

## FALSE-POSITIVE SEROLOGICAL TESTS FOR SYPHILIS IN PREGNANCY

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Chronic biologic false-positive serological reactions (BFP) for syphilis are observed frequently in the so-called collagen diseases, especially in systemic lupus erythematosus (SLE). It has also been observed that BFP reactions can precede the development of manifest SLE by many years (7). A special risk group is formed by young women. Harvey (6), for instance, found only one male among the 31 patients who during follow-up developed SLE or in whom this disease was suspected. A good means of collecting a series of women at risk of SLE is to study women attending antenatal clinics. This source probably forms the most unbiased group that elucidates the significance of the BFP reactions as a warning sign of future development of SLE or of other autoimmune disorders.

In Finland practically all pregnant women are examined at antenatal clinics and the serological tests are performed in a few laboratory centres only. This communication reports the results of the antenatal serological screening performed during 1963-1967 at the State Serum Institute, Helsinki.

### Material and Methods

During the years 1963-1967 a total of 141,043 sera from pregnant women were examined at the State Serum Institute, Helsinki. The blood samples were taken at the antenatal clinics before the beginning of the fourth month of pregnancy. One blood sample was taken during each pregnancy unless the first sample gave a reactive re-

sult in the VDRL slide-flocculation test which was used as the screening procedure. A reactive serological result has been included in the calculations only once during each pregnancy. The reactive results obtained as controls for reactive sera examined in 1962 have been excluded.

A questionnaire on possible syphilitic infection, the basis for diagnosis, the duration of the disease and treatment as well as other diseases during pregnancy was sent to the clinicians for every seroreactive patient.

Facilities for TPI testing were available during the entire study period. The TPI test was performed only at the request of the examining doctor and involved 104 sera. These requests were as frequent in cases with known syphilis as in cases in which no information about syphilis was available. The FTA-ABS test was available for routine use from June 1966. After this date all VDRL reactive sera sent for treponemal tests were examined with both TPI and FTA-ABS tests. The treponemal antibody tests were requested more frequently in 1966 and 1967 than in previous years. Deep-frozen sera were available for 29 of the TPI non-reactive sera taken during 1963-1966. These were also checked with the FTA-ABS test.

The TPI test was carried out by the techniques of Nelson and Mayer (10) and Nelson and Diesendruck (9) with minor modifications. The FTA-ABS test was performed according to the provisional technique of the Venereal Disease Laboratory

Table 1. Results of the VDRL-screening of 141,043 sera in the study period 1963-1967

Year of study	Number of sera examined	VDRL reactive pregnant women	
		Number	per thousand
1963	26,181	62	2.37
1964	28,506	57	2.00
1965	28,286	51	1.80
1966	29,170	26	0.89
1967	28,900	36	1.25
Total	141,043	232	1.64

Table 2. Information about syphilis and the results of the treponemal antibody tests in pregnant women

Information about syphilis	Number of cases	Tests for treponemal antibodies Reactive/Performed
Congenital syphilis	74	26/26*
Recent acquired syphilis	16	7/8**
Previous diagnosis and treatment of acquired syphilis	16	6/6
Reactive serology in the husband	2	0/0
Total	108	39/40

\* In two cases the TPI test was non-reactive and the FTA-ABS test reactive.

\*\* In one case of primary syphilis both the TPI and FTA-ABS tests were non-reactive and in another the TPI test was non-reactive and the FTA-ABS test reactive.

of the Communicable Disease Center, USPHS, Atlanta, Georgia (1965). The VDRL test was performed according to standard technique (12) and using Sitolipin antigen (13).

## Results

The number of sera tested in each year of the study and the frequency of reactive sera are presented in Table 1. There were altogether 232 cases reactive in the VDRL test. The mean frequency of reactive sera during the study period was 1.64 per thousand. In seven instances a reactive re-

sult was obtained during two successive pregnancies.

A total of 108 of the 232 patients had a history of present or past syphilis. This information together with the results of the treponemal antibody tests are presented in Table 2. There were altogether 16 cases of recent syphilis. Not a single case of recent syphilis was diagnosed in 1963. The four following years revealed four, seven, three and two cases, respectively. These fluctuations may be seen in relation to the total number of new cases reported in Finland during the same period. Both groups of figures had their peaks in 1965.

Tests for treponemal antibodies were performed in 40 cases with clinically diagnosed syphilis or in 38 per cent of the series with information about syphilis. The TPI test was reactive in 24 out of 26 cases of congenital syphilis, in all six cases of old acquired syphilis and in six out of eight cases of recent syphilis. The FTA-ABS test was reactive in one case of primary syphilis and in both cases of congenital syphilis, non-reactive in the TPI test.

There were altogether 124 VDRL reactive cases in whom no information about syphilis was available. In thirteen cases, or 10 per cent, the reactivity of the VDRL tests was of proven transient nature (Figure 1). Among the thirteen patients with proven transiently reactive VDRL test, there was one case in which the reactive VDRL test was observed during two successive pregnancies and two non-reactive results were obtained between the pregnancies. This patient had a reactive TPI test and for this reason was believed to have in the past had either congenital or acquired syphilis.

In Figure 1, the patients in whom the treponemal antibody tests were performed are treated separately from those not examined by these tests. Fifty-nine of the 64 cases in which the treponemal antibody tests were performed had presumably chronic reactive VDRL test. Thirty-one of these were reactive and 28 non-reactive in the treponemal antibody tests. The data from the group in which the treponemal antibody tests were performed were used

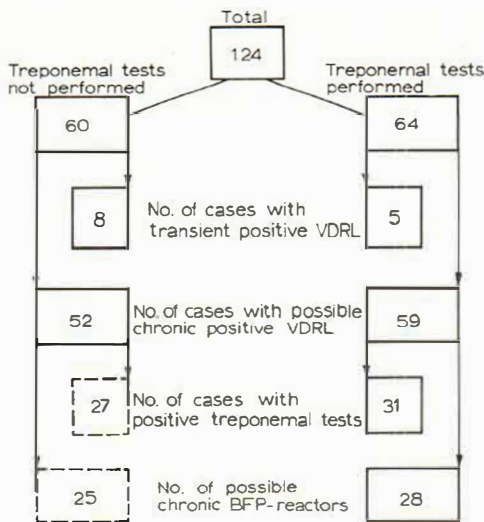


Fig. 1. Results of treponemal antibody tests in pregnant women with no information about syphilis. (Figures surrounded by dotted lines are calculated on the basis of the findings in the group in which the treponemal tests were performed.)

to calculate the probable numbers of patients with syphilitic and false-positive reactions in the group which was not examined by these tests. Among the 52 cases with presumably chronic reactive VDRL test and not examined by the treponemal antibody tests the calculated figures for syphilitic and false-positive cases were 27 and 25, respectively.

Thus among the 124 VDRL reactive cases with no information about syphilis there were altogether 65 patients with probable transient or chronic BFP reactions. In the entire series of 232 positive reactors this amounts to 28 per cent.

### Discussion

In the present study there were 232 positive reactors in the VDRL test. This corresponds to 1.64 per thousand of the subjects. The variation for different years was from 0.89 to 2.37 per thousand. These figures are only about one tenth of those obtained in 1935-1945 by Penttinen (11) and slight-

ly lower than those reported by the Chief Medical Officer for 1955 (5) and Loc (8).

The proportion of false-positive results varies greatly in different studies and depends on the frequency of syphilis in the population under study. Boak *et al.* (1) reported that 73 per cent of the reactive STS results found in pregnant women were false-positive. On the other hand, Wilkinson and Sequeira (14), the British Co-operative Clinical Group (2) and Eng (4) give figures between 18.6 and 27.5 per cent for false-positivity.

In the above studies the distinction between syphilitic and false-positive results has been made on the basis of the available clinical information and the TPI test. However, it is also believed that the TPI test can be non-reactive in old treated syphilis (3). This means that some of the patients with reactions considered on the basis of a non-reactive TPI tests as false-positive can still have had syphilis.

The FTA-ABS test is reported to be more sensitive than the TPI test (3). In the present series there were nine cases in which the TPI test was non-reactive and the FTA-ABS test reactive. One of these patients had early primary syphilis, two had been treated for congenital syphilis and in the remaining six cases no information about syphilis was obtained. The specificity of the FTA-ABS test has not yet been fully appraised, but on the basis of knowledge available it cannot be excluded in the present study that the majority of cases with a reactive FTA-ABS test and a non-reactive TPI test had had syphilis.

In the present series 28 per cent of the reactive VDRL results in pregnant women were probably false-positive. The follow-up of these women will show if they have a greater danger of developing systemic lupus erythematosus than women who do not show biological false-positive reactions during pregnancy.

### SUMMARY

Reactive serological tests for syphilis were studied in a series of 141,043 sera from pregnant women examined during 1963-

1967 at the State Serum Institute, Helsinki.

There were altogether 232 women who had a reactive VDRL test during pregnancy. Clinical information and treponemal antibody tests revealed that 28 per cent of these or 0.46 per thousand examined pregnant women probably had false-positive VDRL results, either transient or persistent.

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