Carbenicillin in the Treatment of Gonorrhea in Males

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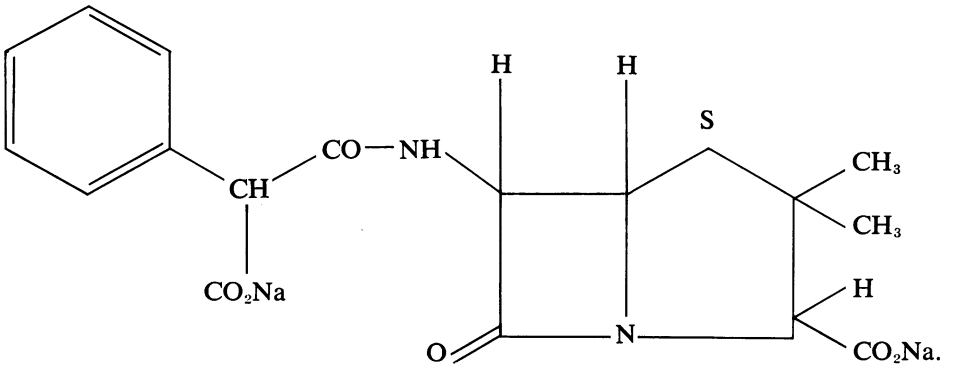
A PILOT STUDY to evaluate the effectiveness of carbenicillin, a semisynthetic injectable penicillin, in treating males with acute gonococcal urethritis was made July 6–September 7, 1971, at the Central Health District Venereal Disease Clinic, Oakland, Calif.

Disodium carbenicillin (*A*) was developed as a benzyl penicillin derivative with substitution by an isonizable functional group in the alpha position:



This antibiotic has been reported to possess greater in vitro activity against gram-negative organisms than existing penicillins (*1*).

The efficacy of carbenicillin in the treatment of gram-negative organisms has been attested to by many investigators (*2,3*). In addition, the reported in vitro activity (minimal inhibition concentration) of carbenicillin against *Neisseria gonorrhoeae* (*4*) created an interest in evaluating this antibiotic in clinical gonorrheal infections. The results of the evaluation of the effectiveness of two dosage schedules of carbenicillin on 140 males with acute gonococcal urethritis are reported here.

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Method and Materials

The presence of *N. gonorrhoeae* is clinically suspected in males when a purulent urethral discharge follows sexual exposure. A presumptive diagnosis was made in all instances by demonstrating *N. gonorrhoeae* in a gram-stained smear of the urethral exudate. The diagnosis of gonorrhea was confirmed by isolating the organism by using a Thayer-Martin culture (*5*) and was subsequently substantiated biochemically.

Patients were assigned randomly to two treatment groups. Group A received 2 grams of carbeni-

cillin and group B, 4 grams. The injections were made into one or both buttocks. All doses were administered intramuscularly during one session.

The age range of patients in group A was 20–54 years, and in group B, it was 21–60 years. The mean age was 28 in group A and 26 in group B. At the followup examination, specimens for culture were obtained from the urethral meatus. Patients who failed to return for reexamination at the specified time (between the second and fourth days after initial therapy) were omitted from the study. Treatment was considered a failure if, when the patient was reexamined, there was laboratory evidence of persisting *N. gonorrhoeae*. These patients were then given a broad-spectrum antibiotic.

Results

A total of 140 male patients were studied—70 patients in group A and 70 in group B. Only 53 patients in each group (76 percent), however, completed the study and could be evaluated. Of the 34 patients who were dropped, 23 failed to return for followup examination; seven returned after the final date for reexamination; and four patients had to be dropped because their initial cultures were negative. The actual dropout rate based on those patients who failed to return for followup reexamination was 16 percent for group A and 17 percent for group B (table 1).

Table 1. Patients dropped from study following carbenicillin therapy, by reason

Reason for dropping	Group A (2 grams)		Group B (4 grams)	
	Number	Percent	Number	Percent
Admitted to study.	70	100	70	100
Total dropped.....	17	24	17	24
Failed to return for followup examination.....	11	16	12	17
Returned after final reexamination date	3	4	4	6
Initial culture negative.....	3	4	1	1

Table 3. Reported side effects associated with intramuscular injections of carbenicillin

Side effects	Group A (2 grams)		Group B (4 grams)	
	Number	Percent	Number	Percent
Total completed study.....	53	100	53	100
Pain at site of injection.	44	83	46	87
Mild.....	15	28	4	8
Moderate.....	16	30	17	32
Severe.....	13	25	25	47
Vertigo or syncope...	4	8	3	6
Diarrhea.....	1	2	0	0

The 2-gram dose of carbenicillin was curative in 94 percent. The 4-gram dose, however, was effective in 96 percent of those who completed the study (table 2). The difference in cure rates between the two groups was not statistically significant (0.95 level of significance, Fisher's exact test).

Adverse reactions occurred in 98 patients of the 106 who completed the study. The most frequent complaint was pain at the site of injection—83 percent in group A and 87 percent in group B. This was followed by vertigo or syncope—8 percent in group A and 6 percent in group B. One patient had diarrhea which was thought to be unrelated to the parenteral carbenicillin.

Patients reported that the intensity of the pain at the injection site varied from mild to severe. Forty-seven percent of the patients receiving the two injections of carbenicillin (2 grams each) reported severe pain as compared with 25 percent of those administered the single injection (table 3). Other investigators have also reported that patients complained of pain at the site of intra-

Table 2. Results of therapy with carbenicillin given intramuscularly to men with gonococcal urethritis, July 6–September 7, 1971

Variant	Total		Group A (2 grams)		Group B (4 grams)	
	Number	Percent	Number	Percent	Number	Percent
Patients who completed study.....	106	100	53	100	53	100
Cured.....	101	95	50	94	51	96
Treatment failures.....	5	5	3	6	2	4

NOTE: 34 patients were omitted because they either failed to return for reexamination, returned after the final reexamination date, or had a negative culture.

muscular injections as a frequent side effect (*6,7*). (Schaeper (*8*) has suggested that the addition of 1 ml. procaine to the carbenicillin solution will overcome this painfulness.)

Discussion

It is difficult to evaluate therapeutic agents in a public health venereal disease clinic. Drugs that require oral administration are likely to be poorly absorbed. Although erratic absorption can be overcome somewhat by administering large and frequent doses, clinical experience has shown that few patients can be relied on to take all the tablets or capsules prescribed. The need for an injectable antibiotic as an alternative to penicillin intramuscular therapy has been presented in earlier works (*9,10*). The results of this study clearly indicate that carbenicillin therapy for gonorrhea in men is effective.

The usefulness of carbenicillin in treating acute gonococcal urethritis in males is certainly supported. Further controlled studies are needed to establish if carbenicillin is an alternative choice for patients with gonorrhea resistant to treatment with aqueous procaine penicillin G.

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SUPPLY REFERENCE

(*A*) Disodium Carbenicillin (Geopen ®): J. B. Roerig Division, Pfizer, Inc., New York, N.Y. 10017.

NELSON, MORTON (Public Health Services, Alameda County (Calif.) Health Care Services Agency): *Carbenicillin in the treatment of gonorrhea in males. Health Services Reports, Vol. 87, October 1972, pp. 762–764.*

In a study conducted from July 6 through September 7, 1971, at the Alameda County Health Care Services Agency, Central Health District Venereal Disease Clinic in Oakland, Calif., 2- and 4-gram schedules of parenteral carbenicillin were compared in the treatment of 106 men with gonorrhea.

The cure rates, as determined by culture, were 94 percent for the 53 patients who received the 2-gram doses and 96 percent for the 53 patients administered the 4-gram doses.

Adverse reactions were reported with both treatment regimens, pain at the injection site being the most common side effect–83 percent of the group given 2-gram doses and 87 percent of the group given 4-gram doses.

The difference in the rates of cure was statistically significant at the 0.82 level by Fisher's exact test. The results indicated that carbenicillin is a useful agent for the treatment of male gonococcal urethritis, but control studies with intramuscularly aqueous procaine penicillin G are needed before definitive conclusions can be made as to the efficacy of carbenicillin in the treatment of penicillin-resistant gonorrhea infections.