A NOTE ON THE COURSE OF REAGIN TITRES IN CHRONIC BIOLOGIC FALSE POSITIVE REACTORS*

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It is well known that some sera giving false positive reactions with the standard serological tests for syphilis (STS) show a pattern which is very seldom found in syphilitic sera, while in other falsely reacting sera the strength or pattern of the STS give no clue to specificity. Less attention seems to have been paid to the *course* of the STS titres in chronic positive STS reactors who are negative with the *Treponema pallidum* Immobilization Test (TPI).

Material

Eleven patients fulfilling the three criteria listed below have been examined in this laboratory.

- (1) Positive STS observed for 2 years or more.
- (2) One or more negative TPI tests.
- (3) No clinical signs or history of syphilis.

Two of these patients (Cases 3 and 7) are included in a study of pregnant women (Eng, 1959).

Methods

The following two quantitative STS were used as a routine:

- (1) Bordet - Wassermann Complement - Fixation Test (WaR) (cardiolipin-lecithin-cholesterol-antigen).
- (2) Meinicke Clarification Test II (MKR) (cardiolipin-lecithin-balsam of Tolu-antigen).

Technique for WaR Titration.—First tube serum dilution 1:5 (diluent: saline), and further doubling dilutions for each successive tube. Each tube given a titration score according to the degree of haemolysis (4 = complete inhibition of haemolysis, 0 = complete haemolysis).

Technique for MKR Titration.—First tube serum undiluted, second tube dilution 1:2 (diluent: pooled MKR-negative serum), and then doubling dilutions as for WaR. Each tube given a titration score according to the degree of

clarification (4 = complete clarification, 0 = no clarification). For both reactions the titre value is given as the sum of the titration scores; the titre value thus runs roughly parallel to the logarithm of the reagin content in the serum.

The WaR or MKR titres of a patient are said to be constant if the difference between the highest and the lowest titre value observed is two whole dilution-steps or less, *i.e.* less than nine.

Results

The material is briefly presented in Table I (opposite). The maximum observation time was 8 years, the minimum 2 years. One patient had an increasing, and one a falling WaR titre, and in six the WaR titre was constant. Two patients had negative WaR tests in all samples, and in one patient the course of the WaR titre was indefinable because of repeated zone phenomena.

Three patients had increasing MKR titres and in five the MKR titres were constant.

In three patients all the specimens were positive in the WaR *only*, reactions of this type being, in our experience, nearly always non-specific.

A decreasing titre has thus been found in only one patient. The three patients with increasing MKR titres (Cases 1, 2, and 3) were all found among those observed for the longest time. The MKR titres in these three patients are shown graphically in the Figure (opposite). In all of them the MKR titres have increased despite earlier anti-syphilitic treatment (see below).

Table II (overleaf) illustrates the findings in Cases 2 and 3. The reactions in the first sample from Case 3 had a "non-specific" appearance, but in the last two samples, the STS pattern aroused no suspicion about the specificity, the titres in both tests being high and concordant. (Tests on sera showing "abnormal" STS-patterns like the first one from this patient are

* Received for publication November 4, 1958.

TABLE I

TIME OF OBSERVATION, COURSE OF STS TITRES, AND ANTI-SYPHILITIC TREATMENT IN ELEVEN TPI-NEGATIVE, CHRONIC POSITIVE STS REACTORS

Case No.	Sex	Age (yrs)	Standard Tests for Syphilis				Anti-syphilitic Treatment
			Period of Observation (yrs)	Total No. of Samples	Course of Titres		
					WaR	MKR	
1	F	48	8	10	†	Increasing	One course of penicillin (1950)
2	F	34	8	5	Constant	Increasing	Two combined courses of penicillin and arsphen chloride (1950) One course of penicillin (1953)
3	F	39	7	3	Increasing	Increasing	Two courses of Penicillin (1950 and 1957)
4	F	72	7	2	Constant	Constant	One course of penicillin (1952)
5	F	40	6	6	Constant	Constant	One course of treatment (1952)
6	F	71	6	4	Constant	Negative*	No treatment
7	F	36	5	5	Constant	Constant	Probably no treatment
8	M	51	3	4	Constant	Negative*	No treatment
9	M	51	3	2	Negative*	Constant	No treatment
10	F	29	3	5	Decreasing	Negative*	One course of treatment (1953)
11	M	41	2	6	Negative*	Constant	No treatment

* Negative means that all samples have been negative in the test concerned.

† Titre course difficult to estimate because of zones in several samples.

FIGURE.—Course of titre in Meinicke Clarification Test in three TPI-negative chronic positive STS reactors (Cases 1, 2, and 3). All three received anti-syphilitic treatment in 1950.

TABLE II
COURSE OF STS TITRES IN TWO TPI-NEGATIVE, CHRONIC
POSITIVE STS REACTORS

Case No.	Date	Titre	
		WaR	MKR
2	17. 7.1950	12	3
	25. 7.1950	14	2
	29. 1.1953	11	9
	9. 8.1955	10	8
	23. 1.1958	Serum anti-complementary	20
3	13. 9.1950	8	Negative
	28. 8.1957	19	15
	8.11.1957	16	15

always repeated, to exclude technical errors.) Case 2 displayed a similar tendency, the MKR being significantly weaker than the WaR in the first samples but not in the last ones.

Table I shows that six patients had received anti-syphilitic treatment, all of them early in the observation period, four patients had had no treatment and in one case only scanty information could be obtained (probably no treatment had been given).

A clinical diagnosis was made in five patients:

Case 1: Chronic cystopyelonephritis, anaemia.

Case 2: Rheumatoid arthritis and suspected disseminated lupus erythematosus.

Case 4: Circulatory failure, vascular hypertension, and crural ulcers.

Case 6: Psychosis.

Case 8: Peptic ulcer.

Summary and Conclusions

Although our series of cases is very small, it suggests that many TPI-negative, chronic positive STS reactors differ sharply from syphilitics in the course of the reagin titres. Of eleven reactors observed for 2 years or more, three had clearly increasing titres in the Meinicke Clarification Test, all being among those who had been observed for the longest time (8 and 7 years), and the MKR titres having increased in them all despite earlier anti-syphilitic treatment.

Wilkinson (1954) has reported a case of presumably false positive WaR- and Kahn reactions, in which the titres increased strongly during several years.

If other laboratories would examine the course of the STS titres in such reactors, valuable information should be obtained.

Many chronic biologic false positive STS reactors suffer from a collagen disease (Moore and Lutz, 1955; Miller, Brodey, and Hill, 1957). It is a not unreasonable hypothesis, that in these patients the clinical symptoms and the false positive reactions stem from a common cause. It seems worthwhile to continue the observation of the STS titres in chronic false positive reactors even after the nature of the reactions has been established.

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