# THE WASSERMANN TEST IN PATIENTS AFFECTED WITH MALARIA IN THE TROPICS.

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## INTRODUCTION.

With regard to the influence of malarial infection on the Wassermann test some controversy prevails:

Wassermann and Lange (1913) refer to Meyer and Bonfiglio who, working in Italy, obtained a positive reaction in 80 per cent. of the cases where the blood contained parasites; in some of their cases positive reactions were obtainable for several months after the disappearance of fever and parasites. For this reason Wassermann and Lange advise to put every case, coming from a malaria-infected country and showing a positive reaction, under quinine treatment and to repeat the test after a lapse of six weeks.

Schoo (1910), Zschucke (1913), de Haan (1913), Meyerstein (1917) and others also obtained a considerable number of positive reactions. Schoo obtained 22 positives out of 38 cases; in several of his cases the blood was free from parasites and there had been no fever for many days. Zschucke, using the Brendel-Müller modified method, obtained 14 positives out of 17 fresh cases.

De Haan experimented at Batavia, Java, on the same class of patients as ours but used Wassermann's original method. His investigations being founded on a sound basis, it is to be regretted that his work was curtailed. He sought especially to discover how long the test would continue positive. With the exception of two cases, his examinations were only continued for three weeks, consequently his results were unsatisfactory. He obtained 63 positive results in a series of 153 cases (40 Europeans and 113 natives). Of the Europeans nine were positive and 31 negative. Of the natives 51 were positive and 62 negative. Among the 60 positives were 29 cases wherein syphilis could be excluded, these latter were examined at regular intervals for some time. Of six cases of benign tertian only two were still positive after 17 days. Of 23 cases of subtertian fever eight were negative and 15 were still positive after 24 days. Of the latter only two were examined again after 40 and 49 days and still found to be positive.

Meyerstein (1917) does not state the number of cases he examined, they were mostly cases of benign tertian and he concludes that: (1) the strongest reaction is found on the fifth to eighth day, 70 to 80 per cent. of malaria

cases being positive; (2) a positive result after the tenth day is very rare; (3) with quinine treatment the positive result disappears; (4) disappearance of the positive result during quinine treatment does not mean definite cure of the malaria, but cases which continue positive (syphilis being excluded) must be considered as uncured.

Sutherland and Mitra (1915) consider malaria to have little influence on the Wassermann test. They examined 32 cases of benign tertian and 18 of subtertian fever. Though they only took blood for the test during the fever and in nine cases obtained a positive result, they come to the perhaps somewhat rash conclusion that a positive result occurs sometimes while the fever lasts, but that in chronic cases no influence is exerted upon the Wassermann reaction. It would be sufficient to wait a week after the disappearance of the plasmodia from the blood, after which the Wassermann test would be reliable.

de Jong (1919) came to a similar conclusion. We cannot, however, discuss his results, since we have only had access to a review of his paper.

## OUR INVESTIGATIONS.

None of the papers on the Wassermann test in malaria mention a quantitative result of the test and none give sufficient data regarding the time during which a positive result persisted.

Therefore we carried out our tests (1) during the fever while there were plasmodia in the blood; (2) after one or two weeks of a good quinine-arsenic treatment; (3) at regular intervals until negative results were obtained; (4) two complete tests were carried out in each case, one with heated (56° C.) and one with unheated serum.

As described in a previously published paper (1919) we use alcoholic extract of human heart. The strength of the complement is determined and a complement-unit established. The test is carried out with one, two, four and eight times the complement-unit. Human serum is used in the same amount as the extract. Of every case we recorded the race to which the patient belonged, the kind of plasmodium, the type of fever, if quinine was used while the blood was taken, and data bearing on possible syphilis or yaws and relapses of malaria.

Possibly syphilitic cases were only recorded when the Wassermann reaction became negative. Here we took for granted that a positive result in syphilis will not become negative in a short time without antisyphilitic treatment. We only considered cases as free from syphilitic infection after thorough investigation; even slightly dubious cases were always excluded. All cases were treated by one of us in the wards of the Tropical School. Apart from natives, our records relate to but three Europeans (syphilitics being barred).

As most of the tests had to be made after the men left hospital we only tested soldiers because we could call them up again when required. Owing to considerable shifting about of men constituting the Batavia garrison we

lost many cases before their test became negative. In such cases we used the decrease of strength in the reaction as an index upon which, in part, to base our conclusions.

**Europeans** (3 cases). With heated serum all gave negative results. With unheated serum all gave positive Wassermann reactions which became negative after two, three and eight weeks.

**Natives** (41 cases). With heated serum 21 were positive and 20 negative. With unheated serum 38 positive and three negative. Only three natives yielded a completely negative result with the Wassermann test.

*Strength of Wassermann test in malaria.* With heated serum, two cases reached our final limit (+ 8) (Nos. 31 and 40).

With unheated serum, we obtained higher values than with heated, as we generally do with this method.

*Period during which a positive result persists.* With heated serum strong positive reactions persisted for a considerable time (Nos. 24, 26, 27, 28, 29, 31, 34) often more than three months. Mostly the strength of the reaction decreased (Nos. 27, 29, 31, 34).

With unheated serum, often the lapse of five to six months is insufficient to yield a negative result (Nos. 19, 23, 25, 27, 29).

*Benign tertian and quartan fever.* Out of 12 cases tested with heated serum four gave positive and eight negative results. Of the positive cases three were negative within 14 days, and one was still positive.

With unheated serum all 12 were positive, eight became negative and four remained positive.

*Subtertian fever.* With heated serum, out of 31 cases 17 were positive and 14 negative. Of the positive cases, four became negative after two, seven, six and eight weeks respectively. Many of them were examined not longer than two weeks after the fever, hence there might have been more negatives if we had been able to examine them again. With unheated serum only three were negative and 28 positive. Here too it must be considered that many could not be examined after two weeks had lapsed from when the fever ceased.

The degree of splenic enlargement was without influence on the strength of the reaction. Subtertian fever seems to give stronger and more persistent positive results than benign tertian and quartan fever. Europeans do not seem to give a positive result so frequently as natives, at least not with heated serum; this may be due to the frequent chronicity of malaria in natives. We are inclined to believe that the long persisting positive Wassermann reaction is a result of defective treatment.

All cases got 15 grains of quinine hydrochl. twice a day with liquor Fowleri 5 to 15 minims three times a day for 14 days. After that period they left the hospital and were supposed to get 15 grains of quinine twice a week for three months, but it is very doubtful that this course of treatment was actually pursued. Better treatment would perhaps have yielded more negatives and in a shorter time.

The great number of positive results obtained with Wassermann tests in natives naturally arouses suspicion that hidden endemic syphilis, acquired and congenital, may have existed amongst them. Now (1) a tremendous degree of infection would have to prevail if out of specially picked persons, without any sign or history of syphilis, 50 per cent. yielded positive results for syphilis by the ordinary Wassermann test; (2) we (1919) carried out the same test on natives of the same kind, *i.e.* healthy subjects that were, as far as we could ascertain, free from syphilis and malaria; these subjects were used to test our Wassermann with unheated serum in our search for non-specific reactions. In 21 native soldiers, using the ordinary Wassermann test with heated serum, *all* yielded negative results. With unheated serum nine tests were negative and 12 positive, the strength of the positive cases not exceeding + 1. We next tried other natives and obtained similar results. Out of 35 cases 34 were negative and one yielded a slightly positive reaction with heated serum. With unheated serum 21 were negative and 14 gave slightly positive results.

Syphilis is rather common in Java and the results mentioned are of course not to be considered as showing the degree of infection, they merely afford evidence that our results with malaria are not impugned by the presence of hidden syphilis. When we compare the results obtained with malaria, where 50 per cent. were positive (heated) and 95 per cent. positive (unheated) with mostly strong reactions up to + 8, while with the non-malarious natives none was positive with heated and only slightly positives occurred with unheated serum, anybody can see that it is the malaria and not hidden syphilis that is giving the difference.

## CONCLUSIONS.

As a result of our investigations, in connection with those of de Haan, we feel entitled to draw the following conclusions:

(1) In many cases malarial infection causes a positive reaction to be obtained with the Wassermann test; 50 per cent. positives were obtained in natives whereas in Europeans no rate could be determined because of the small number of cases available.

(2) The reaction may even attain a maximum.

(3) A positive reaction may persist for three to six months; it may also persist as long in thoroughly treated patients but the reactions obtained in such cases are as a rule rather weaker.

(4) The positive reaction vanishes as a rule under quinine treatment.

(5) The Wassermann test with unheated serum almost always gives a positive result in both natives and Europeans affected with malaria.

(6) The Wassermann test with unheated serum yields positive results for longer periods and gives stronger reactions in natives than in Europeans.

(7) The difference which we (1919) found between Europeans and natives when we applied the Wassermann test with *unheated* serum (viz. that, when

## *Table recording Wassermann Tests carried out on 44 persons.*

| Number | Europeans | Natives | Syphilis | Framboesis | Kind of parasites: Tertiana | Quartana | Tropica | 1st W.R. Date | Inactivated | Not inactivated | 2nd Date | Inactivated | Not inactivated | 3rd Date | Inactivated | Not inactivated | 4th Date | Inactivated | Not inactivated | 5th Date | Inactivated | Not inactivated | 6th Date | Inactivated | Not inactivated | 7th Date | Inactivated | Not inactivated |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | × | . | 1915 | – | + | . | . | 25. iii. | – | +4 | 26. iii. | – | +2 | 15. iv. | – | – | . | . | . | . | . | . | . | . | . | . | . | . |
| 2 | × | . | – | – | + | . | . | 23. iv. | – | +1 | 6. v. | – | – | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 3 | × | . | 1915 | – | . | . | + | 20. v. | – | +2 | 3. vi. | – | +8 | 1. viii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . |
| 4 | . | × | – | – | + | . | . | 20. v. | – | +2 | 17. vi. | – | – | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 5 | . | × | – | – | + | . | . | 20. v. | +2 | +4 | 3. vi. | – | +4 | 1. viii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . |
| 6 | . | × | – | – | + | . | . | 10. vi. | – | +2 | 8. vii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 7 | . | × | + | – | + | . | . | 24. vi. | – | + | 8. vii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 8 | . | × | – | – | + | . | . | 24. vi. | – | + | 8. vii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 9 | . | × | – | – | + | . | . | 25. ii. | – | +2 | 4. iii. | – | +1 | 12. iii. | – | +2 | 28. iv. | – | +2 | 28. v. | – | +2 | . | . | . | . | . | . |
| 10 | . | × | – | – | + | . | . | 3. vi. | +1 | +4 | 17. vi. | + | +2 | 1. viii. | – | +2 | . | . | . | . | . | . | . | . | . | . | . | . |
| 11 | . | × | – | – | + | . | . | 17. vi. | +2 | +4 | 8. vii. | – | +3 | 1. viii. | – | +3 | . | . | . | . | . | . | . | . | . | . | . | . |
| 12 | . | × | – | – | + | . | . | 15. vii. | +1 | +2 | 1. viii. | +2 | +4 | 30. ix. | +2 | +2 | . | . | . | . | . | . | . | . | . | . | . | . |
| 13 | . | × | 1917 | – | . | + | . | 23. iv. | – | +1 | 6. v. | – | +4 | 13. v. | – | +4 | 1. viii. | – | – | . | . | . | . | . | . | . | . | . |
| 14 | . | × | – | – | . | . | + | 25. ii. | – | +2 | 4. iii. | – | +2 | 9. iv. | – | +2 | 13. v. | – | +4 | 1. viii. | – | – | . | . | . | . | . | . |
| 15 | . | × | – | – | . | . | + | 4. iii. | ± | +2 | 11. iii. | – | + | 1. iv. | – | – | . | . | . | . | . | . | . | . | . | . | . | . |
| 16 | . | × | – | – | . | . | + | 4. iii. | +1 | +3 | 12. iii. | + | +2 | 26. iii. | + | +2 | 28. iv. | – | +1 | 28. v. | – | +1 | 1. viii. | – | – | . | . | . |
| 17 | . | × | – | – | . | . | + | 26. iii. | – | +4 | 15. iv. | – | + | 23. iv. | – | – | . | . | . | . | . | . | . | . | . | . | . | . |
| 18 | . | × | – | – | . | . | + | 26. iii. | – | +4 | 6. v. | – | +4 | 1. viii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . |
| 19 | . | × | – | – | . | . | + | 26. iii. | – | +1½ | 6. v. | – | +4 | 30. ix. | – | +1 | . | . | . | . | . | . | . | . | . | . | . | . |
| 20 | . | × | – | – | . | . | + | 26. iii. | – | +2 | 7. iv. | – | +2 | 6. v. | – | +4 | 1. viii. | – | – | . | . | . | . | . | . | . | . | . |
| 21 | . | × | – | – | . | . | + | 26. v. | – | + | 10. vi. | – | +2 | 1. viii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . |
| 22 | . | × | – | – | . | . | + | 17. vi. | – | +2 | 8. vii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 23 | . | × | – | – | . | . | + | 25. ii. | – | +2 | 26. viii. | – | +2 | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 24 | . | × | – | – | . | . | + | 25. ii. | +4 | +7 | 11. iii. | +4 | +4 | 1. iv. | +4 | +4 | 7. v. | +4 | +8 | . | . | . | . | . | . | . | . | . |
| 25 | . | × | – | – | . | . | + | 25. ii. | ± | +2 | 4. iii. | ± | +2 | 12. iii. | +1 | +2 | 26. iii. | ± | +2 | 28. iv. | – | +2 | 28. v. | – | +4 | 1. viii. | – | +1 |
| 26 | . | × | – | – | . | . | + | 4. iii | +2 | +4 | 11. iii. | +2 | +4 | 26. iii. | +2 | +2 | 28. iv. | +1 | +4 | 25. v. | +3 | +8 | . | . | . | . | . | . |
| 27 | . | × | – | – | . | . | + | 4. iii. | +2 | +4 | 12. iii. | +4 | +4 | 26. iii. | +4 | +4 | 13. v. | ± | +4 | 3. vi. | ± | +4 | 30. ix. | ± | +1½ | . | . | . |
| 28 | . | × | – | – | . | . | + | 4. iii. | +4 | +6 | 19. iii. | +4 | +4 | 15. iv. | +4 | +6 | . | . | . | . | . | . | . | . | . | . | . | . |
| 29 | . | × | – | – | . | . | + | 4. iii. | +2 | +4 | 12. iii. | +2 | +4 | 26. iii. | +2 | +4 | 30. ix. | + | +2 | . | . | . | . | . | . | . | . | . |
| 30 | . | × | – | – | + | . | + | 6. iv. | – | +2 | 8. iv. | – | +1 | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 31 | . | × | – | – | . | . | + | 28. v. | +4 | +4 | 10. vi. | +8 | +8 | 1. viii. | +1 | +8 | 30. ix. | +1 | +2 | . | . | . | . | . | . | . | . | . |
| 32 | . | × | – | – | . | . | + | 3. vi. | +2 | +4 | 10. vi. | + | +2 | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 33 | . | × | – | – | . | . | + | 3. vi. | – | +4 | 26. vi. | – | + | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 34 | . | × | – | – | . | . | + | 10. vi. | +4 | +8 | 26. iv. | +2 | +8 | 20. viii. | +2 | +4 | 30. ix. | +2 | +4 | . | . | . | . | . | . | . | . | . |
| 35 | . | × | – | – | . | . | + | 17. vi. | + | +1½ | 1. vii. | + | +1½ | 30. ix. | +1 | +2 | . | . | . | . | . | . | . | . | . | . | . | . |
| 36 | . | × | – | – | . | . | + | 8. vii. | + | +2 | 22. vii. | – | +4 | 20. viii. | – | +2 | 30. ix. | – | +2 | . | . | . | . | . | . | . | . | . |
| 37 | . | × | – | – | . | . | + | 15. vii. | +4 | +4 | 1. viii. | +4 | +8 | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 38 | . | × | – | – | . | . | + | 15. vii. | – | +2 | 22. vii. | – | +4 | 1. viii. | – | +2 | 30. ix. | – | +2 | . | . | . | . | . | . | . | . | . |
| 39 | . | × | – | – | . | . | + | 15. vii. | +3 | +8 | 1. viii. | +4 | +8 | 30. ix. | +4 | +8 | . | . | . | . | . | . | . | . | . | . | . | . |
| 40 | . | × | – | – | . | . | + | 22. vii. | +4 | +8 | 1. viii. | +8 | +8 | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 41 | . | × | – | – | . | . | + | 22. vii. | +1 | +4 | 5. viii. | + | +2 | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 42 | . | × | – | – | . | . | + | 24. vi. | – | – | 8. vii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 43 | . | × | – | – | . | . | + | 24. vi. | – | – | 8. vii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |
| 44 | . | × | – | – | . | . | + | 15. vii. | – | – | 22. vii. | – | – | . | . | . | . | . | . | . | . | . | . | . | . | . | . | . |

healthy and non-syphilitic, Europeans always give negative results, while natives sometimes give positive results) is probably a sequel of malaria.

For practical purposes we would establish the following rules:

I. *In a heavily infected malarial country a positive Wassermann reaction cannot be considered as due to syphilis if there is no special evidence in favour of syphilis.*

II. *If after a good quinine treatment a positive Wassermann reaction becomes negative or distinctly weaker, without antisyphilitic treatment, probably the positive Wassermann was a sequel of malaria.*

III. *Especially in natives a positive Wassermann reaction does not permit of conclusions without careful consideration; a positive result with unheated serum is in such cases almost useless, a negative result of course will be as valuable as elsewhere.*

IV. *In natives, a Wassermann test conducted with heated serum within three months from an attack of malaria is of little value for the diagnosis of syphilis. To consider a test made not more than a week after the attack as advised by Sutherland and Mitra is certainly wrong.*

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