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THE FLUORESCENT TREPONEMAL ANTIBODY-ABSORPTION TEST (FTA-ABS) IN TREATED LATENT AND LATE SYPHILIS

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Since Hunter *et al.* (7) introduced the FTA-ABS test in 1964, several authors (1, 2, 4, 6, 9, 17) have stressed the high sensitivity of the test in all categories of syphilis. However, the patients on which the evaluations of the FTA-ABS test in old syphilis have been based, have, with few exceptions, not been clearly defined as to the actual type and stage of the late disease, obviously because the studies have been performed on the basis of laboratory material with insufficient clinical data being available. Likewise, some of the reports provide no information as to whether the patients had been treated or not—which is essential—. It has, therefore, been considered most important from a scientific viewpoint to evaluate the sensitivity of the test in relation to a clinically well-documented series of old treated syphilis and to compare the results with those of other treponemal and nontreponemal tests.

Material and Methods

Our material consisted of 163 clinically well examined syphilitic cases (23 males and 140 females), 59 of whom had been treated for latent syphilis, 95 for neurosyphilis and nine for late benign syphilis. In addition to positive reagin tests (STS) for syphilis before treatment, the following diagnostic criteria were fulfilled:

In 29 cases of latent syphilis the diagnosis was based on the presence of infectious syphilis in the partner. In the remaining 30 patients (all females) the diagnosis was verified by congenital syphilis of their children. Six patients still had distinct scars after the primary lesion and five after condylomas. In all but six cases the cerebrospinal fluid had been examined to exclude neurosyphilis.

The 95 cases of neurosyphilis had before treatment, a positive Wassermann and/or Cholesterol-Wassermann test in the cerebrospinal fluid. These old-fashioned tests are rather insensitive, and a positive test result in the cerebrospinal fluid is therefore highly indicative of neurosyphilis (see 5, p. 24). The neurosyphilis was asymptomatic in 60 cases and of meningovascular type in 17 cases; tabes was present in 10 cases and paralytic dementia in eight cases. Of the patients with tabes two had additionally atrophy of the optic nerve.

All the nine cases diagnosed as late benign syphilis had had gummatous skin lesions before treatment.

All the patients—except seven treated with heavy metal therapy and/or induced malaria—had been treated with longacting PAM (procain-penicillin in oil with aluminium monostearate). The total dosage varied in the majority of the cases between 6.0 and 12.0 mega-units procain-penicillin. In 18 cases the dosage was lower and in 19 cases higher. Before treatment with penicillin 67 of the patients had received heavy metal therapy and 22 had been treated with induced malaria. All patients who had received less than 6.0 mega-units of penicillin

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belonged to this group. The majority of the patients with latent syphilis had not received antisyphilitic therapy before in late latency.

Until this restudy the average post-treatment period was 16 years for patients with treated latent syphilis, 12 years for patients with treated neurosyphilis, and 10 years for patients with treated late benign syphilis.

The average age of the patients in this restudy was 47 years in the group with latent syphilis as well as in the group with neurosyphilis, and 59 years in the group with late benign syphilis.

Serological Tests

Comparative testing of all sera consisted of the FTA-ABS test, the Reiter Protein Complement-Fixation (RPCF) test, the Kolmer Complement-Fixation test, and the VDRL slide test. In addition the TPI test was carried out in 148 cases. The RPCF, Kolmer and VDRL tests were performed according to the 1959 Manual of serological tests for syphilis (18).

The FTA-ABS test was carried out at the State Serum Institute, Helsinki,[1] according to the provisional technique published in 1965 by the USPHS Venereal Disease Research Laboratory (16). The fluorescein-tagged antiserum used in the test recognized the immunoglobulins gamma-G, gamma-M and gamma-A.[2] The reaction was visualized with a Reichert ultraviolet microscope equipped with a HBO-200 mercury lamp and appropriate filters. Intensity of fluorescense was estimated, using a scale from — to 4+. A fluorescense of 1+ was recorded as positive. If the serum was doubtfully positive or negative, the test was always repeated. A repeatedly doubtful positive serum was recorded as negative. A 1+ serum was used as a control.

The TPI test was in 110 cases performed at the State Serum Institute, Helsinki,[1] and in 38 cases at the State Serum Institute, Copenhagen. At the State Serum Institute, Helsinki, the techniques of Nelson and Mayer (14) and Nelson and Diesenbruck (13) were used. The test was carried out twice on each serum sample. If there was great discrepancy between the results, the test was performed once more. A 20 per cent immobilization on at least two occasions was regarded as positive.

At the State Serum Institute, Copenhagen, the TPI test was performed according to the technique described by Nielsen (15), subsequently modified, however, so that complement : serum : treponema suspension was used in the ratio 40 : 10 : 50.

Results

The test results in the groups with latent syphilis or neurosyphilis are presented in Fig. 1 and the FTA-ABS and TPI test results in the 148 TPI-tested cases in Table 1. FTA-ABS positivity and TPI negativity was shown by one of 19 males and by 14 of 129 females. Four of them had not received penicillin treatment at all and five less than 6.0 mega-units, the main treatment consisting of heavy metal therapy and/or induced malaria.

Treated Latent Syphilis

The FTA-ABS test was positive in 54 out of 59 cases, i.e. 92 %. The corresponding figure for the TPI test was 81 %, for the RPCF test 69 %, for the Kolmer test 58 % and for the VDRL test 54 %. In 10 cases the FTA-ABS test gave a positive result although RPCF and the two reagin tests were negative. These 10 sera were all subjected to the TPI test, which was positive in six and negative in four cases. These four patients had received antisyphilitic treatment already in early latency, but the length of the post-treatment period did not particularly differ from the average in the group with latent syphilis.

Two of the five FTA-ABS negative cases, treated 16 and 19 years previously, were negative in all tests including TPI. Of the other three, two were positive in TPI and RPCF, the third one being negative in TPI, although positive in RPCF and the reagin tests. All these five patients had been treated already in early latency.

Treated Neurosyphilis

Ninety-one of the 95 cases treated for neurosyphilis were positive in the FTA-

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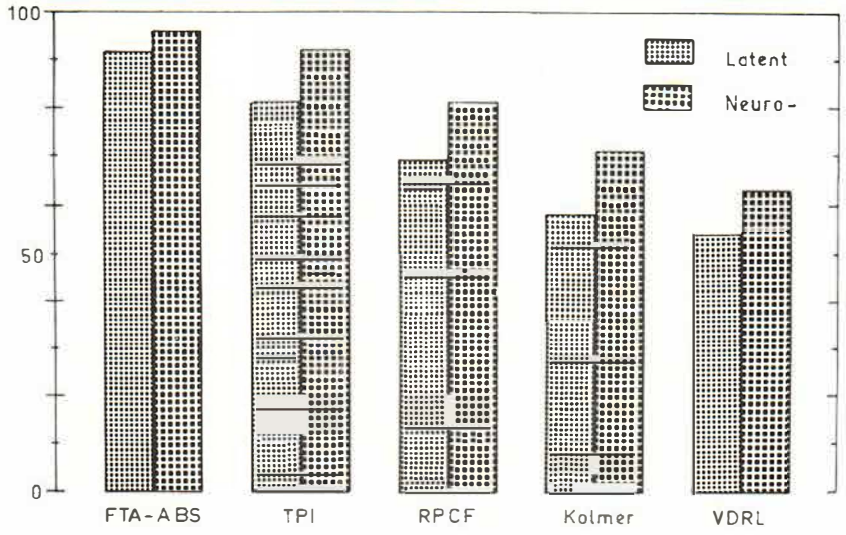
[2] The antigen was obtained partly from the Difco Laboratories and partly from the Sylvana Company, Millburn, New Jersey. The sorbent was obtained from the Difco Laboratories.



PERCENTAGE OF POSITIVE TEST RESULTS IN 59 CASES OF TREATED LATENT SYPHILIS AND 95 CASES OF TREATED NEUROSYPHILIS.

Table 1. *Results of the FTA-ABS and TPI tests in 129 females and 19 males with treated latent or late syphilis*

Stage	FTA—ABS+ TPI+	FTA—ABS+ TPI—	FTA—ABS— TPI+	FTA—ABS— TPI—	Total
Females					
latent syphilis	45	7	2	3	57
late benign s.	5	1	–	–	6
neurosyphilis	57	6	2	1	66
Males					
latent syphilis	–	1	–	–	1
late benign s.	3	–	–	–	3
neurosyphilis	15	–	–	–	15
Total	125	15	4	4	148

ABS test. This represents 96 % of the series. The TPI test was positive in 91 %, the RPCF test in 81 %, the Kolmer test in 71 % and the VDRL slide test in 63 % of the cases. Seven of the FTA-ABS positive patients were negative in both the RPCF test and the reagin tests. Of these three were positive and three negative in the TPI test. The test was not performed in one case.

Of the four FTA-ABS negative patients, three belonged to the asymptomatic (60 cases) and one to the symptomatic group (35 cases). Two of the patients were positive in the RPCF test although negative in the reagin tests. One of the RPCF-positive patients was subjected to the TPI test, which gave a positive result. Of the two remaining cases one was positive in the TPI and the Kolmer test whereas the other one was negative in all tests including TPI. This patient, a woman aged 49, had been treated with 9 mega-units of penicillin 11 years prior to the restudy.

Treated Late Benign Syphilis

All nine cases were positive in the FTA-ABS test. One of them, a woman aged 61 and treated 29 years previously, was negative in all other tests including TPI. The remaining eight cases were all positive in the TPI test. Four patients were negative in the RPCF test and two in the VDRL and the Kolmer test, each.

Discussion

Our results indicate that the FTA-ABS test is highly sensitive also in old treated cases of syphilis. In each of the three categories of syphilis considered in this restudy the FTA-ABS test showed a higher sensitivity than the other treponemal (TPI and RPCF) and the nontreponemal (VDRL and Kolmer) tests.

The FTA-ABS test gave a positive result in 92 % of the patients with treated latent syphilis. This is in conformity with the report by Knox *et al.* (9), who in a corresponding series found a sensitivity of 91 %. Bradford *et al.* (2) and Deacon *et al.* (4) found a slightly higher sensitivity, 93.5–94 %.

Several authors (1, 2, 3, 4, 6, 20) have investigated the sensitivity of the FTA-ABS test in late syphilis, in which also cases of neurosyphilis are included. Data regarding the sensitivity of the FTA-ABS test in neurosyphilis separately, has hitherto been given only by one of us (10). The results were based on a series of 56 treated neurosyphilitic cases, 93 % of whom were positive in the FTA-ABS test. In the present study the FTA-ABS test revealed a sensitivity of 96 %. The small difference in sensitivity is probably due to differences in the diagnostic criterias used in the two studies.

The series of cases with treated gummatous syphilis was small. However, in this group also, the sensitivity of the FTA-ABS test was superior to that of the TPI, the RPCF, and the reagin tests.

A total of 18 patients included in this study were positive in the FTA-ABS test although negative in the RPCF and the reagin tests. Sera from 17 of these were subjected to the TPI test, which gave a negative result in eight cases, originating equally from all diagnostic categories included in this study, i.e. also from the neurosyphilitic group. Of 148 TPI-tested cases not less than 15 showed FTA-ABS positivity and TPI negativity.

It may be asked: Is the high sensitivity of the FTA-ABS test achieved at the expense of its specificity? As the present health status of the patients was known only in a few number of cases, it cannot be excluded that some of them may have developed diseases of autoimmune or infectious origin subsequent to their syphilis and causing antibody production not related to treponemes. If proportionally more women than men were FTA-ABS positive and TPI negative, this should support the assumption that the FTA-ABS is not always positive because it is very sensitive but because it is nonspecific. Depending on the selection of the series, the study does not, however, allow any conclusions in this regard. Most of the patients were namely syphilitic mothers treated at the Kumpula State Hospital in the years after the Second World War, and the number of male patients was small. In our opinion, however, the positive result in the FTA-ABS test is more likely to be true than the negative result in the TPI test.

In four of the 148 TPI-tested cases the result in the TPI test was negative although the serum gave a positive result in one or both of the reagin tests, and in two of these patients the FTA-ABS test was positive. If the specificity of the FTA-ABS test in the future will be definitely settled, the test could serve as a valuable supplement to the TPI test in differentiating BFP reactions from syphilis. As a negative TPI test and positive reagin tests, a pattern usually interpreted as a BFP reaction, are not so unusual in successfully treated old syphilis, such a supplement to TPI would reduce the BFP series reported by several authors (see 11, 19).

The FTA-ABS test gave a negative result in nine cases, four of whom belonged to the neurosyphilis group. Of the nine cases, three were negative in all tests performed,

whereas of the remaining six cases five were positive in the RPCF, and four in the TPI test, but which was not performed in one case. In addition, two of the patients were positive in one or both of the reagin tests. The negative result in the FTA-ABS test can perhaps be explained by technical errors because even though the sera in question were retested with the same result, the same batch of antigen was used. It is improbable that these cases were falsely TPI and/or RPCF positive, especially as clinical and laboratory examination revealed no symptoms of autoimmune disease.

This study suggests that no treponemal test is infallible in old treated syphilis. However, the high sensitivity of the FTA-ABS test—providing that the specificity of the test proves to be of the same order (see 8, 12)—justifies its use as a confirmatory test for syphilis. In FTA-ABS negative but reagin positive cases the further use of the TPI and RPCF tests is recommended, since even if the RPCF test is relatively insensitive in cases with old syphilis, it sometimes detects treponemal antibodies in cases where the TPI and FTA-ABS tests fail (5). The battery of three treponemal tests will make the diagnosis of BFP more certain than the use of a single treponemal test. However, it must be borne in mind that even such a battery of treponemal tests may fail in persistently STS-positive cases of old treated syphilis (see 10).

SUMMARY

The authors studied the sensitivity of the FTA-ABS test in old treated syphilis and compared it with that of other treponemal and nontreponemal tests.

The series consisted of 163 clinically well-documented cases, 59 of whom had been treated for latent syphilis, 95 for neurosyphilis, and nine for late benign syphilis. All except seven had been treated with longacting penicillin PAM. The average post-treatment period varied in the different diagnostic categories from 10 to 16 years. Comparative testing consisted of the FTA-ABS test, the Reiter Protein Complement-Fixation (RPCF) test, the Kolmer Complement-Fixation test and the VDRL slide test. In addition, the TPI test was carried out in 148 cases.

In all diagnostic categories studied the sensitivity of the FTA-ABS test was higher than that of the other tests performed. It reached, in the latent group 92 % and in the neurosyphilis group 96 %. The corresponding figures for the TPI test were 81 and 91 %, respectively. In 18 cases the FTA-ABS test gave a positive result although the RPCF and the reagin tests were negative and in eight of these cases the TPI test was also negative. On the other hand, the FTA-ABS test was negative in nine cases, six of whom showed reactivity in some of the other tests performed.

It is concluded, that the high sensitivity of the FTA-ABS test justifies its use as a confirmatory test for syphilis provided the specificity proves to be of the same order. In FTA-ABS negative but reagin positive cases the further use of the TPI and RPCF tests is recommended.

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