

# TREATMENT OF UNCOMPLICATED GONOCOCCAL URETHRITIS IN MALES WITH TWO DOSES OF AUGMENTIN, SIX HOURS APART

‡ Lim Huat Bee  
‡ Trinh Phang

## SYNOPSIS

To effectively control gonorrhoea, especially in regions where resources are limited and surveillance inadequate, an ideal regimen should be at least 95% curative both to PPNG and non-PPNG, inexpensive, easily administered (preferably orally) and in a single dose and without major toxic or allergic side-effects. Augmentin 3.25 gm taken orally in two doses six hours apart, gives an effective cure rate of 100% with minimal gastrointestinal side effects in 69 patients who were followed up for tests of cure. Some patients (especially patients with venereal diseases) may be unreliable to take the 2nd dose of medicine and the author recommends further trials to be carried out with single dose of Augmentin 3.25 gm plus probenecid to see if the same results can be achieved.

## INTRODUCTION

This study was undertaken to assess the effect of Augmentin 3.25 gm taken in two doses six hours apart in the treatment of uncomplicated gonococcal urethritis in males. Augmentin 3.25 gm is a formulation containing 3 gm amoxycillin and 250 mg clavulanic acid. Failure of amoxycillin alone in the treatment of gonococcal urethritis is due to the enzymes Beta-lactamase that degrades amoxycillin, lowering its concentration to a level that is inadequate to exert any anti-bacterial effect. The clavunate component of Augmentin inhibits most of the Beta-lactamase that can inactivate amoxycillin (1). It does so by competitive inhibition that takes effect very rapidly, and by an enzyme inactivation mechanism that takes place more slowly leading in many instances to a permanently inactivated enzyme (2). A single dose of Augmentin 3.25 gm was found to have an overall cure rate of 89%, 73% if due to penicillinase-producing *Neisseria gonorrhoeae* (PPNG), in the treatment of uncomplicated gonococcal urethritis (3). In this study a double dose of the drug gave a cure rate of 100%.

Klinik Perubatan Lim (Kulit)  
14-A, Lorong Abu Siti  
Penang, Malaysia

Lim Huat Bee, MBBS, Dip Derm (Lond),  
Dip Ven (Lond)

Mrs Trinh Phang, BA, MT (ASCP)

**MATERIALS AND METHODS**

This is a single blind prospective clinical trial of 94 consecutive male patients with uncomplicated gonococcal urethritis attending a private clinic in Penang. Patients with a history of penicillin allergy were excluded.

At the initial visit, intraurethral specimens of urethral discharge were collected using platinum bacteriological loops and smears examined microscopically. A separate specimen was taken for immediate culture on Thayer Martin medium containing vancomycin, colistin, and the anti-fungal agent, nystatin. The culture plates were incubated in a candle jar at 36°C for one day. If no growth was obtained after 24 hours, the plates were reincubated for another 24 hours. An oxidase test and gram stain were performed on colonies suspected of being gonococci. Confirmation of *Neisseria gonorrhoeae* was performed by the Phadebact co-agglutination test technique. The agar plate diffusion method was used to determine the antibiotic sensitive pattern of all isolates. Penicillin susceptibility was tested using discs containing 10 units of penicillin G. Where the inhibition of growth was less than 20 mm in diameter, a Beta-lactamase test was done, using the iodometric method (4).

At the initial visit, all patients with positive results from direct microscopy were each given orally a sachet containing 3.25 gm Augmentin in powder form dissolved in a glass of plain water; another similar dose was taken six hours later after leaving the clinic. They reported 48-72 hours after taking the second dose of Augmentin for physical examination and cultures of urethral specimens. Where no discharge was present, intra-urethral scrappings were performed. The criteria for failure of treatment was positive smear or culture in patients without further sexual contacts after treatment. All patients had been advised to abstain from sexual activity for two weeks after therapy.

**RESULTS**

A total of 94 patients were studied: 39 (41%) were PPNG and 55 (59%) were non-PPNG. The age distribution of the patients is shown in Table I. The clinical presentation of the patients is shown in Table II. 93 out of 94 (98.9%) patients presented with urethral discharge and this was the commonest complaint. 69 patients (73.4%) complained of dysuria, while 26

(27.7%) complained of increased frequency of micturition. 25 patients (26%) did not come for follow up for tests of cure, and hence had to be excluded from further study, leaving 69 patients for final assessment. With double dose Augmentin regime a cure rate of 100% was obtained (Table IV). Following treatment, no serious side-effects or adverse reactions were noticed in all the patients.

**TABLE I**  
Distribution of 94 male patients with gonococcal urethritis by age

Age group — years	Number	Percentage
19 and below	2	2.1
20 — 29	52	55.3
30 — 39	31	33.0
40 — 49	9	9.6
Total	94	100

**TABLE II**  
Clinical presentation

Clinical presentation	Number of patients	Percentage
Urethral discharge	93	98.9
Dysuria	69	73.4
Frequency of micturition	26	27.7

**TABLE III**  
Percentage of Penicillinase-producing *Neisseria gonorrhoeae* (PPNG)

Number of Isolates	Number Tested		
	PPNG	Non-PPNG	Total
94	39 (41%)	55 (59%)	94 (100%)

**TABLE IV**  
Results of treatment

Total number of cases	PPNG			Non-PPNG		
	Defaulted	Failure	Success	Defaulted	Failure	Success
94	12	0	27	13	0	42

## DISCUSSION

*Neisseria gonorrhoeae* is usually sensitive to penicillin and its analogues and it is still the drug of choice in the treatment of gonorrhoea in many parts of the world. The Centre for Disease Control of the United States recommends, as a first line treatment for uncomplicated gonorrhoea, the use of either procaine penicillin (4.8 mega units intramuscularly) as a single dose combined with 1 gram of probenecid orally or ampicillin 3.5 grams or amoxycillin 3.0 grams with 1 gram of probenecid orally (5). However, both chromosomal resistance (that leads to relative resistance to penicillin), and the emergence of a new strain of gonococcus that produces penicillinase (PPNG) in South East Asia pose serious problems.

In July 1977, the Ministry of Health, Malaysia first reported the appearance of PPNG. Since then, the number of PPNG cases has gradually increased and a recent study in Malaysia showed 35% of the gonococcal isolates to be PPNG (6). In the Philippines, clinical isolates from bacteriologically positive cases revealed 40 to 50% to be Beta-lactamase secretors (7). Hence a failure rate of at least 35% is to be expected if penicillin and its analogues are used in the treatment of gonococcal urethritis in South East Asia. Augmentin, the aminoglycosides spectinomycin and the 2nd and 3rd generations cephalosporins are highly effective and on epidemiological grounds should replace penicillin as the first choice antibiotic. This recommendation is not without its hazards and care must be taken to monitor the development of chromosomal resistance. Rajan (personal communication) found a failure rate of 8 to 10% of PPNG cases to kanamycin in Singapore, while the author found a similar failure rate of 8% with non-PPNG and 20% with PPNG (6). Also the discontinuation of penicillin and its analogues may see a resurgence of early syphilis (8, 9).

A single dose of Augmentin 3.25 gm was found to have a cure rate of 89% in uncomplicated urethritis in males (3). In this study by repeating the same dose 6 hours later, the cure rate improved to 100%.

Augmentin has the added advantage of efficacy against PPNG infections, good acceptance by patients, can be taken orally and has low toxicity. It is also effective against incubating syphilis (8, 9). However, it has the inconvenience of having to be taken in 2 doses, six hours apart to achieve 100% cure rate. Some of the patients may not take the 2nd dose after leaving the clinic. Recent work on a few patients by the author suggests that the same result could be

achieved with a single dose of Augmentin 3.25 gm plus 1 gm probenecid, and the author recommends that further trials be carried out with this single dose combination regime.

## ACKNOWLEDGEMENTS

The authors wish to express grateful thanks to Beecham Pharmaceuticals United Kingdom for all the help given in this study, and also for supplying the Augmentin used in this trial. Our grateful thanks also go to Professor T.J. Danaraj for his encouragement and helpful criticism in this paper. In addition the authors would like to acknowledge herein our gratitude to Lam Wah Ee Hospital for allowing us to use its facilities to carry out the microbiological tests for the purpose of this research. Our thanks also to Miss Chin Seow Hwa for her capable assistance in the conduct of this research.

## REFERENCES

1. Miller J.M., Baker C.N., Thornsberry C.: Inhibition of Beta-lactamase *Neisseria gonorrhoeae* by sodium clavulanate. *Antimicrobial Agents and Chemotherapy* 1978; 14:794-6.
2. Reading C.: The biochemistry and mode of action of Augmentin. *Proceedings of an International Symposium, Montreux, Switzerland 17th July 1981 Excerpta Medica Amsterdam.*
3. Lim V.K.E., Bakar R.: Single dose oral amoxycillin and clavulanic acid in the treatment of gonococcal urethritis in males. *Med. J. Malaysia* 1982; 36:235-8.
4. World Health Organisation Technical Report Series No. 616 *Neisseria gonorrhoeae* and gonococcal infections: Technique for the detection of Beta-lactamase producing strains of *N. gonorrhoeae*. Geneva: World Health Organisation 1978.
5. Centre for Disease Control Sexually Transmitted Diseases Treatment Guidelines 1982; 31:37S-39S.
6. Lim H.B.: Kanamycin in the treatment of gonococcal urethritis in males. *Med. J. Malaysia* 1983; 38:182-4.
7. LaO L.M., LaO M.L.M.: A combination of amoxycillin and clavulanic acid in the treatment of acute male penicillinase resistant gonorrhoea in the Philippines. *Proceedings of an International Symposium Montreux, Switzerland 17th July 1981. Excerpta Medica Amsterdam.*
8. Rajan V.S.: Gonorrhoea Control: Keeping ahead of resistance. *Medical Progress July 1982: Vo. 9. No. 7 p. 9.*
9. Schroter A.L., Turner R.H., Lucas J.B., Brown W.J.: Therapy for incubating syphilis — Effectiveness of gonorrhoea treatment. *J Am Med Assoc.* 1971; 218:711-3.