Outpatient treatment of syphilis with penicillins

We would like to draw the attention of colleagues to a proposed change in the recommended dosage for bemethamine penicillin (Triptopen) when used in late syphilis. Following discussions with one of us (PCG) the manufacturers (Glaxo Laboratories) are seeking approval from the Department of Health that the current approved dosage of two vials weekly¹ be replaced with a recommended dosage of one vial administered twice weekly for three weeks. This is because blood levels produced by the latter regime can be shown to be above 0.03 u/ml immediately prior to the next dose² whilst no such confirmation is available for the existing recommendations.

Triptopen is currently the only licensed penicillin product suitable for routine outpatient treatment of syphilis. This follows the commercial demise of alternative long acting penicillin preparations. It is true that these or similar products remain available under Section 13¹ of the Medicines Act 1968 on a "named patient" basis. However, the use of non-licensed products is fraught with difficulty, as treatment is usually required to commence immediately on diagnosis, so the delay which may occur in obtaining "named patient" supplies would be unacceptable (unless manufacturers bend the rules and accept retrospective names) and, in addition, the release of patient names in these circumstances may be in breach of the anonymity demanded by the National Health Service (Venereal Diseases) Regulation 1974.

The use of a non-licensed product in favour of an effective licensed product may produce medicolegal problems for the prescriber in the event of an adverse event occurring (Medical Protection Society, personal communication).

The new dosage recommendations for Triptopen should remove the previous uncertainty concerning the maintenance of adequate blood levels during the treatment of late syphilis and will present prescribers with a licensed source of penicillin suitable for the outpatient treatment of late syphilis.

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- 1 Triptopen Data Sheet. ABPI Data Sheet Compendium 1989-90.
- 2 Data on File. Glaxo Laboratories.

MATTERS ARISING

Gastrointestinal obstruction associated with Chlamydia trachomatis

The paper by Pegg and Owen¹ describing a case of gastrointestinal obstruction associated with *Chlamydia trachomatis* in an 18 year old female brought a similar case to our minds.

An 18 year old schoolgirl presented with an acute intestinal obstruction. Operation revealed a peritonitis with adhesive bands running from the omentum to the Fallopian tubes with bilateral salpingitis and tubo-ovarian abscesses. Her post-operative history was rather stormy and 4 years later she is still troubled by low abdominal pain and menorrhagia.

Because of the operative findings the patient was referred to the Special Treatment Clinic and aspects of her history not revealed before were voiced. She had had only one boy friend with whom she had her first and only sexual contact several weeks before the onset of her symptoms. No protection had been used. The boy friend, an older student resident in the United Kingdom, had a history of recent chlamydial urethritis.

Initial post-operative vaginal specimens were negative but later testing produced a positive reaction for *Chlamydia trachomatis*. The patient also developed a vaginitis with plaques which yielded *Candida albicans*. Both conditions responded to specific treatment.

This young lady missed a crucial years schooling and has suffered symptoms on and off for 4 years following the single unprotected contact with a thoughtless young man.

The consequences of infection with chlamydia in females can be devastating, and as Pegg and Owen warn the possibility of such a cause for adhesive small bowel obstruction or unexplained peritonitis should be considered.

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- 1 Pegg DJ, Owen AWM. Gastrointestinal obstruction associated with *Chlamydia trachomatis*. *Genitourin Med* 1990;66:26-7

Post-gonococcal urethritis: a double blind study of doxycycline

I read with interest, the recent article by McLean *et al*¹ entitled "Post-gonococcal urethritis: a double-blind study of doxycycline vs placebo", describing the significant reduction of postgonococcal urethritis (PGU) by the addition of a course of tetracycline to standard single dose treatment for urethral gonorrhoea in heterosexual men.

I would be interested to know, however, the number of patients with PGU who returned for a second follow-up at 28 days and in spite of receiving doxycycline, continued to show evidence of PGU; and the management offered to those 30 patients who at the 1st follow-up, were still found to have PGU in the doxycycline group. It would be useful to know the number of men in whom *C trachomatis* was not isolated in the PGU and non-PGU group, who were consorts of women with chlamydial infection. Also, it is not mentioned in the article whether the study population has been advised to abstain from sexual intercourse during the follow-up period and the number of men in the PGU and non-PGU group who followed this advice.

Moreover, doxycycline was ineffective in 30 (26.8%) men in the treatment group (N = 112), and 50 (48%) men in the placebo group would have had unnecessary medication had they been given routine tetracycline in conjunction with single dose therapy for genital gonococcal infection. In other words, 37% (80/216) men in this study would have received a potentially hazardous medication without any benefit. This should concern us all, more so in the light of emerging plasmid and chromosomal mediated resistant strains of *N gonorrhoeae*, which may have serious implications in the future. This concern has been shared in the recent editorial of this journal² in which it has been suggested that widespread use of tetracyclines may be contributing to this problem. *C tra-*

chomatis might have been isolated from 11 men in this group (N = 80) but they could effectively be identified by routine test for chlamydial infection.

In addition, has the time come to review the definition of PGU and should we not exclude those patients who are proven to have genital chlamydial infection, from this condition? It seems neither justifiable nor scientific to include such a specific and proven clinical entity under the umbrella of a rather non-specific condition like PGU or non-specific urethritis (NSU). The current DHSS coding system (KC 60) for patients attending genitourinary medicine clinics, in this respect, has shown a move in the right direction.

I agree with the authors that routine test for genital chlamydial infection should always be performed and as shown in the survey by the Royal College of Physicians Committee on Genitourinary Medicine³ this facility is very widely available. Interestingly only one fifth of the clinicians in this survey, thought that patients with gonorrhoea should be given anti-chlamydial treatment.

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McLean, Evans, and Azadian reply: Concern about the possible over use of tetracycline in the routine management of patients with gonococcal infection was one of the reasons for our study. Since the study began tetracycline resistance in gonococci has been increasingly reported.^{1,2}

With regard to Dr Mandal's enquiries about the further management of patients in the doxycycline-treated group, of the 30 patients with PGU at first follow-up, management consisted of oxytetracycline for one

week in 24, erythromycin stearate for one week in one, and no antibiotic therapy in five. Interestingly, of the five patients who were not given further antibiotic therapy, three failed to reattend for follow-up and two had no evidence of PGU on follow-up.

Of the 30 patients with PGU at first follow-up, 22 (73%) returned for second follow-up at approximately 28 days. Of the 22, 10 (45%) continued to have evidence of PGU despite antibiotic therapy as outlined above. These patients were given further courses of oxytetracycline or erythromycin and either had apparent cure (7) or failed to reattend (3).

Patients were advised by both the doctor and the health adviser to abstain from sexual intercourse until apparent cure, but it was impossible to be sure if this advice had been followed in all cases.

We are unable to give information on the chlamydial isolation rates in female partners from this study.

The terminology of urethritis remains controversial. The term non-specific urethritis (NSU) is unhelpful and should probably be discarded. However, "umbrella" terms such as non-gonococcal urethritis (NGU) and PGU will remain necessary until chlamydial testing becomes universally available and until the aetiology of the remaining cases of urethritis becomes known. We would not propose further confusion in terminology by referring to NGNCU (non-gonococcal, non-chlamydial urethritis).

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Recurrent genital tract infections: a result of induced immunosuppression?

Sonnex¹ has reviewed various studies examining the immunopathogenesis of recurrent genital tract infection. Although the author did not mention bacterial vaginosis (BV), we believe that this syndrome may, to some degree, compromise normal mucosal immunity.

We found that in women without BV, the endogenous vaginal lacto-

bacilli were coated with IgG and IgA, whereas the bacteria found in the vaginal fluid of women with BV had either an IgA coating or no coating at all.² In addition, tests indicate that IgG and IgA proteases are produced by some strains of *Bacteroides melaninogenicus* and *B. asaccharolyticus* isolated from women with BV.³ Another study has shown that some bacteroides antigens are able to retard polymorphonuclear leukocyte locomotion.⁴

As the *Bacteroides* spp. constitute a significant component of the vaginal flora of women with BV,⁵ the potential for altering the local immune responses appears significant.

These observations may be related to the pathogenesis of BV. Further, the reduction in the immune defences of the vaginal mucosa is likely to be linked to treatment failures found in recurrent or recalcitrant BV. Also worth consideration is the possibility that an immuno-compromised mucosa may make the host more susceptible to agents such as chlamydia and papillomavirus.

Further assessment of these observations is necessary before the full effect of BV on vaginal mucosal defences can be defined.

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Correction The Notice (*Genitourin Med* 1990;66:307) should have been headed "Northern Genito-Urinary Physicians Colposcopy Group".