
**ABSORBED FLUORESCENT TREPONEMAL ANTIBODY (FTA-ABS) TEST**

**COMPARISON WITH THE FTA-200 AND TPI TESTS ON 1,056 PROBLEM SERA**

BY

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Deacon and Hunter (1962) have shown that the fluorescent treponemal antibody (FTA) test detects two separate antibodies in syphilitic sera. One, a group antibody, reacts with other treponemes, such as the Reiter organism, *Treponema microdentium*, and *Treponema zuelzerae*, as well as with *Treponema pallidum*, presumably because of an antigen shared in common by these organisms. Removal of group antibody from syphilitic sera by absorption with Reiter treponemes allows the detection of a second antibody which is thought to be specific for *T. pallidum*. Group antibody is present in low titres in the majority of normal, non-syphilitic sera, possibly being produced in response to the presence of commensal treponemes in the body. Wilkinson and Rayner (1966) have shown that it also occurs in the course of syphilitic infection and that, except in secondary syphilis, it appears to preponderate over the antibody specific for *T. pallidum*. This has also been found to occur in infections with yaws (Wilkinson, unpublished data).

In the FTA-200 test described by Deacon, Freeman, and Harris (1960), sera are tested at a dilution of 1 in 200 which is above the threshold of group antibody found in the great majority of non-syphilitic sera. Despite the sensitivity of the indirect fluorescence technique, this dilution reduces the potential sensitivity of the method and various means have been advocated for the removal of group antibody from sera so that tests can be made for the presence of the antibody specific for *T. pallidum* alone. This has been done by absorption of sera with intact Reiter treponemes, by a sonicate of these organisms or by a heated filtrate of a culture of Reiter treponemes (Hunter, Deacon, and Meyer, 1964; Hunter, 1964; Betz, 1966; Deacon, Lucas, and Price, 1966; Knox, Short, Wende, and Glicksman, 1966). The use of intact or ultrasonically disintegrated Reiter treponemes presents technical difficulties, but the heated culture filtrate can be prepared in sufficient quantity and its reactivity standardized and so was used in the present investigation.

**Material and Methods**

**Sera**

Tests were made on all sera sent to the laboratory for TPI tests during a period of 4 months. These were "problem" sera, usually referred because tests for reagin had been found positive in other laboratories. FTA-200, Reiter protein complement-fixation (RPCF), cardiolipin Wassermann reaction (CWR), and VDRL slide tests were also performed. During the period reviewed there were 1,056 sera on which valid results had been obtained by all six tests.

**FTA-ABS Test**

This was performed according to the technique recommended by the Venereal Diseases Research Laboratory, Communicable Disease Center, Atlanta, Ga. (Report, 1968). The fluorescein-conjugated anti-human gamma globulin serum and the sorbate were prepared in the laboratory. The latter had a working titre of 1 in 3; at this dilution it completely abolished the reactivity of a non-specific control serum which gave +++ fluorescence at a dilution of 1 in 25 in saline but did not significantly reduce the fluorescein given by a known positive serum. The tests were read on a Reichert Zetopan microscope using a 2 mm. BG 12 exciter filter and appropriate barrier filters. Sera giving definite + + + + fluorescence at a dilution of 1 in 25 in saline were considered reactive. Tests were repeated on sera giving borderline readings between + and + + +, if these were confirmed, the results were also classed as reactive.

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Results

A comparison of the results of the TPI test with those of the two fluorescence tests is given in Table I.

If the TPI results are taken as the standard for comparison, positive and doubtful results being grouped together as reactive, there was overall agreement between the TPI and FTA-200 in 78\% of the sera and between the TPI and the FTA-ABS test in 92\% of the sera. 622 sera were reactive in the TPI test; of these, 77\% were reactive in the FTA-200 and 96\% in the FTA-ABS test. These results show clearly that the FTA-ABS test is considerably more sensitive than the FTA-200, even in the group of 59 sera which gave doubtful TPI results, the FTA-ABS was found reactive in 51 (86\% of the sera) but the FTA-200 gave only 39 (66\%) positive results.

In the group of 434 sera which gave negative TPI results, the FTA-200 was read as reactive in 83 instances, many of these being borderline reactions. The FTA-ABS was also found reactive in 39 of these and with a further 25 sera on which the FTA-200 was negative. Examination of the clinical information—often very scanty—supplied with these sera gave the results summarized in Table II.

<table>
<thead>
<tr>
<th>TPI</th>
<th>Positive 563</th>
<th>Doubtful 59</th>
<th>Negative 434</th>
</tr>
</thead>
<tbody>
<tr>
<td>FTA-200</td>
<td>Positive 443</td>
<td>Negative 120</td>
<td>Positive 39</td>
</tr>
<tr>
<td>FTA-ABS</td>
<td>Pos. 441</td>
<td>Neg. 2</td>
<td>Pos. 107</td>
</tr>
</tbody>
</table>

**Table II**

**CLINICAL INFORMATION AVAILABLE ABOUT PATIENTS WHOSE SERA GAVE NEGATIVE TPI BUT POSITIVE FLUORESCENCE TESTS**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Cases</th>
<th>FTA-200 + FTA-ABS</th>
<th>FTA-200 - FTA-ABS</th>
<th>FTA-200 + FTA-ABS</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of Syphilis or Yaws Lesions possibly Syphilitic or Diagnosis of Syphilis No information</td>
<td>19</td>
<td>8</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>24</td>
<td>8</td>
<td>3</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>14</td>
<td>12</td>
<td>39</td>
<td></td>
</tr>
</tbody>
</table>

From these data it appears that in a proportion of these patients there was clinical evidence to substantiate the reactive fluorescence tests. Nineteen of these gave a definite history of previous syphilis or yaws; the FTA-200 test was positive in nine but the FTA-ABS test was positive in all but one.

The TPI test has found its most useful application in the differentiation of clinically latent treponemal disease from biological false positive reactions with tests for reagin. Although a positive TPI test is good evidence of treponemal disease, past or present, failure to demonstrate immobilizing antibody does not exclude such infection with the same degree of certainty because the antibody appears rather late in the primary stage and may be absent in a minority of long-standing cases. Tuffanelli, Wuepper, Bradford, and Wood (1967) re-examined 100 patients who had been presumed to be biological false positive reactors on the basis of one or more negative TPI tests. Fifty of these had negative TPI and FTA-ABS tests; in 38, although the TPI was again found negative, the FTA-ABS test was positive and in seven of these patients clinical evidence of late syphilis was found. The remaining twelve patients were found to have positive TPI and FTA-ABS tests and six showed clinical evidence of late syphilis. The authors consider that the FTA-ABS test should be used to identify chronic BFP reactors because of its high sensitivity. Lassus, Mustakallio, Aho, and Putkonen (1967) have also re-examined 57 patients classed as chronic BFP reactors because of negative TPI tests. They found that sera from six of these gave weakly reactive and one a reactive FTA-ABS test; they consider that these seven patients should not be regarded as definite BFP reactors because of these findings.

In the present series there were 171 sera in which the TPI test was negative but one or more of the tests for reagin positive, and a further seventeen on which the Reiter protein complement-fixation test was also positive. On purely serological grounds, therefore, these reactions might be suspected of being falsely positive. The FTA-ABS test was found positive in thirteen of the former group and in eight of the latter. The available information...
ABSORBED FLUORESCENT TREPONEMAL ANTIBODY (FTA-ABS) TEST

TABLE IIIA
CLINICAL INFORMATION AVAILABLE ABOUT THIRTEEN PATIENTS WHOSE SERA GAVE NEGATIVE TPI TESTS BUT POSITIVE FTA-ABS AND REAGIN TESTS

<table>
<thead>
<tr>
<th>Case No.</th>
<th>RPCF</th>
<th>VDRL</th>
<th>CWR</th>
<th>FTA-200</th>
<th>FTA-ABS</th>
<th>Clinical Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>R4</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>R1</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>-</td>
<td>R2</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>WR</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>-</td>
<td>WR</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>-</td>
<td>R2</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>-</td>
<td>WR</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>-</td>
<td>WR</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>11</td>
<td>-</td>
<td>WR</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>12</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>13</td>
<td>-</td>
<td>R1</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Clinical Data
- ? chronic BFP reactor
- Contact of primary syphilis
- West Indian male. Penile sore 6 wks ago. Contact has vaginal ulcer
- Coloured male, treated for ? early syphilis 1965
- Male aged 65. Diabetic
- Male aged 30. Diabetic and diabetes mellitus
- Male aged 35. Prior history of syphilis
- Female, Husband had syphilis 40 yrs ago
- Male, penile sore. Various recent exposures
- Male aged 77. Similar results on second serum
- Female, arthritis metacarpophalangeal joints. Similar results and positive TPI (63 per cent. s.i.) on second specimen
- Mental disturbance. Treated for “VD” many years ago
- Coloured pregnant female
- Female aged 64. Choroiditis and absent ankle jerks

WR = Weakly reactive.

TABLE IIIB
CLINICAL INFORMATION AVAILABLE ABOUT EIGHT PATIENTS WHOSE SERA GAVE NEGATIVE TPI TESTS BUT POSITIVE FTA-ABS, REAGIN, AND REITER PROTEIN COMPLEMENT-FIXATION TESTS

<table>
<thead>
<tr>
<th>Case No.</th>
<th>RPCF</th>
<th>VDRL</th>
<th>CWR</th>
<th>FTA-200</th>
<th>FTA-ABS</th>
<th>Clinical Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>WR</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>R2</td>
<td>+</td>
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<td>0</td>
<td>+</td>
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<td>+</td>
<td>WR</td>
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<td>0</td>
<td>+</td>
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<td>4</td>
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<td>+</td>
<td>+</td>
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</tr>
<tr>
<td>6</td>
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<td>+</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>+</td>
<td>R2</td>
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<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Clinical Data
- Pregnant. Similar results on second specimen
- "Suspicious" STS in previous pregnancy 8 yrs ago. No treatment given then
- Female West Indian. Pregnant. ? yaws scars on legs
- Female aged 60. ? syphilis
- Male aged 51. History of treated syphilis in the past
- Male aged 60. Poor arterial blood supply, R. arm
- Darkground positive primary syphilis
- Pregnant, no antenatal care. Child clinically normal

WR = Weakly reactive.

about these patients is shown in Tables IIIA and IIIB (above).

In the thirteen patients listed in Table IIIA, a diagnosis of treponemal infection is thought probable in eight (Cases 2, 3, 4, 7, 8, 10, 11, and 13) and in three of the eight patients described in Table IIIB (Cases 3, 5, and 7).

37 specimens of cerebrospinal fluid were examined by the FTA-ABS and TPI tests. Complete agreement was found, nine specimens being positive and 28 negative by both methods.

To assess the performance of the FTA-ABS test in normal individuals presumed to be free from treponemal disease, sera from 107 blood donors were tested. All gave negative results with the RPCFT, CWR, and VDRL tests and the FTA-ABS tests were all found to be negative.

Discussion
The FTA-ABS test is technically no more difficult to perform than the FTA-200 test. The results obtained in this series of problem sera show that the absorption procedure considerably enhances the sensitivity of the test without compromising its specificity. Deacon and others (1966), in a survey of 2,252 sera, showed that the FTA-ABS test at least equaled the TPI test in sensitivity in tests on sera from patients with untreated and treated syphilis at all stages. They found it considerably more sensitive than the TPI in untreated and treated primary syphilis. Three sera (0.8 per cent.) from 384 presumed normal patients gave positive FTA-ABS tests at one of the laboratories participating in the study, but these were found to be negative when re-tested in the authors' laboratory. Garner, Grantham, Collins, and Roeder (1968) have compared the FTA-ABS test with the TPI on 841 problem sera and found 95.1 per cent. agreement; discrepancies in which the FTA-ABS test alone was positive were mainly found when testing sera from patients with primary syphilis or with a history of treated syphilis. Harner, Smith, and Israel (1968) reported on the use of the absorbed test in the investigation of 1,985 patients in whom late ocular or neurosyphilis was to be excluded; they found it reactive in 41 per cent., but the TPI
Our thanks are due to Messrs C. J. Storey and H. Ferguson for their technical assistance and to Lt.-Col. R. C. Stewart, R.A.M.C. College, Millbank, for supplying donor sera.

REFERENCES


Le test fluorescent de l'anticorps absorbé du treponème (FTA-ABS)

Comparaison au test fluorescent de l'anticorps du treponème 200 (FTA-200) et au test de l'immmobilisation du treponème (TPI) sur 1,056 séums présentant des problèmes sérologiques

Résumé

(1) Les résultats du test FTA-ABS et ceux du test FTA-200 sont comparés à ceux du test TPI faits avec 1,056 séums présentant des problèmes sérologiques.

(2) Le test FTA-ABS a été trouvé comme étant beaucoup plus sensible et aussi beaucoup plus spécifique que le test FTA-200.

(3) Une concordance complète entre les tests FTA-ABS et TPI a été trouvé en examinant 37 spécimens du liquide céphalo-rachidien. Aucun résultat positif n'a été rencontré quand 107 séums obtenus de personnes normales ont été soumis au test FTA-ABS.

Summary

(1) The results of the FTA-ABS test and FTA-200 test are compared with those of the TPI test on 1,056 sera presenting serological problems.

(2) The FTA-ABS test was found to be considerably more sensitive and to be more specific than the FTA-200 test.

(3) Complete agreement between the FTA-ABS and TPI tests was found on 37 specimens of cerebrospinal fluid. No positive FTA-ABS test results were found on sera from 107 presumed normal persons.

was reactive in only 29 per cent. of the 1,298 sera tested by it. 126 sera gave negative TPI but positive FTA-ABS test results; on clinical grounds these patients were thought to have syphilis. Atwood, Miller, Stout, and Norins (1968) re-examined 67 patients who had been diagnosed and treated for latent or late syphilis 13 years previously on the basis of positive TPI and reagin tests. The TPI test was found to have reversed to negative in seven of these patients, all with late latent syphilis, but the FTA-ABS test was positive in all save one, who was also TPI-negative.

The results obtained in the present study on a very selected group of sera have confirmed the high sensitivity of the absorbed test and suggest that it has an acceptable level of specificity. It has proved of considerable value in the investigation of "problem" sera and it is thought that it should supersede the less sensitive FTA-200 test. Used in conjunction with tests for other antibodies produced in treponemal infection (reagin and RPCF antibody), it should be most helpful in assessing the specificity of reactions in problem sera and materially reduces the numbers of sera on which TPI tests are needed.

As yet there is no published information on the nature of the active principle in the sorbing agent. The heated culture filtrate is a very crude product, and although it works well in practice, further studies with a view to its isolation and purification are desirable. Work by Király, Jobbágy, and Kováts (1967) suggests that absorption of sera by Reiter treponemes may not necessarily remove reactivity with all other cultivable treponemes so that a sorbing agent prepared from a wider range of these organisms might be advantageous.
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