

AN INVESTIGATION UPON THE INFLUENCE OF MALARIA ON THE WASSERMANN REACTION.

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Introduction.

THE special committee upon the standardisation of pathological methods appointed by the Medical Research Committee recommended selected standard methods of performing the full original Wassermann test.

While working on a special malaria research for the War Office under the direction of Colonel Sir Ronald Ross, it was suggested by Brevet-Colonel L. W. Harrison that it would be of great value to test a series of malaria cases by one of the standard Wassermann methods used for the diagnosis of syphilis. The technique employed in this series of observations on malarial sera is that described by Harrison¹⁹ in the special report on the Wassermann test, Series 14, published by the Medical Research Committee.

The following is an account of previous experimental work done by using the Wassermann test in malaria.

(a) Authors Who Obtained Positive Wassermann Results in Malaria.

1. Boehm (1909) states that only recent cases of malaria gave a positive Wassermann reaction, and that these became negative when the parasites were no longer present in the peripheral blood.

2. Schoo (1910) reported upon 38 cases of tertian malaria and 22 gave a positive reaction. Syphilis as far as possible was excluded.

3. Meier and Bonfiglio (1910) were of the opinion that as long as malaria parasites were present in the blood the Wassermann reaction was positive and advocated that no case in which syphilis was suspected should have the test performed until after three months free from malarial fever.

4. Professor Wassermann (1910), in an address before the British Medical Association, gave it as his opinion that the test ought not to be done in suspected cases until the patient had been free from malaria for three months.

5. Ferrari and Gioseffi (1911) obtained 16.6 per cent. of positive reactions in cases of malaria clinically not syphilis, and they confirmed Boehm's observations that the reaction disappeared after quinine treatment.

6. Zschucke (1913) applied the Müller Brendal modification of the test to 17 cases of malaria and only 3 gave negative results. At the same time Da Rocha-Lima applied the ordinary test to 7 of these cases and only obtained one positive result which, on standing, became negative.

7. J. de Haan (1913) conducted experiments on the sera of 163 cases of acute malaria and reported a positive result in 63 cases. Eleven of these cases, previously positive, became negative after quinine treatment. He diagnosed 27 of his cases as syphilis clinically, and states that it is not clear why all cases of acute malaria do not give a positive reaction.

8. Sutherland and Mitra (1915), in a series of experiments on 50 cases of malaria, obtained positive results during the acute attack of the disease, but not in chronic cases. They advise that the blood be clear of parasites for a week before doing the test for syphilis.

9. Thompson (1916) on several occasions found the test positive in malaria during the time of the fever, but these became negative when the temperature fell and the parasites disappeared from the peripheral blood.

10. Hirsch (1917) examined 78 cases all with malarial parasites in the peripheral blood, and 28 gave positive results. Five remained positive after three weeks' treatment with quinine.

11. De Jong and Martin (1917) concluded that if the blood was not drawn at or near the paroxysm of an attack of malaria the test was of diagnostic value in syphilis.

12. Meyerstein (1917) declared that the Wassermann reaction (particularly when using ethereal-heart-extract of Lesser) was often positive in tertian malaria during the first

few days after an attack of fever. After the tenth day of fever he seldom obtained a positive result. He stated that the Wassermann reaction depended on, but did not completely coincide with, the presence of malarial parasites in the blood and that the reaction became negative simultaneously with the disappearance of the parasites under the influence of quinine.

13. Prins (1918) advocated that patients with malaria should have six weeks' quinine treatment before the Bordet-Wassermann test was done for the diagnosis of syphilis.

14. Craig (1918) reports in his recent book on "The Wassermann Test" that he obtained positive results in five cases of tertian malaria during the paroxysm, the blood becoming negative at the afebrile periods. This author, however, definitely states that the occurrence of a positive reaction in malaria, even during the paroxysm of the fever, is comparatively rare, for he has examined many cases with negative results, and other investigators report similar experiences.

(b) Authors Who Found the Wassermann Reaction Negative in Cases of Malaria.

15. Cziknawerow (1909) examined 13 cases of malaria, all of which gave negative results.

16. Manu Muscel and Vasiliu (1910) in 12 cases of malaria, some acute and others chronic, found all were negative.

17. Bates (1912) in Panama used Noguchi's modification of the Wassermann test in 164 cases of malaria, and obtained 37 positive results; of these 30 were certainly infected with syphilis.

18. Fletcher (1914), using the technique of Browning, Cruickshank, and McKenzie, examined 50 cases of malaria, all with parasites in the blood, and all gave negative results. He found that fresh unheated sera gave slight positive reactions and he thought the large number of positive results obtained by others was due to the various modifications of the test used by them.

20. Mathis and Heymann (1915), using the Wassermann method as employed at the Pasteur Institute of Lille, reported negative results in 21 cases of malaria.

21. Kimura (1917) found the reaction negative so constantly as to lead to the presumption that the test is of diagnostic value in syphilis.

Factors Responsible for the Conflicting Results.

It is evident that the term Wassermann test has been employed in a very loose sense. Many writers have not even taken the precaution of describing the method used. The contradictory results and consequent confusions which have arisen since 1909 have undoubtedly been caused by different laboratory workers using a variety of methods, some of which certainly must have been unreliable. In addition to this it must be recognised that in many cases latent syphilis is difficult to exclude, even when the aid of a specialist accustomed to the clinical aspects of this disease is solicited.

We can classify the findings of other observers into four groups:—

(a) Those who have found the Wassermann reaction positive when malaria parasites were present in the blood, and found that the reaction persisted in some cases after several weeks' treatment with quinine.

(b) Authors who found that the Wassermann was positive only when malaria parasites were present in the peripheral blood.

(c) Those who obtained positive results only during the paroxysm of the fever, and even then only in a few cases.

(d) Those who found the Wassermann universally negative in all cases of acute malaria.

With regard to groups (a) and (b), it is now certain that two factors were responsible for the results obtained—namely, an unreliable technique and undiagnosed syphilis. Bates (1912) and Fletcher (1914), using the technique of Noguchi and that of Browning, Cruickshank and McKenzie, obtained universally negative results in cases of malaria, and most of these were acute cases with parasites present in the blood. On the other hand, Craig (1918) obtained five positive results in tertian malaria during the paroxysm of the fever. He, however, states that a positive Wassermann reaction in malaria, even during the paroxysm of the fever, is comparatively rare. We consider that the coexistence of syphilis in any given series of patients is certainly not "rare."

In summing up the literature, therefore, it seems clear that the cases of malaria credited with giving a positive Wassermann reaction are extremely rare.

TABLE SHOWING THE AUTHORS' RESULTS OF THE WASSERMANN TEST ON THE SERA OF MALARIA CASES.
(These observations were made at the Rochester Row Military Hospital, and the test carried out was that used in the routine diagnosis of syphilis.)

(a) Cases of Malaria giving Negative Wassermann.

No. of cases.	Type of infection.	Period at which serum was examined.	Remarks.	Result of test.
2 cases	<i>P. vivax</i> numerous in the blood.	During rigor, cold stage. No quinine.	Numerous previous attacks.	—
1 case	" " "	" " " "	Numerous relapses and previous attack of subtertian malaria, (i.e., <i>P. falciparum</i>).	—
1 case	<i>P. vivax</i> present in the blood. 3200 parasites per c.mm.	Blood taken immediately after rigor had ceased. T. 105° F. No quinine.	Several previous relapses.	—
2 cases	<i>P. vivax</i> present in the blood. All stages of growth, 14,736 parasites per c.mm.	Rigor 1 hour previously. T. 103° F. No quinine.	Several relapses.	—
2 cases	<i>P. vivax</i> present in the blood. 10,304 parasites per c.mm. In one case chiefly young rings and $\frac{1}{2}$ and $\frac{1}{4}$ grown parasites.	Rigor 2 hours before blood was drawn. T. 103° F.	7 attacks of malaria in France.	—
1 case	<i>P. vivax</i> present in the blood. Parasites 16,800 per c.mm.	Blood taken 12 hours after rigor. No quinine.	Many relapses previously.	—
3 cases	<i>P. vivax</i> present in the blood. Heavy infections and parasites at all stages of development.	Rigor night before. No quinine.	Numerous previous relapses.	—
2 cases	<i>P. vivax</i> numerous parasites.	Rigor 24 hours before.	Numerous relapses.	—
3 cases	" " "	Rigor 2 days ago. No quinine. Taken before 2nd rigor.	" "	—
1 case	" " "	Rigor 3 days ago. No quinine.	" "	—
1 case	<i>P. vivax</i> present in the blood.	Rigor 4 days ago. No quinine.	Many relapses.	—
10 cases	<i>P. vivax</i> present in the blood. All heavy infections.	Last rigor 3 to 7 days ago. No quinine.	Numerous previous relapses.	—
1 case	<i>P. vivax</i> present.	No rigor for 8 weeks. No quinine.	Several relapses.	—
5 cases	<i>P. vivax</i> present in the blood.	All cases had 10 gr. quinine 2 hours before serum was examined.	Numerous previous relapses.	—
3 cases	" " "	All had received two doses of quinine, 10 gr. each dose.	Numerous relapses.	—
2 cases	" " "	Quinine 8 gr. daily for two days.	Quinine 2 gr. 4 hours daily.	—
1 case	" " "	Very chronic case.	Very numerous attacks. Spleen 3 in. below costal margin.	—
1 case	<i>P. vivax</i> . No parasites present at time blood was taken.	Chronic case of malaria.	Numerous attacks; long courses of treatment. Spleen 4 in. below costal margin.	—
1 case	<i>P. vivax</i> .	Five weeks' quinine treatment.	Numerous previous attacks. Spleen 1 in. below costal margin.	—
2 cases	<i>P. falciparum</i> . Sexuals only present (i.e., crescents).	No quinine recently.	Both had numerous attacks. One had spleen 3 in. below costal margin.	—
2 cases	<i>P. falciparum</i> . Asexual and sexual parasites present in large numbers.	" "	Numerous attacks of malaria.	—
2 cases	<i>P. vivax</i> and <i>P. falciparum</i> . Mixed infection.	Long courses of treatment; no parasites in blood when examined.	" " "	—
1 case	<i>P. falciparum</i> . Asexual parasites numerous in the blood. No sexuals.	No quinine. (A comatose case followed by death.)	Numerous attacks.	—
2 cases	<i>P. falciparum</i> . Both had asexuals and sexuals. Crescents in one case 4936 per c.mm. In other 748 per c.mm.	One case never treated with quinine. Both very anæmic. The other case has no quinine recently.	One case infected in Salonika, the other in E. Africa.	—
70 cases	<i>P. vivax</i> . Parasites not present in blood, except in case of three which had a few sexuals. Three cases <i>P. falciparum</i> ; no parasites present in the blood.	Blood serum examined at all stages of quinine treatment from 4 days to 2 months of 30 gr. a day.	These were all cases with numerous relapses. First attack dating from 3 years to 6 months ago, and infected in France, Egypt, Palestine, German East Africa, Salonika, and Mesopotamia.	—

(b) Cases of Malaria in which the Wassermann was Positive and were afterwards Diagnosed by Mr. Mills as Syphilitic.

1 case	<i>P. vivax</i> present in the blood.	Blood taken when T. 104° immediately after rigor.	Examined by C. H. M. Old case of syphilis treated in India.	+
1 case	<i>P. vivax</i> . No parasites present.	15 days quinine, 30 gr. a day.	Examined by C. H. M. Patient confessed having syphilis.	+
1 case	<i>P. vivax</i> present in blood at time of examination.	15 gr. of quinine 4-hourly for 1 day.	Examined by C. H. M. and found to be a tertiary syphilitic.	++
2 cases	<i>P. vivax</i> .	Both treated with quinine. One for 2 days, 60 gr. a day. The other had had no treatment.	Examined by C. H. M. and both had evidence of congenital syphilis.	++
3 cases	<i>P. vivax</i> .	One case had long course of quinine. The second had 30 gr. for one day. The third had <i>P. vivax</i> (sexuals) and 9 days quinine 30 gr. a day.	All examined by C. H. M. Two cases were tertiary syphilitics. No. 3 had definite congenital syphilitic stigmata.	++

Notes of Cases with Positive Wassermann Reaction.

CASE 1. Wassermann positive.—Treated for secondary syphilis in India in 1913, receiving three injections of "606" and approximately nine months' mercurial treatment by the mouth and 12 intramuscular injections of grey oil. Patient has noticed no clinical relapses. Superficial scar of mental chancre; no cutaneous lesions; right anterior pillar of fauces scarred, also posterior pharyngeal wall; no active mucous membrane lesions. Reflexes normal. Syphilis (treated)—Wassermann recurrence.

CASE 2. Wassermann strong positive.—Penile sore in 1912. Treated for three months with mercurial pills at St. Thomas's Hospital. No treatment since. (a) One definitely infiltrated scar in dorsum coronal

sulcus; (b) circular scar left side corona glandis; no loss of tissue. Well-marked leucoderma and melanoderma of neck, anterior folds axillæ and over iliac crests. Diffuse alopecia posterior third of scalp. Each posterior pillar of fauces converted into "pearly" band of scar tissue, the left being bound down to posterior pharyngeal wall. Reflexes normal. Tertiary syphilis.

CASE 3. Wassermann strong positive.—Preputial chancre removed by circumcision 1901. Marked superficial glossitis with accompanying leucoplakia; leucoplakia mucous membrane both cheeks; faint leucoderma and melanoderma of neck. Tertiary syphilis.

CASE 4. Wassermann strong positive.—No evidence, clinically, of acquired syphilis; family history unreliable. Bossing of frontals, middle third of face atrophic. Faint rhagades at angles of mouth.

High arched palate. Incisors removed; last upper molars exhibit marked doming of cusps (Moon's malformation). Considerable exaggeration of normal fissures of tongue. Antero-internal surface of tibia protuberant. Chronic painless synovitis both knee-joints. Reflexes normal. Patient considered to be a congenital syphilitic.

CASE 5. Wassermann positive.—No evidence clinically of acquired syphilis; family history unobtainable (orphan). Bossing of frontals; saddle-shaped nose; mid third of face atrophic. High arched and asymmetrical palate. Well-marked Moon's molars (upper). Supernumerary cusps to upper incisors; tongue deeply fissured. Old osteitis and periostitis both tibiae. Reflexes normal. Patient considered to be a congenital syphilitic.

CASE 6. Wassermann strong positive.—No evidence clinically of acquired syphilis. Youngest of family of 10. Two eldest died in infancy; third had "convulsions" in infancy; fifth "hard of hearing"; eighth had "inflammation of his eyes" at age of 14. Patient has well-marked bossing of frontals; rhagades angles of mouth. Nose depressed and flattened laterally. Upper incisors widely spaced and slightly pegged. Very typical Moon's molars (upper). Central nebula right cornea from old interstitial keratitis (at age of 16). Genu valgum. Reflexes normal. Congenital syphilitic.

CASE 7. Wassermann strong positive.—Penile chancre 1890, with considerable non-suppurative painless inguinal adenitis. Patient remembers no rash or sore throat. Was treated with mercurial pills for one month only; lotio nigra to chancre. Scar of chancre present in dorsum of coronal sulcus with no loss of tissue. Has had several attacks of herpes preputialis; no cutaneous lesions. Scarring from previous ulceration each anterior pillar of fauces. Circinate superficial scarring right side soft palate. Extensive leucoplakia mucous membrane right cheek; one ulcerated fissure right lateral margin of tongue. Reflexes normal. Tertiary syphilis.

CASE 8. Wassermann strong positive.—Scar of old chancre in right frenal angle and scar of sinus right inguinal region from suppurating adenitis of approximately 12 years ago. Multiple pigmented scars outer surface middle third left leg. All very supple with regular circinate outlines. Considerable loss of tissue. Bossing from old periostitis antero-internal surface lower third right tibia. Fixed scarring over left sterno-clavicular articulation from previous "breaking-down" peri-articular gummata. Interstitial and superficial glossitis. Reflexes normal. Patient looks considerably older than his actual age. Tertiary syphilis.

Reliability of the Wassermann Reaction in Malaria.

In our series of 130 cases of definitely diagnosed malaria, examined at every possible stage of the infection, it will be noted that only eight were positive, and in these we were able definitely to diagnose syphilitic infection in each case.

The patients came from different parts of the world, and thus infections with many different strains of parasites were tested. In the above series we have cases from France, Egypt, Palestine, Mesopotamia, India, German East Africa, Salonika, and West Coast of Africa. Some of these had suffered from as many as 30 attacks of fever or more during a period of three years.

The blood was examined by us at every stage of the disease, from the paroxysm onwards. Blood containing asexual parasites (*P. vivax*) in numbers of 14,000 per c.mm. or more, gave a negative Wassermann. Similarly a case of *P. falciparum* infected with over 4000 sexuals (crescents) per c.mm. of peripheral blood was also negative, and cases of chronically enlarged spleens due to malaria, which had been treated or untreated with quinine, also gave a negative reaction. In fact, in no case could it be said that malaria *per se* gave rise to a positive reaction.

In this series of experiments on the sera of malaria cases, we thus definitely can state that by using the Wassermann method as conducted at the Rochester Row Military Hospital for the diagnosis of syphilis, we need not be influenced by a previous history of malarial fever, nor even by the presence of malarial parasites in the blood. It is true that Craig found that a few cases of malaria gave a positive reaction during the paroxysm of a fever, but it is unlikely that blood in such a case would be drawn at that time for a complement-deviation test, and this may therefore be excluded. Moreover, we were unable to corroborate this.

19. Harrison (1918) points out that serum in itself, even fresh unheated serum, is sometimes anti-complementary, and Browning and McKenzie state that sera which have stood for some days develop increased anti-complementary powers, although they may have been heated previously. In these experiments it was found that if the malaria serum was not heated it tended to give a positive reaction, and it was also noted that serum, if kept for two days even after being heated on some occasions, gave positive results, probably due to contamination. An important point definitely established in this series of observations is that the presence of quinine in detectable quantities in the serum in no way affects the Wassermann reaction in syphilitic cases. This was proved by examination of serum by Staff-Sergeant Nierenstein, D.Sc., Ph.D.

Exclusion of Possibility of Syphilis being Present.

In perusing the literature upon this subject we are forcibly struck by the very unsatisfactory and generally totally inadequate investigations pursued in order to exclude the possibility of the patient being a syphilitic, acquired or congenital, since upon this fact the entire value of the research depends. The absolute exclusion of syphilis in a patient is by no means such a simple clinical proposition as one might be led to infer from the cursory allusions to it by some of the writers mentioned above.

Very frequently in a venereal clinic we are confronted with a positive Wassermann test, taken as a routine, in a patient exhibiting a lesion which is clinically and microscopically non-specific, for instance, say a scabetic papule on the penis. A more thorough systematic examination at the first attendance would have revealed that the patient was a tertiary syphilitic.

Syphilitic Involvement of Parenchyma of Central Nervous System.

Cases occur in which there is extensive syphilitic involvement of the parenchyma of the central nervous system, yet which exhibit practically no clinical signs or symptoms—e.g., the incipient G.P.I. We know that an active gummatous process about the general tissues has never yet been observed in such a case, nor the scarring of such a process. The history frequently given in these cases is that the primary sore was never noticed, having usually been trivial, and sometimes masked by an accompanying gonorrhoea. The secondary rash, if observed, is often of a transient erythematous roseolar variety, lasting but a few days, and leaving no scarring. It is a hard-and-fast fact that when the parenchyma (as opposed to the supporting structures, i.e., meninges and vessels) of the central nervous system takes the brunt of the syphilitic invasion the general tissues of the body escape. To repeat, the scar of a gumma has never yet been observed about the general tissues in a case of G.P.I., and just prior to its onset no clinician deprived of laboratory methods could detect that the patient was syphilitic.

On the other hand, where the general tissues exhibit extensive recurrent gummatous foci—e.g., nodular cutaneous syphilide, interstitial glossitis or orchitis, &c.—the parenchyma of the central nervous system most frequently escapes and a normal cerebro-spinal fluid is often obtained. Although digressing somewhat, the point we wish to emphasise is this—that in the majority of cases of early syphilitic involvement of the parenchyma of the central nervous system a very careful and thorough clinical examination is always absolutely necessary and an examination of the cerebro-spinal fluid imperative, in order to detect that the patient is a syphilitic. Such a case may for intervals even give a negative Wassermann in the blood serum.

Supposing that such a case contracts malaria, we consider it probable that his syphilitic infection might not be detected, and that his blood Wassermann would therefore be considered as due to the malaria. Were his blood Wassermann found to be negative at the onset and to become positive as his general resistance became lowered subsequently—then the case would go down as proof that malaria *per se* gives a positive Wassermann reaction in a patient.

Non-recognition of Congenital Syphilis.

Congenital syphilis is very liable to pass undetected as such, and therefore swell the number of fallacies when a large number of malarial patients are submitted to the Wassermann test. There seems to be a tendency amongst medical men who are not specially concerned in syphilology to connect the clinical picture of congenital syphilis only with those gross lesions classically depicted in "the good old text-books of surgery"—i.e., bossing of the frontals, saddle nose, rhagades, Hutchinson's teeth, interstitial keratitis, scabbard-shaped tibiae, deafness, convulsions, epilepsy, juvenile tabes, &c.

We wish to emphasise here that a patient may be a definite congenital syphilitic even when exhibiting none of these stigmata, and that were he to be submitted to the most thorough examination his syphilis would not be detected without the aid of the Wassermann test. We have seen cases during the war of interstitial keratitis supervening on a local lowering of resistance, such as air concussion, actual blow, conjunctivitis from foreign body and from gas, occurring between the ages of 22 to 29,

in which we were unable to detect any other clinical evidence suspicious of congenital syphilis beyond, perhaps, the doming of the cusps of a solitary molar tooth. The physique and mentality were excellent. The Wassermann was persistently a strong positive. In some cases the unaffected eye became subsequently involved and went through the phases of a typical attack.

One might describe here the case of a surgeon, aged 29, who, whilst operating upon a non-syphilitic patient, received a splash of pus into one eye which was immediately washed out with some too strong perchloride of mercury lotion (1:1000). The resulting chemical conjunctivitis resolved, but was subsequently followed by an attack of interstitial keratitis in that eye. He was then examined for evidence of congenital syphilis—a possibility entirely unsuspected hitherto. His Wassermann reaction was strongly positive with other corroborative evidence.

Now if any of these cases had contracted malaria prior to the interstitial keratitis we are positive that syphilis would not have been suspected, and malaria would have been held responsible for the production of a strongly positive Wassermann reaction. It is well to point out that of the eight cases in our series giving a positive Wassermann reaction three were found on examination to be congenital syphilitics, a fact hitherto unnoticed in their military career.

Undetected Cases of Acquired Infection.

Numbers of acquired cases occur where the patient is entirely ignorant of his having been infected with syphilis; these come under the observation of the medical man if the severity of the secondary manifestations become such as to necessitate the patient seeking advice. It frequently happens that the patient only presents himself for examination after certain proprietary "blood mixtures" have failed to disperse the lesions. (There are many in whom the secondary lesions are trivial, and these resolve spontaneously undetected.) The type of case, by no means as rare as the literature might lead one to suppose, is that in which inoculation occurred on the tonsil, tongue, or fossa navicularis of the urethra. As an illustration it was found at Rochester Row Military Hospital, over one period of 18 months, that the incidence of a chancre in the fossa navicularis was 1 in 14 of the total admissions for primary and secondary syphilis; and the primary sore was by no means infrequent on the lip, tonsil, tongue, and finger in the order given in a period of four years.

The number of cases that have attained the age of, say, 40 and onwards before syphilis is diagnosed for the first time upon the development of an active gummatous process convinces one that many must pass entirely undetected. A large number might pass unsuspected should they develop, say malaria, at an earlier date while presenting no gross lesions. It is only reasonable to suppose that the number of syphilitics, especially females, who carry their infection to the grave undetected, must be considerable.

We are convinced that the further this investigation proceeds, in the hands of careful clinical observers, upon the behaviour of the Wassermann reaction in the various diseases other than syphilis and yaws, the more light will be thrown upon the number of undetected syphilitics, and it will not be assumed so lightly as hitherto that these other diseases are responsible for the reaction.

A positive Wassermann reaction in malaria demands that syphilis be excluded by a most careful and searching inquiry.

Authors' Conclusions.

1. The Wassermann reaction conducted according to a recognised standard method does not give a positive reaction in malaria at any stage of the disease.

2. If a positive Wassermann reaction is obtained in a case of malaria it is either due to undiagnosed syphilis or to faulty technique.

We wish to tender our grateful thanks to all the staff at Rochester Row Military Hospital for their kindness. Colonel Harrison, D.S.O., officer in command, Rochester Row; Captain D. Thomson, pathologist; and Mr. Noël Clarke gave us every facility and help, and it is wholly due to them that these observations were made possible. Captain T. Gardner, R.A.M.C., and Dr. Jamieson on the malaria research staff gave invaluable assistance.

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WASSERMANN TESTS:

THE OCCURRENCE OF VARIATIONS IN THE RESULTS OF SUCCESSIVE TESTS; THE CLINICAL APPLICATION OF THE DATA.*

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THE clinical value of the positive Wassermann reaction as a "specific" indication of syphilis is now generally accepted. This statement, of course, applies to the performance of the test under adequately controlled conditions.¹ The subject, however, assumes another aspect when an attempt is made to draw conclusions for the control of treatment, &c., from quantitative differences in the reaction.

Quantitative Differences in the Reaction.

Owing, probably, to the fact that few observers test the reaction with a sufficient series of varying quantities of complement, it has not been widely recognised how variable the results are when the same specimen of serum is examined repeatedly. An indication of this fact is afforded by scattered observations on "paradoxical" reactions—i.e., the obtaining of a positive result on one occasion and a negative on another with certain sera. But the importance of such variations has not been recognised as affecting the value of the results of those who grade the positiveness of the reaction, e.g., by a series of plus signs, &c. Also it has not been sufficiently realised that conclusions regarding the state of a patient can scarcely be drawn from the result of repeated tests unless a definite positive reaction is replaced by a definite and repeatedly obtained negative. On the contrary, a number of observers (see Boas²) base conclusions on minor quantitative differences in consecutive examinations. Thus there is the danger of imbuing the reaction with an illusory attribute of precision in the quantitative sense.

A consideration of the fact that, other constituents apart, different guinea-pigs' sera are used as a source of complement, as well as different specimens of red corpuscles in the hæmolytic system on successive occasions, should entail a cautious attitude; but we shall indicate later that the sources of discrepancy are probably even more extensive. In the report furnished to the Medical Research Committee³ the conclusions which we had reached in this matter were stated as follows:—

"It has been found as the result of many years' routine tests with longer series of tubes than those above noted (i.e., more than three amounts of complement for each specimen of serum) that no single amount of complement, measured either by volume or by hæmolytic doses, will serve as a criterion for positive, owing to slight or no lysis occurring with it or for negative, owing to complete lysis occurring with it. This is due to the following facts:—(a) The absence of any fixed relationship between hæmolytic power and deviability on the part of different specimens of complement; (b) the difference between the amount of complement necessary to cause complete lysis and the amount which causes only a trace of lysis, varies greatly with different complements when the same antigen and the

* A report to the Medical Research Committee.

(Continued from previous column.)

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