A Review of the Literature of Syphilis in Infancy and Childhood

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Since the last Review slight advances have been made here and there but, as a whole, our conception of syphilis has been changed but little. The same questions are debated and the same conflict of opinion is manifest. It is not the purpose of this review to notice every article published, but rather only so many as will serve to demonstrate efficiently the trend of present thought. Nevertheless, the general plan of the previous review has been adopted without other alteration.

SOLUTIONS FOR INJECTIONS

On the whole, the ancient methods of preparing the arsenical remedies for injection still prevail. The only noteworthy modification is Taege's method of procuring an absolutely sterile salt solution. He first rid the water of any calcium, magnesium, manganese or iron which it may contain by adding an alkali, allowing the mixture to stand twenty-four hours and then filtering. The glass or crockery vessel to be used is scrubbed out with strong hydrochloric acid. Then a mixture of 2.5 gm. strong, hydrochloric acid and 1 gm. sodium chlorid is poured in. Next, a 1 per cent. alcoholic solution of phenolphthalein and a solution of sodium chlorid are added, drop by drop, until a distinctly pink color is produced. A sterile normal salt solution results which will keep for months without change, uncovered. The salvarsan can be dissolved easily in the acid solution and later can be neutralized, avoiding, however, overalkalization in the process.

THE THERAPY OF SYPHILIS

Passing to the consideration of the therapy of syphilis, we shall find no such comparative agreement. The dosage, the therapeutic indications and the method continue to be much disputed.

Dreyfus advises the employment of salvarsan in from 1 to 1.5 per cent. solution.

Schmitt* advocates, by implication, concentrated solutions. He says that according to the evidence there is danger in submitting a diseased circulatory apparatus to the sudden strain of the dilute solution with its consequent increase in the bulk of the circulating medium.

Simon recommends the cautious administration of small doses of salvarsan in old syphilis, incompletely or carelessly treated with large doses at some previous time, in cases of secondary syphilis, and in cases in which meningitis has been demonstrated by lumbar puncture. Otherwise a troublesome and even fatal Herxheimer reaction may be excited. He reports a case in which the reaction caused a fatal edema of the glottis. Simon says 0.2 gm. is an average primary dose for adult patients. If the temperature or the spinal fluid shows no ill effects, subsequent doses may be gradually but cautiously increased.

Nicholas and Mutot agree with Simon that the initial dose of salvarsan should be small and that subsequent doses should be increased gradually and cautiously. They calculate the normal dose on the basis of 0.01 gm. salvarsan, or of 0.015 gm. neosalvarsan, to each kilogram of body weight. The maximum dose of salvarsan however, should not exceed 0.6 gm. and of neosalvarsan, 0.9 gm. Two courses of five or six injections each, one injection each week, may be employed, the second course commencing one or two months after the first.

Leir's abortive method consists of the combined use of neosalvarsan and of a soluble mercurial salt. He first injects the mercurial and, a little later, the neosalvarsan. This preliminary treatment is followed by weekly injections of neosalvarsan for five or six weeks, and by about twenty injections of mercury salicylate at two or three day intervals. If possible the primary sore is excised or at least cauterized. In secondary syphilis he advocates weekly injections of from $\frac{1}{2}$ to 1 per cent. suspensions of mercury salicylate or, if the tonsils show signs of recurring disease, of the bichlorid or succinamid.

Krefting believes in large doses of salvarsan. Three to five injections, he says, given at intervals of two weeks, will cure primary syphilis. In secondary syphilis eight to fifteen doses may be required. No rule of treatment can be formulated, however, save that it must not stop with the production of a negative Wassermann. In his opinion salvarsan therapy has no contraindications.

*Footnote 10.
Hell is convinced that the most efficient method of treating congenital syphilis is by combining inunctions or intramuscular injections of mercury with intravenous injections of salvarsan. He insists, however, that it is important to add to this treatment hygiene and breast milk feedings. He uses either daily inunctions of mercury for from four to six weeks, with a bath after every sixth treatment, or biweekly injections of from 0.003 gm. to 0.005 gm. of the bichlorid (mercuric chloride 1, sodium chloride 10, distilled water 100). The mercurial course is followed by a series of four or five weekly intragluteal or intravenous (into the temporal vein) injections of from 0.005 gm. to 0.15 gm. of neosalvarsan in concentrated solution. A second combined course is given a few months later, succeeded, perhaps, by a third or even by a fourth. Hell never gives salvarsan by intramuscular injection because of the danger of necrosis.

Leir reports that all patients treated solely with mercury had recurrence.

According to de Aja neosalvarsan in small doses is beneficial in many cases in which it was once supposed to be contraindicated; for instance, in hereditary syphilis, in nerve syphilis, in aortitis and aneurysm with cardiac compensation and, often, in renal disease. Nevertheless, he concludes neosalvarsan can not safely be prescribed, indiscriminately by every one or for every one.

Wechselmann, too, says that nephritis is no bar to arsenotherapy, provided only that the kidneys are functionally active. If albuminuria is present, he would advise a primary course of intrafascial injections of neosalvarsan before administering it intravenously.

Schmitt's deductions, drawn from an analysis of von Mentberger's book, are that in certain directions arsenotherapy demands care. Patients with circulatory or other grave diseases should be treated cautiously and never in the ambulatorium. The salvarsan solution should be alkaline, as acid solutions predispose to embolism of the lungs. Hepatic complications, even if no more than the passive congestion of heart disease, require especial caution. Too large dosage or too frequently repeated injections may cause fatal renal damage. In the presence of already irritated or crippled kidneys, salvarsan should not be given. The possibility must be remembered that a local Herxheimer reaction may cause a disseminated miliary tuberculosis by its effect on a preexisting, localized focus or produce dangerous symptoms in malignant tumors seated over vital parts. In nerve syphilis salvarsan must be administered early and in repeated,

11. Metberger: Two Hundred and Seventy-Four Deaths from Salvarsan.
fractional dosage. It must not be used if meningitis exists. Salvarsan and mercury may be used in combination.

On the other hand, Wechselmann says that salvarsan and mercury should not be combined, as the result is harmful in at least 50 per cent. of the cases. Fischer, likewise, says that the administration of mercury after preceding salvarsan injections may cause death.

**SALVARSAN ACCIDENTS**

Simon says that every active antisyphilitic remedy is liable to excite a serious Herxheimer reaction. Schmitt, already quoted, says that salvarsan accidents are due, in larger part, not to the mercury used in combination, but to toxemias produced by overdosage. A smaller part is to be explained by personal idiosyncrasy. The danger is especially great in nerve syphilis for, unquestionably, neurorecurrences have increased with the use of salvarsan and in spite of every effort to avoid them. Fordyce writes that intensive salvarsan treatment which does not cure tends to promote the development of a state of anaphylaxis and to increase the liability to severe, local manifestations. The late vascular symptoms he attributes to a state of allergy, but questions the theory that nerve syphilis is an anaphylactic phenomenon. He is inclined to believe that it is due to the extension of a primary, meningeal process, seated on the posterior roots between the ganglia and the cord, which causes a degeneration of the afferent fibers and eventually an ascending tract degeneration in the cord. Nicholas and Mutot found that serious complications, even coma and death, were more frequent after salvarsan therapy, especially if the solution was acid. To the best of their observation, the primary administration of mercury does not lessen liability to salvarsan accidents. Schmitt could find no satisfactory explanation of the part played by salvarsan in the production of fatal metabolic disturbances, or of fatal results in cases of status thymolympaticus or of diabetes. He also found no explanation for the large number of cases which develop signs of meningeal irritation, epileptiform attacks or coma after salvarsan. Many alleged salvarsan deaths, Schmidt decided, had no foundation in fact. Fischer would require a necropsy record to be submitted in proof with every claim of death by salvarsan. As regards fatal encephalitis hemorrhagica, in 6,000 necropsies, he rarely encountered a case which could, with justice, be laid at the door of salvarsan.

WHY EFFICIENCY VARIES

Takahashi* studied, experimentally, the fate of salvarsan in the tissues. His conclusions were as follows:

1. Salvarsan produces an extensive necrosis of all tissues at the site of its injection. Regurgitation, in animals, occurs, in about 350 days, by a preliminary process of acute inflammation. Fourteen days after the injection, a leukocytic infiltration walls off the injected mass. Gradually the necrotic process is replaced by the granulation tissue of chronic inflammation growing inward from the periphery.

2. The elimination of the injected, insoluble salvarsan has three reactive stages. The primary stage is of necrosis, in which the lymphatics carry away a certain amount. In the succeeding, second stage, the walled-in foreign substance is changed into collections of coarse, opaque globules, which can be dissolved with difficulty. If an abscess forms, some globules are discharged with the pus. In the third stage giant cells invade the remaining mass and take it up. In man such regenerative processes require not less than 400 days.

Stühmer15 endeavored to trace the injected substances in the tissues by means of a color reaction. Rabbits were used for the experiment. He concluded that neosalvarsan was the most evenly distributed substance and alkaline solutions of salvarsan a close second. Salvarsan, in acid solution, was most abundant in the lung tissue, which seemed to filter it out. Concentrated alkaline solutions were similarly filtered. Concentrated neosalvarsan solutions, on the other hand, distributed the drug uniformly throughout all the tissues of the body. Infiltrations occurred in lung, liver and spleen, rapidly and equally. Storage depots were formed which, in the case of salvarsan, freed small amounts to the bloodstream for three days and, in the case of neosalvarsan, for about twenty-four hours. A large proportion of the salvarsan was eliminated unchanged, by way of the kidneys and the intestinal tract. The latter fact suggested that the symptoms of toxemia might be due to the oxidation of the drug in the intestine, during intestinal disturbances, with resorption of the poisonous product. Stühmer found, also, that repeated injections increased the capacity of the storage depots. Salvarsan seemed to respect the nervous system, but neosalvarsan exhibited a special affinity for the meninges. The result gives a practical hint as to the choice of a remedy in meningeal involvement.

Schümaker† discovered a new test for salvarsan in the urine. During the course of a quantitative, colorimetric urinalysis, he observed that salvarsan answered to all the classic requirements of a true dye. It was absorbed by animal charcoal. It contained (two) aromatic rings, a chromophore (a group of doubly bound atoms, in this instance,

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† Schümaker: Dermat. Wschnschr., 1914, lix, 1295.
As=As—), and auxochrome groups (which can form salts). Therefore, both physically and chemically salvarsan must be considered a true dye.

The discovery furnishes fresh confirmation of Wassermann's theory that the therapeutic activity of remedies composed of combinations of dye stuffs and poisons is due to the ability of the dye to lead the poison to the diseased cells. This action occurs, however, only when the poison is an essential part of the dye, and not merely an addition to it which can be easily split off. For example, in toluolazo, mercury, silver, salicylic acid, the mercury is not an essential part, but is added to a side chain, so that when the substance is injected into the body, it is easily split off. The dye reaches the diseased cell but the mercury does not. In salvarsan, on the contrary, the arsenic is an essential part of the dye substance and can not be so separated. Consequently it reaches the cell with the dye. Its therapeutic efficiency obviously depends on the ability of its dyestuff guide to penetrate the microorganisms against which the drug is directed. Those which stain most easily are the most susceptible to the destructive action of the arsenic, to wit, the spirochetes of syphilis, anthrax bacilli, the spirilla of recurrent fever, etc. The organisms which resist the stain are uninfluenced by the arsenic; for instance, the waxy envelope about the bodies of the bacilli of tuberculosis is impermeable to the salvarsan dye. It follows that against tubercular disease salvarsan is powerless.

NEW REMEDIES

Salvarsan natrium is a modification of old salvarsan, which is supposed to be superior to neosalvarsan. It is described by Wechselmann as follows: Salvarsan natrium contains 20 per cent. arsenic, the same amount as neosalvarsan. Like the latter, on exposure to the air it changes to a brown color and becomes less soluble and more toxic. It is more soluble than salvarsan and, by so much, easier to use. In eighteen months Wechselmann encountered but four instances of the so-called anaphylactic reaction, all mild. He found the new remedy safe in all stages of syphilis, with doses of 0.3 gm. to 0.45 gm., and suitable for office administration. Two or three injections, one every week, may be given up to a total of forty or fifty. Recurrences were rare. Eruptions, usually resistant to mercury, yielded to persistent salvarsan natrium therapy. In old syphilis the effect on the Wassermann reaction of the blood and of the cerebrospinal fluid varied from prompt to none. For injection Wechselmann prefers 1 per cent. dilutions to the more concentrated.

Dreyfus has used salvarsan natrium with great success in over 450 cases, in from 1 to 1.5 per cent. concentration and in doses rarely exceeding 0.45 gm. Sometimes the drug was used alone, sometimes in
conjunction with mercury. If used alone, it was injected three times a week. If combined with mercury, it was given but twice a week. Over 100 ambulant cases were treated without accident, the patients being required, however, to rest until the morning following the injection. Reactions sometimes occurred, but were never more than slight, transient rises of temperature, diarrhea or attacks of vomiting.

Loeb\textsuperscript{16} considers salvarsan natrium as efficient as old salvarsan. His method was to give intravenous injection of salvarsan natrium once a week and intramuscular injections of the mercury salicylate twice a week for a period of four or five weeks.

Pulvis fluens hydrargyr i is a mercurial powder proposed by Unna\textsuperscript{*} as a substitute for the less easily prepared and more disagreeable mercurial ointment. It is made by rubbing up metallic mercury with a lycopodium powder, previously soaked in oil of turpentine, in the presence of much air and loosely combined oxygen. The powder which results from the process may be used as such or as an ointment base.

A new method for old remedies was invented by Fischel and Hecht,\textsuperscript{17} who obtained intensive mercurial effects by injecting a dose of from 0.015 gm. to 0.04 gm. of mercuric chlorid or of the oxycyanid of mercury (1 to from 200 to 400 c.c. solution) into the cubital vein every three to eight days until eight injections had been given.

**SUMMARY OF ARSENOThERAPY**

A few assert that arsenotherapy is efficient without the aid of mercury. This is contradicted by the fact that the search for newer remedies is continued and by the greater prevalence of the combined method. The advocates of arsenotherapy maintain that the method is harmless and is not responsible for the alleged deaths. The opponents answer that, granting the method is falsely accused of death in some cases, the proponents have never produced satisfactory proof of innocence in the remainder; even admitting that the arsenicals merely set a preexisting process in train which causes the death of the patient, the admission of itself proves the method dangerous; and, furthermore, it can not be denied that neurorecurrences have increased with increased arsenotherapy.

Regarding its liability to produce the Herxheimer reaction and the state of anaphylaxis, the debate is about even. Finally, we fail to find in the literature any agreement, even among the advocates of arsenotherapy, as to what constitutes the most efficient dose or concentration. Nicholas and Mutot concluded that while the arsenicals are of unde-

\textsuperscript{16} Loeb: Deutsch. med. Wchnschr., 1916, lxii, 325.
\textsuperscript{*} Unna: Dermat. Wchnschr., 1915, lx, 337.
\textsuperscript{17} Fischel and Hecht: Arch. f. Dermat. u. Syph., 1913-1914, cxviiii, 813.
niable value they lose in efficiency if not combined with mercury, and that in spite of all dispute, mercury and the iodids still retain their former position and value.

SEROLOGY

Ravaut\textsuperscript{18} gives the results of his investigations of the value of the serum test. One result was to convince him that in many quarters too much stress is laid on its evidence. He does not deny any part of its claim to value. He merely deplores the prevailing tendency to regard the test reaction as a mathematical certainty, when the facts justify nothing of the sort. The test, admittedly, possesses many sources of error. Ravaut's experiments bring some into strong prominence. Assuming for the purpose of the argument that the serum test is infallible, Ravaut turned his attention to the personal element in the interpretation, to the influence which personality exerts. Three identical samples were sent to three different serologists and the interpretations of the test reactions compared. He found that 61 per cent. agreed, 36 per cent. varied from positive to doubtful or negative, and 3 per cent. differed absolutely. It was noticeable that the reports conflicted less in tests of avowed syphilitics than of nonsyphilitics.

Ravaut challenges the claim of invariable accuracy for the Wassermann test. He has seen positive reactions persist for years in numbers of instances, despite most vigorous treatment and although no other symptom ever developed. On the other hand, he has seen cases of ocular, cutaneous or visceral disease, unquestionably syphilitic, in which the reaction was invariably negative. Ravaut also claims that there are various conditions which may create a false positive reaction in nonsyphilitic serums, as, for example, injections of autoserum. Of fourteen nonsyphilitics, previously negative, after experimental injections of arsenobenzol 35 per cent. gave positive reactions. Ravaut freely admits that a positive Wassermann test usually means active syphilis and that a negative test does not prove the contrary; but he claims that, while it is desirable to convert a positive reaction into a negative by treatment, it is sometimes impossible. In such cases Ravaut ignores the test and bases his prognosis on other clinical factors. He believes that not even a positive Wassermann reaction can always be accepted if it is not confirmed by other symptoms or evidence.

Keyes\textsuperscript{19} insists that the diagnosis of syphilis should not be made on the sole evidence of a Wassermann test. He argues that such methods are illogical. The test is admittedly nonspecific; its results depend too

\textsuperscript{18} Ravaut: Errors in the Interpretation of the Wassermann Reaction, Ann. de derm. et de syph., 1914, Series 5, v, 285.

much on the technic and too often manifest utterly inexplicable vagaries. Although all agree that a negative test does not disprove the existence of active disease and, much less, that it assures future immunity, a number of alleged cases of reinfection have been reported whose sole foundation was a former negative Wassermann.

Weisenburg\(^{20}\) says that the Wassermann reaction cannot be made to dominate the diagnosis, even though its great value can be granted without reserve. As a matter of fact, the serum reaction is only a single symptom. Its presence or its absence is a no more indispensable factor in the clinical diagnosis than is any other single symptom. The serum test method has not yet shown why we should discard the ancient dictum that one symptom does not constitute a diagnosis.

Frühwald\(^{21}\) has demonstrated by animal experimentation that the blood of syphilitics may contain and may transmit to animals the virus of syphilis, although its serum reaction is consistently negative.

Heimann\(^{22}\) accepts the evidence of the positive Wassermann test if it can be shown that it has not been influenced by certain nonsyphilitic states which, notoriously, tend to falsify the reaction. On the other hand, the negative test is so regularly in error during certain stages of syphilis and in the presence of many other extraneous factors that it can never be accepted without reserve.

Uhle and Mackenney\(^{23}\) tested the reliability of the Wassermann reaction from the clinician’s standpoint. Seven different serologists, employing different methods, were selected to test the 325 specimens from 292 persons. In every instance identical serums were sent to at least three of the seven operators. The reports were then compared. From 2.5 to 18.1 per cent. of normal and nonsyphilitic persons were reported positive, the percentages varying with the operator. The percentage of positive reports ranged, according to the test method, from 50 to 100 per cent. Five of the seven serologists agreed in 47 per cent. of their total results. It was noteworthy that the serologists who most consistently reported positive tests which clinical expectancy confirmed also most consistently returned doubtful or negative reports when the clinical evidence was doubtful or negative. In 21 per cent. of the total reports there was full agreement; 10 per cent. disagreed completely, and in 61 per cent. of the total reports not more than four conflicted in any one case. The specific antigens gave the smallest number of discrepancies.

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positive tests, except in two cases. On the other hand, their reactions were most often confirmed by the clinical evidence. It seemed to make no difference in the accuracy of the reaction whether the specimen was collected in sterile or unsterile containers, whether or not the blood was contaminated by virulent strains of the typhoid bacillus, of the Staphylococcus pyogenes-aureus or of the streptococcus; whether the specimen was one or several days old; or whether the blood was drawn when the stomach was full or when it was empty. So far as a few cases could show, acidosis did not seem to influence the reaction.

Glomset\textsuperscript{24} accepts the unsupported evidence of the serum test without hesitation.

Kolmer and Schamberg\textsuperscript{25} conclude that the Wassermann method is not sensitive enough. They often obtained a positive result with cholesterinized serums when, by the Wassermann method, they got a negative. They believe that the sensitized serums furnish reliable proof of the presence of active disease. Nevertheless, they advise that the results should be analyzed in the light of the history and of the clinical signs. Confirming their claim of its greater delicacy, the cholesterin reaction was less easily converted to negative by treatment than the Wassermann.

Hell\textsuperscript{7} questions the absolute accuracy of the Wassermann test in its prognosis of congenital syphilis. He found it difficult to change the positive reaction of congenital syphilis to negative even by energetic treatment. He inferred that in congenital cases a positive Wassermann test may not invariably indicate active disease.

**CUTANEOUS TESTS AND OTHERS**

Noguchi's cutaneous luetin test has been well received in this country, though not abroad. Sherrick\textsuperscript{26} reports that both syphilitic and nonsyphilitic cases gave positive cutaneous reactions to luetin inoculation if potassium iodid or any other iodin-containing substance had not been administered just before, at the same time or shortly after the performance of the test.

Klausner\textsuperscript{27} includes in his article an interesting review of the general subject of cutaneous tests. Pallidin is a substance obtained by Fischer's method of making extracts from lung tissue.\textsuperscript{28} Klausner's


\textsuperscript{27} Klausner: Pallidin Cutaneous Test, Arch. f. Dermat. u. Syph., 1914, cxix, 444.

\textsuperscript{28} Equal parts of the saline and of tissue, by weight, ground up with glass, centrifugalized, heated to 60 F. for twenty-five minutes, and phenol (carbolic acid) added to make 0.5 per cent.
estimate of its value is as follows: 1. In syphilis, preparations made from tissue rich in spirochetes by a similar technic also give positive cutaneous reactions. 2. A positive reaction is a local, inflammatory infiltration, which reaches its height in thirty-six to forty-eight hours after the inoculation. 3. The pallidin test is specific for syphilis, and especially for the tertiary and late hereditary forms. 4. In precocious, malignant syphilis the reaction is often positive or negative in correspondence to the Wassermann reaction. 5. Visceral gummas are positive to the pallidin test. 6. In cases of parenchymatous keratitis the pallidin test is more often positive than the Wassermann. 7. Gummas of the periosteum and cachexia are often negative to pallidin. 8. Tertiary syphilis and the late, hereditary disease yield a higher percentage of positive reactions to pallidin than to the Wassermann test. Treatment does not greatly influence the pallidin reaction, although if intensive it does sometimes cause it to disappear. Pallidin may excite a positive allergic reaction where previously the serum reaction was negative. The reaction to pallidin is to be interpreted as a phenomenon of anaphylaxis.

Fränkel and Thiele investigated the coagulation test for syphilis, proposed by Hirschfield and Klinger. Nonsyphilitic serum was found to coagulate within fifteen minutes, the time varying with the method employed. Syphilitic serum exhibited a delayed coagulation. The coagulation test, which depends on fixation of the complement, appeared to correspond in most instances to the Wassermann test. Brant drew similar conclusions from his experience with 500 tests. He reports that as a rule the results of the coagulation method and of the Wassermann agreed. When they differed, the history and the clinical signs favored the coagulation test.

Pfeiler and Scheyer recommended the employment of hemolysin and hemagglutinin as indicators of complement fixation in syphilis and as a parallel method to the Wassermann. They reported several cases of suspected syphilis in which these methods were positive when the Wassermann was negative.

CILIA A DISTINGUISHING MARK OF TREPONEMA

Fontana reports a new method of staining by means of which he succeeded in demonstrating that the treponema possess cilia. He estimates that the length varies from one to seven times that of the windings of the organism; that the cilia occur in both straight and spiral forms; that they may be at one or at both ends of the organism;

that they are exceedingly thin; and that, though they stain weakly, they nevertheless stain sufficiently to be photographed. Most specimens of cilia do not end in a point but in a more or less well-developed, club-shaped swelling, three or four times as thick as the cilia itself, which stained moderately well. This last observation Fontana considers unique.

**MANIFESTATIONS OF CONGENITAL SYPHILIS**

De Aja\(^{33}\) believes that congenital syphilis is in reality extraordinarily frequent. His cases varied in age from 8 to 53. Examples of the so-called late or adult syphilis were not rare. Usually the history in such cases revealed the existence of syphilis in the parents. Their own most frequent symptom of the inherited infection was disease of the long bones. De Aja believes that these cases of late manifestations of inherited syphilis are frequently unrecognized, because the observer fails to take into account every factor connected with the lesions, the symptoms and the history and because he does not comprehend how frequent inherited syphilis really is or how it may make itself manifest.

In their discussion of the manifestations and the diagnosis of congenital syphilis Soldin and Lesser\(^ {34}\) manifest that comfortable reliance on the unvarying truth of the Wassermann reaction which Ravaut so deplored. The writers examined a large number of infants and children who were admitted to the hospital for nonsyphilitic diseases and who, therefore, showed none of the ordinary signs of syphilitic inheritance. In such cases snuffles were never pronounced, skin rashes were few, and epitrochlear glands were barely palpable. Enlargements of the spleen or liver were the most important symptoms of their syphilitic inheritance. Many children showed not the slightest sign of syphilis, not even a positive serum reaction. Nevertheless, Soldin and Lesser unhesitatingly proclaimed them syphilitic because their mothers invariably yielded positive tests. They concluded that in children, even when corroborative evidence fails, bare suspicion is sufficient reason for testing the mother's blood. If the result is positive, the child must be regarded as a victim of inherited syphilis.

Haberman\(^ {35}\) calls attention to the fact that although syphilis may be one of the great inherited causes of degeneracy, it is not the sole cause. Therefore, to avoid harmful error, the possibility of a nonsyphilitic origin can never be ignored.

Vignoli-Lutati\(^ {36}\) maintains that many cases in which the enlarged cervical glands break down and produce scars are wrongly attributed

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to tuberculosis. Yet no proof of tuberculosis has ever been demonstrated. Because of their occurrence in association with congenital syphilis, because tuberculosis has not been proved and because the symptoms respond promptly to antisyphilitic treatment, Vignoli-Lutai is convinced that the true cause is not tuberculosis, but inherited syphilis.

TRANSMISSION OF SYPHILIS

Glomset is of the opinion that the syphilitic virus may be transmitted to the fetus by way of the placenta and that the infection usually occurs late in gestation.

Fordyce states that the manner of fetal infection is indirect, that is, through the mother; that the later the stage of the disease in the mother, the greater chance that the fetus will escape; and that he believes that the spirochetes pass from the mother through the placenta to the blood of the child.

As has just been noted, Soldin and Lesser maintain that even though the offspring show no visible signs and even though they manifest negative Wassermann reactions, the positive serum tests of their mothers is sufficient to prove that the children are syphilitic. The lack of evidence in the children, they say, is due to immunization during intrauterine life, with a consequent prevention or hindrance to the further development of spirochetas in the offspring.

Trinchese has collected data concerning congenital syphilis from various sources, which he interprets as follows:

1. It is impossible for the fetus to immunize the mother (Colles' law). Paternal infection of the fetus, alone, does not exist. Moreover the fetus has never been shown to possess immunizing substances.

2. The immunization of the fetus by the mother (Profeta's law) is not an infallible occurrence. 3. The earlier the infection of the fetus, the more rapid the development of a septic syphilitic process which is fatal within six months. 4. The mother may have a positive Wassermann and the fetal tissues may abound in spirochetes, and yet the fetal reaction will be negative, because the fetus builds no reaction substance until about its eighth month. After the eighth month the fetal blood for the first time begins to respond positively.

5. If infection occurs in the last weeks of gestation, the infant may possess neither clinical symptoms nor a positive serum reaction, because the time permitted the spirochetes for incubation has been too short. Such cases were once considered immune. In fact they are the cases in which the late manifestations of inherited disease develop.

6. If the mother is syphilitic, neither the absence of clinical signs nor of a positive serum reaction is

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positive proof of health. 7. Four possible eventualities confront the offspring of syphilitic mothers, which in the order of their gravity are clinical freedom and a negative test; clinical freedom and a positive test; clinical signs and a negative test; clinical signs and a positive test. The last is inevitably fatal.

We have considered above the possibility of transmission only by the mother with a positive Wassermann reaction. Frühwald’s experimental inoculation of a syphilitic rabbit’s testicle indicates that the blood of a syphilitic mother, without either visible signs or a positive Wassermann reaction, may, nevertheless, be infectious.

The advent of the Wassermann test has not caused Keyes to alter his views concerning the marriage of syphilitics. He can see no reason for changing the old rules.

Heimann will not consent to the marriage of syphilitics so long as the serum reacts positively; so long as a sufficient period has not elapsed, without symptoms, after disappearance of the positive reaction under adequate treatment; or so long as the serum gives a positive response to provocative injections of salvarsan.

Nicholas and Mutot recommend the retention of the old rules concerning syphilitic marriages.

**SUMMARY**

Three broad conclusions may be drawn from this exposition of the literature on the subject of syphilis:

1. Today all parties concede the right of the arsenicals to a place in the sun of syphilitic therapeutics. Nor does the concession invalidate the claim that mercury and the iodids have lost nothing of their original worth (Nicholas and Mutot).

2. The Wassermann and the other serum tests are seated more firmly in their original position as efficient aids to diagnosis, but have failed signally to deprive clinical methods of their old importance.

3. In short, the newer methods of diagnosis and of treatment have strengthened our hands immeasurably. The older methods have held their own. Combined, they mark a noteworthy advance in the subject of syphilis which neither could accomplish alone.

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