EFFECT OF TETRACYCLINE ON THE DURATION OF A RAISED ANTISTREPTOLYSIN-O TITRE IN RHEUMATIC FEVER

BY

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Patients with rheumatic fever may often show prolonged high titres of antistreptolysin-O (ASO) despite a 10-day course of penicillin in bactericidal dosage at the onset. It has been suggested that penicillin used thus in the treatment of rheumatic fever, while eradicating the Group A beta-haemolytic streptococcus, may not affect the L form of streptococcus (a PPLO sensitive to tetracycline) which appears to manufacture streptolysin-O (Freimer, Krause, and McCarty, 1959) and might possibly therefore produce continuing antigenic stimulation even in penicillin-treated hosts.

We therefore decided to compare ASO titres over a period of 6 months in two groups of patients:

- (1) A test group treated for 3 weeks with tetracycline;
- (2) A control group not so treated.

Both groups were given a bactericidal dose of penicillin at outset.

Design of the Trial

Material.—Thirty patients with rheumatic fever, who fulfilled the Rheumatic Fever Committee diagnostic criteria (1957), were admitted to the trial. All cases of chorea and those who had had previous hormone therapy were excluded.

The patients could be of any age, but the duration of the illness from the onset was less than 2 months in all of them. The erythrocyte sedimentation rate was raised above 20 mm./hr (Westergren) in all cases.

The patients were allocated by random selection into two groups, the test group and the control group.

Therapy.—Both groups received the following treatment:

- (1) Benzathine penicillin 1.2 mega units intramuscularly on the first day.
- (2) Oral prophylactic penicillin G 200,000 U. twice daily during the stay in hospital and thereafter.

TABLE I
RESULTS IN THE TWO GROUPS

Group	Case No.	ASO Titre					
		0 wks	3 wks	6 wks	9 wks	3 mths	6 mths
Control	1	200	500	500	< 200	< 200	200
	2	1,250	1,250	500	—	500	333
	3	500	500	200	—	< 200	200
	4	500	200	500	—	200	< 200
	5	1,250	2,500	1,250	333	< 200	200
	6	200	500	200	200	200	200
	7	200	500	500	333	200	200
	8	500	1,250	833	—	—	< 200
	9	500	< 200	500	500	200	500
	10	1,250	833	333	—	200	—
	11	200	500	500	—	—	—
	12	500	500	333	333	—	333
	13	500	500	200	200	200	500
	14	200	500	200	—	200	—
	15	200	200	333	200	—	200
Test	1	500	200	500	500	—	—
	2	2,500	200	500	833	500	200
	3	1,250	200	200	—	200	200
	4	500	200	500	200	500	500
	5	500	1,250	500	200	—	200
	6	1,250	500	500	200	200	200
	7	200	200	200	200	—	333
	8	333	333	200	200	200	—
	9	500	500	500	500	500	200
	10	333	500	333	200	200	—
	11	833	833	1,250	833	500	200
	12	200	200	200	200	—	200
	13	500	—	833	833	200	200
	14	500	500	833	1,250	500	333
	15	333	200	500	—	—	200

TABLE II
COMPARISON OF MEAN ASO TITRES IN CONTROL AND TEST GROUPS

Group	Time of Estimation	0 wks	3 wks	6 wks	9 wks	3 mths	6 mths
Control	Mean ASO Titre* ..	3.6	4.0	3.5	2.5	1.9	2.3
	No. of Cases	15	15	15	8	11	12
Test	Mean ASO Titre* ..	4.0	3.0	3.6	3.3	2.6	1.9
	No. of Cases	15	14	15	13	10	12

* Tubes in the titration series were numbered consecutively from 1 to 6 < 200, 200, etc. Values shown at each interval are mean tube number for each group.

- (3) Becosym 1 tablet three times a day for 21 days.
- (4) Salicylate 60-80 gr. daily for at least 6 weeks or according to the individual needs.

The test group also received:

- (a) 11 years or over: Tetracycline 2 g. daily for 2 days and then 1 g. daily for 19 days.
- (b) 10 years and under: Tetracycline 1 g. daily for 21 days.

Methods.—ASO titres were estimated on admission and then at 3-weekly intervals during the stay in hospital and after discharge for 6 months from the start of the trial. The method instituted in this hospital by Dr. E. J. Holborow was used throughout (Johnson, 1955). Streptolysin-O Reagent (Difco Laboratory) and Standard Antistreptolysin-O 200 units/ml. (Colindale Laboratory) were used for estimations.

Analysis of Results

Statistical analysis of the results (Table I) showed that in both groups the original mean ASO titres were similar ($P=0.4$) and that after 6 months there was still no significant variation ($P=0.3$). There was a slight difference at 3 weeks, the mean ASO titre being lower in the test group ($P=0.1$), but at 6 weeks and after both groups were again similar (Table II). Thus, even if there were any effect from the tetracycline, it was not maintained.

It was therefore concluded that tetracycline had no significant effect on the persistence of a raised ASO titre.

Summary

Thirty patients satisfying the diagnostic criteria for rheumatic fever were allocated by random selection into two groups. Both groups were treated similarly with initial bactericidal and continuing prophylactic doses of penicillin, but the test group received in addition a 3-week course of tetracycline in an attempt to eliminate any continuing streptolysin production, such as might perhaps come from the L forms of streptococcus.

ASO titres were estimated on admission to the trial and subsequently at 3-week intervals for a period of 6 months.

At the conclusion of the trial no significant difference was observed in the ASO titre between the control and the test group.

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L'effet de la tetracycline sur la durée du titre élevé de l'anti-streptolysine-O dans la maladie de Bouillaud

RÉSUMÉ

Trente malades répondant aux critères diagnostiques de la maladie de Bouillaud furent divisés en deux groupes égaux et similaires. Les deux groupes furent traités de la même manière par des doses bactéricides d'abord et prophylactiques ensuite de pénicilline, mais le groupe expérimental reçut de plus une cure de 3 semaines de tetracycline afin d'éliminer toute production de streptolysine, par exemple celle pouvant dériver de la forme L du streptocoque.

L'ASO (anti-streptolysine-O) fut titrée dès l'admission à l'essai et toutes les trois semaines pendant six mois.

A la fin de l'expérience on ne trouva pas de différence significative dans le titre de l'ASO entre les deux groupes.

El efecto de la tetraciclina sobre la duración de las cifras altas de la antistreptolisina-O en la fiebre reumática

SUMARIO

Treinta enfermos respondiendo a los criterios de fiebre reumática fueron repartidos en dos grupos iguales y similares. Ambos grupos fueron tratados del mismo modo con penicilina, primero en dosis bactericidas y luego profilácticas, pero el grupo experimental recibió además tetraciclina durante 3 semanas para eliminar toda posible producción de estreptolisina, tal como la creada por la forma L del estreptococo.

La ASO (antistreptolisina O) fué determinada al comienzo de la investigación y cada tres semanas durante seis meses.

Al cabo de la investigación no se encontró diferencia significativa en las cifras de la ASO entre el grupo experimental y el grupo testigo.