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THE VALUE OF THE WASSERMANN REACTION

AS INDICATED BY POSTMORTEM INVESTIGATION IN
THREE HUNDRED AND THIRTY-ONE CASES
AT BELLEVUE HOSPITAL*

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When the Wassermann reaction was introduced, it was widely embraced as marking the end of all diagnostic difficulties in syphilis. In addition, it caused to be included in the already comprehensive domain of syphilis conditions that previously were regarded as independent or doubtful affections, and it promised to lay the foundations of a new eugenics by the exposure of latent but transmissible syphilis in either or both prospective participants in an otherwise desirable procreative venture. As time progressed, instances began to multiply in which the reliability of the reaction was brought into question. By this time, however, the serology of syphilis had become identified with almost every thought devoted to the contemplation of this far-reaching disease; and while, at the present moment, it still occupies a place of profound importance in the study of syphilis, there seems to be a growing tendency to moderate those views which once were attacked only on a charge of heresy.

In the pathologic laboratories at Bellevue Hospital we have used the Wassermann reaction in the diagnosis of syphilis for a period of nearly seven years, during which time about 75,000 serums have been examined, representing a total of nearly a hundred thousand reactions, the cholesterin-fortified antigen having been exclusively employed for the first four years, and both the cholesterin and the crude alcoholic antigens for the past three years. From the outset the Wassermann laboratory has been under the supervision of pathologists who, with their assistants, have been specially trained in serologic work. Every effort has been made to safeguard the accuracy of the reports. In view of the doubt concerning its reliability as a diagnostic sign of syphilis, not only in our own labora-

tory but elsewhere, we have attempted to correlate the results of the Wassermann reaction with postmortem findings, keeping constantly before us the fundamental conception that syphilis is an inflammatory process, that it is characterized by definite and diversified structural alterations, and that without anatomic changes there is no syphilis. However indispensable this conception may be as a point from which to start and around which to build, the pathologist whose routine brings him into intimate and frequent contact with postmortem investigation can scarcely remain insensible to the fact that certain anatomic changes in subjects of suspected syphilis are sometimes exceedingly difficult to interpret, not only in the organs as they come under orderly examination at necropsy, but also in the subsequent microscopic investigation of individual tissues, even when special methods of differentiation are employed.

There were 331 cases in which the results of the Wassermann reaction were correlated with the anatomic findings in the same subjects investigated postmortem. In 204 cases no anatomic signs of syphilis were detected at necropsy, and the Wassermann reaction during life was negative, or was reported as "weakly positive" or "doubtful." The cholesterin-fortified antigen was used in every case. In 158 cases both the cholesterin and alcoholic antigens were employed. In a considerable number of cases, as will be shown later, no syphilis was demonstrable at necropsy, and yet the Wassermann reaction during life was positive. Of the latter cases it may be said, of course, that syphilis was present, but that we failed to find it at necropsy. The possibility of overlooking syphilitic lesions in isolated cases is not to be denied. However, it is not fair to assume that we overlooked syphilis in one series of cases in which the Wassermann reaction during life was positive without assuming that we overlooked it in another series in which the reaction during life was negative. In those instances in which the Wassermann reaction was positive, we employed exactly the same methods of excluding syphilis at necropsy as were employed in those cases in which the Wassermann reaction during life was negative; and we assume that we were no more frequently guilty of error in one series than in the other, particularly since the results of the Wassermann reaction, whether negative or positive, had nothing whatever to do with the postmortem exclusion of syphilis, the absence of which was postulated purely on the basis of failure to detect the naked eye changes by which the disease is characterized. We repeat that, in the absence of demonstrable syphilis, the existence of syphilis is not to be denied. We do not feel called on, however, to admit more than a small percentage of failures in view of the universally recognized fact that syphilis

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is a disease of ambitious anatomic proportions and that, while it may undergo modifications spontaneously or under treatment, it usually does so at the expense of structural legacies which, in the majority of cases, are characteristic and readily identified at necropsy.

Unfortunately, it was not practicable for us to subject every tissue to special methods of staining

designed to bring out the *Spirochaeta pallida*. Such an investigation, in the absence of otherwise recognizable syphilitic lesions, might have been of value in helping to avoid mistakes. With other pathologists who have investigated the question at length, one of us (Symmers) has secured only negative results in a numerically and otherwise comprehensive series of

TABLE 1.—CASES ON WHICH REPORT IS BASED

Cholesterin Antigen	Alcoholic Antigen	Necropsy Findings	Cholesterin Antigen	Alcoholic Antigen	Necropsy Findings
Positive	Negative	No signs of syphilis	Strongly positive	Not used	No signs of syphilis
Positive	Negative	No signs of syphilis	Strongly positive	Not used	Tabes
Positive	Negative	Atrophic pretibial scars; hepar lobatum	Strongly positive	Not used	No signs of syphilis
Positive	Negative	No signs of syphilis	Strongly positive	Not used	No signs of syphilis
Positive	Negative	No signs of syphilis	Strongly positive	Not used	No signs of syphilis
Positive	Negative	No signs of syphilis	Strongly positive	Not used	No signs of syphilis
Positive	Not used	Ulcerative cutaneous syphilids	Strongly positive	Not used	No signs of syphilis
Positive	Not used	Syphilitic aortitis; adenopathy	Strongly positive	Not used	Congenital syphilis
Positive	Negative	No signs of syphilis	Strongly positive	Not used	Syphilitic aortitis
Positive	Negative	No signs of syphilis	Strongly positive	Not used	Syphilitic aortitis with aneurysm
Positive	Negative	No signs of syphilis	Strongly positive	Not used	Chancre; adenopathy
Positive	Not used	No signs of syphilis	Strongly positive	Not used	No signs of syphilis
Positive	Not used	Smooth indurative atrophy of tongue, with scarring of epiglottis	Strongly positive	Not used	No signs of syphilis
Positive	Not used	No signs of syphilis	Strongly positive	Not used	Gumma of heart; syphilitic aortitis
Positive	Not used	No signs of syphilis	Strongly positive	Not used	No signs of syphilis
Positive	Not used	Penile scar; syphilitic orchitis and aortitis	Strongly positive	Not used	Syphilitic aortitis
Positive	Negative	Syphilitic aortitis	Strongly positive	Not used	No signs of syphilis
Positive	Negative	No signs of syphilis	Strongly positive	Not used	Gumma of heart; syphilitic aortitis
Positive	Negative	Syphilitic aortitis and valvulitis	Strongly positive	Not used	No signs of syphilis
Positive	Negative	No signs of syphilis	Strongly positive	Not used	Syphilitic aortitis
Strongly positive	Negative	No signs of syphilis	Strongly positive	Not used	No signs of syphilis
Strongly positive	Not used	No signs of syphilis	Strongly positive	Not used	Syphilitic aortitis
Strongly positive	Negative	No signs of syphilis	Strongly positive	Not used	No signs of syphilis
Strongly positive	Negative	No signs of syphilis	Strongly positive	Not used	Gumma of heart; syphilitic aortitis
Strongly positive	Negative	No signs of syphilis; miliary tuberculosis	Strongly positive	Not used	No signs of syphilis
Strongly positive	Not used	Syphilitic orchitis	Strongly positive	Not used	Pigmented pretibial scars; syphilitic aortitis
Strongly positive	Not used	Syphilitic aortitis	Strongly positive	Not used	Syphilitic aortitis; hepar lobatum
Strongly positive	Not used	Syphilitic ostitis and periostitis	Strongly positive	Not used	Syphilitic aortitis; aneurysm of aorta; gummas of liver; penile scar
Strongly positive	Not used	No signs of syphilis	Strongly positive	Not used	Hepar lobatum; indurative atrophy of tongue
Strongly positive	++++	Syphilitic orchitis and aortitis	Strongly positive	Negative	No signs of syphilis
Strongly positive	Negative	Hepar lobatum; syphilitic orchitis	Strongly positive	Not used	No signs of syphilis; ulcerative pulmonary tuberculosis
Strongly positive	Negative	Syphilitic aortitis; paresis	Strongly positive	++++	Congenital syphilis
Strongly positive	Negative	No signs of syphilis	Strongly positive	Negative	No signs of syphilis
Strongly positive	Negative	Syphilitic leptomenigitis	Strongly positive	Not used	Syphilitic aortitis
Strongly positive	+++	Syphilitic aortitis	Strongly positive	Not used	Syphilitic orchitis; indurative atrophy of tongue
Strongly positive	Negative	No signs of syphilis	Strongly positive	Not used	No signs of syphilis
Strongly positive	Negative	No signs of syphilis	Strongly positive	Not used	No signs of syphilis; ulcerative tuberculosis of lungs
Strongly positive	Negative	Scars on shins; laryngeal cicatrices	Strongly positive	Not used	No signs of syphilis
Strongly positive	Negative	Syphilitic aortitis and valvulitis; penile scar; smooth atrophy of tongue.	Strongly positive	Not used	Congenital syphilis
Strongly positive	++++	No signs of syphilis	Strongly positive	Not used	No signs of syphilis; general miliary tuberculosis
Strongly positive	Not used	No signs of syphilis	Strongly positive	Negative	Mucous patches on palate
Strongly positive	Not used	Syphilitic osteomyelitis tibiae	Strongly positive	Negative	Syphilitic aortitis and valvulitis; syphilitic cerebral endarteritis
Strongly positive	+++	No signs of syphilis; cancer of uterus	Strongly positive	Not used	No signs of syphilis
Strongly positive	Negative	No signs of syphilis	Strongly positive	Not used	Syphilitic leptomenigitis, cerebral endarteritis
Strongly positive	Not used	Syphilitic aortitis	Strongly positive	++++	Syphilitic aortitis
Strongly positive	+++	Syphilitic aortitis	Strongly positive	++++	Syphilitic aortitis, pharyngitis, laryngitis and glossitis
Strongly positive	Negative	Pretibial scars; syphilitic aortitis; general lymphadenopathy	Strongly positive	++++	Generalized cutaneous syphilids; mucous patches; adenopathy
Strongly positive	Negative	No signs of syphilis	Strongly positive	++++	No signs of syphilis; epithelioma with extensive metastases
Strongly positive	Negative	Pretibial scars; syphilitic aortitis; general lymphadenopathy	Strongly positive	Negative	No signs of syphilis
Strongly positive	Negative	No signs of syphilis	Strongly positive	++++	No signs of syphilis; carcinomatosis
Strongly positive	Negative	No signs of syphilis	Strongly positive	Negative	Syphilitic aortitis
Strongly positive	Not used	Syphilitic aortitis	Strongly positive	++++	Syphilitic leptomenigitis; syphilitic aortitis
Strongly positive	Not used	No signs of syphilis	Strongly positive	++++	Congenital syphilis
Strongly positive	Not used	No signs of syphilis	Strongly positive	++++	Syphilitic aortitis with aneurysm
Strongly positive	Not used	No signs of syphilis	Strongly positive	+++	Congenital syphilis

known syphilitic tissues stained for spirochetes by the older method of Levaditi, including sclerotic lesions at the base of the tongue, syphilitic cirrhosis of the liver, chronic interstitial orchitis, syphilitic aortitis, gummas and sclerotic chancres. Even in active syphilitic lesions, efforts to demonstrate spirochetes by the same method are by no means uniformly fruitful. For example, in a case of syphilis recently investigated at necropsy in Bellevue Hospital, the skin was the seat of a generalized eruption, there were mucous patches in the mouth, and the scar of the chancre was still visible on the penis. The patient died of an acute exudative glomerulonephritis about seven weeks after syphilitic infection, and the body was submitted to necropsy a few hours after death, so that conditions appeared to be propitious for the demonstration of spirochetes in silver preparations. Sections of all the organs, including the skin lesions and the chancre, were stained and examined with care, but spiral microorganisms could not be identified. It appears, therefore, that the use of this method, while desirable in certain instances, is not always free from disappointing results, even in known syphilitic tissues. In the active chancre and in other virulent lesions of acquired syphilis, and in the organs of those dead of congenital syphilis, notably in the suprarenal capsule, swarms of spirochetes are often to be shown by the older method of Levaditi. In late syphilitic lesions, such as aortitis and orchitis, the demonstration of spirochetes is an exceedingly precarious undertaking, and pitfalls are frequent in the forms of minute tissue fibrils which become impregnated by silver and present an alluring resemblance to spirochetes, so that the microscopist who ventures to lay the foundations of a newer pathology of syphilis on the interpretation of spiral forms in sclerotic tissues sponsors a method whose hazards are at least fascinating.

The difficulty at Bellevue Hospital is furthermore increased by the fact that, in some instances, the written permission for necropsy is necessarily worded in such fashion as to preclude the examination of certain viscera, notably the organs of the head and neck, thus making it impracticable, in a small percentage of cases, to exclude lesions in localities in which it is known that syphilitic changes are of common occurrence. In by far the greater number of cases, however, we have been enabled to conduct complete necropsies, and in these, as in the restricted cases, we are always on the alert for signs of syphilis. Moreover, there are circumstances in which the pathologist, no matter what his training or experience may be, is apt to overlook the structural defects of syphilis. By taking all these things into consideration, and by excluding questionable necropsy reports, we feel that we have succeeded in arriving at certain conclusions which are accurate within the limitations imposed by biologic vagaries and by a human tendency to err. As far as the worth of the Wassermann reaction is concerned, we may be permitted the observation that we have no theories to defend, merely facts to present as we have found and interpreted them, and we shall hope not to leave it to be read between the lines that our technic has precipitated certain exceedingly regrettable mistakes.

Excluding the 204 instances in which one or both antigens gave a negative reaction and in which no signs of syphilis were found at necropsy, together with certain doubtful cases, Table 1 shows the cases

on which this report is based. The results of an analysis of these cases may be expressed as in Table 2.

In order to arrive at an intelligent interpretation of the result of the Wassermann reaction, it is necessary to start with an anatomic conception of syphilis, and any definition of the disease which is not founded on an anatomic basis is obvious sophistry. Every known sign of syphilis, from the chancre through the gamut to the scar, is explicable as a purposeful reaction to injury. The Wassermann reaction, on the other hand, is a biologic phenomenon which occurs in certain syphilitic subjects and, in these circumstances, it is a symptom of value. It is not a specific reaction, however, but occurs in conditions other than syphilis, and it does not always occur in syphilis.

To the clinician, the interpretation of the results of the Wassermann reaction is of moment only so far as it permits him to arrive at a correct conclusion as to the absence or existence of the anatomic changes of syphilis in the body. We should not be guilty of such a glaring platitude were it not for the fact that the clinician who invokes a Wassermann reaction to aid

TABLE 2.—RESULTS OF ANALYSIS OF CASES IN TABLE 1

Positive Results with the Cholesterinized Antigen: 96 cases
Positive in 20
Syphilis in 6 (30 per cent.)
No syphilis in 14 (70 per cent.)
Strongly positive in 63
Syphilis in 30 (47.5 per cent.)
No syphilis in 33 (52.3 per cent.)
Very strongly positive in 13
Syphilis in 9 (69 per cent.)
No syphilis in 4 (30 per cent.)
Positive Results with the Alcoholic Antigen: 15 cases
Syphilis in 11 (73 per cent.)
No syphilis in 4 (26 per cent.)
Results from the Use of Both Antigens in 49 Cases
Cholesterin positive in 12; alcoholic negative in all; signs of syphilis positive in all.
Cholesterin strongly positive in 12 (44 per cent.); alcoholic negative in 6, positive in 6; signs of syphilis positive in all.
Cholesterin strongly positive in 15 (55 per cent.); alcoholic negative in 12, positive in 3; no syphilis in any.
Cholesterin very strongly positive in 8; alcoholic positive in all; signs of syphilis positive in all; cholesterin very strongly positive in 2; alcoholic positive in both; no syphilis in either.
Negative Results in Positive Syphilis
Cholesterinized antigen negative in 21 (31.3 per cent.) of 67 cases of syphilis.
Syphilis indolent, possibly healed, in 9 (42.5 per cent.).
Syphilis active in 12 (57 per cent.)
Alcoholic antigen negative in 18 (56.2 per cent.) of 32 cases of syphilis.
Syphilis indolent, possibly healed, in 7 (38.8 per cent.)
Syphilis active in 11 (61 per cent.)

him in visualizing syphilitic changes in the deeper parts not uncommonly neglects to search for anatomic lesions in localities in which the senses are ready to yield definite information. We refer to those superficial and detectable changes in the skin and mucous membranes and elsewhere that lend themselves to purposes of diagnosis and that, unlike the Wassermann reaction, are specific, and reveal syphilis stripped of its uncertainties and artificialities. Previous to the introduction of the Wassermann reaction, the pathologist who had occasion to inquire of the attending physician or of the intern as to the clinical evidence of syphilis in the body under investigation almost invariably received a reply quoting the patient's denial or admission of infection. At the present moment the same question equally often elicits a statement referring to the substance of the Wassermann report. It is practically an unknown incident, in our experience, to receive any voluntary reference to the existence of a scar in the genital region that might be interpreted as a healed syphilitic lesion, to atrophic pigmented scars in the pretibial skin, to roughening of the anterior border of the tibia or thickening of its periosteum, to superficial lymphadenopathy, to

increased consistency and diminished sensitiveness of one or both testicles, to indurative atrophy of the base of the tongue, leukoplakia and the like, and scarring and deflection of the epiglottis, to scars of the pharyngeal vault, to perforation of the nasal septum, to the presumptively syphilitic nature of aortic regurgitation, to the ophthalmoscopic signs of chorioretinitis pigmentosa, and similar discoverable signs of syphilis, any one or any combination of which, as the case may be, is less apt to lead one astray than the results of a Wassermann reaction. These and like signs were sought by the clinicians of the generation that passed with Delafield and the elder Janeway; but the generation that holds the responsibility of the future is being inculcated with an almost reverential respect for artificial methods that neither clinician nor pathologist can explain or control.

CONCLUSIONS

1. Depending on the antigen employed, the Wassermann reaction in the living patient, as carried out at Bellevue Hospital, gives a negative result in from 31 to 56 per cent. of cases in which the characteristic anatomic signs of syphilis are demonstrable at necropsy.

2. The Wassermann reaction in the living patient is positive in at least 30 per cent. of cases in which it is not possible to demonstrate any of the anatomic lesions of syphilis at necropsy.

THE DIAGNOSIS OF INFARCTION OF THE ENTIRE SPLEEN

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Total infarction¹ or necrosis of the spleen has received little attention in medical literature. Even the larger systems of medicine devote only a line to its consideration. From scattered reports of colliquative necrosis, coagulation necrosis, thrombosis of the splenic vein, etc., it is evident that a definite symptomatology is associated with these specific affections of the spleen. The purpose of this paper, in addition to adding four instances of total infarction or necrosis of the spleen to the literature, is to point out the possibility of the diagnosis of this condition.

The symptoms are pain, tenderness in the left hypochondrium, enlargement of the spleen, occasionally fever, and vomiting of blood due to rupture of dilated gastric veins. A glance at the literature reveals the regularity with which these symptoms are recorded. The added examples in this report are a repetition of the former.

Whenever the spleen becomes totally infarcted, enlargement occurs, the weight varying from 300 to 1,300 gm., and the dimensions reaching such proportions as 25 by 15 by 8 cm. The enlargement in all of the new cases reported here was noted on physical examination, but was often misleading, it being assumed that such an enlargement must be due to a leukemia or other condition. This fallacy is demonstrated by the fact that infarction of the spleen may

result in a huge enlargement, such as occurred in no less than ten instances in this report.

Pain in the left hypochondrium likewise is present, though variation in the site of the pain differs somewhat. In three cases the pain was described as diffuse throughout the abdomen, then localizing in the left hypochondrium, and in a fourth as "in the region of the stomach." The character of the pain varied from a dull ache to a sharp colic, with all degrees of gradation between. The pain is usually superficial and spontaneous, but may be deep and provokable. It is frequently exaggerated by changes in position, and may radiate along the phrenic nerve or into the left shoulder.² A sensation of weight in the left hypochondrium was often complained of, a violent hauling to the left exaggerated by inspiration, or a tingling, shooting or beating sensation in the same region.³ The pain is probably due to irritation or interference with the structures immediately surrounding the spleen, since this organ is not very sensitive. Total infarction of the spleen may occur, however, without any pain, as in one case here reported and in three of those in the literature.

Tenderness is usually associated with the pain, and is present in the left hypochondrium. The tenderness may come on suddenly and may continue for many days, or there may be occasional tenderness in the left side.⁴

The presence of fever apparently depends on the disease to which the spleen alterations are concomitant. When this is due to an obstruction of the splenic vessels by thrombi or emboli that are sterile, fever is absent. But after the spleen has undergone degenerative changes, bacteria which were already present⁵ or which make their entrance from some source such as the colon⁶ multiply rapidly, the organ finally resembles a bag of pus, and fever occurs. In one of the four cases here reported, the *Proteus mirabilis*, in another the colon bacillus was isolated from the spleen, and in each instance a rise in temperature of from 1 to 2 degrees was present intermittently. Many times the splenic changes result from or are accompanied by inflammatory changes elsewhere in the body, and under such conditions the fever is often attributable to such factors. In one of our instances a gangrenous cystitis, in another a suppurative pyelophlebitis and in a third an amebic dysentery was present and would account for the rise in temperature.

The vomiting of blood, bright red at times, and resembling coffee grounds at others, is of frequent occurrence. It was present in one of our instances and in several from the literature. Ewald⁷ recorded an example of a large spleen resulting from a thrombosed splenic vein, the patient dying as the result of a hemorrhage from the stomach. Following the hemorrhage there was a marked reduction in the size of the spleen. The reasons for bleeding from the stomach following splenic infarction or necrosis are well known, and have been substantiated by experiments. The splenic changes are accompanied by extensive anastomoses between the splenic and gastro-epiploic vessels. The dilatation of these gastric veins often becomes extreme, and the possibility of their rupture

1. The term "total infarction" is here used because the condition is discussed in the literature, as a rule, under this title. Strictly, total infarction is very rare, most infarcts being "mixed," the blood by imperfectly anastomosing vessels infiltrating the edges to make a red margin about the place of more total infarction. "Infarction of the entire spleen" is, therefore, a better term.

2. Lefevre: Bull. Soc. anat. de Paris, 1848, p. 193.

3. Durand, M.: Contribution à l'étude des infarctus de la rate, Lille, 1903, Mason.

4. Sandby: Brit. Med. Jour., 1908, 2, 1155.

5. Carrière and Vanverts: Arch. d. méd. exper. et d'anat. pathol., 1899, 11, 48.

6. Balacescu: München. med. Wehnschr., 1901, 48, 35.

7. Ewald: Deutsch. med. Wehnschr., 1913, 39, 398.