

# A CRITICAL STUDY OF THE WASSERMANN AND LUTETIN REACTIONS DONE SIMULTANEOUSLY ON 500 CASES.\*

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The following report is based principally upon some as yet unfinished investigations in which we were engaged at the University of Texas Medical School at Galveston. The object of these is to determine the percentage of the negro race which is infected with syphilis. The present paper, therefore, is simply a branch, as it were, of this work, but we feel that such a report is justifiable for several reasons, chief of which is the vital interest of both of these reactions to the profession as a whole, and more especially since some doubt has recently been cast upon the specificity of the luetin reaction, particularly by Sherrick, of Minnesota. (J. A. M. A., 1915, LXV 399.)

Before reporting the details of our observations it would perhaps be well to describe briefly the technique which we have employed. The Wassermanns in the following cases were done according to Noguchi's technique, using the anti-human hemolytic system instead of the anti-sheep system of the original Wassermann test. The blood for the Wassermanns is taken and the luetin given to every negro patient admitted to the John Sealy Hospital as a routine. This is done as soon after admission as possible. The luetin is given according to Noguchi's technique, namely: 0.07cc, or about two minims, intradermically. The luetin used in the majority of these tests was obtained from the Rockefeller Institute for Medical Research through the kindness of Dr. Noguchi, to whom we wish now to express our appreciation. The remainder was obtained from H. K. Mulford & Co. All of these tests, both the luetins and the Wassermanns, were done and interpreted by myself. In interpreting both of these

reactions we have endeavored to be as conservative as possible, calling only those Wassermanns positive which showed a fixation of at least 75%. We have considered only those luetins positive which showed a definite, indurated papule of at least 4mms diameter, which persisted for at least four days after the injection. The majority of our positive luetins were clear-cut and offered no room for doubt. There was a certain unpleasant number of borderline cases, however, in which we were in doubt. These we have considered negative. The most troublesome luetin for us to interpret has been a small (2-4 mms.), hard, indurated papule with little or no redness or inflammatory reaction, lasting for a day or so and then disappearing. Another confusing reaction which we have noticed, especially with the luetin furnished by Mulford, has been a small, pin-head sized, seropurulent bleb, appearing usually about twelve hours after the injection and persisting usually for one or two days. There is no inflammatory areola about these blebs, nor is there, as a rule, any induration. We have been unable to determine any relation between these reactions and syphilis. Our feeling is that they are probably bacterial in origin. Regarding bacterial infection in the luetin reactions: unless the lesions just described were bacterial we have had but two such infections. Both of these were typical abscesses, containing pus and staphylococci, and could in no way be confused with a positive luetin reaction. In all of our luetins we have sterilized the skin before injecting with 95% alcohol alone. In both of the cases in which infection occurred the luetin used in the test had been kept in a warm room for several days. It is only necessary to see one such case of infection in order to be able to distinguish it readily from a positive luetin reaction.

In the following report we shall attempt to study several features of our reactions. First, the relation of the positive luetins to the positive Wassermanns. Second, can the luetin be used as a substitute for the Wassermann reaction? Third, is the luetin reaction specific? Fourth, is the Wassermann reaction specific? Before proceeding further I wish to present the following protocol of our cases:

\*Read in Section on Medicine, Southern Medical Association, Ninth Annual Meeting, Dallas, Texas, Nov. 8-11, 1915.

## PROTOCOL NO. 1

Wassermanns and luetins on the same patient at the same time	
Total number positive Wassermanns.....	138
Total number positive luetins.....	111
Both Wassermanns and luetins positive.....	66
Both Wassermanns and luetins negative.....	112
Positive Wassermanns and negative luetins.....	72
Positive luetins and negative Wassermanns.....	45

At first glance at these tables the most striking characteristic is the comparatively small number of cases which show a positive reaction to both the Wassermann and the luetin reaction. Only about half of our positive cases showed a positive reaction to both tests.\* There were more positive Wassermanns than positive luetins. Regarding the complementary value of these tests we have been especially interested. What percentage of the so-called doubtful Wassermanns will be cleared up by a positive luetin? Our experience has been that the two reactions are, in fact, of considerable complementary value. About one-third of our doubtful Wassermanns were on patients who gave positive luetins, while about the same number giving doubtful luetins gave positive Wassermanns.

Regarding the negative luetin reactions in those who are clinically syphilitic, we are able to substantiate the findings of all who have had much experience with this test, namely, that the luetin is apt to be negative in untreated primary or secondary syphilis, while the Wassermann is usually more strongly positive at this stage than at any other time. The incidence of the positive luetins varies, therefore, directly with the age of the infection, while the incidence of the positive Wassermanns varies inversely with the age of the infection. We have also noted another point in regard to the luetin reaction in syphilitics which we have not heretofore seen mentioned. This is a phenomenon somewhat resembling the negative tuberculin (Von Pirquet) reactions in patients who are very far advanced in the disease of tuberculosis. We have noted a number of cases of undoubted syphilitics in all stages of the disease, including the tertiary, who were greatly emaciated or who were about to succumb to the disease, in whom the luetin reaction was entirely negative. Such cases will, however, give a good Wassermann

reaction almost invariably. Concerning, therefore, the first question which we have attempted, namely, the relation of the positive luetin to the positive Wassermann reaction, and of both to the clinical findings, we have found the following to be true in this series of cases. Practically all cases of known clinical syphilis react positively to either the Wassermann or the luetin reactions. A negative reaction to both tests, while not absolutely ruling out syphilis, is, of course, of much more value than a negative reaction to either test separately. A negative Wassermann reaction is of much more significance than a negative luetin reaction. The Wassermann reaction is of much greater value than the luetin reaction in the diagnosis of syphilis.

Regarding the question of whether the luetin test is specific for syphilis, we have been particularly interested recently. Until a few months ago the luetin reaction, so far as I am aware, has been regarded by every one who has used it at all frequently as specific for syphilis alone. Recently, however, several observers have reported that positive reactions could be obtained in syphilitics by the injection into the skin of other substances than luetin. Positive reactions could be obtained with ordinary liver extract, with peptone, agar-agar and other proteids instead of the extract of the *spirochaeta pallida*. These reactions were not, however, so marked as a rule as were those given by the pallida extract. Sherrick has, moreover, recently reported that he is able to obtain a positive luetin in 99% of all individuals, regardless of whether they have syphilis or not, by the preliminary administration of potassium iodide in sufficient quantities (40 to 60 grains per day for several days). We had ourselves, at one time, been great believers in the so-called provocative treatment for bringing out a positive luetin in a suspected case. To a suspected or doubtful case who had given a negative or a doubtful luetin, and who we thought ought to have a positive one, we would give potassium iodide and mercury for several days, usually a week, and then do another luetin. This procedure we found so exceedingly satisfactory, and our clinical judgment was proven correct in so many cases, that

\*Approximately 25% of these had had potassium iodide before or during the test.

we ourselves had begun to suspect that our diagnostic ability was too good to be true, when Sherrick published a report of his cases.

During the past several months we have been endeavoring to either confirm or refute the claims of Sherrick experimentally. Our experiments were conducted as follows: First, all cases in whom we were able to investigate the medication before and during the administration of the luetin were investigated. This series consisted of about four hun-

#### PROTOCOL NO. 2

The relation of positive luetin reactions to the administration of potassium iodide and to the presence of clinical syphilis, in 400 cases:

	No. having	
	K	I
Syphilitics with positive luetins.....	72	37
Syphilitics with negative luetins.....	42	2
Clinical non-syphilitics with pos. luetins....	39*	36
Clinical non-syphilitics with neg. luetins....	227	6

\*Including 30 selected cases of non-syphilitics.

dred cases. A glance at our second protocol, consisting of the four hundred cases which we have been able to study in such a manner, will show that the majority of our positive luetins were on patients who had had potassium iodide at some time before the interpretation of the test. We have also found the delayed reaction to have been frequently present in these treated cases. The second step in our investigation of the effects of potassium iodide has been to select all cases admitted who had negative Wassermanns and who had no clinical signs of syphilis. An abso-

#### PROTOCOL NO. 3

Total number of patients having K. I.\* during the luetin test or before the test... 81  
Number giving positive luetins..... 68  
Number giving negative luetins..... 13\*\*\*

\*We have considered only those cases having grs. XX. or more per day.

lutely negative history was obtained in all. This series consists of some thirty patients. After the negative luetin had been obtained we waited two weeks and then began the administration of potassium iodide, 15 grains t.i.d., increasing in some cases to 30 grains t.i.d. All of this series gave positive reactions, and all except five gave severe reactions. Finally the test was done on myself in the same way and a beautiful positive reaction obtained, while several previous ones had been negative. We have been able in a few of these cases (six) to do still another luetin test several weeks after the positive one had been obtained, and after

the potassium iodide had been discontinued. Three of these six cases gave good positive reactions one week after the discontinuance of the potassium iodide. One gave a weak positive reaction. Four of the six were negative to the luetin test two weeks after the discontinuance of the medication, while two were still positive. One was still positive at the end of the fourth week, becoming negative after six weeks, however.

The question immediately arises, as a result of such findings, as to whether the luetin reaction has any value at all. A study of our cases, and of many others reported, will, however, show that many do react to the luetin without the exhibition of any medicines whatever, and that the majority of cases so reacting give strong evidences of clinical syphilis. As we have said, syphilitic individuals may react to the injection into the skin of many foreign substances, while a normal individual will fail to react. In the same way patients saturated with potassium iodide will react to many other substances than luetin which are injected into the skin. It would seem possible, therefore, as has been suggested by others, that the infection with the spirochaeta pallida produces a special change or sensitization of the skin analogous to that produced by the action of potassium iodide. Regarding the reaction of the skin during the administration of other medicines we are unable to speak definitely. We feel sure, however, from our statistics, that neither mercury nor salvarsan alone will produce a positive reaction. We have noticed in the study of our medications, however, that a number of otherwise negative patients had been on protiodide of mercury for some time before the luetin was obtained. As a result of this work with the luetin reaction, therefore, and of a study of its relation to the administration of potassium iodide, we conclude that it is not a specific reaction for syphilis in the true sense of the word, but that, if the proper precautions are taken, especially as to the previous administrations of medicines, not only of potassium iodide but of all medicines, it is of value in the diagnosis of syphilis.

Finally, what conclusions have we drawn from this work as to the actual working value of the Wassermann reac-

tion? It is, in the first place, our belief that the Wassermann reaction is of great diagnostic value when properly done and interpreted. And by this I mean interpreted by the man who has studied the case, by the clinician, and done by a trained laboratory man with whom he is personally acquainted, and in whom he has confidence, and not by a man whom he has never seen and about whose methods he knows nothing. The joker in the statement, which is usually made by the laboratory men, and especially by the so-called "commercial laboratories," that "a positive Wassermann reaction means syphilis," is, in my opinion, the omission of a description of the technique used in the reaction. There are almost as many kinds of Wassermann techniques as there are stars in heaven. An investigation will show that hardly any two men do their Wassermanns alike. If it is borne in mind by the clinician that there is a personal element in the doing of a Wassermann reaction and that an accommodating laboratory man can by proper titration, or rather by improper titration of the reagents, make a negative or a doubtful reaction become positive at will, he will more readily realize, perhaps, the importance of a careful selection. Moreover, just as Wassermann techniques vary, so do the interpretations as to what constitute positive and negative reactions. The remedy for this state of affairs is, of course, a standardization of the Wassermann techniques, so that one technique can be used by all to the exclusion of all other methods. This remedy is perhaps distant, but will probably come. The other remedy, which all can apply, but which, unfortunately, too many do not apply, is the more careful consideration of clinical findings and of clinical judgment with a more careful selection of the laboratory man. In other words, the report of a positive Wasserman reaction should be considered as a symptom and not as a diagnosis in itself.

#### DISCUSSION.

Dr. J. J. Terrill, Temple, Texas.—I have been very much interested in this paper from a clinical standpoint. It is a paper well worth thinking of, and there are many points in it that deserve further emphasis. The doctor has mentioned the possible effect of potassium iodid in bringing out a positive Iustin reaction. I wish to mention the possible effect of potassium iodid

upon the Wassermann reaction. It has been taught that the administration of iodids and mercury will provoke a Wassermann reaction in cases that did not previously give it. We tried the administration of potassium iodid to provoke such a reaction, and it provoked so many of our patients we were uncertain about the results. So we took a series of ten individuals, with negative histories, and in which we got negative Wassermanns, and administered ten grains of potassium iodid every three days for several days, and had a Wasserman reaction, the blood being examined by the Nogouchi technic. We found, without exception, upon the first day after discontinuing the three-day treatment with potassium iodid the blood gave the same reaction. In other words, if one interprets with X's they would vary between 2 plus to complete fixation. In those individuals with negative Wassermanns previously and with negative histories, on leaving off the potassium iodid, these all cleared up at the end of five days and showed a negative reaction, and that has raised a strong doubt in my mind as to the value of the so-called provocative reaction. I simply offer that as a suggestion. If the provocative reaction is shown to be reliable, I feel a sufficient space of time, not less than seven, but better, fourteen days, should elapse after the use of potassium iodid or mercury before the Wassermann reaction is tested.

The question of the interpretation of the results of the Wassermann in my mind is either a positive or negative reaction. There is no question but that a doubtful reaction which is gotten ought to be regarded as such and re-examinations made and considered with the clinical history. Every Wassermann should be interpreted in the light of the clinical history. Any practitioner who allows a laboratory man to make a diagnosis of syphilis for him from the Wassermann reaction will get into shallow water and run into the rocks sooner or later.

#### A PLEA FOR UNIFORMITY IN THE WASSERMANN REACTION.\*

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The Wassermann reaction, one of our most valuable methods of establishing the existence or non-existence of syphilis in an individual under observation, has re-

\*Read in Section on Medicine, Southern Medical Association, Ninth Annual Meeting, Dallas, Texas, Nov. 8-11, 1915.