

Correspondence

"THE TYRANNY OF THE WASSERMANN TEST": A BENEVOLENT DESPOTISM *

To the Editor:—The torch-bearers of enlightenment, who condemned Copernicus, probably retired from judgment chamber to refectory with a satisfied inner glow at their well administered coup de grace. In passing we may muse on how Copernicus still lives, while his calumniators are forgotten, for the outstanding truth persists that the earth swings about the sun precisely as the martyred scientist intimated. The drama just sketched has been repeatedly enacted on the stage of human philosophy, and will, without doubt, continue to be with varying settings, so long as conclusions arise on feeble foundations.

Within the past few years it has become increasingly popular to anathematize the Wassermann test. The paper to which this article is a reply is a fair example of how this sport is conducted. It levels no new shaft, but since the field for this particular display of archery is *THE JOURNAL OF CUTANEOUS DISEASES*, the attack possesses a certain extrinsic force. For this reason alone, it is deemed necessary to counter, and may it here be stated that, though the protagonist believes that a scientific battle may be sharp, his weapons are not maliciously personal. If at times the argument should seem to be ad hominem, it is in spite of a desire to play cricket and because, in order to bring out definite points, it is necessary to select a specific article for analysis.

It is not intended to dedicate a panegyric to the Wassermann test, but to oppose the doctrine that it is tyrannous. Any tyranny connected with it is rather a reflection of that greater tyranny inherent in the limitations of human reasoning. Dr. Lisser postulates eight conclusions. The first, second and fifth are palpable. The other five are not, and it is purposed to illustrate what different inferences might have been drawn by the author of the paper under discussion from his own data. To simplify the structure of the present paper, the debatable conclusions will be employed as captions.

"The negative Wassermann means exactly nothing. (a) It does not prove the absence of syphilis, because negative tests occur in cases urgently requiring treatment. (b) Therefore it cannot denote a cure in treated cases."

As a matter of fact, the negative Wassermann test means a great deal. It means precisely one of three things: (1) that the patient is cured; (2) that the case is latent; (3) that because of some peculiarity in the infectious-protective mechanism, the test fails to be positive. It is infinitely simpler to assume that the test is worthless than to try to discover the explanations of its being negative in a given instance. So comfortable an assumption exemplifies the tyranny of human inertia.

The negative Wassermann test indicates that the patient is cured when, after adequate treatment and for a prolonged period—say for two years—it has remained negative. A serologic cure obviously is not to be assumed if, under the conditions just laid down, there is clinical activity. In other words,

* Lisser, H.: The Tyranny of the Wassermann Test, *J. Cutan. Dis.* **37**:754 (Nov.) 1919.

the trite fact is here reiterated that the Wassermann reaction is precisely one symptom of syphilis and nothing else, and its presence or absence has the same practical value as the presence or absence of any other one symptom of the disease. Suppose a patient presented himself with a gumma of the forearm which vanished under treatment, and a gumma of the hard palate appeared later. No one would state such an absurdity as "A healed gumma of the forearm means exactly nothing: (a) It does not prove the absence of syphilis, because healed gummas occur in cases urgently requiring treatment; (b) therefore, it cannot denote a cure in treated cases." And yet this exactly parallels Dr. Lisser's third conclusion, and a gumma and a serologic test have the same practical, if not biologic, significance. But, if the patient's gumma had been cured, and he never showed any other evidence of syphilis, including a negative Wassermann test, the disappearance of the gumma would indicate a cure. Does not the fading of the secondary eruption indicate a tendency to cure? Does not the disappearance of any single symptom or sign of the disease indicate such a tendency? It does. Then why does not a negative Wassermann test have the same significance, provided all controlling factors support the belief?

The negative Wassermann test may simply indicate latency. Is this astonishing? We are all sufficiently familiar with the fact that syphilis vacillates between periods of activity and quiescence. We see these remissions with and without treatment. The history of the ordinary gumma dramatically may prove this. Why then may not the negative Wassermann test prove latency? Why, indeed, may not all the symptoms of the disease, including the Wassermann test, vanish during latency? As a matter of fact, they do; and it is for this reason that no one regards a case as cured, except after critical and prolonged observation.

Lisser continues, in his third conclusion, "Therefore, it cannot denote a cure in treated cases." Had Lisser said, "Therefore, it may not denote a cure," there could have been no ground for debate. As a matter of fact, it may and can denote a cure. Prolonged observation—clinical and serologic—supplies the acid test. The entire literature on reinfection abundantly proves that it not only may, but can and often does, denote a cure. Admittedly, often, a negative Wassermann test is found in active syphilis. This is so in the early primary stage, at times in the tertiary stage, and particularly often in neurosyphilis. In the last group of diseases, the spinal fluid will usually supply the blood deficiency. Often, too, the test is absent in malignant syphilis. This furnishes some idea of what was meant when the writer stated that a negative Wassermann test in active syphilis might indicate a peculiarity in the infectious-protective mechanism. The test, as all other symptoms and signs of the disease, is related to the swerving balance between the protective agencies of the host and the aggressive agencies of the parasite. In cases of frank syphilis urgently requiring treatment, with a negative test, the lacking sign may be of first-rate significance as to the host's inadequate powers of resistance. Would the negative test in such instances mean "exactly nothing?" Actually, it would appear to mean a great deal.

Dr. Lisser italicizes "If one patient having a negative test nevertheless requires active treatment, how can it follow that another one be cured because his test is negative?" It is long since any one has so contended. Dr. Lisser is tilting at windmills, and perhaps some Dulcinea is applauding. But he distorts the facts, which are that in certain groups of cases properly con-

trolled, the negative test does denote a cure; in others, equally well controlled, it denotes latency; in still others, it denotes neither, but a probable failure in the protective mechanism of the host. In short, the negative test never denotes "nothing," but always indicates a problem to be solved, and no mean problem that dare be dismissed by an indolent negation.

Nor is it true that any syphilographer worthy of the name is ready "to build systems of treatment on the negative test." He is willing to construct such systems on the vanishing of signs of syphilitic activity, and the negative test properly construed and interpreted is among these signs. As will be shown, it is a mighty subtle and valuable one.

"A positive Wassermann reaction means syphilis, but not necessarily active syphilis."

It is impossible to agree with this in any respect. In the first place, the Wassermann test may be positive in nonsyphilitic diseases, notably yaws and nodular lepra. Let us ignore this, however, for these conditions are easily excluded. But the positive reaction in syphilis definitely means active syphilis. If, as Lisser correctly states, the phenomenon is a resistance reaction, it follows that there must be something to resist, a concept which, regarded either way, postulates activity. Thus Lisser is "hoist by his own petard." It is not the reaction that is to be overcome, but its exciting agents—in other words, the parasite to which it denotes resistance. It is easy to agree with Lisser and Wile that the attempt to convert positive into negative Wassermann tests is "chasing a shadow," provided the test is worshiped as a totem-pole. Disregarding such scientific paganism (an example of the tyranny of idolatry) it is not the shadow we should pursue, but the substance of which this shadow is a distinct hint. The Wassermann test is the resistance shadow of the active process which is the resisted substance. If the substance is destroyed, the shadow will automatically disappear. Let the proper quarry then be pursued!

If the test may prove negative in active syphilis, and if Warthin's observations, which are convincing beyond peradventure, hold, it is extremely doubtful whether syphilis can be pathologically actually cured. In view of this, by what oblique mental process can it be concluded that a positive reaction may be present in the cured individual? A *reductio ad absurdum* may be permitted. The Wassermann reaction is a resistance phenomenon. Thus there is something to resist. If this something were eliminated, the reaction would automatically disappear, but in spite of all therapeutic effects, this cannot invariably be consummated. It may possibly be wiser not to overcome the test, since there is nothing to overcome anyway, even though it does indicate resistance to a cause no longer extant. This *vers libre* is precisely what is embraced in the concept of a resistance reaction to a provocation that has ceased to be.

Dr. Lisser's subterfuge that a positive test does not necessarily indicate active syphilis is remarkable. It may tax his ingenuity to illustrate the meaning of resistance to inaction. What is the nature of a resistance reaction to an inactive pathologic process? If the positive test indicates syphilis at all, it must, by Lisser's own conception, mean active syphilis and no arbitrary subtleties can cloud the fact.

"Treatment should be entirely independent of the Wassermann reaction because negative Wassermann reactions sometimes occur prematurely during treatment, while positive Wassermann reactions frequently persist long after clinical cure."

Discussion of this statement will depend on definitions of concepts and assumptions, before the conclusion itself may be approached. Precisely what is meant by the Wassermann test becoming "prematurely negative" is mysterious. If it is negative it means that, for the time being, perhaps even permanently, it is negative, because latency or cure has been effected, either in the natural course of the disease or therapeutically. It is safer to assume that very early in the disease the negative test indicates inactivity rather than cure, and to continue treatment. In an instance of this sort the inactivity may be practically interpreted as an encouraging tendency on the patient's part to withstand his infection. Perhaps Lissner has seen cases in which the test has become inactive, other objective evidences of the disease persisting, even under therapy. This would be strictly premature. But who would have the test performed under these hypothetical circumstances? Certainly no astute syphilographer. Thus, this hypothesis may be dismissed. And what is meant by "the positive Wassermann test being present long after a clinical cure"? What is a clinical cure? It is an illusory disappearance of signs detectable by the physician's senses. What physician would assert that this means anything? Lissner is assuming more than the combined experiences of the world's physicians would warrant, if he recognizes a cure simply because he can detect nothing by the crude methods of physical diagnosis. It is just here that a positive test is a control of unparalleled value.

Therefore, it is contended that the treatment should not be independent of the test, but in a large measure guided by it. For, as the test fades, a power becomes evident in the patient to respond to therapy, and if it persists, such power exists either not at all, or only in a restricted degree. In a clinician's judgment the test may be disregarded, but it may not be ignored, and the writer makes bold to assert that if he had syphilis he would continue to be treated as long as he exhibited a Wassermann reaction. He would "chase the shadow" until he got the substance. An extensive experience with syphilitics leads the writer to assert that patients are not depressed by a positive reaction, and a similar experience with human nature justifies the view that a patient would be depressed by a sense of neglect on the part of the physician. Just what constitutes an "excess of treatment" is not quite clear, but granting that there may be such a thing, it would be a safer risk than under-treatment, even if the only guide were a persistent Wassermann reaction. If it is not excessive to treat early syphilis with a negative test for three or four years, at what point does the treatment become extravagant in a patient with an occult syphilis and a positive test? Perhaps Lissner will be able to specify this point. If treatment should be entirely independent of the test, and if, as a diagnostic sign it is totally unreliable—a conclusion inherent in Lissner's point of view—why does not Lissner say that the procedure is worthless? Why does he not discard the test entirely? It is for the reason that he does not think it is worthless, as he indicates, and that he would not dare to try to dispense with it.

"Once the diagnosis of syphilis is positively established, the fewer Wassermann tests done the better, both for the peace of mind of the patient and the physician."

This statement needs a certain amount of deciphering. The phrase "When the diagnosis of syphilis is positively established" leaves the mind uncertain as to whether Lissner includes the test among his diagnostic factors. If he does not so include the test, many of his diagnoses must be open to criticism, or we more modest syphilographers are franker in confessing our clinical limita-

tions. If he is willing to make his diagnosis without recourse to serologic aid, his opinion as to what is and what is not syphilis would be so unsubstantial as to throw out the value of his views with regard to the consistencies and inconsistencies of the test. If he admits the value of the test up to the moment that a diagnosis is "positively established," at what moment thereafter does the test lose its diagnostic worth?

If Lissner can indicate no such period, precisely what number of tests should be done? In other words, what is the significance of the phrase "the fewer Wassermann tests done the better"? What, indeed is the reasonable minimum—one test a month, one a year, one a decade? In what relation to symptoms or to treatment? Precisely how is the peace of mind of the patient subserved by this vague—"the fewer the better"? Will the patient be satisfied with the physician's admonition to go along happily because his medical advisor intuitively senses a cure? As a matter of fact, it is better for a patient to realize the unpleasant certainty of a positive test than to be in suspense. A tyro in psychology would understand the greater repose inherent even in bad news that is positive, than in the alleged tranquility of unsupported optimism.

The peace of mind of the physician might be enhanced by ignoring the test, for a subtle source of disquietude would be removed. This lulling security would have the philosophic value accruing to the ostrich who buries his head, and by blotting out the world to his vision concludes that the world has ceased to be. When this species of defense fails the ostrich, he resorts to his next great weapon—speed a-foot. By courting "peace of mind" the physician would either evade or escape his problem, according to the expediency of shutting it out or fleeing from it. But the fact remains that the Wassermann test exists, and is to be regarded in syphilis as of the same first-rate importance as any other sign of the disease. Would Lissner disregard a recurrent gumma "both for the peace of mind of the patient and the physician"?

This concludes the analysis of Lissner's summing up. Lest it be thought that the present paper is too blind an endorsement of the Wassermann test, the writer will add a few remarks indicating what appear to him to be its liabilities and assets. The liabilities are numerous. Some are avoidable, others not. The avoidable ones are due to carelessness, or improper training on the part of the serologist. If the warnings and strictures of such writers as Kolmer and Ottenberg were heeded, purely technical faults would be largely overcome.

The unavoidable sources of error are more numerous and subtle. Impurities in the glassware, time and method of incubation, nature of antigen, dilution of complement, are factors indicating elusive phases of the technic that have been pointed out in the works of the two serologists already mentioned. Nor is the test in a restricted sense specific, for it is not spirochetes that are employed as antigen. Thus, the phenomenon must be defined as a nonspecific complement fixation test usually indicating active syphilis, provided certain other diseases have been ruled out. It is understood that it may normally be negative in the early initial period, and during any period of latency throughout the disease. With these exceptions, a positive test indicates active syphilis, and a negative test, cured or latent syphilis. It must further be reemphasized that it may be negative in malignant syphilis, neurosyphilis and at times in tertiary syphilis.

In these apparent contradictions lie the limitations of the procedure. In active syphilis there may be no evidence of the disease, except the positive test. The physician is thus confronted with the task of determining the

seat of the malady. If a careful physical examination reveals no changes in the heart, vessels, kidneys, liver, alimentary tract, bones, or nervous system, it is difficult to translate the evident facts of an active process into terms of diagnosis, prognosis and treatment. Conservatism requires, however, that treatment be given indefinitely to forestall future injury to the patient. The object is not the paltry endeavor to render the test negative, purely a pursuit of shadows, but to prevent greater inroads on the host by the parasite.

The negative test indicates, as repeatedly stated, cure, latency, a stage of the malady too early for serologic recognition, or a total absence of the disease. Which of these obtains in a given case is again a problem involving nice discrimination. A cure may be assumed if the test is negative, and if other objective evidence of the disease is wanting after adequate treatment over a number of years, and after prolonged subsequent observation and control without treatment. Latency may be assumed if the test is negative early in the disease, and here, regardless of the negative test, treatment should be continued. There can be no confusion caused by a negative test in the primary stage, for the dark field comes to the rescue. Absence of syphilis may be assumed if the test is negative, and if there are neither history, symptoms, nor signs of the disease. Deficiency in immunization explains the negative test in malignant and tertiary syphilis.

What has so greatly obscured the issue has been a wide tendency to make synonyms of the Wassermann test and syphilis. The reaction is actually but one sign of the disease, and the numerous attributes of the Wassermann test are subject to the same influences and have the same diagnostic and therapeutic value as any other single, objective feature of the malady. If this were only understood, many of the apparent inconsistencies of the reaction would be eliminated. Finally, then, it may be permitted to paraphrase Lissner's conclusions as follows:

1. A positive Wassermann test is undoubted evidence of active syphilis, yaws and nodular lepra having been excluded.

2. Since it constitutes such evidence, it is a subtler sign of the disease than the ordinary objective phenomenon. Not all lesions, however, associated with the positive test are syphilitic. Thus, a syphilitic with gastric carcinoma, corns, acute lobar pneumonia, beriberi, cerebrospinal meningitis, scabies, lupus vulgaris or any of the acute exanthemata, et cetera, would give a positive reaction, but these conditions would not be syphilitic. Mastering such facts, and not railing at them, is the test of a true syphilographer.

3. The negative test means: (a) absence of the disease, (b) latency, (c) recovery, (d) a period too early in the initial stage for the formation of antibodies, (e) deficiency in immunization. It is for the syphilographer to make a proper interpretation.

4. It is a resistance reaction; hence, it indicates active syphilis.

5. Regardless of a negative or positive reaction, a patient should be treated adequately for syphilis, according to the state of the disease and the age of the patient. The younger the patient, the longer should the treatment be continued, because of the greater number of years ahead of him in which the sequelae of the disease may develop. This is a fine phase of syphilography too little understood.

6. Treatment should be guided by the Wassermann reaction, but should not be prejudicially influenced by optimism at its too early conversion to a negative reaction. There is no clinical cure without a serologic cure, for the test is one of the important signs of the disease.

7. When the diagnosis of syphilis has been established, enough Wassermann tests should be performed to serve as an aid to the physician in his management and views of the case. This will subserve his conscientious efforts, and he will not be misled into a sense of false security by evading an unpleasantly subtle reminder of his therapeutic limitations.

8. The Wassermann test should be employed as an adjuvant to clinical judgment, which is synonymous with common sense.

9. Thus viewed, the Wassermann test will be divested of its fancied tyranny and become a docile servitor of the syphilologist.

WALTER JAMES HIGHMAN, M.D., New York.

"URTICARIA PROBABLY DUE TO SYPHILIS"

To the Editor:—I have read with interest Dr. Lester Hollander's article on "Urticaria Probably Due to Syphilis," which appeared in the January number of the ARCHIVES. The author says that "in the present literature no pruriginous lesions have as yet been attributed to syphilis." I would refer him to two valuable contributions by Hazen, one published in *The Journal of the American Medical Association* 67:1650, 1916; the other in *The American Journal of Syphilis* 1:750, 1917. Reference to the complication may also be found in Hazen: Syphilis, The C. V. Mosby Co., St. Louis, 1919, p. 155. In a series of 100 cases, Hazen found the Wassermann reaction positive in 33 per cent., and in every instance antisyphilitic treatment was followed by the disappearance of the urticaria. During the past two years, I have made it a point to subject every case of persistent urticaria to a serum test, and while I have no available statistics, it is extraordinary how many of these patients suffer from syphilis.

RICHARD L. SUTTON.