

Terramycin for Nongonococcic Urethritis And Reiter's Disease

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The oral antibiotics, aureomycin, chloramphenicol, and terramycin, are perhaps the most effective drugs so far discovered for the treatment of nongonococcic urethritis, although there are at present insufficient data to assess their relative efficiency, both in nonspecific urethritis as a whole and in those forms in which virus inclusion bodies and/or pleuropneumonia-like organisms may be found in Giemsa-stained urethral scrapings.

Using aureomycin, Finland and co-workers (1) successfully treated 2 patients, and Willcox and Findlay (2) likewise had success with 3 of 4 patients, it being noted that pleuropneumonia-like organisms which were present in the urethral scrapings before treatment subsequently disappeared. Harkness (3) also succeeded in curing 7 out of 10 patients with this drug.

More recently, Chen and Dienst (4) reported the cases of 5 patients who improved or recovered when treated with 3 to 6 gm. of chloramphenicol. Of 12 male patients treated by Findlay and Willcox (5) with 3.0 to 15.75 gm. of chloramphenicol given over a period of 3 to 21 days, virus inclusion bodies were found before treatment in 6 and pleuropneumonia-like

organisms in 5. The disease was clinically resistant in 2, and 3 patients relapsed. Pleuropneumonia-like organisms disappeared from all patients, but the inclusion bodies persisted or recurred in 4, all of whom were considered clinical failures. The successes included 1 patient with Reiter's disease who was given 15.75 gm. of chloramphenicol over a 3-week period. On the other hand, Harkness (6) quoted Harman (personal communication) as having treated unsuccessfully 1 patient having Reiter's disease with this drug, although Korb and Brown (7), also in a single case, had steady improvement after treatment with aureomycin.

The present paper concerns the use of terramycin, an orally administered antibiotic prepared from *Streptomyces rimosus*. Twenty male patients with nonspecific urethritis, including two patients with Reiter's disease, and six female consorts were treated. The work has been controlled by the examination, both before and after treatment, of Giemsa-stained urethral scrapings.

Male Cases

Of the 20 patients treated, the urethritis was uncomplicated in 15, in 1 it was complicated by epididymitis, in 1 by chronic prostatitis, in 1 by cystitis, and in 2 by Reiter's disease. The average age was 33.9 (extremes 23 to 44) years. Treatment previously had been given to 9 patients (some patients have had more than one drug): 5 had received sulfonamides (after treatment 3 were still virus positive); 4 had received penicillin (3 were still virus positive after treatment); and 3 had received chloramphenicol, one with aureomycin in addition, after

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which treatment 2 were found to be virus positive. One man, previously untreated, was receiving cortisone for rheumatism.

Before treatment with terramycin, 14 patients showed inclusion bodies and 6 did not. Both patients having Reiter's disease showed inclusion bodies, and these patients were also the only 2 to show pleuropneumonia-like organisms. Routine tests were performed to exclude gonorrhea and syphilis, and Giemsa-stained urethral scrapings were examined before and repeatedly after treatment. A routine urethral culture on blood agar was made before and after treatment on 12 of the patients.

Except for 1 patient who was given 3 gm. of terramycin over 5 days, 1 patient who was given 3.75 gm. over 4 days (which dosage was dictated by toxic effects), and 1 patient with Reiter's disease who failed to respond and therefore received 19.25 gm. in two uninterrupted courses over a 14-day period, the remainder of the 20 patients received 6 to 12 gm. of terramycin over 5 to 7 days.

Results

Clinical. All patients except one having Reiter's disease responded clinically.

Cultural. The organisms grown on urethral cultures bore no relationship either to the severity of the condition of the patient or to the outcome of treatment. Cultures were performed on 12 patients and the organisms reported before and after treatment in the number of cases concerned are shown in table 1.

Giemsa-stained scrapings. Before treatment 14 patients showed inclusion bodies, 2 with pleuropneumonia-like organisms in addition, and 6 showed neither. The 6 patients with negative test results were observed without evidence of relapse for 1 to 10 post-treatment checks: 1 patient at the fourteenth post-treatment day, and the remainder of the patients over 33 to 128 post-treatment days. The 14 patients showing inclusion bodies before treatment had 1 to 10 post-treatment checks: 3 patients at 6 to 14 days; the remainder, between 23 and 98 days. The one patient with Reiter's disease who did not respond clinically and another patient whose condition was complicated by prostatitis were pathologic failures, the inclusion bodies persisting in spite of treatment

Table 1. Findings in urethral cultures of 12 patients with nongonococcal urethritis, before and after treatment with terramycin

Type of organism	Number of patients	
	Before treatment	After treatment
<i>Staphylococcus albus</i>	10	8
<i>Staphylococcus aureus</i>	1	0
Coliforms.....	3	1
Streptococci.....	1	0
Diphtheroids.....	4	3
Saprophytes.....	1	2

with terramycin. The pleuropneumonia-like organisms disappeared at once from the 2 patients in whom they were found.

Complicated Cases

Five of the fourteen virus positive cases were complicated and are considered in greater detail.

Two patients had Reiter's disease. One, a man with a history of two previous attacks, showed conjunctivitis of 8 days' duration, an effusion into the right knee joint, and a painful elbow. Both virus bodies and pleuropneumonia-like organisms were demonstrated in the urethral scrapings. The patient was given 250 mg. of terramycin orally three times daily but, on the third day, his symptoms increased in severity and he was admitted to the hospital. Some days later the course of terramycin was resumed but there was no clinical improvement (sedimentation rate, 55 mm. in 1 hour), and the virus bodies persisted in the urethral scrapings even after 19.25 gm. had been given. The pleuropneumonia-like organisms, however, disappeared at once and the patient's urethral discharge and urine cleared. Virus bodies were still detected 52 days after the onset of treatment in spite of three sessions of artificial fever induced by intravenous typhoid-paratyphoid A and B (T. A. B.) vaccine. He was discharged from the hospital 47 days after the onset of treatment and, when seen at 67 days, no inclusion bodies were observed.

The second patient with Reiter's disease had had four previous attacks within 6 years. At the time of examination there was an abacterial

urethritis with pronounced keratoderma of the penis, but no other signs. Both virus bodies and pleuropneumonia-like organisms were demonstrated in the urethral scrapings. Preliminary local treatment with Castellani's paint for 1 week was applied unsuccessfully to the penis. The patient was then given 6 gm. of terramycin orally, over a period of 6 days. The urethritis cleared up at once and the keratosis improved dramatically, although it took virtually 26 days for the keratosis to disappear without the use of other methods. Neither virus bodies nor pleuropneumonia-like organisms could be demonstrated at any of four post-treatment checks over a period of 49 days. The wife of the patient also was examined but no inclusion bodies or pleuropneumonia-like organisms were found; it was stated that marital intercourse had not taken place during the previous 6 months.

One case of urethritis was complicated by epididymitis. Only *Staphylococcus albus* and diphtheroid organisms were demonstrated in culture, but inclusion bodies were observed in scrapings taken immediately before and during a course of 8 gm. of terramycin given over a period of 6 days. The urethral discharge disappeared at once, the epididymis ceased to be tender, and the swelling rapidly resolved. Moreover, at two post-treatment checks at 16 and 23 days, respectively, after the onset of treatment, no virus bodies were demonstrated either in the urethral scrapings or in the prostatic secretion. The female consort, although clinically normal, also showed inclusion bodies, which disappeared after 5 gm. of terramycin had been given over 5 days.

One case of a mild urethritis was complicated by a chronic prostatitis. Numerous pus cells were observed in the prostatic smear, and virus bodies were also observed. This patient, who had no history of conjunctivitis or keratosis, was under treatment with cortisone for an infected arthritis of the fingers and rheumatic pains in other parts of the body, which were controlled by this drug. After treatment with 12 gm. of terramycin over a period of 6 days, the pus disappeared from the prostatic smear, as did the inclusion bodies. Although only a negligible amount of pus was noted 22 days after treatment, the virus bodies had returned.

A further case of urethritis showing inclusion bodies was complicated by cystitis. Coliform organisms and *S. albus* were grown on culture. After 8 gm. of terramycin had been given orally over 6 days the urethritis and cystitis cleared, the coliforms disappeared from the urine, and no inclusion bodies could be observed in the urethral scrapings. The patient remained well throughout six post-treatment examinations over 56 days.

Female Cases

Eight female consorts, the average age of whom was 26.6 (extremes 19 to 44) years, were also examined. Although present in the remainder of the female patients, virus bodies were not found in two patients: One, whose consort had a nonspecific urethritis without virus bodies in the urethral scrapings, possessed a large, clean cervical erosion; and the other, the wife of a man with Reiter's disease but who denied sexual intercourse for a period of at least 6 months, had vaginal thrush. These patients were not treated. Of the six in which inclusion bodies were found, two had clean, apparently almost healed, cervical erosions, one had a mild vaginitis which responded clinically to carbarsone pessaries, although these had no effect on the virus bodies which were seen in subsequent smears, while the genitalia of three appeared normal in every way.

The immediate male consorts of four were known to be virus positive, one was virus negative, and the nature of one was unknown, although the young female concerned claimed that she had given nonspecific urethritis to three men in 2 years. These women, except one who had toxic symptoms and received only 2.5 gm. of terramycin over 2 days, received 5 to 8 gm. over 3 to 6 days and were observed for 7 to 87 days. The results of post-treatment smears of one are unknown, four responded satisfactorily, and one was a failure. The failure, who had no clinical signs although she complained of somewhat heavy and premature menstrual periods, was the wife of a man who had relapsed three times after chloramphenicol treatment and once later after penicillin. After a course of terramycin, however, he apparently responded.

Table 2. Results of terramycin treatment of 20 patients with nongonococcal urethritis and 6 female consorts

Nature of the urethritis	Number of patients					
	Treated	Observed	PPLO positive	Clinical failure (resistant)	Pathological failure	Failure rate (percent)
Virus positive.....	Male.....14	19	2	1	3	15.8
	Female.....6					
Virus negative.....	Male.....6	6	0	0	0	-----
	Female.....0					
Total.....	26	25	2	1	3	12.0

¹ The 1 clinical failure was also a pathological failure.

Cultures from the urethra and cervix were performed on four patients, and these showed coliforms, *S. albus*, and/or diphtheroid organisms both before and after treatment.

Toxic Effects

Of the 26 patients treated, 9 complained of side effects, which were mild in 7 and severe in 2, necessitating the termination of treatment in a husband and his wife. Six complained of diarrhea or looseness of stools, 4 of nausea or vomiting, 1 of water brush, 1 of headache, 1 of feeling sleepy, 1 of sore throat, and 3 of soreness or irritation within or near the rectum. Most of these symptoms were trivial in nature.

The results of treatment with terramycin are shown in table 2.

Summary and Conclusions

Twenty patients with nongonococcal urethritis including two patients with Reiter's disease, and six of their female consorts, were treated with 3.0 to 19.25 gm. of terramycin. The clinical results were excellent as only one, a case of Reiter's disease, proved refractory. Twenty of these patients showed inclusion bodies in Giesma-stained urethral scrapings before treatment, and apart from the one clinical failure who was also a pathological failure, all but two of the patients became negative with treatment. Likewise the pleuropneumonia-like organisms were banished from the scrapings from the two

patients having Reiter's disease in whom they were found.

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