A NOTE ON THE SPECIFICITY OF CARDIOLIPIN AND STANDARD ANTIGENS IN TESTING SERA FOR SYPHILIS*

BY
I. N. ORPWOOD PRICE

London

Comparative serum testing by the Wassermann reaction using cardiolipin and standard antigens was reported by Price and Wilkinson (1950). Test results on 5,124 sera were reviewed and it was concluded that cardiolipin antigen was appreciably more sensitive than the standard antigen (Harrison and Wyler technique), as it detected a higher proportion of cases of early primary syphilis and also remained positive in cases of treated syphilis long after other tests had reverted to negative. In the testing of problem sera sent to the V.D. Reference Laboratory, cardiolipin antigen was more specific than the standard antigen (940 sera tested). In the case of sera obtained from a V.D. clinic and a general hospital this was not apparent.

Cardiolipin and standard Wassermann antigens at their optimal titres were used to test 2,876 sera in parallel by Price and Wilkinson (1952), by the Whitechapel technique (Price, 1950).

The sera came from three sources:

(1) Whitechapel Clinic (1,007 sera);
(2) London Hospital (879 sera, of which 424 were from antenatal patients);
(3) Other laboratories (990 sera sent to the V.D. Reference Laboratory for investigation).

It was concluded that cardiolipin antigen was more sensitive than the standard antigen when sera from treated syphilitic patients were tested, but owing to insufficient data no opinion was offered concerning the performance of these two antigens with sera from patients suffering from primary syphilis.

The authors also stated that cardiolipin antigen gave more non-treponemal reactions than standard antigens when routine sera were tested.

It was apparent that it was necessary to re-investigate the question of the occurrence of non-treponemal reactions when testing sera with cardiolipin and standard Wassermann antigens. It was thought that any discrepancies in the occurrence of non-treponemal reactions would be thrown into higher relief if "problem sera"† rather than routine sera were tested in parallel by the two antigens. Problem sera, when received, are routinely tested in parallel by means of both the standard and cardiolipin Whitechapel Wassermann reactions, Price's precipitation reaction (P.P.R.), and the Kahn test. Each serum, when sent to the laboratory, is accompanied by a clinical history and any relevant details appertaining to the patient. It was decided to examine the results of testing serial unselected sera received during a period of 2½ years. In all, the serological and clinical records of 8,750 sera were scrutinized. The conclusions are recorded below.

Non-Treponemal Reactions

These were obtained with:

(1) Standard antigen, 139 (1-69 per cent.).
(2) Cardiolipin antigen, 169 (1-92 per cent.).
(3) Both antigens, 91 (1-04 per cent.).

It will be seen that over half of the sera (91) gave non-treponemal reactions when tested by either antigen, but it was found that 48 sera (non-reactors when cardiolipin was used) gave non-treponemal reactions with standard antigen. In like manner, 78 sera (non-reactors to standard antigen) yielded non-treponemal reactions with cardiolipin antigen. From this it is inferred that the liability to obtain non-treponemal reactions is somewhat greater when cardiolipin antigen is used (0-23 per cent.). It might well be argued that such a result may be due to the type of reaction employed (complement fixation) and in particular to the variety of technique (Whitechapel W.R.) used. Therefore, it was resolved

† Those which had given anomalous results when tested by other laboratories and which had been sent to the V.D. Reference Laboratory for investigation.

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to test sera in parallel with precipitation tests for syphilis, using a cardiolipin-type antigen (V.D.R.L. Chamblee) and an alcoholic extract of the ox heart type of antigen (P.P.R.).

Non-Treponemal Reactions with Problem Sera.
—In all, 1,886 problem sera were tested using the above reactions with the following results:

(1) P.P.R., 11 (0-57 per cent.).
(2) V.D.R.L., 117 (6-2 per cent.).

The figures show that the chances of obtaining non-treponemal reactions with problem sera are approximately ten times greater when using V.D.R.L. cardiolipin antigen than when using P.P.R. antigen. This difference seemed to be rather large, and it was decided to ascertain whether these results were due to the type of sera tested or to the type of reactions employed.

Non-Treponemal Reactions with Routine Sera.
—3,097 routine sera were tested in parallel using the V.D.R.L. test and P.P.R., with the following results:

(1) P.P.R., 5 (0-002 per cent.).
(2) V.D.R.L., 74 (0-02 per cent.).

These figures show that approximately the same ratio of non-treponemal reactions is obtained when either problem or routine sera are tested, and that, therefore, the type of antigen used and not the particular group of sera tested was responsible for the diversity of results.

Clearly, therefore, the liability to obtain non-treponemal reactions is greater when using cardiolipin-type antigens in the sero-diagnosis of syphilis than when the ordinary unpurified alcoholic extracts of ox heart (standard antigens) are used. In the case of complement fixation, when using the Whitechapel technique and cardiolipin antigen formula, this liability is roughly 1:5 to 1, and with precipitation tests using V.D.R.L. cardiolipin antigen this propensity is much greater, approximately 10 to 1.

During recent years there has been a tendency to increase the sensitivity of tests for syphilis without due regard to specificity, and it is time that a reorientation of the value of sensitivity as against specificity should be undertaken. Kahn (1950) has already stated that he believes that a lowering of the sensitivity levels of present day sero-diagnostic tests may prove to be a step in the right direction. During this work one aspect of this problem was investigated, namely, the relative sensitivities of cardiolipin antigens as against standard antigens when sera from treated syphilis were tested by both types of antigen. The figures are taken from the same groups of sera tested in parallel in which the occurrence of non-treponemal reactions was noted. Furthermore, they refer only to the disagreements between results. When the complement-fixation technique was used it was found that of the 8,750 sera tested nine (0-1 per cent.) were positive with standard antigen and negative with cardiolipin antigen, whilst 215 (2-5 per cent.) were negative with standard antigen but positive with cardiolipin antigen. Using the precipitation tests, the problem sera (total 1,886) yielded seven (0-37 per cent.) positive reactions which were negative with the V.D.R.L. cardiolipin reactions, and 162 (8-6 per cent.) which were negative with P.P.R. but positive with the V.D.R.L. test. With routine sera (total 3,097) a similar pattern was obtained; five (0-16 per cent.) sera were positive with the P.P.R. but negative when using V.D.R.L. antigen, and 96 (3-1 per cent.) were negative with the P.P.R. but positive when tested with V.D.R.L. antigen.

Thus it would appear that with the more sensitive cardiolipin antigens there is a greater liability to non-treponemal reactions.

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