GONORRHEAL URETHRITIS IN MEN TREATED WITH ONE ORAL DOSE OF METHACYCLINE

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SUBSTITUTION of various groups on the basic tetracycline molecule has resulted in a family of antibiotics with varying pharmacological activities. Methacycline (6-methylene oxytetracycline), developed by Blackwood (*1*) and produced commercially by Pfizer Laboratories as Rondomycin, is effective against a wide range of bacterial infections. Methacycline has an inhibitory concentration for *Neisseria gonorrhoeae* equivalent to that of tetracycline (*2*). It is readily absorbed from the gastrointestinal tract. It reaches a maximum concentration at about the fourth hour and declines to a negligible amount in about 24 hours. Eighty percent of methacycline is bound in human serum, but this situation is easily reversed. Methacycline has essentially the same spectrum of antimicrobial activity as the other tetracycline derivatives but is more potent.

Marmell and co-workers (*3*) and Morton and Higson (*4*) have established the effectiveness of methacycline in the treatment of gonorrhea. However, their studies employed regimens requiring multiple oral doses. Oral medication for treating gonorrhea is desirable because painful injections are eliminated, there is no need for large number of syringes, and a large clinic load can be readily handled. One-dose therapy, given in a clinic, is desirable because patients frequently do not complete a longer course of oral, self-administered therapy.

The need to test new antibiotics for treating gonorrhea is dictated by the waning efficacy of penicillin. While penicillin remains the preferred treatment, the dosage has escalated in a period of 20 years from 300,000 units of long-acting forms to 2,400,000 units of short-acting penicillin (*5*). Furthermore, an increasing percentage of the population is now found to be hypersensitive to penicillin and requires treatment with alternate antibiotics.

Trials of newer drugs are essential to establish the best alternate to penicillin and to indicate which therapy may be the first choice in the future.

Materials and Methods

Men coming for treatment of urethral discharge at Fulton County Health Department, Atlanta, Ga., were selected on the basis of having a urethral exudate which on stained smear demonstrated typical intracellular diplococci. Their ages ranged from 14 to 53 years. This study was conducted between January 1, 1967, and March 30, 1967.

Exudates from patients with positive smears were collected by intraurethral scraping with a 2-mm. platinum wire loop and was immediately inoculated on culture plates of Thayer-Martin selective medium (Baltimore Biological Laboratories, IsoVitalex enrichment, with vancomycin, colistin, and nystatin) (*6*). Presumptive identification of *N. gonorrhoeae* was made on the basis of typical colonial morphology, oxidase reaction, and gram stain. Sugar fermentation studies were not routinely carried out. The

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Thayer-Martin culture was negative for only 24 of 289 patients who had a positive stain smear. The 24 negative cultures may indicate nongonococcal urethritis or failures in culturing technique.

Routine serologic tests for syphilis were done for all patients, and each patient was examined for evidence of primary or secondary syphilis.

The first 97 patients received 600 mg. methacycline, the second 95 patients 900 mg., and the next 97 patients 1.2 gms. Patients were asked to return in 24 hours, but were included in the study if they returned within 96 hours. Patients returning with signs and symptoms more than 96 hours after the initial visit were presumed to be reinfected. At followup, smears were made if exudate was present and intraurethral scrapings for culture were taken from all patients. All patients were told to return if symptoms recurred. None of the persons treated were retreated at the first followup visit.

Emesis appeared to be a problem for the first few patients treated. Thus, each group was divided in half; the first half was instructed to take methacycline with their next meal and the second was told to take the methacycline immediately, regardless of the period of time since the last or before the next meal. Many persons in the second half of each group were fasting. The purpose was to determine if a meal influenced either the emesis or the cure rate.

Results

The results achieved with the various dosages are summarized in table 1. All patients were instructed to return if signs or symptoms recurred. Thirty-four patients who returned between 96 hours and 2 weeks had positive cultures. Twelve had received a 600-mg. dose, 15 a 900-mg. dose, and seven a 1,200-mg. dose.

Table 2. Effect of taking methacycline to treat gonorrhea with and without meals, by size of dose, Fulton County, Ga., January 1–March 30, 1967

Dose and when taken	Patients with positive culture and followup	Patients with positive culture within 96 hours	Emesis
600 mg.:			
With meal	46	3	2
Without meal	45	7	2
900 mg.:			
With meal	45	3	4
Without meal	43	4	0
1,200 mg.:			
With meal	40	0	1
Without meal	46	2	4

Table 2 summarizes the groups according to whether the methacycline was taken with a meal or not.

No relationship between age, race, number of previous infections, or duration of symptoms and failure of the treatment was found in the patients who returned with clinical evidence of gonorrhea within 2 weeks of treatment. No cases of concomitant syphilis were noted.

In this study only one of the 19 failures was married. In a previous study the number of persons in the failure group who were married was greater than expected (Gonorrheal urethritis in males treated with one oral dose of ampicillin. Unpublished report by D. G. McLone, T. E. Billings, and J. F. Hackney).

Discussion

There are several ways to approach these data. For the purpose of this study the criteria for diagnosis were clinical signs and symptoms of gonorrhea, positive smear of urethral exu-

Table 1. Results with various doses of methacycline to treat gonorrhea, Fulton County, Ga., January 1–March 30, 1967

Dose	Number of patients with—				Percent failure
	Positive smear	Positive culture	Positive culture and followup	Positive culture 96 hours	
600 mg	97	91	68	10	14.7
900 mg	95	88	54	7	12.9
1,200 mg	97	86	55	2	3.6

date, and positive culture of urethral exudate. The criteria for cure were disappearance of signs and symptoms, negative urethral smear if exudate was present, and negative culture of urethral exudate within 96 hours posttreatment.

If the patient returned within 4 days of treatment and had a positive urethral smear, he was classified in the failure group since reinfection can be considered negligible in this period. Nineteen patients had a positive culture using the Thayer-Martin medium on followup. This method assumes that all positive smears after 4 days are the result of reinfections. The calculated cure rate among those who did return was 96.4 percent for those receiving 1.2 gms. of methacycline.

The rate of emesis with methacycline is independent of dosage and not related to whether or not methacycline was taken with meals. The overall emesis rate was about 5 percent. Contrary to what has been noted in other studies involving tetracycline derivatives, taking methacycline with meals did not alter the cure rate. No other adverse reactions were noted with methacycline.

Summary

Clinical evaluation of methacycline in the treatment of gonorrhea was conducted from January 1, 1967–March 30, 1967, at the Fulton County Health Department, Atlanta, Ga. The study involved 289 men who came for treatment at the clinic. A negative smear and culture were used as the criteria for cure.

The schedule of one oral dose of 1,200 mg. resulted in a cure rate of 96.4 percent. The rate of emesis was not influenced by dosage or meals. Age, race, marital status, and taking methacycline with meals did not alter the cure rate.

Based on these findings, methacycline is an acceptable alternative to penicillin in the treatment of gonococcal urethritis in males.

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