SEROLOGICAL TESTS FOR TREPOНЕМАЛЬ INFECTION IN LEPROSY PATIENTS

AN EVALUATION OF THE FLUORESCENT TREPOНЕМАЛЬ ANTIBODY ABSORPTION (FTA—ABS) TEST*

BY

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Much has been written about the biological false positive (BFP) reaction demonstrated by reagin tests applied to sera from patients suffering from leprosy. It is well known that a BFP reaction is in all but a very small minority of cases proved or disproved by recourse to specific tests for treponemal infection, i.e. the Treponema pallidum immobilization (TPI) test and/or the fluorescent treponemal antibody absorption (FTA-ABS) test.

The FTA-ABS test is not as specific as the TPI test and therefore not as well fitted for demonstration of BFP sera as the TPI test (Fribourg-Blanc and Niel, 1967). The TPI test, still the most specific serological test for the diagnosis of treponemal infection (Wilkinson and Rayner, 1966), is largely confined to specialized laboratories because of cost and technical difficulties; by contrast, the FTA-ABS test is less expensive, simpler to perform and all reagents required can be purchased commercially. With care and experience reproducible results can be obtained. For these reasons the FTA-ABS test is likely to become the test of choice for confirmation of BFP reactions in those areas of the world where a laboratory performing the TPI test is not within easy access.

This study was undertaken on sera from leprosy patients, to compare the results of the TPI and FTA-ABS tests on those sera which had shown BFP and non-specific reactive results to the more conventional tests for treponemal infection.

Material and Methods

Sera were obtained from 270 patients at the Central Luzon Sanitarium and the Leprosy Research and Training Center Skin Clinic, the Philippines. The sera all came from persons suffering from the lepromatous form of leprosy, 244 being from the leprosarium and 26 from more recent cases attending the skin clinic.

A control group of 250 sera was examined from the normal, i.e. non-leprosy, population of Manila.

The ages of the leprosy patients varied from 15 to 79 years. There were 203 males and 67 females. The duration of treatment of the leprosy extended from a maximum of 22 years for some patients in the leprosarium to no treatment at all in seven patients attending the skin clinic. Apart from this information their past medical histories were unknown to us.

The following tests were performed on each serum received: cardiolipin Wassermann reaction (CWR), Venereal Disease Research Laboratory (VDRL) test, Reiter protein complement-fixation (RPCF) test, Treponema pallidum immobilization (TPI) test, a fluorescent treponemal antibody (FTA-200) test, and the fluorescent treponemal antibody absorption (FTA-ABS) test. Where discrepancies occurred between the results of the various tests, these were repeated to confirm the original result.

Results

A total of 270 sera from leprosy patients was tested, 218 of which gave non-reactive results to all six tests; 195 sera came from patients in the leprosarium and 23 from patients attending the skin clinic. Thus, of the patients with lepromatous leprosy, sera from 52 gave reactive results to some or all of the tests for treponemal infection.

A reactive TPI test result was taken to indicate treponemal infection. Sera from fifteen patients were reactive to this test, indicating that these patients had a treponemal infection as well as leprosy. Sera from three of these fifteen patients gave reactive results to all six tests performed.

A further two sera gave reactive results to all except the RPCF test. The CWR gave a non-reactive test result with only three sera. Both the CWR and RPCF test results were non-reactive and the other four reactive with five sera. One serum was reactive to all except the reagin detection tests.

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and one gave reactive results to the TPI, FTA-200, and FTA-ABS tests only (Table I).

**TABLE I**  
SERAS FROM FIFTEEN LEPROSY PATIENTS SHOWING SEROLOGICAL EVIDENCE OF TREPONEMAL INFECTION

<table>
<thead>
<tr>
<th>No. of Sera</th>
<th>Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CWR</td>
</tr>
<tr>
<td>3</td>
<td>R</td>
</tr>
<tr>
<td>2</td>
<td>R</td>
</tr>
<tr>
<td>3</td>
<td>NR</td>
</tr>
<tr>
<td>5</td>
<td>NR</td>
</tr>
<tr>
<td>1</td>
<td>NR</td>
</tr>
<tr>
<td>1</td>
<td>NR</td>
</tr>
</tbody>
</table>

R = reactive  
NR = non-reactive

Considering a biological false positive reaction to be indicated by a reactive result to a reagin detection test but a non-reactive result to a treponemal test, biological false positive reactions were shown by 22 sera (8.1 per cent.); all came from patients at the leprosarium. Two of these sera, from females aged 17 and 46 years, were reactive to the CWR only. Of the remaining twenty sera which were reactive to the VDRL test only, ten were from females aged 19 to 58 years, and ten from males aged 19 to 50 years. No serum in this group was reactive to both reagin detection tests (Table II).

Non-specific reactive results to the RPCF test were given by two sera only, both being from male patients aged 19 and 30 years in the leprosarium. One serum was reactive to the RPCF test only and the other was reactive to the RPCF and VDRL tests only. Both these sera gave non-reactive results to the TPI and FTA-ABS tests (Table II).

Sera from eleven patients were reactive to the FTA-200 test but non-reactive to the TPI and FTA-ABS tests. Of these eleven sera, two were also reactive to the VDRL test; these sera were from a female aged 41 years and a male aged 37 years, both at the leprosarium. Of the remaining nine sera, two were from males aged 30 and 31 years attending the skin clinic and seven from patients at the leprosarium (two females aged 22 and 38 years and five males aged 17 to 37 years). The results with the eleven sera in this group were regarded as non-specific reactions to the FTA-200 test (Table II).

The TPI test was non-reactive and the FTA-ABS test reactive with sera from two patients; one from a male aged 34 years was reactive to the FTA-ABS test only and the other from a male aged 29 years was reactive to both the VDRL and FTA-ABS tests (Table III).

**TABLE III**  
TEST RESULTS ON TWO SERA SHOWING DISCREPANCIES IN TPI AND FTA-ABS TESTS

<table>
<thead>
<tr>
<th>No of Sera</th>
<th>Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CWR</td>
</tr>
<tr>
<td>1</td>
<td>NR</td>
</tr>
<tr>
<td>1</td>
<td>NR</td>
</tr>
</tbody>
</table>

In the control group of 250 sera, 241 were non-reactive to all six tests. Of the remaining nine sera, one was reactive to the TPI and FTA-ABS tests only, seven to the RPCF test only, and one to the FTA-200 test only. The reactive results to the RPCF and FTA-200 tests were considered to be non-specific.

**Discussion**

It is an accepted fact that leprosy and treponemal infection can co-exist and that the prevalence of treponemal infection in lepers is similar to that in the population from which they are drawn. In this survey a reactive TPI test result has been
FTA-ABS TEST IN LEPPERS

21

taken to indicate treponemal infection and other test results have been compared with it. In the sera from the group of leprosy patients studied, the prevalence of treponemal infection was 5·6 per cent. By contrast, definite evidence of treponemal infection was found in only one specimen from the control group.

Thus the prevalence of treponemal infection among the leprosy patients was probably not a true indication of prevalence in the community as a whole because of variation in socio-economic background, chance of exposure to treponemal infection, e.g. yaws, and the unequal grouping together of patients in a leprosarium compared with their normal spread through the community as a whole. There was complete agreement between the results of the TPI and FTA-ABS tests in this group of leprosy patients.

Leprosy, especially the lepromatous form, is well known to be associated with BFP reactions. In our group, sera from 22 out of 270 patients with lepromatous leprosy (8·1 per cent.) showed BFP reactions, i.e. reactive results to reagin detection tests and non-reactive results to treponemal tests. These reactions were commoner in females (12 of 67) than in males (10 of 203) in the leprosy group.

The incidence of reported BFP results in sera from leprosy patients has varied greatly. Nelson (1952) tested sera from seventy patients at the leprosarium in Carville, Louisiana, and found that 46 sera gave BFP reactions. Foster and Kerchan (1966) reported 8 per cent. BFP reactions in 87 patients with lepromatous leprosy in Uganda. As the TPI test was not available to them they accepted as showing BFP reactions, those sera in which a positive Wassermann reaction was unsupported by a positive RPCF test result. In this regard it is of interest that two sera in our group reacted to reagin detection tests and to the TPI, FTA-200, and FTA-ABS tests, but not to the RPCF test (Table I).

That the VDRL test among the two reagin tests was reactive in all sera except two in Table I agrees with the concept that the VDRL test is more reactive than the CWR for specific as well as for non-specific antibodies. This was confirmed by the results in Table II.

Sera were regarded as giving non-specific reactions to the RPCF and FTA-200 tests when these results were unsupported by a reaction to the TPI test. Only two out of 270 sera from the leprosy patients showed non-specific reactions to the RPCF test. This finding differs from that of Azulay, Pinto, Deane, Rocha, and Azulay (1967) who reported a relatively large number of non-specific reactions to the RPCF test.

There were 4·1 per cent. non-specific reactions to the FTA-200 test. In contrast to the other non-specific and BFP reactions in our group of sera, a higher proportion of non-specific reactive FTA-200 tests occurred with sera from the skin clinic than from the leprosarium. However, as the number of sera tested from the skin clinic was small, no valid conclusions could be drawn from this. The FTA-200 test showed reactivity with eleven sera and the FTA-ABS test was non-reactive with all these eleven sera, possibly because the FTA-ABS test was less reactive and thus seemed to be more specific. The only properly specific test is the TPI test.

The TPI and FTA-ABS test results showed close agreement, the only discrepancy being with two sera which were reactive to the FTA-ABS test and non-reactive to the TPI test. One of these sera was reactive to the VDRL test also. Both patients were males aged 29 and 34 years respectively. On enquiry, Dr. J. Dizon, Chief of Disease Intelligence in Manila, informed us that neither patient had a history of syphilis or yaws, or any clinical signs suggestive of infection. That the VDRL test was reactive is perhaps an indication of a BFP serum. Király, Jobbágy, and Kováts (1967) showed that the Reiter treponeme alone did not always remove all group antibody from all sera. As a result of this work it is felt that a reactive FTA-ABS test, when all other tests (i.e. CWR, VDRL, RPCF, and TPI test) are non-reactive, must be viewed with caution.

The order of percentage agreement of each test in relation to negative results to the TPI test in the leprosy sera listed in Tables II and III and the 218 non-reactive sera (altogether 255 sera) was as follows:

<table>
<thead>
<tr>
<th>Test</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CWR, RPCF, and FTA-ABS</td>
<td>99 per cent</td>
</tr>
<tr>
<td>FTA-200 test</td>
<td>95·2 per cent</td>
</tr>
<tr>
<td>VDRL test</td>
<td>90·6 per cent</td>
</tr>
</tbody>
</table>

With the fifteen TPI positive sera listed in Table I, the TPI, FTA-200, and FTA-ABS tests were of equal sensitivity, followed by the VDRL test (13 of 15), the RPCF test (7 of 15), and finally the CWR (5 of 15). These findings are summarized in Table IV (overleaf).

This overall pattern of specificity and sensitivity of the FTA-ABS test on sera from patients with lepromatous leprosy indicates that it is able to replace the TPI test in detecting BFP reactions and non-specific positive results to tests for treponemal...
infection. The FTA-ABS test should be of use in those areas where the TPI test is not available.

**Summary**

Serological tests for treponemal infection were carried out on 270 patients with lepromatous leprosy and 250 normal controls, from the Philippines. All sera were subjected to the Cardiolipin Wassermann reaction, the Venereal Disease Research Laboratory test, the Reiter protein complement-fixation test, the fluorescent treponemal antibody test, the fluorescent treponemal antibody absorption test, and the *Treponema pallidum* immobilization test. A reactive TPI test result was taken as evidence of treponemal infection and all other test results were compared with it.

Sera from 5·6 per cent. of the leprosy patients showed evidence of treponemal infection. BFP reactions occurred with 8·1 per cent. of leprosy sera, the VDRL slide flocculation test being responsible for the majority of these. Non-specific reactive results to the RPCF and FTA-200 tests are discussed. Special attention was given to evaluating the FTA-ABS test against the TPI test. They were found to be of almost equal specificity and of equal sensitivity.

It is concluded that, where the TPI test is not available, the FTA-ABS test can replace it in detecting BFP and non-specific reactions to serological tests for treponemal infection in sera from patients with the lepromatous form of leprosy.

The authors are grateful to Dr. J. H. Hirshman, Assistant Director of Health Services, World Health Organization, Manila, who arranged for the collection and transport of the sera studied; and to Dr. Paulino Garcia, Secretary of Health, Manila and the members of his staff who so willingly co-operated with us. Our appreciation is also due to Dr. T. Guthe, Chief, Venereal Disease and Treponematoses Section, W.H.O., Geneva, for helpful suggestions during the preparation of this paper.

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**REFERENCES**


Les tests sérologiques de l'infection causée par les tréponèmes chez les lépreux

Evaluation du test fluorescent de l'absorption de l'anticorps du tréponème (FTA-ABS)

**RÉSUMÉ**

Les tests sérologiques de l'infection causée par les tréponèmes ont été faits chez 270 malades de lépre lépromateuse et 250 te moins normaux des Philippines. Tous les sérum ont été soumis à la réaction Wassermann cardiolipine, aux tests VDRL, fixation du complément de la protéine de Reiter, fluorescent de l'absorption de l'anticorps du tréponème et à celui de l'immobilisation de *Treponema pallidum*. Un résultat positif au test TPI avait été accepté comme preuve d'une infection par le tréponème et tous les résultats des autres tests comparés à ce dernier.

Le sérum de 5,6 pour cent des lépreux montrait des preuves d'infection par le tréponème. Des réactions biologiques pseudo-positives avaient eu lieu chez 8,1 pour cent des sérum des lépreux, les tests de flocculation VDRL slide étant responsable de la majorité de ceux-ci. Les résultats réactifs non-spécifiques aux tests RPCF et FTA-200 sont discutés. Une attention spéciale avait été portée en évaluant la comparaison entre le test FTA-ABS et le test TPI. On a trouvé qu'ils étaient d'une spécificité presque égale et d'une sensibilité égale.

Il est conclu que, là où le test TPI ne peut être fait, le test FTA-ABS peut le remplacer pour révéler les réactions BFP et celles non-spécifiques aux tests sérologiques de l'infection causée par le tréponème dans les sérum des malades atteints de lépre lépromateuse.

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**Table IV**

<table>
<thead>
<tr>
<th>Result</th>
<th>Test</th>
<th>CWR</th>
<th>VDRL</th>
<th>RPCF</th>
<th>FTA-200</th>
<th>FTA-ABS</th>
<th>TPI</th>
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<tbody>
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<td>Non-reactive</td>
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<td>Percentage Agreement</td>
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<td>95-2</td>
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<tr>
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<tr>
<td>No. of Sera</td>
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<td>13</td>
<td>7</td>
<td>15</td>
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<tr>
<td>Percentage Agreement</td>
<td>33·3</td>
<td>86·7</td>
<td>46·7</td>
<td>100</td>
<td></td>
<td></td>
<td>100</td>
</tr>
</tbody>
</table>

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