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THE TREATMENT OF ANTENATAL AND CONGENITAL SYPHILIS *

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The problem of antenatal and postnatal syphilis is one of the largest in the entire field of medicine, not only because it concerns nearly every specialty, but also because of its wide social and economic importance. As is well-known, syphilis is the most frequent cause of abortions and stillbirths, statistics ranging from 20 to 50 per cent. Williams, in his series of 10,000 pregnancies, holds the disease responsible for 26 per cent. of the fetal deaths between the end of the seventh month of gestation and the two weeks prior to delivery. Routh arrived at about the same figures in his computations, stating that, in urban populations, 25 per cent. of the miscarriages and stillbirths are due to this infection. When the fetus survives and is brought into the world, suffering from latent or active syphilis, its personal handicaps, as well as its being a burden to the family and, only too often, to the community, have to be reckoned with.

We are, however, more optimistic for the future because our more efficient methods of treatment and investigation are reducing not only fetal mortality but also the number of cases of active congenital syphilis. We have cooperated for some time with a number of maternity institutions, and the infrequency of actively syphilitic infants has been a matter of surprise to us. The explanation, of course, is simple. Practically all maternity hospitals today are thoroughly investigating their prospective patients to determine the presence of a syphilitic infection. A careful history is taken as to the outcome of previous pregnancies and a blood examination is made in all cases. Even where the serologic findings are negative, if there is any suspicion of the disease, syphilitic treatment is given, it being believed better to err on the side of safety. At the Vanderbilt clinic, we have had a great many women referred to us with positive blood reactions. Some give a history of infection dating from the time of their marital ties, but by

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far the larger number can supply no such data. In these, the most frequent story is one of repeated abortions or miscarriages, followed later by a stillborn child or the birth of a premature infant which died shortly after from malnutrition and feeble development. We make it a rule in cases in which the only symptom is a positive serum reaction to have the test corroborated in different laboratories, as we are fully aware of the danger of relying on one laboratory examination and of the fact that a normal pregnant woman's blood may give a strongly positive reaction with the cholesterinized antigen.

We have found that from 25 to 35 per cent. of the patients referred to us by maternity hospitals, because of a strongly positive reaction with cholesterinized antigen alone give a negative Wassermann reaction with all methods when they report several weeks after delivery and remain negative on repeated examination.

THE IMPORTANCE OF EARLY TREATMENT

Does treatment early in pregnancy prevent abortions or miscarriages and insure the birth of a healthy nonsyphilitic infant? We can answer this question in the affirmative. It is important, however, to begin treatment early. Little can be expected if we delay until the last weeks of gestation, as illustrated by the subjoined case:

CASE 1.—History.—R. E., colored, aged 19, pregnant seven months, was referred to the clinic Feb. 2, 1921, for treatment. She gave no history of infection, had had no abortions and presented only a + + + + Wassermann reaction. She received four injections of arsphenamin, 0.3 gm. at weekly intervals, and mixed treatment. February 21, she gave birth to a girl weighing 4 pounds and 2 ounces (1870 gm.). The blood from the cord gave a + + + + reaction; and ten days later, from the heel, a + + + + reaction. The physician in charge reported that at birth the liver and spleen were not palpable.

The infant did not gain in weight. When the infant was 42 days old, a small ulceration appeared on the labium majus and oozing of blood was observed from the small stab in the left heel, which had never closed. The child now became distinctly jaundiced, vomited, and had gray, chalky stools; the spleen was enlarged, and the liver slightly enlarged; the heart and lungs were negative. On the forty-fourth day, whole blood was injected subcutaneously, but the bleeding continued from the heel and labium and two hematomas appeared above the knees. Blood examination revealed: hemoglobin, 65 per cent.; red blood cells, 3,650,000; white blood cells, 12,200; polymorphonuclears, 52 per cent. On the forty-sixth day, the infant died.

Necropsy Findings.—We are indebted to Dr. W. C. Johnson, pathologist to the Sloane Hospital, for the necropsy report. Baby E., girl, aged 46 days; weight 1,950 gm.; length 46 cm. Anatomic Diagnosis: (1) congenital syphilis, (2) syphilitic hepatitis, (3) syphilitic splenitis, (4) anemia, (5) jaundice, (6) melena, (7) injected blood (therapeutic), (8) ulcer of labium, (9) involution of thymus, (10) hemorrhage in parathyroids, and (11) fractures of ribs (6, 7, 10, right side).

The body was that of a poorly nourished, apparently full-term infant. Rigor and lividity were present. The skin was pale and markedly jaundiced. The scalp, eyes and ears appeared normal. There was no discharge from the nose, and no fissures around the mouth. The anus was normal. There was a small yellow patch with a blackish crust on the left labium majus. The navel appeared completely healed and normal.

There was no fluid or exudate in the peritoneal cavity. The umbilical vein was still open. The mesenteric lymphnodes were enlarged.

The pleural cavities were normal. There was a large collection of clotted blood in the left pectoralis major. The muscles were pale. The pericardial cavity contained a normal amount of clear, bile tinged fluid.

The thymus weighed $1\frac{1}{2}$ gm., was very soft and had much loose tissue around it.

The heart was normal in size, and there were no epicardial hemorrhages. The muscle was pale. The foramen ovale still showed a small opening and the ductus arteriosus was not fully closed. There were no valvular lesions.

The lungs weighed 40 gm. They appeared well aerated. There were no pleural hemorrhages. Both lungs felt soft, crepitated slightly, and were pale white except for small, reddish patches along the posterior part of the lower lobes. There was slight emphysema along the anterior margins. The trachea and bronchi contained reddish brown, slimy material.

The thyroid was pale and rather small.

The parathyroids were all enlarged and dark red, possibly hemorrhagic.

The tongue appeared normal.

The esophagus contained reddish brown material resembling partly digested blood. This appears to be the same material as that in the trachea.

The stomach contained bloody material.

In the small intestines, there was blood stained mucous throughout the lower 68 cm.

The pancreas was not enlarged.

The spleen was markedly enlarged, weighing 42 gm. The capsule was smooth and tense. The cut surface was rather firm and dark red.

The liver was slightly enlarged, weighing 129 gm. The capsule revealed a few patches of thickening. The cut surface was greenish brown, fairly uniform in appearance. The gallbladder and ducts appeared normal.

The suprarenals together weighed 3 gm., and showed no hemorrhages.

The kidneys together weighed 21 gm. The surfaces were pale. The cut surfaces showed a slightly thickened cortex, but were otherwise normal.

The ureters were slightly dilated at their upper parts. The bladder, uterus and adnexa were normal.

The epiphyseal lines at the knee joint were slightly thickened and bile-stained.

The spinal cord appeared normal.

The brain was pale but otherwise normal.

The sixth, seventh and tenth ribs on the right side were fractured and showed some callus formation.

The middle ears, sutures and fontanelles were normal.

Microscopic Examination.—The heart was normal.

Some lobules of the lungs were emphysematous and others atelectatic. In the latter areas, the alveoli contained mononuclear cells and erythrocytes. The alveolar walls generally appeared more cellular and less vascular than normal. There was no definite fibrinosis.

The liver cords, which were rather large, were separated by a moderate amount of diffuse cellular fibrous tissue. Some of the liver cords were necrotic and were invaded by polymorphonuclear leukocytes. Many of the hepatic cells contained numerous coarse granules or masses of brown pigment. Some of the hepatic cords had numerous nuclei arranged near their centers, giving them the appearance of giant cells. New blood formation was not increased. The portal canals and their contents revealed nothing significant. The capsule was normal. The capsule of the spleen was slightly thickened. The malpighian bodies were small and indistinct. The pulp presented a very confused picture. The pulp cords were thickened and contained numerous mononuclear cells as well as red cells.

The kidneys were practically normal.

Examination of the suprarenals revealed congestion of the inner part of the cortex and medulla. The cells of the inner part of the cortex were separated from each other.

The pancreas was practically normal. In some places, there was a small amount of interstitial fibrosis.

Examination of the thymus revealed that the lymphoid tissue was considerably diminished and the reticulum was more prominent than normal.

Examination of the thyroid revealed that the acini were well developed and many contained colloid.

There were no changes of any significance in the stomach and intestines.

The uterus was normal.

In the ovaries, there were several rather large, and one cystic follicle.

The fallopian tubes were normal.

In the mesenteric lymphnode, the lymphoid tissue was greatly decreased. The lymph sinuses were packed with large phagocytes, many of which contained lymphocytes.

There was no evidence of inflammation in the navel.

The lesion on the labium was a superficial ulcer with necrosis and slight leukocytic infiltration.

Levaditi Sections: There were no organisms in the kidneys.

Examination of the suprarenals revealed numerous spirochetes in and around the medulla.

No organisms were found in the spleen except a few around one of the larger blood vessels.

A few spirochetes were found in the lungs.

No spirochetes were found in the pancreas.

A few were present in the lymphnodes.

There were very few organisms in the thymus.

In the liver, spirochetes were present in enormous numbers.

The ovary was negative.

In the heart, there were a moderate number of the organisms.

COMMENT

Had this mother been seen during the early period of her gestation and treated systematically, we feel confident that she would have been delivered of a full-term, healthy baby. In the treatment of these patients we follow a regular plan of giving from six to eight injections of arsphenamin or neo-arsphenamin, the former in doses of from 0.3 to 0.4

gm., the latter in doses of from 0.45 to 0.6 gm., at weekly intervals, together with mercuric salicylate or mercuric chlorid, 1 grain, once a week for from twelve to fifteen injections. As a rule, pregnant women tolerate the treatment well and without bi-effects. When the mercurial injections are especially painful or give rise to abdominal cramps, we discontinue them and administer mercury or mixed treatment by mouth. If the remedies are well tolerated, treatment is continued interruptedly during the entire period of pregnancy. Of course, the kidneys and other organs are carefully watched for the development of toxic symptoms. While many of the infants from such mothers are without clinical or serologic evidence of the infection, we have not been able to reduce the positive findings in many of the mothers to negative. The reason for this is that many of them have had their infection a number of years and the usual difficulty to reverse the blood reaction applies here. Infants born of treated mothers have been carefully examined for cutaneous or visceral syphilitic manifestations and have now been followed serologically for years with negative results. Whether they will develop active signs of the disease in later life is a question that time only can decide.

A PROBLEM IN IMMUNOLOGY

How is it possible for a mother with a positive Wassermann reaction to give birth to a baby with a negative reaction? Do our immunologic theories offer an explanation, or does the anatomic barrier interposed by the placenta play the chief rôle? We believe the former offer a more satisfactory solution, and we are not inclined to regard as significant the view that the placenta acts as a filter, because of the contradictory findings presented. To account for a healthy infant which began its development with the strongly positive blood of its mother and continued to be nourished with it during its entire existence in utero, Routh's theory of the action of chorionic ferments might also apply.

According to Williams, a positive maternal blood does not necessarily imply the existence of fetal syphilis, nor do the findings in the fetal blood at birth necessarily give positive information. This, also, has been our experience, for we have seen well-developed infants at birth give a ++++ reaction with blood from the cord, but ten days later give a negative one, which subsequently remained persistently negative both serologically and clinically. We, therefore, do not believe that we can attach much significance to the reaction at birth in the absence of other data. Williams has also found infants, with a negative Wassermann reaction at birth and a syphilitic placenta, develop a positive reaction later, with clinical manifestations. These

fluctuations in the sero-reaction of early congenital syphilis, therefore, demand a frequent repetition of the test. Occasionally, we see syphilitic babies, with a ++++ Wassermann reaction at birth which becomes negative ten days later and then positive after a week or two, as in the following case:

CASE 2.—History.—Baby F. was born in one of the maternity hospitals, of a mother who had a strongly positive Wassermann reaction. At delivery, a specimen of blood was taken from the umbilical cord and sent for serologic examination. This was reported + + + +. The infant was a full-term baby but weighed less than 4 pounds (1,800 gm.), and was immediately placed in an incubator. Examination at birth and daily thereafter for a week failed to reveal any lesions of a syphilitic nature. The blood taken from the longitudinal sinus ten days after birth was reported negative. At this time a lesion appeared about the anus and distinct snuffles developed.

There was difficulty in feeding the infant, and its weight had increased slightly. Local rubbings of mercurial ointment were ordered and kept up daily. We saw the child for the first time on the thirty-first day after birth. It weighed then 4 pounds and 2 ounces (1,870 gm.), was feeble and shriveled looking, and had a marked coryza. The skin of the body presented no lesions except around the anus, where an infiltrated annular patch, of dusky red hue, was present. A Wassermann test on that day from the longitudinal sinus was reported + + + + by two different laboratories. On the fifty-seventh day, the infant died.

Necropsy Findings (Report by Dr. Johnson).—Baby F., a boy, aged 57 days, weight 2,000 gm., length 49 cm. Anatomic Diagnosis: (1) acute peritonitis, with inflammation of tunicae vaginales; (2) congenital syphilis (lesions in liver, spleen and pancreas); (3) jaundice, and (4) malnutrition.

The body was that of a poorly nourished colored infant. Rigor mortis was absent. There was slight jaundice. The eyes and ears appeared normal. A whitish material came from the nose. There were no fissures around the nose or mouth. The fontanelles were wide open and the sutures were not closed. The abdomen was distended. The navel appeared normal. The scrotum was large and edematous; the skin over it was slightly reddened. Around the anus were several small, nearly healed fissures. The palms and soles appeared normal. There was some peeling of the epidermis around the wrists, ankles and knees. There were no hemorrhages or eruptions on the skin.

The peritoneal cavity contained a small amount of turbid yellowish fluid in which were lumps and flocculi of whitish material resembling fibrinopurulent exudate. Some of these flocculi were scattered over the coils of the intestine and also on the capsules of the liver and spleen. The serous surfaces were rather dull and pale. There was no localization of the peritonitis, no adhesions, and no local indications of its origin.

The pleural cavities contained no fluid, exudate or hemorrhage.

The pericardial cavity contained a normal amount of fluid showing bile coloration.

The heart was normal in size. The foramen ovale and ductus arteriosus were closed. There were no hemorrhages or valvular lesions.

The lungs were pale pinkish, were well expanded and showed no definite lesions.

The larynx, trachea and bronchi were normal.

The thymus weighed 2.5 gm., was very small but of good consistency

The liver weighed 110 gm., was pale and somewhat jaundiced; otherwise it showed no definite lesions.

The spleen weighed 10 gm. No abnormality was noted.

There were no lesions noted in the gastro-intestinal tract and pancreas.

The kidneys together weighed 29.5 gm. They were pale but showed no other changes.

The suprarenals together weighed 3.5 gm. They appeared very small and showed no lipoid material.

Examination of the genitals revealed that the processus vaginalis still communicated with the peritoneal cavity through a small opening on each side. The cavities were rather large and contained fibrinopurulent material. The tunica vaginalis was thickened. The testes appear slightly swollen and reddened.

The epiphyseal lines at the knee appeared practically normal. In the upper end of the shaft of the tibia on both sides, adjacent to the epiphyseal lines, a small part of the cortex and medulla were replaced by a homogeneous whitish material, softer than the cartilage of the epiphyses. The symmetry of these lesions and the absence of any inflammatory reaction made them appear to be congenital anomalies or defects of development.

There were no gross lesions in the brain. The head was 30.7 cm. in circumference.

Microscopic Examination.—The heart was normal.

In the lungs some lobules were emphysematous; others contained a moderate amount of albuminous precipitate and a few large and small mononuclear cells. There was no fibrosis.

Examination of the liver revealed that the capsule was normal. The portal canals showed an increase of fibrous tissue and slight cellular infiltration. Scattered through the lobules were several small patches of fibrosis. There was no necrosis. There was a considerable amount of blood cell formation.

The kidneys were practically normal.

Examination of the spleen revealed that there was an exudate on the capsule, consisting of fibrin with mononuclear cells and leukocytes. The capsule itself showed a slight leukocytic infiltration. The malpighian bodies were distinct and of moderate size. The venous sinuses were distinct and only partly filled with blood. Many large mononuclear cells containing brown pigment were present. The pulp cords were wide and were packed with red cells. Throughout the pulp there was a definite increase of connective tissue in the form of small strands.

In the suprarenal, the cells in the inner part of the cortex were small and separated. Many were necrotic or autolyzed.

In the pancreas there was a moderate interstitial fibrosis with loose cellular connective tissue. Otherwise the gland appeared practically normal.

In the thymus, the lymphoid cells in the cortex were considerably diminished in number. Large mononuclear cells were relatively abundant.

Examination of the testicles revealed that the serous cells of the tunica vaginalis had disappeared and the surface was covered with a thick layer of fibrin, beneath which the connective tissue was infiltrated with leukocytes and mononuclear cells. The subcutaneous tissue of the scrotum showed edema and the exudate of the fibrin.

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Sections of lesions of the anus showed practically nothing but crusts on the surface, beneath which the epithelium had healed.

Levaditi sections of all organs, including the brain and spinal cord, were negative for spirochetes.

COMMENT

This case is interesting because the child had a + + + + Wassermann reaction and syphilitic lesions in the viscera, and yet the examination was negative for spirochetes after a careful search.

It is a common clinical fact that the tendency to transmit the disease lessens with the age of the infection. We frequently see women with strongly positive reactions, who have had no treatment whatever, give birth to healthy offspring with a negative blood reaction or to infants with alternating positive and negative reactions.

STATISTICS IN ONE HUNDRED AND FORTY CASES

We have had under observation, during the last year and a half, 140 children who were born of mothers with a strongly positive Wassermann reaction, but whose own reactions are negative clinically and serologically, the latter on repeated testing.

There were twenty-seven female white children, forty-one female black children, thirty-six male white children, and thirty-six male black children.

The age on admission in eighty-seven children ranged from 3 weeks to 6 months; in the rest from 6 months to 9 years.

The Wassermann reaction of blood from the umbilical cord of twenty-two of the younger infants gave a positive test in nineteen. The Wassermann reaction on admission to the clinic and repeated several times thereafter was negative in all of the 140 children.

Syphilis was admitted by nineteen fathers; it was denied by one or both parents in 121 cases; of these, twelve fathers admitted gonorrhea. The age of the infection when admitted by the father ranged from three to sixteen years. The number of years the parents had been married ranged from less than one year to eighteen years; five of the children were illegitimate.

The Wassermann reaction was obtained in sixty-six of the fathers; in thirty-six it was positive; in thirty negative; of the latter, five had had treatment for syphilis. Seventy-four fathers refused or were unable to come for a test. The Wassermann reaction was positive in all of the mothers; 133 had a + + + + reaction; three had a + + + and four a + + reaction.

Forty-three mothers gave a history of abortions or stillbirths; ninety-seven gave no history. Sixty mothers had had no other children; sixty-four had other children whose reactions were negative; five had other children who were syphilitic, and eleven had both healthy and

syphilitic children. Forty-eight of these women had had no antenatal treatment; twenty-five had had internal treatment only; sixty-one had had partial treatment with arsphenamin and mercury, and six only had had prolonged treatment with these drugs.

NONSYPHILITIC CHILDREN OF SYPHILITIC PARENTS

The question frequently arises as to what should be done with infants with a negative Wassermann reaction born of parents with a positive Wassermann reaction, and it is difficult at times to render a decision. One often sees the statement that the children of syphilitic parents should be treated whether symptoms are present or not and regardless of a negative Wassermann reaction. This, in our opinion, is an unnecessary hardship, and we favor instead keeping them under surveillance for several years after we have satisfied ourselves, in the absence of clinical manifestations, that the blood and spinal fluid are negative.

Can a patient with a negative Wassermann blood reaction and a positive spinal fluid reaction transmit the disease? In answer we quote the subjoined case.

CASE 3.—Mrs. G. H., white, aged 25, whose previous history was indefinite was delivered at the Sloane Maternity Hospital of a baby weighing 4 pounds and 13 ounces (2,180 gm.). The Wassermann reaction of the blood from the umbilical cord was + + + +. Examination by the resident physician at birth revealed no evidence of syphilis. The blood from the longitudinal sinus ten days later was strongly positive. The baby had now developed distinct snuffles and an eruption on the buttocks consisting of lesions of various types, impetiginous, bullous and infiltrated papules. There were no anal or mouth lesions. The clinical diagnosis was in favor of syphilis. Another specimen of blood was sent to two different laboratories and again reported strongly positive. The mother's blood before delivery and after the birth of the child was negative; twenty days later, examined in two different laboratories, it was again reported negative. Clinical investigation failed to disclose any signs of syphilis. She was then given a provocative injection of arsphenamin, but the blood remained negative. A spinal puncture was now made and the fluid found positive in all phases.

As she had been deserted by her husband some time before entering the hospital, we were unable to extend our investigations to him. In this instance, of course, we cannot exclude paternal syphilis. Again, it is possible that the mother was suffering from an old neurosyphilis, the infection dating prior to her marriage, although she disclaimed any knowledge of it.

QUESTION OF LIKELIHOOD OF TRANSMISSION IN NEUROSYPHILIS

Are patients with neurosyphilis more likely to transmit the disease to their offspring than those in whom the nervous system is spared? We think not. This we judge from the large number of cases we have observed in which both wife and children had escaped infection. Most of these patients, however, had not married until quite an

interval had elapsed since their infection, namely, from ten to fifteen years. On the other hand, a case such as the one presented herewith is not unusual:

CASE 4.—Mr. J. W., white, aged 35, acquired syphilis at the age of 18, for which inunction treatment was carried out in a systematic fashion for two years. He married at the age of 22, his wife giving birth two years later to a healthy child. He is at present under treatment for an advanced tabetic condition, with all the signs of degenerative changes in the posterior columns of the cord. His blood Wassermann reaction is strongly positive and the spinal fluid is also strongly positive in all phases. He has four children, 11, 8, 5 and 3 years of age. The youngest was born after the patient had complained of neurologic symptoms. They are all negative clinically and serologically. The wife also had a negative Wassermann reaction both in the blood and the spinal fluid.

QUESTION OF MARRIAGE

When is it safe for a patient who has had a syphilitic infection to marry? From our experience in the past, we believe a person who has had active syphilitic treatment, is free from all clinical evidence, has a negative spinal fluid and whose blood has been negative for two years may be permitted to marry. Recently, we were called on for an opinion in the subjoined case:

CASE 5.—P. Y. was under our care for an extragenital infection acquired about six years previously. The chancre was not recognized, and he was treated surgically until secondary manifestations made their appearance, at which time we first saw him. He received arsphenamin and mercuric salicylate, in all twenty intravenous injections and thirty intramuscular injections in two courses. The Wassermann reaction had been negative for more than five years, tests having been taken at six-month intervals after the second year. He was instructed to have a lumbar puncture, but for business and family reasons he was unable to have this done. He then married, and his wife recently gave birth to a premature baby, weighing about 5 pounds (2,260 gm.). The skin, mucous membranes and viscera were carefully examined for clinical evidence of syphilis, but none was found. A specimen of blood was not taken by the attending physician for fear of arousing the mother's suspicions. However, the placenta was sent to a private laboratory for microscopic examination and the pathologist reported that he found spirochetes in the tissue.

COMMENT

With all the negative data we have in the father's case, we are inclined to doubt the accuracy of the report. We are told by pathologists with experience in placental tissue work that it is an exceedingly difficult task to find spirochetes and that often one is not rewarded until hundreds of sections have been studied, even when active manifestations of the disease are present in the child. There, of course, remains the possibility that the mother was syphilitic. This was ruled out only clinically, but in the case of the child there was likewise no

clinical evidence of the disease, other causes besides syphilis being responsible for prematurity. Would it be possible for a husband whose Wassermann reaction has been repeatedly negative for five years to infect his wife? We do not deny that a patient may harbor spirochetes in the testicles and have a negative blood reaction, but we are not inclined to believe that one who has been treated thoroughly and whose blood has been continuously negative for five years is likely to transmit the disease.

DEMONSTRATION OF SPIROCHETES IN PLACENTA

To illustrate how difficult it is to demonstrate spirochetes in the placenta even when they are abundant in the viscera, Dr. Johnson's report on Baby A. is appended.

CASE 6.—History.—The child, a boy, was born at the eighth month of gestation of a mother and father having strongly positive Wassermann reactions, and lived only four days. It weighed 1,700 gm. The anatomic diagnosis was: (1) congenital syphilis; (2) maceration, and (3) prematurity.

Necropsy Findings.—The body was well developed and showed no external abnormalities except softening of the head, and peeling of the epidermis in places over the trunk and extremities. Rigor mortis was absent.

The peritoneal cavity contained some reddish brown fluid.

The pleural cavities were normal.

The pericardial cavity contained a normal amount of fluid, which was rather turbid.

The thymus was small and soft.

The heart was normal in size and showed no lesions except that the myocardium was pale and soft.

The lungs were normal in size, pale, soft and not aerated.

The thyroid gland was normal.

The gastro-intestinal tract showed no gross lesions.

The pancreas showed no gross lesions.

The spleen was much enlarged, pale, brownish-red in color. On the capsule there was a slightly whitish coating, apparently fibrin. The cut surface was brownish red and rather soft.

The liver was slightly enlarged and quite soft. On section, the cut surface had a uniform pale brownish-red color.

The gallbladder and ducts were normal.

The suprarenals showed no gross lesions.

The kidneys were pale, but otherwise normal.

The ureters and bladder were normal.

The testicles were in the scrotum and appeared grossly normal.

The epiphyseal lines at the lower end of the femur and the upper end of the tibia did not appear widened or irregular, but there was a yellowish discoloration extending for some distance into the marrow of the shaft.

The brain was very much softened and no gross lesions could be found.

Microscopic Examination.—The organs for the most part manifested advanced decomposition and could hardly be recognized histologically. The lung showed

slight thickening of the interalveolar septums, which appeared edematous rather than fibrous. The alveolar epithelium was not recognizable. Many alveoli contained a network of fibrin threads.

Levaditi Sections: Spirochetes were present in large numbers in the lung, liver, spleen and suprarenal. The pancreas showed a moderate number.

On cross examination the placenta, which weighed 400 gm. (nearly one-fourth of the weight of the fetus), appeared pale and was thicker than normal in proportion to its size. No macroscopic infarcts or calcified areas were noted. The umbilical cord was thick and appeared edematous.

Microscopic examination of the placenta revealed that the chorionic villi, teased out in salt solution, appeared thicker and less vascular than normal. Stained sections showed the villi enlarged, with greatly diminished vascularity and an infiltration of the stroma with a moderate number of mononuclear cells. *Levaditi* sections which were stained along with the fetal organs showed no spirochetes in the placenta, umbilical cord or fetal membranes.

Diagnosis.—Syphilis of the placenta was diagnosed.

METHOD OF TREATMENT

Since our preliminary report in November, 1920, on the treatment of congenital syphilis with intramuscular injections of neo-arsphenamin and mercuric chlorid, our confidence in the method has grown, and we are decidedly encouraged as to the ultimate outcome in these small patients. Our work has been greatly hampered because of the enormous difficulties encountered in obtaining the cooperation of mothers as to reporting weekly. After active lesions have disappeared and the child looks healthy and gains in weight, indifference sets in or the address is changed to another quarter of the city, and the visits are discontinued. In spite of efficient social service and follow-up work, treatment has been interrupted in a number of cases, or we have failed to induce the mothers of new patients to begin treatment. If we had had hospital facilities we feel that more might have been accomplished, and our natural timidity in increasing the dosage might have been overcome sooner.

From the results obtained, however, we believe that it is the method of choice. We are led to this belief by the rapid disappearance of all clinical signs, the improvement in the nutrition of the child, its steady gain in weight and the reversal of a positive Wassermann reaction to negative. In the literature one frequently sees the claim that a positive Wassermann reaction in congenital syphilis cannot be changed. Of forty-seven children with positive reactions who have received one course or more of treatment, fourteen gave negative reactions on repeated examination. Among those who still gave a ++++ reaction, we have several in whom the blood became negative after one course of treatment and then positive again after the period of rest. In the case of the older children, the reaction is not so easy to influence. The same problems, therefore, present themselves as in the adult with

acquired syphilis. The infection must be attacked early and treatment must be prolonged to bring about a continuously negative Wassermann reaction.

Originally we gave 0.075 gm. of neo-arsphenamin to infants from 3 to 8 weeks old, at weekly intervals; 0.1 gm. from 2 to 6 months; 0.15 gm. from 6 months to a year, and from 0.15 to 0.2 gm. from 1 to 2 years, in a course of six injections, followed by a rest period of from four to six weeks. We are now giving from six to eight injections to the course and make the initial dose 0.1 gm. for infants from 2 to 12 weeks old; 0.15 gm. from 3 months to 9 months; 0.2 gm. from 1 to 2 years, and 0.25 to 0.3 gm. for children 3 years old. The mercuric chlorid, too, we have increased to from ten to twelve injections to the course, at intervals of a week, and the dosage as follows: 1/10 grain for children from 2 weeks to 6 months old; 1/8 grain from 6 months to 1 year; 1/7 grain from 1 to 2 years; 1/5 grain from 2 to 3 years, and 1/4 grain for those more than 3 years old.

Just as in acquired syphilis, the treatment must be individualized and the intervals lengthened or the dosage changed if indications arise. The urine should be examined at frequent intervals, as occasionally a trace of albumin is found, but this quickly subsides when the drug is discontinued. We believe two full courses each, with proper intervals, should be given, regardless of a negative reaction, and possibly a third course of mercury. In very feeble infants, it is better to initiate the treatment with mercury, giving about eight injections before the administration of neo-arsphenamin.¹ To date, we have had no abscesses even in undernourished infants with a poorly developed musculature. No reactions from the drugs have been noted in the dosage given, except an occasional trace of albumin after the mercury.

The eye, neurologic and spinal fluid examinations should be carried out as in the case of adults.

SUMMARY OF EIGHTY-EIGHT CASES

We summarize herewith the data on the cases of eighty-eight children who have come to us within the last fifteen months with evidence of syphilis.

There were eighty-eight children with clinical or serologic evidence of syphilis: thirty-four female, white; eighteen, female, black; twenty-six male, white, and ten male, black.

1. It is important to use neo-arsphenamin which is especially prepared for intramuscular injection and is neutral in reaction. That put up for intravenous use is slightly alkaline and when injected into gluteal muscles is apt to be followed by tissue necrosis or abscess formation.

We would also like to emphasize the necessity of using only sharp needles for these treatments. As a rule, they are not sharp enough when delivered by the manufacturers and should be sharpened on a fine oil stone by the operator.

The age, on admission, in twenty-three ranged from 3 weeks to 6 months; in eight from 6 to 12 months; in fourteen from 1 to 2 years; in forty-three from 2 to 12 years. The Wassermann reaction obtained from the blood of the cord in nine of the infants was + + + +.

The Wassermann reaction on admission to the clinic was positive in all eighty-eight children. Clinical manifestations were present in twenty; in four there were skin lesions; in six visceral lesions; three had a marked epiphysitis; five had interstitial keratitis and one child was partially deaf. Twelve children received two courses or more of neo-arsphenamin and mercury intramuscularly; thirty-five have had one course; thirty have had less than one course; eleven failed to report for treatment.

Clinically all visible lesions yielded promptly to treatment.

Serologically, the Wassermann blood reaction is negative in fourteen; in twenty it is still + + + +. The reaction of several of these had been negative but it became positive again because of failure to continue treatment; in three cases the reaction is + + +, in two, + +, and in one, +. The remainder have not been examined since treatment was begun. (We have omitted from this series a number of older children whose reactions have become negative after intravenous treatment with arsphenamin combined with mercury intramuscularly.)

In fifty-nine cases, infection was denied by one or both parents, but two fathers admitted gonorrhea. In twenty-nine fathers, a history of syphilis was obtained. The age of the infection in these varied from 2 to 15 years. The number of years the parents had been married ranged from one to sixteen. Thirty-three fathers gave a strongly positive Wassermann reaction; thirteen a negative; forty-two we were unable to examine. Seventy-four mothers gave a strongly positive reaction; two a negative. In twelve we could secure no data as they were either dead or divorced. Fifteen mothers gave a history of miscarriages or stillbirths; sixty-one gave no such history; in the case of twelve mothers we could obtain no data. Thirty-one mothers had had no other children; in twenty-six cases, the other children all gave negative Wassermann reactions; in thirteen all gave positive reactions, and in eighteen both negative and positive. Eight of these women had had only partial antenatal treatment with arsphenamin and mercury; seven had had internal treatment only; sixty-one had had none, and twelve we could learn nothing about.

CONCLUSIONS

1. Every prospective mother should receive a routine Wassermann examination.

2. The proper treatment of a syphilitic mother during pregnancy will undoubtedly result in the birth of a healthy infant.

3. Every infant born of a mother or father with syphilis should have a Wassermann test made at birth; again two weeks later, then every four weeks up to six months, and after that every three months up to two years. If the reaction is negative with all these tests and no clinical signs have appeared, the baby has in all probability escaped the infection.

4. A certain number of infants born of mothers with strongly positive reactions give a positive cord reaction, but subsequently all tests are negative, and they fail to show any clinical manifestations of the infection. They should, however, be kept under observation for at least two years.

5. Occasionally an infant with active clinical signs of syphilis will give negative serologic findings, usually only temporarily. The clinical diagnosis should always take the precedence over the laboratory diagnosis and proper treatment should be instituted.

6. In the treatment of our patients having congenital syphilis we have adopted as the method of choice the systematic intramuscular injection of neo-arsphenamin and mercury. We not only have had good clinical results but we also have been able to obtain negative reactions in fourteen of our infants out of a total of forty-seven with + + + + blood reactions, when the treatment was begun within the first few months. This to our minds proves that systematic treatment begun early, in the first week or two where possible, will result in the clinical and serologic cure of the infant.

ABSTRACT OF DISCUSSION

DR. WILLIAM ALLEN PUSEY, Chicago: I would like to express my great appreciation of this paper. I have gotten in a state of mind where I almost hate to hear a paper read which takes up the treatment of syphilis, because so many things are given as established facts that violate my clinical conceptions of what happens and has happened in syphilis. I was gratified to find that this paper did not in any way violate the conceptions that a good many of us have gathered after seeing the disease through many years.

On the subject of prenatal and postnatal treatment, it seems to me the paper represents very good end-results. It is a much better experience than we formerly had, and one which I am ready to believe is entirely within the facts.

DR. RICHARD L. SUTTON, Kansas City, Mo.: I, too, wish to express my appreciation of this excellent paper. The use of arsphenamin and neo-arsphenamin by intramuscular injection has always appealed to me, and when the drugs are properly administered by this route, I consider it far superior to the intravenous method.

DR. HAROLD N. COLE, Cleveland: I have not obtained as good results in the prenatal treatment. I have had women in the hospital for the entire period of time and have given thorough treatment, but I have had a great many

babies that within two or three months would again show evidence of the disease. I have had no single + + + + Wassermann reactions, but have found mucous patches, and so on, and have been somewhat discouraged as to curing them.

In treating the babies, we use neo-arsphenamin and give it intravenously. By employing a fine pointed needle, we have no difficulty at all in administering a dose of 0.1 c.c. per kilogram. It is marvelous what will happen in the case of some of the babies that are about to die. In some cases, the injection of neo-arsphenamin into the vein will, within twenty-four hours, make an altogether different baby. There is no question that you can do much with neo-arsphenamin in the case of congenitally syphilitic babies that is impossible with mercury alone.

DR. JAY FRANK SCHAMBERG, Philadelphia: The observation made by Drs. Fordyce and Rosen that children born of syphilitic parents may give a positive Wassermann reaction from the umbilical cord blood which may subsequently become negative is of considerable importance, because I am sure that the average physician would be likely to interpret such a finding at the time of birth as definite evidence of syphilis. On the other hand, I think it is the experience of many of us that children born of known syphilitic parents, and who exhibit negative reactions at birth, may commonly develop within two or three years positive Wassermann reactions or other evidences of syphilis; these evidences may not be the classic manifestations of the disease, but they may merely show a persistent anemia or a persistent subnormal weight which will not be overcome by anything except syphilitic treatment. I cannot but believe that such patients harbor spirochetes. I am sure that there are throughout the country tens of thousands of persons who have congenital syphilis which is entirely unsuspected, and I should like to emphasize the point that we must not regard the offspring of syphilitic parents as free of syphilis because of a negative Wassermann reaction at birth or even during the first year. I have seen such children subsequently develop symptoms that have yielded only to antisyphilitic treatment.

DR. JOHN A. FORDYCE, New York: To answer Dr. Sutton's question, as to why we use neo-arsphenamin instead of arsphenamin, our reason is that it is less painful to the children. The method was devised at the clinic because of the ineffective methods of treating congenital syphilis, very inefficient mercury rubs usually being employed in these cases. Our results with the new method I think have proved that it is easily applied and is certainly efficient in curing a larger percentage than the older methods. It has been used in the Babies' Hospital by Dr. McLean, and in other institutions, and all have been much pleased with the results. It is much less dangerous than the intravenous method or that of introducing the solution into the longitudinal sinus. With the latter accidents occur, unless the work is in skilled hands.

I agree with Dr. Schamberg that there are many children going about who are syphilitic and who are harboring spirochetes. When they are cured, we cannot tell. Our work is too recent to permit the expression of any dogmatic opinion, but we hope it will be taken up by other members of the Association.

DR. WILLIAM ALLEN PUSEY, Chicago: How much more painful are the injections than those of mercuric chlorid?

DR. ISADORE ROSEN, New York: In reply to Dr. Pusey's question as to whether the babies have much pain: The babies cry while being treated but stop a few

minutes after they are returned to their mothers and apparently seem comfortable. We have given neo-arsphenamin intramuscularly to adults for the purpose of determining the amount of pain. They compare the pain to that of an ordinary intramuscular injection of mercury.

To answer Dr. Cole with regard to the treatment through the longitudinal sinus: I have seen photographs of pathologic specimens of brains (in the laboratory of Dr. Johnson of the Sloane Hospital) showing the results of treatment through the longitudinal sinus. There was a diffuse infiltration of the cortex with the drug, probably caused by some unavoidable accident during injection.

At the present time there are six institutions in New York City that have organized clinics for the treatment of congenital syphilis along the lines outlined by Dr. Fordyce and myself, and we hope in the near future to hear their reports.