

Fluorescent treponemal antibody absorption (FTA-ABS) test in yaws

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The pathogenic treponemes, *T. pertenue* and *T. pallidum*, produce similar antibodies in the serum of a person infected with either organism. Thus sera from patients with yaws react similarly to sera from syphilitic patients in the conventional tests for syphilis and in the *Treponema pallidum* immobilization (TPI) test.

The most recent test developed for the detection of syphilis is the fluorescent treponemal antibody absorption (FTA-ABS) test of Hunter, Deacon, and Meyer (1964). This was introduced as a simpler, less costly procedure than the TPI test, which could be performed in a non-specialized laboratory and was as specific as the TPI test for treponemal infection. The FTA-ABS test was a refinement of the less specific fluorescent treponemal antibody (FTA-200) test, which detects both group and specific antibodies in syphilitic sera. The non-pathogenic and the pathogenic treponemes all share common or group antigens which can cause the production of group antibody. Thus false reactive FTA-200 test results can be due to the presence in the serum of group antibody to non-pathogenic treponemes. The pathogenic treponemes have group and specific antigens, the specific antigens being shared by the pathogenic treponemes alone. In the FTA-ABS test, sorbent, an extract of the non-pathogenic Reiter treponeme, is used to remove group antibody from the serum and leave only specific antibody. This specific antibody is theoretically the one detected in the FTA-ABS test. The FTA-ABS test has been compared by various laboratories with the TPI test, an established specific test for syphilis, and has shown reasonable agreement (Johnston and Wilkinson, 1968; Garner, Grantham, Collins, and Roeder, 1968).

The present study has been undertaken to compare the results of the FTA-ABS test with those of the TPI test in sera from persons living in areas where yaws is a common treponemal infection.

Materials and methods

Sera were examined from 848 persons living in New Guinea and the tropical north of the Northern Territory of Australia. Active yaws had been diagnosed in some of

those in each area. There was no evidence of venereal syphilis in the communities from which the sera examined were drawn. No cases of cardiovascular, neurosyphilis, or congenital syphilis were seen. Some of the subjects had clinical evidence of old yaws lesions.

The following tests were performed on each serum: cardiolipin Wassermann reaction (CWR), Venereal Disease Research Laboratory (VDRL) test, Reiter protein complement-fixation (RPCF) test, *Treponema pallidum* immobilization (TPI) test, and a fluorescent treponemal antibody absorption (FTA-ABS) test. In performing the FTA-ABS test, two modifications were made to the technique described in the 'Manual of Tests for Syphilis, 1969' (US PHS, 1969). Tween 80 was not used and the anti-human globulin was diluted to titre in 0.04 per cent. Evans blue in phosphate buffered saline as recommended by Fry and Wilkinson (1963). These two alterations are normal procedure in fluorescent treponemal antibody tests in our laboratory. A reading of + intensity of fluorescence was considered reactive. Where this agreed with the TPI test result, the FTA-ABS test was not repeated. If any discrepancy was observed between TPI and FTA-ABS test results, both were repeated.

Results

The TPI test has been used as the standard for comparison for the FTA-ABS test. The results of both tests are compared in Table I.

TABLE I Comparison of results of TPI and FTA-ABS tests on 848 sera being tested for yaws

| | Reactive | | Non-reactive | |
|--------------|----------|----|--------------|-----|
| TPI test | 579 | | 269 | |
| FTA-ABS test | 556 | 23 | 46 | 223 |

Agreement between the TPI and FTA-ABS tests was shown by 779 (91.9 per cent.) of the 848 sera examined. Of these 223 sera were non-reactive and 556 sera reactive to both tests. 579 sera were reactive in the TPI test of which 556 (96.0 per cent.) were also reactive in the FTA-ABS test. Of 269 sera non-reactive in the TPI test, 223 (82.9 per cent.) were non-reactive in the FTA-ABS test.

In 69 (8.1 per cent.) of the sera, the results of the TPI and FTA-ABS tests did not agree; 23 sera gave

reactive results to the TPI test and non-reactive results to the FTA-ABS test. Table II compares the results of the CWR, VDRL, RPCF, TPI, and FTA-ABS tests on these sera. The eight sera which were reactive in the CWR, all gave low titre results.

TABLE II Results of serological tests on 23 sera in which TPI test was reactive and FTA-ABS test non-reactive

| No. of sera | CWR | VDRL | RPCF | TPI | FTA-ABS |
|-------------|-----|------|------|-----|---------|
| 3 | — | — | — | R | — |
| 5 | — | — | R | R | — |
| 6 | — | R | — | R | — |
| 1 | — | R | R | R | — |
| 8 | R | R | R | R | — |

There were 46 sera which gave non-reactive TPI and reactive FTA-ABS test results. The reading of the intensity of fluorescence in this group was + in 41 sera and ++ or greater in five. These five sera comprised three in which the FTA-ABS test only was reactive, and two in which the CWR, VDRL, and RPCF tests gave reactive results. A comparison of the results of the CWR, VDRL, RPCF, TPI and FTA-ABS tests on these 46 sera is shown in Table III. There were twenty sera which gave reactive results to the FTA-ABS test only. Of the other 26 sera which gave non-reactive TPI and reactive FTA-ABS test results, six were reactive in reagin detection tests, fourteen in the RPCF test, and six in the reagin and RPCF tests. Clinical signs of yaws were shown by one of the 46 patients in this group (Table III).

TABLE III Results of serological tests on 46 sera in which TPI test was non-reactive and FTA-ABS test reactive

| No. of sera | CWR | VDRL | RPCF | TPI | FTA-ABS | Clinical signs of yaws | No signs of yaws |
|-------------|-----|------|------|-----|---------|------------------------|------------------|
| 20 | — | — | — | — | R | — | 20 |
| 14 | — | — | R | — | R | — | 14 |
| 4 | — | R | — | — | R | — | 4 |
| 1 | R | — | — | — | R | — | 1 |
| 1 | R | R | — | — | R | — | 1 |
| 6 | R | R | R | — | R | 1 | 5 |
| Total | | | | | | 1 | 45 |

Discussion

The FTA-ABS test on the group of sera from yaws areas showed an agreement with the TPI test of 91.9 per cent. This compares favourably with its performance in problem sera being tested for syphilis, where results were also related to the TPI test; an agreement of 92.7 per cent. has been reported by Johnston and Wilkinson (1968) and of 95.1 per cent. by Garner and others (1968).

The sensitivity of the FTA-ABS test in relation to the TPI test in our group of sera being tested for yaws was 96.0 per cent. This also compares favourably with the 96.4 per cent. reported by Johnston and Wilkinson (1968) in a group of problem sera being tested for syphilis. Thus the sensitivity of the FTA-ABS test is apparently the same in syphilis and yaws. However, the specificity of the FTA-ABS test on the same sera as related to the TPI test was only 82.9 per cent.

Of the 23 sera which were reactive in the TPI and non-reactive in the FTA-ABS test, 22 came from persons who had no clinical signs of yaws. The remaining serum was from a person who had one leg grossly shortened by scar tissue. This serum also gave reactive CWR, VDRL, and RPCF test results. The reactive TPI test results given by these 23 sera indicated that they all came from persons who had or had had yaws. The serological picture presented by the low titre CWR and the VDRL and RPCF test results supported a serological diagnosis of long-standing or 'old' yaws.

There were five sera in which the FTA-ABS test result was reactive with a reading of ++ or greater intensity of fluorescence and the TPI test result was non-reactive; three of these sera were also non-reactive in the reagin and RPCF test results. These three sera were drawn from the following subjects:

- (1) A child who showed no clinical signs of yaws but who lived in a village where there were other children who showed serological evidence of yaws, but no clinical signs;
- (2) An adult who showed no clinical signs of infection but lived in a group where one-sixth of the population had clinical yaws, but no active lesions;
- (3) An adult who showed no clinical signs of infection but lived in an area with a high prevalence of yaws.

These three persons had obviously all been exposed at some time to yaws. It can easily be argued that the child probably has an early infection and that the two adults were 'old' cases of yaws, in which the immobilizing antibody is absent as it is in a minority of cases of long-standing syphilis (Johnston and Wilkinson, 1968), along with a natural decrease in reagin and group antibody. However, as Rathlev (1968) pointed out, it is extremely unwise to make a diagnosis of treponemal infection on the result of one serological test only, especially the FTA-ABS test, in the absence of clinical signs of infection in the individual. Thus no definite conclusion can be reached on the interpretation of the FTA-ABS test results on these three sera. The remaining two sera which gave reactive results to the FTA-ABS test of ++ or greater intensity of fluorescence and non-

reactive TPI test results, also gave reactive CWR, VDRL, and RPCF test results. One of these sera came from a subject with a tropical ulcer of the ankle and lesions around the knees (? yaws), and the other from a subject who showed no clinical signs of yaws. It seems probable on clinical grounds that the former was an early case of yaws in which the immobilizing antibody was not yet detectable; whether the second was an early or an old case of yaws could not be determined.

Sera from 41 persons gave non-reactive results to the TPI test and reactive readings of + intensity of fluorescence, which held on repeat, to the FTA-ABS test. None of them showed clinical signs of yaws. Király, Jobbágy, and Kováts (1967) showed that Reiter treponemes did not always remove all group antibody from serum. In seventeen sera, reactive to the FTA-ABS test only, the sorbent may not have been completely effective in removing all group antibody, thus accounting for the persistent + intensity of fluorescence in the FTA-ABS test result. In a further fourteen sera, the effectiveness of the sorbent in removing group antibody is also in question, as these sera gave reactive RPCF test results as well as a persistent + FTA-ABS test result. Of the remaining ten sera in the group, six were reactive in one or both reagin detection tests and four were reactive in both reagin tests and the RPCF test. On serological grounds and in view of the absence of clinical signs of yaws, these results may well have been falsely positive, but no definite conclusion could be reached in this regard.

The main problem encountered in this survey was that of sera showing a persistent + intensity of fluorescence in the FTA-ABS test and a non-reactive TPI test result, in the absence of clinical signs of yaws. Of the 556 sera which gave both reactive TPI and FTA-ABS test results, 210 were found to give a + intensity of fluorescence in the FTA-ABS test. Thus, the level at which a FTA-ABS test result was considered to be reactive could not be upgraded to a ++ intensity of fluorescence.

Our results leave the impression that more needs to be known about the FTA-ABS test in yaws, especially when unsupported by the TPI test result and when there are no clinical signs of infection, past or present. The interpretation of isolated reactive FTA-ABS test results, especially those showing + intensity of fluorescence, might possibly be clarified if a sorbent containing an extract of other treponemes as well as the Reiter treponeme were available.

Summary

The results of the FTA-ABS test were compared with those of the TPI test on sera from 848 persons living

in areas where yaws is a common treponemal infection. The results of the two tests agreed in 91.9 per cent. of the sera.

The sensitivity of the FTA-ABS test in relation to the TPI test was 96.0 per cent. and the specificity 82.9 per cent.

In 69 sera (8.1 per cent.) the results of the FTA-ABS and TPI tests did not agree. These are discussed in detail.

It is felt that more information is required about the FTA-ABS test in yaws, especially because in many areas its results will have to be interpreted without the support of a TPI test and probably without a very comprehensive clinical picture of the patient.

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L'épreuve de l'anticorps fluorescent tréponémique avec absorption (FTA-ABS) dans le pian

SOMMAIRE

Les résultats du FTA-ABS ont été comparés à ceux du TPI sur le sérum de 848 sujets vivants dans des régions où le pian est une infection tréponémique commune. Les résultats des deux épreuves furent concordants pour 91,9 % des sérums.

Par rapport au TPI, la sensibilité du FTA-ABS fut de 96,0 % et sa spécificité de 82,9 %.

Les résultats du FTA et du TPI furent en désaccord pour 69 sérums. Ces cas sont discutés en détails.

On considère qu'une meilleure information est requise sur le FTA-ABS dans le pian, particulièrement parce que, dans beaucoup de régions, ses résultats devront être interprétés sans le soutien de l'épreuve TPI et probablement sans que l'on dispose d'une observation clinique complète du malade.