

Single-dose oral treatment of gonorrhoea

TO THE EDITOR *British Journal of Venereal Diseases*

SIR—May we comment on single-dose oral therapy with ampicillin for gonorrhoea? To find a successful treatment of gonorrhoea using the shortest effective course has been the aim of many investigators. 'One-shot treatment' or 'one-dose oral therapy' has claimed and continues to claim many advocates. Epidemiologically it is useful to have such a method; but as a general recommendation for the treatment of an infective disorder, wisdom dictates a cautious approach. We have not found 'one-shot' or 'one-dose' treatment for gonorrhoea safe in the long run or in the short term.

Since there have been many claims for the use of 'one dose oral' ampicillin therapy (Groth and Hallqvist, 1970; and more recently Willcox and others, 1973), we conducted a pilot trial at two hospital clinics in 1972. The object of this small trial was to compare the ampicillin (plus probenecid) treatment, which had begun to be recommended more widely, with the orthodox intramuscular procaine penicillin treatment.

Alternate cases of acute uncomplicated gonorrhoea in men were treated with either one dose of oral ampicillin 2 g. plus 1 g. probenecid, or with three daily injections of intramuscular penicillin 0.9 m.u. plus 1 g. probenecid by mouth on the first day. The patients were diagnosed routinely by the typical appearance of Gram-negative intracellular diplococci in the urethral smears. A satisfactory response to treatment was assessed partly by the disappearance of symptoms and signs in the patient, but more critically by noting two clear urines 1 week after treatment. Two institutions were used for our small trial, since the clientèle differed slightly in each although the medical staff was the same.

Material

71 men were treated (36 at Guy's Hospital and 35 at the Miller Hospital); 35 received the standard course of three daily injections of procaine penicillin with probenecid, and 36 received the single oral dose of ampicillin with probenecid swallowed in the clinic before leaving.

Those treated with procaine penicillin were of a similar age group and ethnic group to those receiving ampicillin. In neither group was re-infection a factor, so far as could be ascertained.

A small number failed to return, one on the ampicillin and three on the procaine penicillin régime, and these were not included among those showing a satisfactory response.

Results

The results are given in the Table.

TABLE *Results of treatment of 71 men*

Hospital	Therapy		Response	
	Ampicillin	Procaine penicillin	Success	Failure
Guy's	21	15	10 11	11 4
Miller	15	20	5 15	10 5

Judged by the criteria outlined above, of 36 patients treated with ampicillin, fifteen (42 per cent.) responded and 21 (58 per cent.) failed to respond. The response was better at Guy's Hospital than at the Miller Hospital.

Procaine penicillin was more successful. Of 35 patients so treated, 26 (74 per cent.) responded, and nine (26 per cent.) did not.

After treatment gonococci were seen in smears in only a few cases, and there was no difference in this respect between the two groups.

Discussion and conclusion

The purpose of this pilot study was to compare the ability of the two forms of treatment to produce evidence of resolution of inflammation in acute gonorrhoea. A good response was shown by absence of signs and symptoms and especially by an absence of signs in the urine. The signs in the urine (held for 2 hours) probably offer the most sensitive index at present of continuing urethral inflammation or of healing.

The matters of relapse and re-infection in treated gonorrhoea are sufficiently difficult, not only to unravel clinically and microbiologically, but in the very nature of their presentation (for example, to what extent and for how long is the gonococcus able to exist in the sub-epithelial layers without appearing on the surface epithelium, quite apart from any factor such as Littritis that may bedevil post-treatment management?). Furthermore, it may be argued that the persistence of inflammatory signs can be due either to cryptic gonorrhoea or to a non-specific urethritis. In that case the effects of these possibilities should be comparable within certain limits in

each group; and the figures for treatment response in each group should approximate more closely than the results show (see Table). For this reason the simple end-point of clear urine after one week was used in the trial to assess the effectiveness of the therapy.

It is therefore on the comparative nature of these results that we have based our opinion of the doubtful efficacy of the one-dose treatment.

Our results with procaine penicillin are approximately in line with those found by other workers using this drug. Our results with ampicillin do not agree with those of several workers, notably Groth and Hallqvist (1970), Willcox and others (1973), Cobbold and others (1973), and Jersild and Svendsen (1973).

Taking our overall experience, therefore, it appears that in 36 patients treated with ampicillin the re-treatment rate was 58 per cent., whereas in those treated with procaine

penicillin it was 26 per cent.

Yours faithfully,
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September 12, 1973

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Elimination of gonorrhoea

TO THE EDITOR *British Journal of Venereal Diseases*

STR—In their letters to the editor, Felton (1973) and Spencer (1973) gave some additional thoughts on the paper 'Potential impact of chemical prophylaxis on the incidence of gonorrhoea' by Lee, Utidjian, Singh, Carpenter, and Cutler (1972).

Felton stated that 'the question of the acceptability of the intravaginal contraceptive compounds (ICC) *vis à vis* other contraceptive and preventive measures is not discussed. It seems to be assumed there is no substantial hindrance to their use by up to 30 per cent. of the population at risk. . . . I agree that the acceptability of the ICC is one of the most important factors if it is to help bring the epidemic of gonorrhoea under control. It was pointed out by Lee and others that a prophylactic programme alone cannot be expected to eliminate the disease. Its greatest value will be obtained by incorporating it into the existing programme of treatment and education. Public health workers have to find ways of convincing potential patients that no single prophylactic agent is 100 per cent. effective. Also, the patients themselves must develop a greater sense of responsibility to protect themselves from infection by employing prophylactic methods.

Felton also pointed out that the Lee model assumes either unlimited partner-change activity or increased partner-change activity in line with an increase in gonorrhoea. This is of course not true. The Lee model employed the constant rate of becoming infected by exposure to an infected partner. It did not put the number of sexual acts per generation into the model explicitly, but this was considered from the point of view

of point-prevalence. It is a census type of measure and it represents the frequency of the disease at a designated point in time (MacMahon and Pugh, 1970).

Factors, such as number of partner-change intercourses and inequality of male and female infectious periods, may 'in reality' help to determine the number of cases at a particular time. However, also 'in reality', the variables may be very difficult to incorporate into a model if, indeed, they can be defined at all. Future inspection of the Felton model will be necessary before the relative merits of the two models can be assessed.

The Lee model may indeed be improved upon, as can any tool. However, as an initial attempt to explain what has been observed and to predict what might be observed with an ICC, this model seems to be a good beginning (Sussman, 1973).

Felton also stated that 'if a higher rate of infection and removal rate had been chosen, the predicted benefit of ICC would have been even more rapid'. This is not precisely true. The predicted benefit of ICC depends on infection rate, removal rate, proportion of usage of ICC by potential patients, and the effectiveness of the ICC. Only if a larger difference between infection rate and removal rate had been chosen, would the predicted benefit of ICC have been more rapid.

At the end of his letter, Felton concluded that ' . . . the use of ICC at the levels of effectiveness put forward by Lee and his co-workers will produce a simple rather than a compound decrease.' According to Webster's New College Dictionary (1973), the term 'compound' by