COMPARISON OF OXYTETRACYCLINE AND CHLORTETRACYCLINE IN THE TREATMENT OF NON-GONOCOCCAL URETHRITIS*†

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Since the wide-range orally administered antibiotics, aureomycin (Finland and others, 1948) and terramycin (Willcox, 1951; Willcox and Findlay, 1952), were first reported as effective in non-gonococcal urethritis the question has arisen of their relative efficacy.

In a previous paper a comparison was made of the relative efficacy of terramycin, aureomycin, chloramphenicol, sulphonamides, streptomycin, and penicillin in non-gonococcal urethritis (Willcox, 1953). In assessing the failures no attempt was made to distinguish between relapse and re-infection, except that all such occurrences noted after a symptom-free period of 3 months were assumed to be re-infections. This period was commonly accepted as an adequate criterion of cure of non-gonococcal urethritis when the disease was treated routinely with sulphonamides. As any extension of this interval after treatment with the antibiotics is concerned more with the possibility of masked syphilis than with uncured urethritis it is considered that this arrangement is reasonable and fair. The results of this previous study are shown in Table I.

TABLE I
COMPARISON OF RESULTS OF TREATMENT OF NON-GONOCOCCAL URETHRITIS IRRESPECTIVE OF DOSE, FOLLOW-UP, OR PREVIOUS THERAPY

Drug	No. Treated	No. Followed-up	Failed within 3 Months	
			No.	Per cent.
Terramycin ..	70	70	14	20.0
Aureomycin ..	62	60	16	26.7
Chloramphenicol ..	65	63	23	36.5
Sulphonamides ..	75	72	27	37.5
Streptomycin ..	103	95	40	42.1
Penicillin ..	85	80	36	45.0
Total ..	460	440	156	35.5 (average)

Thus, clearly, the two most successful drugs were terramycin (oxytetracycline) and aureomycin (chlortetracycline).

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However, closer examination of the data showed that all drugs were more successful in cases not previously treated. This is illustrated in Table II in which the failure rates have been cumulated to compensate for differences in the duration of follow-up.

TABLE II
CUMULATIVE RE-TREATMENT RATES AT 3 MONTHS IRRESPECTIVE OF DOSE IN PREVIOUSLY TREATED AND PREVIOUSLY UNTREATED CASES OF NON-GONOCOCCAL URETHRITIS

Drug	Previously Treated			Previously Untreated		
	Cases Treated	No. Failed	Cumulative Percent. Failed at 3 Months	Cases Treated	No. Failed	Cumulative Percent. Failed at 3 Months
Terramycin ..	25	9	46.2	45	5	12.9
Aureomycin ..	29	10	63.3	33	6	25.1
Chloramphenicol ..	29	11	51.4	36	12	43.7
Penicillin ..	15	10	104.1	70	26	53.3
Streptomycin ..	41	18	71.9	62	22	53.8
Sulphonamides ..	20	6	40.0	55	21	63.7
Total ..	159	64	—	301	92	—

Although it is evident that the results of treatment with the antibiotics were clearly much inferior in previously treated cases than in those untreated, the superiority of terramycin and aureomycin in the untreated case was confirmed.

Another important factor was the size of the dose which is recorded in respect of terramycin (Willcox, 1954) in Table III.

TABLE III
CUMULATIVE FAILURE RATES IN PREVIOUSLY UNTREATED CASES OF NON-GONOCOCCAL URETHRITIS GIVEN TERRAMYCIN, RELATED TO DOSE

Dose	No. Treated	Failed	Cumulative Per cent. Failed at 3 Months
Less than 4 g. ..	4	1	50.0
5-6 g. ..	25	4	19.4
Over 6 g. ..	16	0	—
Total ..	45	5	—

It is thus evident that no true comparison of the antibiotics can be made unless previously untreated patients are selected, the same dose given, and the cumulative failure rates calculated. The results of such a comparison are shown in Table IV which gives the cumulative failure rates in previously untreated patients who had received 5–6 g. of the orally administered antibiotics.* It will be noted that, although terramycin and aureomycin were still superior, the numbers of previously untreated cases which received 5–6 g. of the orally administered antibiotics were, in fact, relatively small.

TABLE IV
COMPARISON OF CUMULATIVE RE-TREATMENT RATES
OF PATIENTS NOT PREVIOUSLY TREATED GIVEN 5–6 g.
OF THE ORALLY ADMINISTERED ANTIBIOTICS

Drug	No. Treated	No. Failed within 3 Months	Cumulative Per cent. Failed within 3 Months
Terramycin ..	25	4	19.4
Aureomycin ..	25	5	25.3
Chloramphenicol	15	4	30.5
Penicillin ..	70	26	53.3
Streptomycin ..	62	22	53.8
Sulphonamides ..	55	21	63.7

Harkness (1953) who reported a series of cases of non-gonococcal urethritis in which the effect of terramycin and aureomycin was compared, found terramycin to be superior. It is apparent, however, that in this study no allowances were made for variations in follow-up ("most of the cases under review were observed for at least a month after antibiotic therapy"), and the dose given was not entirely standardized for "in a small number of uncomplicated cases (usually of acute abacterial urethritis) in which resolution appeared incomplete on the fourth day, the course was extended for a further 2 days". Neither is it stated whether the cases under review were previously untreated.

It is significant that the statistical analysis in Harkness's paper was confined to 39 cases treated with each drug, there being five failures in the terramycin-treated group and sixteen failures in the aureomycin-treated group. Although it was concluded from the application of Fisher's method that "the apparent superiority of terramycin was confirmed", no allowance was apparently made for variations in follow-up.

Present Study

In order to make a stricter comparison of terramycin and aureomycin the series of previously untreated cases of non-gonococcal urethritis which

received 5–6 g. of these two drugs, as shown in Table IV, has been enlarged. A further forty patients were treated with 6 g. terramycin, bringing the series total to 65, and a further 82 patients were treated with aureomycin, bringing the total to 107.

Marital Status, Age, and Race.—Of the 122 newly added cases 53 were married and 69 were single: the average age was 30.8 yrs (extremes 18–61); twelve were Negroes and 110 were white.

Previous History.—Only 45 gave no history of venereal disease; the remaining 77 admitted having had eighty attacks of gonorrhoea, 45 of non-gonococcal urethritis, and seven of syphilis between them. Of the twelve Negroes, three denied previous venereal disease, but the remaining nine had had eighteen attacks of gonorrhoea and two of non-gonococcal urethritis between them.

Serology.—The serum tests for syphilis (Wassermann and VDRL or Kahn) were both negative in 120; the Wassermann reaction was negative and the Kahn or VDRL test positive in two. In nine cases the gonococcal complement-fixation test was not done, but out of 113 cases tested it was negative in 105 and positive in eight.

Duration of Symptoms.—The discharge had been noted by the patient before treatment for 0–3 days in 51, for 4–7 days in 38, for 8–14 days in twenty, for 15–21 days in six, for 22–28 days in one, and for over 28 days in six.

Presence of Trichomonas Vaginalis.—Trichomonads were tested for in sixteen cases and found in three (18.75 per cent.). These three patients were all treated with aureomycin: in one the parasite was still present at 2 days and the patient was lost to observation, although the condition was known to have relapsed later; in one the trichomonads disappeared but the urethritis relapsed and was re-treated at 28 days; in one the condition cleared up and remained satisfactory over an observation period of 61 days.

Dysuria.—This was complained of by fourteen of 32 questioned.

Of eighteen married men fifteen (83.3 per cent.) admitted extra-marital intercourse.

Results

The results of the 65 terramycin-treated cases and the 107 aureomycin-treated cases are shown in Table V (opposite).

At 2–3 months the cumulative failure rate in the two series was the same.

Summary

(1) Results of a previously reported study of the efficacy of terramycin, aureomycin, chloramphenicol,

*The usual dose was 1.8 mega units procaine penicillin with aluminium monostearate (PAM) over 3 days; of streptomycin 3–4 g. over the same time, and of sulphonamides 4 g. daily for 5–7 days.

TABLE V

RESULTS OF TREATMENT OF 65 PREVIOUSLY UNTREATED CASES OF NON-GONOCOCCAL URETHRITIS WITH TERRAMYCIN AND 107 CASES WITH AUREOMYCIN

Follow-up	Treatment					
	Terramycin (5-6 g. orally)			Aureomycin (5-6 g. orally)		
	No. Followed-up	Failures including Re-infections	Cumulative Per cent. Failed	No. Followed-up	Failures including Re-infections	Cumulative Per cent. Failed
0	65	—	0	107	—	0
1-7 days	62	1	1.6	101	2	2.0
8-14 days	57	4	8.6	91	5	7.5
15-21 days	51	1	10.6	76	3	11.4
22-28 days	49	1	12.6	71	4	17.0
1-2 months	44	3	19.4	65	4	23.2
2-3 months	33	2	25.5	44	1	25.5
Over 3 months	22	4	—	32	9	—

streptomycin, penicillin, and the sulphonamides in the treatment of non-gonococcal urethritis showed the superiority of terramycin and aureomycin. Similar claims have been made by other workers.

(2) With all the antibiotics personally tested in this previous study the failure rates were higher in previously treated than in previously untreated cases.

(3) The failure rates with terramycin were shown to vary according to the dose given.

(4) When previously untreated patients given 5-6 g. aureomycin or terramycin were compared, terramycin was apparently the more efficacious, but the numbers involved were too small for a valid statistical comparison.

(5) The series of previously untreated patients with non-gonococcal urethritis given 5-6 g. aureo-

mycin or terramycin was enlarged to 107 treated with aureomycin and 65 treated with terramycin.

(6) All relapses and re-infections occurring within 3 post-treatment months were grouped as failures, and incidents occurring after a symptom-free period of 3 months were considered to be re-infections and excluded. When the failure rates in this study are cumulated to allow for differences in follow-up the cumulative failure rates at 3 months for the two drugs are the same.

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