

2. A new Meinicke method described by Ford Robertson and Colquhoun has been tested in 482 cases. The correlation between this and the Wassermann test with serum is of the same degree as with the original method. The use of the antigen prepared for blood in spinal fluid tests leads to an excessive number of false reactions. A special antigen is used for spinal fluids.

3. With this method one half of the positive reactions occur in one tube only. It is shown that this is a source of error, and it is suggested that, by altering the concentration of salt in the antigen emulsions, or the volume of serum in the tubes, the reaction may be turned into a two- or three-tube one with a corresponding increase in accuracy.

4. There are no grounds for abandoning the Wassermann reaction in sole favour of the Meinicke test in the diagnosis of syphilis.

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Note upon the Foregoing Paper.

By W. M. FORD ROBERTSON.

I WISH, firstly, to express my appreciation and thanks to Dr. Thomas for having carried out with manifest care this series of tests with the F.R.C. antigen. The fact, too, that he has been able to correlate the results with a large series of Meinicke tests has added to their value.

The evaluation of discrepancies between the Wassermann and the flocculation tests is usually one of difficulty, as it depends on clinical diagnosis and the reliance placed on one or other test. In framing our observations we have no personal knowledge of the cases, and from considerable experience

have come to rely more on the Meinicke and our flocculation test than on the Wassermann.

(1) MEINICKE KLÄRUNGS REACTION (M.K.R. II).

In the 45 discrepancies we would regard the presumed errors of each test to be equal, having excluded 7 " M.K.R. at fault " examples on the grounds that they should be regarded as negative. Ten " M.K.R. fast " sera are described, and in these we submit that the Wassermann is equally prone to this phenomena. In a series of 30 non-luetic treated cases of our own the results indicated greater sensitivity of the F.R.C. antigen, and I am therefore hesitant to admit that all of the 10 sera described are non-specific. Of the 27 residual disagreements in Dr. Thomas's series, it is unusual to find the Wassermann more sensitive than the M.K.R., and it can only be assumed that the test has been made unduly so in spite of the fact that subsequently with his M.R.C. method only 4 plus-minus reactions occurred that were ultimately deemed false. Another explanation may be sought, however, from the fact that the Wassermann-positive M.K.R.-negative discrepancies occurred almost exclusively in the old treated cases of neuro-syphilis. Here a Wassermann-fast condition seems likely, to which the M.K.R. is much less reactive. It is therefore suggested that the two tests behave differently in late treated lues and that there is perhaps some qualitative difference in the reactivity of the two tests. With the exception of this type of patient, there seems to be little difference in specificity, but that the M.K.R. (F.R.C. modification) is still superior in sensitivity will be seen from the following results in early cases of primary syphilis.

(2) MEINICKE KLÄRUNGS REACTION (FORD ROBERTSON-COLQUHOUN MODIFICATION).

A. *Discrepancies*.—The F.R.C. antigen was adjusted (on the basis of 500 sera) to give a sensitivity approximately 6% lower than the original M.K.R. (*Journ. Ment. Sci.*, 1939, lxxxv, p. 548), specificity being improved without loss of sensitivity.

Examination of 41 cases of early primary syphilis, diagnosed as such by dark-ground examination of the lymph from primary chancre, gave the following comparative results against a Wassermann technique similar to that used latterly by Dr. Thomas, this being run independently at the Public Health Laboratory.

Table I represents the cases in which the F.R.C. antigen became positive prior to the Wassermann.

In 4 cases out of 7 (Nos. 7, 8, 15 and 23) the Wassermann became positive at either the second or third testing. The exact time lag of the Wassermann is uncertain, as daily specimens were not taken, but in one instance, however, it was only twenty-four hours behind (No. 7). In 3 cases (Nos. 1, 20 and 21) the

TABLE I.

Case number.	Date.	F.R.C. antigen.	W.R.	Treatment.
I	2.ii.39	±---	-	None.
	8.ii.39	-DTr.--	-	0.45 NaB and 0.2 bismuth.
7	12.iv.39	+---	-	None.
	15.iv.39	+---	++	1.05 NK and 0.4 bismuth.
8	12.iv.39	+---	-	None.
	15.iv.39	+---	++	0.45 NaB and 0.2 bismuth.
15	8.v.39	++-	-	None.
	9.v.39	+---	+ -	"
	12.v.39	+±-	+ -	1.05 NK and 0.2 bismuth.
20	7.ii.39	±---	-	None.
	10.ii.39	±---	-	0.45 NaB and 0.2 bismuth.
	17.ii.39	----	-	..
21	2.iii.39	-DTr.--	-	None.
	4.iii.39	±---	-	0.45 NaB and 0.2 bismuth.
23	14.xii.38	±---	-	None.
	17.xii.38	±---	-	..
	19.xii.38	..	++	..

Key: -DTr. denotes a slight degree of precipitation without evidence of clarification.

Wassermann failed to become positive after an interval varying from two to ten days. While admittedly our antigen gave only a weak positive in these cases, the findings were verified by a second very similar result. The consistency of these weak reactions is rather striking, whereas Wassermann reactions of this order (± 3 M.H.D. complement) rarely repeat themselves, and are therefore usually regarded as non-specific. In this series the Wyler method gave complete complement fixation either at 3 M.H.D. or 3 and 5 M.H.D. The minor degrees of reaction produced by the F.R.C. antigen are, however, in keeping with such early pathological lesions, prompt treatment having arrested serious secondary involvement. In fact this is so slight in some that the Wassermann failed to detect its reflection upon the patient's serum.

TABLE II.—*Summary of the Comparison in the 41 Cases.*

Positive agreement	22	53.6%
Negative „	12	29.1%
F.R.C. antigen + before Wassermann	7	17.3%
Wassermann + before F.R.C. antigen	0	-

It will be seen that the F.R.C. antigen gave a 17% superior sensitivity. In the light of these results the observations we have made on the M.K.R. discrepancies especially those relating to the luetic cases, appear to us to be even

more relevant, and lead us again to emphasize that the reversed role of superior Wassermann sensitivity shown in Dr. Thomas's paper is exceptional. Nevertheless, we agree with Dr. Thomas that for the present at least the sero-diagnosis of syphilis cannot be undertaken adequately without a Wassermann and a complementary flocculation test. Equal reliance should be placed on each, and the interpretation of discrepancies assisted by clinical data, provocatives and repeated testing.

b. Single tube reactions.—As these were found to be as much as 50% of the positives in his series Dr. Thomas has felt they would be less open to doubt if backed by precipitation in the second tube. He mentions by contrast only 6% of such reactions exhibited by the M.K.R. These findings are in fair agreement with our experience and led us to conclude that the M.K.R. second and third tube reaction with sera giving negative or only weakly positive Wassermann could advantageously be reduced. Thus, we condensed the M.K.R. +++-, ++-- and +--- into a +--, and after much experience are convinced that our single clear tube represents syphilis and can be interpreted with confidence. Table I even shows the significance of ±-- in early syphilis.

As regards tube contamination as a cause of false reactions, we have sometimes observed control tubes so precipitated, but have no reason to suspect that antigen plus serum (0.3 c.c.) has thus been affected. Experiments have shown indeed the remarkable buffering effect of serum to electrolytes. Increasing the NaCl concentration as suggested in order to bring about a two-tube reaction would, in our opinion, endanger the balance of the present colloid system. We are, however, not unaware of the advantage of bringing in some degree of reaction in the second tube, which, from tests already made, seems likely to be accomplished by increasing the serum in the second tube from 0.1 to 0.15 c.c.

We consider that all +-- reactions noted as 400 and 300 are indicative of syphilis, and that ± reactions (200) should be regarded as warranting confirmation. The 100 notation, we agree, should be regarded as negative except in a known or strongly suspected case of syphilis.

c. Cerebro-spinal fluids.—We concur with Dr. Thomas's observations on the question of lipoid concentration and sensitivity. The problems involved are different to those encountered with sera. A special antigen of reduced lipoid content is essential, and with it can be claimed excellent specificity and a sensitivity only slightly inferior to the Wassermann.

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