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MEDICAL MEMORANDUM

Treatment of Gonorrhoea with a Combination of
Probenecid and Sodium Penicillin G among
African Ugandans

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Summary. The results of 4534 patients with uncomplicated gonorrhoea treated with a combination of 1 g of probenecid followed 30 min later by 5.0 Mega units of sodium penicillin G at the Venereal Disease Clinic in Mulago, Makerere University Kampala from August 1969 to May 1970 have been reported. Albeit, 70–80% of the gonococcal strains in the community being resistant to penicillin (partial resistance) a cumulative cure rate of 99% was achieved. This is very encouraging because the schedule is cheap, easily administered and least toxic. Besides, patients, for reasons discussed, fail to attend the clinic regularly so that one single curative dose of treatment is better than several repeated doses.

Résumé. Les auteurs donnent des résultats, du traitement de la bléonorragie non-complicquée, obtenues de l'étude effectuée pendant la période allant d'août 1969 au mai 1970 sur 4534 à la clinique des maladies vénériennes de l'hôpital universitaire de Makerere à Kampala. Chaque patient recevait 1 g de Probenecid suivi, 30 min après, par une injection de 5 millions de Penicillin G. Bien que 70–80% des cas de bléonorragie dans la population sont partiellement résistants à la penicillin, une guérison de 99% était obtenue, ce résultat est fort encourageant car le traitement est non seulement moins cher et moins toxique mais aussi facile à administrer. En plus, bien des patients, pour des raisons discutées ci-dessous, ne fréquentent pas la clinique régulièrement ce qui fait que une seule dose thérapeutique adéquate est beaucoup plus rentable que des doses répétées.

INTRODUCTION

The increasing frequency of gonococcal strains resistant to penicillin is a challenging medical problem all over the world. In the past two decades the curative dose of penicillin has had to be duplicated several folds to meet the increasing resistance.

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In Uganda 70–80% of the gonococcal strains are resistant to penicillin *in vitro* (Phillips *et al.*, 1969). Accordingly large doses of penicillin are necessary to effect cure. Arya & Phillips (1970) tried 2.0–2.45 Mega units of procaine penicillin amongst college students and reported a cure rate of 94%. Olsen & Lomholt (1969) on the other hand employed a combination of 1 g of oral probenecid followed 15–30 min later by intramuscular injections of 5.0 Mega units of sodium penicillin G amongst a Greenland population and obtained a cure rate of 99%. Fifty-six percent of gonococcal strains in this population were resistant to penicillin *in vitro*.

Since August 1969 the Olsen-Lomholt schedule has been employed at the Venereal Disease (VD) Clinic attached to Mulago Hospital, Makerere University Kampala with very favourable results. Reported in this communication is our initial experience with this schedule.

PATIENTS AND METHODS

The patients included in this series were those treated for uncomplicated gonorrhoea at the VD clinic from August 1969 to May 1970.

The clinic is perhaps the oldest clinic in the country. It was started by Keane and collaborators in 1913 and currently it treats over 11,000 patients with urethral discharge annually. The majority of patients are males.

Diagnosis

Every patient presenting with urethral or vaginal discharge was carefully examined and the diagnosis was established by a positive gonococcal smear quickly stained with methylene blue and viewed under the ordinary light microscope for intracellular diplococci. Cultures for the organisms were not performed as facilities for these procedures do not exist in the clinic at the moment.

Treatment

All the smear-positive patients were then given 1 g of probenecid (two tablets of 500 mg Benemid) followed 30 min later by intramuscular injections of 5.0 million units of sodium penicillin G dissolved in 8 ml of 0.5% lignocaine solution to minimize pain. Those who could not tolerate penicillin received a single dose of 2 g of tetracycline if they were males or 2.5 g if they were females.

Before leaving the clinic every patient was briefed on venereal diseases and their hazards, how to avoid them and how vital it was to have adequate treatment. They were also advised to attend regularly for follow-up meanwhile abstaining from sexual intercourse until they were declared cured and fit. Finally they were asked to bring their *bona-fide* contacts for treatment.

Follow-up

All patients (smear-positive and smear-negative) were reviewed every 3–4 days for three consecutive visits. On every visit smear examination was performed. Those patients who had had negative smears in the previous two consecutive visits were discharged. Those who were still smear-positive were given another full course. Patients who failed to attend for follow-up were presumably relieved of their symptoms and were considered cured.

RESULTS

During the 10-month period, 4830 patients with leucorrhoeal discharge attended the clinic. Of these, 4534 (93.9%) were smear-positive for *N. gonorrhoea*. The majority of them were males (ratio M : F = 34 : 1) because the clinic was until recently essentially for males. The age ranged from 15 to 56 years (median 21 years). All the patients were African by race but a majority were Bantus from within and outside Uganda.

Socio-economically most of the patients were from the low income group. The few well-to-do citizens included those who had failed to get cured elsewhere.

Treated group

Of the 4534 treated patients, 4113 (90.7%) were cured after a single shot of treatment (Table 1). Another 6.9% (312 patients) were cured after a second shot as evidenced by

TABLE 1. Distribution of patients according to therapeutic response

	Treated		
	Cured	Failed	Total
Number of patients	4488	46	4534
Percentage	99.0	1.0	100

TABLE 2. Attendances and positive smear results per visit

	Visits			
	Initial	First	Second	Third
Cases with <i>positive</i> smears on their previous visit	4534	421	109	38
Cases with <i>negative</i> smears on their previous visit	—	—	151	8
Total positive smears	4534	421 (9.3%)	260 (5.7%)	46 (1.0%)
Total attendance	4534	2083 (46%)	1300 (28.7%)	827 (18.2%)

smears on the second visit. However, on the same visit another 151 patients (3.3%) who had had negative smears on the previous visit were smear-positive. Most likely these patients were repeaters. On the third visit (i.e. after three or less shots of penicillin) only forty-six patients (1%) were still smear-positive (Table 2). The cause for the failure is being evaluated.

Default rate

The default rate among the 4534 patients was high. Fifty-four percent of the patients failed to turn up for the first follow-up visit. Of the 2083 patients who were seen, 421

patients (20.2%) were smear-positive. Similarly on the second and third visits, 20% of those who turned up were smear-positive. It would appear that mostly patients with symptoms turned up. By the third visit only 18.2% of the original 3534 patients turned up for review.

DISCUSSION

Uganda, like many other developing countries, has limited financial resources, limited manpower and poor technical facilities. Consequently, for any treatment schedule to succeed it must be cheap, easily administered and highly effective. Up till now, penicillin is the drug of choice for the treatment of gonorrhoea. It is cheap and is the least toxic. Besides the resistance exhibited by strains of gonococci towards this drug is merely relative so that when large doses are used complete cure follows.

The schedule currently employed at the VD clinic combines all the above ideals. It is easily administered. Even the most inexperienced members of the team encounter virtually no problems. Furthermore, it is very effective. In spite of the frequency of resistant gonococcal strains in the community being 70–80%, 99% of the patients were cured. Arya & Phillips (1970) on the other hand employing 2.0–2.45 Mega units of fortified procaine penicillin (PPF) and 4–5 g of tetracycline respectively achieved a cure rate of only 94%.

Other workers have also reported very favourable results with the schedule. Oslen & Lomholt (1969) treated 832 cases of gonorrhoea in both males and females in Greenland and achieved a cure rate of 99%. The incidence of partial gonococcal resistance in this area at the start of the campaign was 56% but in a period of 4 years (i.e. 1964–68) the rate dropped to 19%. Gray, Phillips & Nicol (1970) also treated 222 male patients with gonorrhoea in London where 35% of the gonococcal strains are partially resistant to penicillin and obtained a cure rate of 99.5%. A concomitant group of 188 patients given 24 Mega units of procaine penicillin plus Benzyl penicillin (Distaquine Fortified), achieved a cure rate of only 96.9%.

With this schedule, peak levels of penicillin in the serum are rapidly attained, last for a brief period and fall to undetectable levels within 8–10 h. Such is the ideal for the treatment of gonorrhoea and prevents emergence of resistant strains. Long-acting preparations of penicillin fail to attain peak levels early and the low serum levels at the beginning and at the end of the treatment favour the emergence of the resistant strains (Curtis & Wilkinson, 1958).

It has already been suggested that a second attack of urethritis after the 5.0 Mega units of penicillin is more likely to be a re-infection rather than a relapse (Gray *et al.*, 1970). By the same token it is conceivable that most of the patients in this series who required more than one dose were repeaters rather than relapses. The incidence of symptomless carriers amongst the women in Kampala is abominable (Bennett, 1962). Besides, most of the patients attending the VD clinic are young with very little knowledge about venereal diseases, let alone being very little concerned. Some patients even equate gonorrhoea with the common cold which comes and goes without much disability. Perhaps this is a fault of too effective a treatment.

While the above surmise holds true, other possibilities of treatment failure like misdiagnosis of other micro-organisms (Mima-Herellea group of organisms) for *N. gonorrhoea* (Thayer & Moore, 1964), or protection of the gonococci from extra-cellular antibiotics by phagocytic macrophages and columnar epithelial cells (Thayer *et al.*, 1957) cannot be

excluded. Facilities for culture and typing of the organisms are not routinely available at the clinic. Methylene blue and Gram stain are the only aids to diagnosis available at the clinic but these cannot differentiate the Mima-Herellea group of organisms from *N. gonorrhoea* which are morphologically indistinguishable on smear (Thayer & Moore, 1964). The Mima-Herellea group of organisms have never been proved beyond dispute that they cause urethritis, but the fact that they are insensitive to penicillin and that they are usually recovered from urethral and cervical discharges (Thayer & Moore 1964) can make evaluation of gonococcal therapy very complex. Probably these were responsible for the 1% failure rate.

Concerning review of the patients, the results were disappointing. The number dwindled with each visit. Probably this is expected in case of a disease like gonorrhoea which does not cause constitutional disability and whose response to treatment is so dramatic that patients may deem it unnecessary to return for review. Alternatively, some patients could possibly have failed to turn up because they could not reconcile their employment with hospital attendance. Although most of them were young and belonged to the low socio-economical status, a majority of them were workers (labourers and artisans). They therefore find it difficult to convince their employers that they have to attend hospital without running the risk of losing their day's pay. No one would be prepared to miss his pay when he has no pain.

Other patients live far from the clinic and have to catch buses to attend the clinic. Unless they are really having pain they cannot afford to expend their very limited means to attend the clinic. This, as a matter of fact, probably explains why most women do not appear for treatment. A majority of them do not experience pain and are hence symptomless carriers (Catterall, 1970).

Finally, the clinic operates only during the working hours so that even if the patients wanted to attend after working hours they cannot do so. This is, of course, unfortunate but the lacking manpower at the moment does not permit alternative time-tables.

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