passive failure of development, it can be said that such a conception is unscientific and at least many of the cases bear the distinguishing marks of fetal endocarditis. From such observations we are justified in concluding that an infection of the fetus before its organs are formed would necessarily produce some disturbances or anomaly of the organs affected. There is no evidence of such results in cases of congenital syphilis. The morphologic picture is that of fully developed organs reacting to injury in the same manner as in adult disease. In Figure 14 we have a picture of a lung from a normal fetus of 4 months' development. As yet the air cells are not developed. The lung parenchyma consists of bronchial tubes with three or four tubular branches. If we imagine spirochetal infection in such a lung with the amount of anatomic change shown, for instance, in the lung of the case of congenital syphilis—shown in Figure 5—it is difficult to imagine how the development of the air cells could proceed to the perfection shown in the latter case. So it is in the case of all the organs affected, and I think this is strong morphologic proof that infection of the embryo in the present case at least took place after the organs were fully developed, and this would seem to hold good for the great majority of cases.

3. The spirochetes are introduced and multiply in the fetal stage, i. e., after the formation of the organs. This is the stage in which, in view of the facts stated above, we must believe that the spirochetes at least begin to multiply and give rise to inflammatory reaction on the

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34. Loeb, J.: Ueber die Entwicklung von Fisch-Embryonen ohne Kreislauf, *Arch. f. d. ges. Physiol.* **54**:28, 1893.

35. Knowler, H. McE.: Effects of Early Removal of the Heart and Arrest of the Circulation on the Development of Frog Embryos, *Anat. Rec. (Am. J. Anat.)* **1**:161, 1906-1907.

part of the fetal tissues. In the latter part of the period after the decidua reflexa has been absorbed (about the sixth month) we can conceive of the spirochetes as coming directly from the father, penetrating the amnion, the amniotic fluid, and thence going to the fetus by way of the gastro-intestinal tract. By analogy some basis of fact is given to such an hypothesis by the recent researches of Winter, Menge and Walthard,³⁶ in which they find the fetal membranes a frequent nidus for the growth of ordinary bacteria which pass thence through the amniotic fluid into the mouth of the fetus. At this late period, then, we can conceive of paternal transmission resulting in genuine congenital syphilis without necessarily causing infection of the mother. Facts of any great weight, however, in support of this view are not available.

4. The spirochetes are introduced but do not multiply in the germinal stage. They lie latent throughout the germinal and embryonic phases of development, but do not multiply and give rise to tissue reaction until the fetal stage. This is the old theory of "latency" referred to by Ballantyne³⁷ in his excellent work on Antenatal Pathology, as a necessary implication "if we are to accept the hypothesis of germ and sperm infection with syphilis." This period of latency is regarded by some as equivalent to an "incubation" period. It must be remembered, however, that the true meaning of "incubation" involves the multiplication of the organisms. Another conception is that of an inactive "larval" stage, or as recently resurrected by Wile, a "granular" stage. The classic fact used in support of this theory is that it has been demonstrated experimentally that tubercle bacilli introduced into the hen's egg may apparently remain latent in the embryo chick, setting up tuberculosis only after the chick has left the egg. This solitary and perhaps somewhat doubtful experimental success has been a long time awaiting fellow facts to support it, and it seems a slender thread of evidence beside the counter experimental evidence quoted above.

5. We may conceive, as Boulengier³⁸ did, that the mother really contracts syphilis, but that all the strength of the virus is exerted on the very active organs of the fetus (placenta included), which are as it were a most favorable culture medium for it. According to some such view, spirochetes could multiply in the maternal tissues during the

36. Winter, Menge and Walthard, quoted from DeLee, Joseph B.: *The Principles and Practice of Obstetrics*, Philadelphia, W. B. Saunders Company, 1918, p. 842.

37. Ballantyne, J. W.: *Antenatal Pathology and Hygiene: The Fetus*, Edinburgh, 1902, p. 245.

38. Boulengier: *Jour. d. mal. cutan. et syph.* 7:722, 1895.

germinal and embryonic stages and reach the fetus in the fetal stage where at least the great bulk of the tissue reaction would take place. There is a reaction on the part of the maternal tissues, but it is very mild and escapes all tests for clinical detection. That such mild degrees of syphilis—so-called “latent”—do exist is proved by many clearly established facts. It is now well known that the Wassermann test fails in a large number of cases of latent syphilis. Warthin³⁹ has found the incidence of latent syphilis in about one-third of adult necropsies, and many of these cases gave a history of negative Wassermann reactions and negative clinical findings. In a certain number of the cases, spirochetes were demonstrated in such organs as the heart, aorta and testes, without producing any apparent reaction. As Warthin expresses it, only the necropsy reveals that these people are “spirochete carriers,” and have a latent infection of very low virulence. Furthermore, Symmers, Darlington and Bittman,³⁹ not infrequently at necropsy have found positive evidence of syphilis in the vascular system, liver and spleen in cases in which there were negative Wassermann reactions and negative clinical histories. And recently Fraser⁴⁰ has encountered evidence of syphilis of the coronary artery at necropsy in cases in which the Wassermann reaction had been persistently negative and in which all clinical evidence of syphilis had escaped detection.

In the light of these revelations, and especially when they are considered with the biologic and morphologic evidence set forth in the preceding pages, it must be evident that there is little justification for the hypothesis that the syphilitic children of these mothers received their infection by germinal transmission from the father.

The occasional occurrence of apparently healthy mothers giving birth to infected children by syphilitic fathers, and subsequently giving birth to healthy children by fathers free from syphilis, has long been used as an argument in support of the theory of infection by paternal germinal transmission, but this argument is counteracted by the fact that a known syphilitic mother, after giving birth to a syphilitic child, may subsequently bear healthy children. There is another group still more rare in which syphilitic children are born of parents neither of whom have ever shown either clinical or serologic evidence of syphilis. It is possible that here we may be dealing with congenital infection totally unrecognized by the patient. Many cases of congenital syphilis, especially in women, run an unrecognized latent course sometimes throughout a lifetime.

39. Symmers, Douglas, Darlington, Charles G., and Bittman, Helen: The Value of the Wassermann Reaction as Indicated by Postmortem Investigation in Three Hundred and Thirty-One Cases at Bellevue Hospital, *J. A. M. A.* **70**:279 (Feb. 2) 1918.

40. Fraser, Alexander: Personal communication.

SUMMARY

1. The case here reported is one more to be added to those of apparently nonsyphilitic and immune mothers bearing children that have been proved syphilitic.

2. From a review of antenatal pathology and embryology and the morphologic evidence in this case, as indeed in all cases of congenital syphilis, it would appear that infection takes place only after the fetal organs have been formed — a fact which excludes the theory of germinal transmission unless we assume a practically unsupported theory of “larval inactivity” of the infecting organism.

3. From the facts reviewed the most plausible explanation of the 5 per cent. residue of nonsyphilitic and immune mothers of syphilitic children is that these mothers have a mild, low grade form of syphilis.

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