

GONORRHOEAL URETHRITIS IN MALES TREATED WITH ONE ORAL DOSE OF OXYTETRACYCLINE*†

BY

DAVID G. McLONE‡, JAMES D. KILEY§, AND JAMES F. HACKNEY||

Atlanta, Georgia

Gonorrhoea is the most common venereal disease, with an attack rate conservatively estimated at about a million new cases per year in the United States (USPHS, 1965a).

Aqueous procaine penicillin G, in a dose of 2·4 million units, is presently considered the drug of choice for the treatment of gonorrhoea in males (USPHS, 1965b). However, studies *in vitro*, including both cases of therapy failures and those from routine admissions, show that in 1963 and 1964 the concentration of penicillin required to inhibit all strains was up to 15 times greater than that which was adequate in 1955 (Thayer, Samuels, Martin, and Lucas, 1965). The frequency of penicillin hypersensitivity, which is estimated at 10 per cent. and which may be increasing (USPHS, 1961), makes the search for an alternate antimicrobial agent desirable.

An ideal drug would be one which would achieve a cure with a single oral dose, be of low cost, and have no adverse reactions. Parenteral administration is painful, requires large numbers of syringes and needles, and is apt to cause complications at the injection site (McKechnie and Yow, 1960). There is also a greater possibility of sensitizing the patient to the therapeutic agent and of eliciting hypersensitivity reactions in patients previously sensitized by parenteral medication. One-dose therapy, given in a clinic, is attractive because patients frequently do not complete a longer course of oral therapy which depends on self-administration.

Oxytetracycline HCl (Terramycin, Pfizer) in a dose of 1·5 g. orally, based on a short trial with varying dosages, appeared worthy of clinical evaluation. Oxytetracycline is not new to the list of agents useful in the treatment of gonorrhoea. Hendricks, Greaves, Olansky, and five others

(1950), Putkonen (1951), Willcox (1951, 1952, 1953, 1954), Sokoloff (1964), Vander Stoep, Montgomery, and Knox (1961), Shapiro (1962), and Shapiro and Lentz (1963) have investigated its use, but the method of administration and attempts to prove bacteriological cure have not been adequately studied.

The results of treating 161 male patients with acute gonococcal urethritis with one oral dose of 1·5 g. oxytetracycline HCl are described below.

Material and Methods

Male patients presenting themselves for treatment of urethral discharge at Fulton County Health Department, Atlanta, Georgia, were selected on the basis of a urethral exudate, which on stained smear demonstrated typical intracellular diplococci. Their ages ranged from 14 to 53 years.

Exudates from patients with positive smears were collected by intra-urethral scraping with a 2-mm. platinum wire loop. Each exudate was immediately inoculated on a culture plate of Thayer and Martin selective medium (B.B.L., IsoVitalax Enrichment, with Vancomycin, Colistin, and Nystatin) (Martin, Billings, Hackney, and Thayer, 1966). Presumptive identification of *Neisseria gonorrhoeae* was made on the basis of typical colonial morphology, oxidase reaction, and Gram stain. Sugar fermentation studies were not routinely carried out. In only nine out of 161 patients was the TM culture negative. The nine negative cultures may indicate non-gonococcal urethritis or failures in culturing technique.

The first ten patients received 0·5 g. oxytetracycline, the second ten patients received 1 g., and the remaining 141 received 1·5 g. Patients were asked to return in 24 hours, but were included in the study if they returned within 96 hours. Patients returning more than 96 hours after the initial visit with signs and symptoms, were presumed to be cases of re-infection; 75 per cent. of the patients returned within 96 hours. At follow-up, smears were made if exudate was present and intra-urethral scrapings were taken for culture in all cases. All patients were told to return if symptoms recurred. None of the group treated with 1·5 g. was re-treated at the first follow-up visit.

Results

The results achieved with 1·5 g. oxytetracycline HCl are summarized in the Table. The failure rates in the groups treated with 0·5 g. and 1 g. were about 70 and 60 per cent. respectively.

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‡ SA Surgeon (R) (T), Venereal Disease Program, National Communicable Disease Center, Public Health Service, U.S. Department of Health, Education, and Welfare, assigned to the Fulton County Health Department, Atlanta, Georgia.

§ Emory University School of Medicine.

|| Director, Fulton County Health Department, Atlanta, Georgia, U.S.A.

TABLE
RESULTS OF TREATMENT WITH
1.5 g. OXYTETRACYCLINE HCl

No. of Patients	Positive Cultures	Positive Culture and Follow-up	Returned Positive by 96 hrs	Positive Smear or Culture 96 hrs to 14 days
141	132	96	6	15

Of 161 patients, 13 per cent. gave a history consistent with penicillin sensitivity. Two refused to take capsules and were given intramuscular penicillin G, 2.4 mega units. Three developed nausea from the tetracycline and two of these vomited about 2 hours after therapy. One patient was found to have concomitant primary syphilis and was given 2.4 mega units benzathine penicillin.

No correlation between age, race, number of previous infections, or duration of symptoms was found with treatment failures in the patients who returned with clinical evidence of gonorrhoea within 2 weeks of treatment.

Discussion

For the purpose of this study the criteria for diagnosis of gonorrhoea were:

- (1) Clinical signs and symptoms of gonorrhoea.
- (2) Positive smear of urethral exudate.
- (3) Positive culture of urethral exudate.

The criteria for cure were:

- (1) Disappearance of signs and symptoms.
- (2) Negative urethral smear if exudate present.
- (3) Negative culture of urethral exudate within 96 hours of treatment.

If the patient returned within 4 days of treatment with a positive smear, he was considered to be a failure, since re-infection can be considered negligible in this period. Four patients had a positive TM culture on follow-up. Three of these returned in 3 days for re-treatment because of clinical evidence of gonorrhoea and the fourth returned in 4 days. Two patients with negative cultures at follow-up had positive smears on the fourth day. Thus, of the six failures, four were detected by positive TM culture while still asymptomatic at follow-up. This method assumes that all positive smears after 4 days are re-infections. The calculated cure rate was 93.8 per cent. An alternative to this would be to count all 141 patients treated and to consider as failures those with positive smears within 2 weeks of treatment.

A previous study on gonorrhoea in this clinic (Tiedemann, Hackney, Simpson, and Price, 1962) demonstrated that over 90 per cent. of placebo-treated patients returned to the clinic within 2 weeks. In the present series a total of 21 patients

returned with positive smears within 14 days. The cure rate by this calculation was 83.7 per cent. The true cure rate probably lies somewhere between 83.7 and 93.8 per cent.

Three patients out of 161 experienced nausea and two had emesis. These were the only complications noted.

Summary

Oxytetracycline HCl in a single oral dose of 1.5 g. has been found to be an acceptable alternative to penicillin. Considering the increasing rate of penicillin hypersensitivity and the decreasing cost of oxytetracycline HCl, tetracyclines may become the drug of choice in the treatment of gonococcal urethritis in males.

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Le traitement de l'urétrite blennorragique chez les hommes par une seule dose d'oxytétracycline administrée par voie buccale

RÉSUMÉ

Une seule dose d'oxytétracycline HCl de 1,5 g. par voie buccale a été trouvée comme étant une alternative comparable à la pénicilline. Quand on considère l'augmentation croissante d'hypersensibilité à la pénicilline et le prix décroissant de l'oxytétracycline HCl, les tétracyclines pourraient devenir le médicament de choix pour le traitement de l'urétrite blennorragique chez les hommes.