SEROLOGICAL TESTS IN LONG-STANDING CONGENITAL SYPHILIS*

A CASE OF LONG-STANDING CONGENITAL SYPHILIS WITH ONLY TRACES OF
ANTIBODIES IN BOTH THE STANDARD TESTS FOR SYPHILIS (STS) AND THE
TREPONEMA PALLIDUM IMMOBILIZATION TEST (TPI)

BY

JAN ENG

State Institute of Public Health, Sero-diagnostic Department, Oslo, Norway (Director: Otto Hartmann, M.D.)

The TPI test is able to distinguish between specific and non-specific reactions to STS because it is a highly specific test for syphilis and because, in patients with late syphilis, it usually remains clearly positive for a long time after the STS have become completely negative. An exception to the latter rule is reported below.

Previous reports of cases of late syphilis with reactive STS and negative TPI stem chiefly from France. Alline and Béranger (1957) and Rabut (1952) reported small groups of such patients as parts of large series of TPI-tested individuals. These authors did not report the findings upon which the diagnosis of syphilis was founded. The cases described by Roulin and Baelden (1957) included five of TPI-negative late syphilis which gave positive or doubtful reactions with a new complement-fixation test using cardiolipin antigen. All these cases, however, gave completely negative results with all the other STS employed (Kahn, V.D.R.L., Debains, Kolmer). Bolgert and Lévy (1952) reported a series including one tabetic whose blood gave a positive Wassermann reaction and a doubtful negative result to the TPI test (20 per cent. specific immobilization). The authors did not state why the tabes was considered syphilitic in this case. Joulia, Le Coulant, Texier, and Fruchard (1955) described a case of tertiary syphilis (having gumma of the palate and ulcerous-tubercular syphilides which were healed by penicillin therapy) with strongly positive STS and a positive Pallignost test; the TPI test was negative in one blood sample and doubtful to negative in another. Sausse, Borel, Louis, and Pierre (1952) recorded two cases of sero-positive primary syphilis

which became sero-negative after treatment; later on the STS again became positive whilst the TPI remained negative. The same phenomenon, sero-relapse confined to STS, was also described by Delacrétaz (1956) and Périn and Hérrmann-Fournier (1957). The latter authors mentioned the possibility of false positive STS superimposed upon a long-established syphilitic infection.

Because so few reports can be traced in the literature of indubitable cases of late syphilis with the serological pattern under consideration, we feel that the case recorded below merits attention.

Case Report

A woman born in 1898 had been in hospital several times suffering from congenital syphilis, sinusitis, ischialgia, torticollis, and hysteria. She was admitted to Ullevål Hospital, Medical Department VIII, in 1932, when an ophthalmologist observed a slight, diffuse opacity in both corneae, with numerous small opacities in the subcapsular layer of the lenses, several heavily pigmented scars at the periphery of each choroid, and two white scars in the left choroid. Keratitis and long-standing peripheral choroiditis were diagnosed and the ophthalmologist stated that all these pathological changes might be accounted for by congenital syphilis. The patient stated that her sister suffered from a similar type of eye disease.

Two small perforations were seen in the soft palate, and the palatine arch and the fauces were greatly scarred. She had a dental prosthesis in the upper jaw.

Previous blood samples had been examined at the Laboratory of Pathology, Ullevål Hospital in 1932, 1935, 1937, and 1944; all four samples gave a positive Meinicke test, a negative Wassermann reaction and a negative Kahn test.

In 1932 and 1933 the patient received seven injections of bismuth subcarbonate, two of bismuth tartrate, four

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of neosalvarsan and an unspecified amount of potassium iodide. None of the available records yielded any information about additional treatment.

Present Serological Investigations

Methods

STS Technique.—The three following routine tests were used:

- (1) *Bordet - Wassermann Complement - Fixation Test (WaR)* (cardiolipin-lecithin-cholesterol-antigen).
- (2) *Meinicke Clarification Test II (MKR)* (cardiolipin-lecithin-balsam of Tolu-antigen).
- (3) *Wadsworth and Brown's Flocculation Test (W-Br)* (crude beef heart antigen, Wadsworth and Brown, 1936). From Jan. 1, 1959 this was replaced by the V.D.R.L. slide flocculation test (cardiolipin-lecithin-cholesterol-antigen).

All sera were examined with qualitative WaR and MKR, and the reactive sera were re-tested quantitatively.

TPI Technique.—The test-tube contained 0.05 ml. patient's serum, 0.2 ml. undiluted pooled guinea-pig serum, 0.25 ml. *Treponema pallidum* suspension. The WHO III (WHO Reference Pool No. III for TPI test) was tested quantitatively on each testing day. The titres for WHO III usually varied from 320 to 686.

Results

Four blood samples were examined between June, 1958, and January, 1959 (Table).

Samples No. 1 and 3 were completely STS-negative, Nos. 2 and 4 gave a very weak positive MKR, and No. 2 also gave a weak positive W-Br.

Three of the samples (Nos. 1, 3, and 4) were TPI-tested on separate testing days. Nos. 1 and 4

were weakly reactive with the TPI and in No. 3 the TPI was negative. No. 3 was examined on testing days with a relatively low sensitivity of the TPI test (see titres for WHO III in the Table), but unfortunately it contained so little serum that it could not be TPI-tested simultaneously with the other samples.

Samples No. 1 and 4 were tested ten times altogether; in only one instance were all the treponemes immobilized, the remaining nine examinations showing only partial immobilization, *P* varying from 26 to 80 (average 53).

The presence of residual complement was checked by means of sensitized sheep cells after each examination. No anticomplementary activity was demonstrated in any of the three sera.

Discussion and Conclusions

Had the patient congenital syphilis?

She presented three signs which made the diagnosis exceedingly probable:

- (1) Keratitis and long-standing peripheral choroiditis.
- (2) Reactive MKR observed several times during 27 years.
- (3) Weak, but certainly reactive, TPI tests.

Were the present weak positive STS results due to technical errors?

A weak positive MKR was found in two MKR-tested blood samples; each of them were TPI-tested twice (qualitatively and quantitatively) with concordant results. One sample gave a positive W-Br as well. It is therefore certain that the patient's blood contained reagins.

Were the TPI results due to technical errors?

The patient gave negative TPI tests when

TABLE
SEROLOGICAL RESULTS IN FOUR BLOOD SAMPLES FROM A 60-YEAR-OLD WOMAN WITH CONGENITAL SYPHILIS

Serum Sample No.	Standard Tests for Syphilis				Treponema pallidum Immobilization Test (Dates)								
	Dates	WaR	MKR	W-Br	6.6.58	17.6.58	15.12.58	18.12.58	13.1.59	16.1.59	3.2.59	11.2.59	13.2.59
1	5. 6.58	—	—	—	P = 26 ±	P = 100 +					P = 33 ±	P = 44 ±	P = 64 +
2	19.11.58	—	Titre 1	+									
3	24.11.58	—	—	Not readable			a = 84 —	a = 92 —					
4	10. 1.59	—	Titre 1	V.D.R.L. —					P = 73 +	P = 80 +	P = 56 +	P = 52 +	P = 52 +
Titre for WHO Control Serum III→					520	453	Irregular	226	Irregular	640	422	597	640

WaR = Bordet-Wassermann complement-fixation test
MKR = Meinicke clarification test II
W-Br = Wadsworth and Brown flocculation test

P = Per cent. treponemes specifically immobilized
a = Per cent. motile treponemes in the test-tube

examined in a period of lowered sensitivity of the test. The titre for WHO III then observed was 226. This figure ranks among the lowest titres ever seen in this laboratory, but it approximates to the average titres for many other laboratories, and our average titre for WHO III is considered to be remarkably high (Krag, 1958). Our immobilization curves for WHO III show that Sample No. 1 (the result obtained on 17.6.1958 being ignored) and Sample No. 4 had the same reactivity as WHO III diluted from 1:394 to 1:686, and that WHO III in these dilutions gave a negative TPI result on 18.12.1958. The results agree well with the assumption that the variation in the sensitivity of the TPI test was the chief reason for the fluctuation of the TPI results between $-$, $\pm$, and $+$. But the reason why the patient was first non-reactive and then weakly reactive with the TPI was *not* that the sensitivity of the test was too low or that the sera possessed anti-complementary properties. The patient's blood actually contained only small amounts of immobilisin, which could only be detected by means of a sensitive TPI technique.

Were the present weak positive STS results false positive reactions?

This eventuality cannot be entirely excluded but it does not seem very probable. The STS pattern presented by this patient is, in our experience, typical for some cases of late syphilis. Eng and Kornstad (1959) examined twelve blood donors showing the same STS pattern (persistent, very weak

positive MKR-reactions alternating with quite negative ones); eight of the twelve were TPI-positive.

It is easily seen that, if only Samples No. 2 and 3 had been examined (*e.g.* as a part of routine serological screening) and the clinical signs of syphilis presented by the patient had been unknown, the positive STS would have been regarded as non-specific.

More research is required to establish the frequency of exceptions to the rule that the sensitivity of TPI is far superior to that of STS in patients with late syphilis. Apart from cases of primary syphilis, positive STS in conjunction with negative TPI are very probably false positive reactions; but they may occur in congenital syphilis as shown by the case reported above.

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