TREATMENT OF GONORRHOEA WITH STREPTOMYCIN*

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Although a number of papers on the treatment of gonorrhoea with streptomycin have been published during the last four years, few reports have come from Great Britain. Chinn and others (1947) obtained seventy cures out of 72 patients who were given 0.2 to 0.5 g. streptomycin, and Pulaski (1947) reported success in nine cases. Willcox (1948), employing a single injection of 0.2 to 0.6 g. had success in five out of seven cases, and Taggart and others (1949) claimed no less than 76 of 77 patients cured by a single injection of 0.4 to 0.6 g., although smaller amounts were less effective. More recently Salzberg and others (1950) reported cures in seventeen out of eighteen women treated with this drug.

Using the newer, supposedly less toxic, dihydrostreptomycin, Taggart and others (1950) reported 95 out of 104 cured with a single injection of 0.2 to 0.4 g. Jacoby and others (1950) reported cures in 57 out of 66 patients given 0.5 g., and in 69 out of 73 given 1 g., some drug-resistance being noted in the failures. Streptomycin has also been successfully used in gonorrhoeal arthritis by Hirsh and Kurland (1950), and Malhotra (1950).

One of the advantages of treating gonorrhoea with streptomycin is that the risk of masking syphilis is less than with any of the other effective antibiotics. Thus Taggart and others (1949) and Willcox (1948) were able to see *T. pallidum* in syphilitic sores of patients given single injections of 0.5 to 1.0 g. of the drug 24 hours previously. The risk is not, however, entirely absent, for Herrell and Nichols (1945) found spirochaetes temporarily absent in the lesions of four cases of early syphilis treated with 1.2 to 10 g. streptomycin, and Willcox (1950) observed not only permanent disappearance of treponemata but also complete healing of the sores in three syphilitics given 3 to 7 g. streptomycin.

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The disadvantages of streptomycin are its side-effects and the possibilities of drug-resistance. So far there is little evidence that single doses given for gonorrhoea produce more adverse reactions than penicillin, although the injection of streptomycin causes a little more pain—a point to remember in dealing with nervous patients. Nor is there evidence that single injections given for gonorrhoea have prejudiced the later streptomycin treatment of co-existent tuberculosis in the same patient. On the other hand, there is certainly good reason to believe that the gonococcus, like other organisms, readily becomes resistant to the drug, as Jacoby and others (1950) noted in their failures. However, the fact that two drugs, i.e., penicillin and streptomycin, each quite able to deal with the failures of the other, are available, apart from aureomycin, chloramphenicol, and terramycin, means that potentially resistant strains of gonococci can be confronted with an overwhelming superiority of effective drugs.

The effectiveness of the sulphonamides has now declined; Dunlop (1949) noted 176 failures in 205 patients treated in London. Some alternative is therefore required for gonorrhoeal patients in whom the risk of concomitant syphilitic infection is above average. These include persons with suspicious, but repeatedly dark-field negative, sores and a negative blood test, persons with suspicious adenitis, persons with abnormal serum tests for syphilis thought to be possible false-positives, and persons with a history of intercourse with an infectious syphilitic. For such cases single injections of 0.5 g. streptomycin would now appear to be the most hopeful treatment.

Present Investigations

No really large series of cases of gonorrhoea treated with streptomycin has yet been published in Great Britain. During 1948 seven cases of

gonococcal urethritis were treated with a single injection of 0.2 to 0.6 g. streptomycin (Willcox, 1948). From January to July, 1950, a further 55 cases were treated at King Edward VII Hospital, Windsor, and St. Mary's Hospital, London, with a single injection of 0.5 to 1.0 g. This paper reports the total series of 62 patients (47 males and fifteen females). The gonorrhoea was uncomplicated, except in one male case with Cowperitis. The results are summarized in the Table.

Material

Female Cases (15).—These patients were aged 18 to 35 years (average 22.8).

Symptoms.—Five showed mild to marked urethritis, ten mild to marked cervicitis. Gonococci were recovered from the urethral smears of eleven and from the cervix in eight, while cultures from both sites were positive in nine. The Wassermann reaction and Kahn test were negative in all but one, and the gonococcal complement-fixation test was negative in all but two. In addition one patient had vulvar warts and one had latent syphilis.

Therapy.—One woman had been treated with penicillin one week previously for gonorrhoea which had subsequently relapsed, but the remainder had received no prior treatment. One was treated with a single injection of 0.6 g. streptomycin, but all the others received a single injection of 1 g. No toxic effects were noted.

Follow-up.—One patient defaulted at once, but the other fourteen remained under observation and attended for a total of 46 (average 3.7 each) post-treatment examinations for from 4 to 281 (average 96) days. Eight patients attended for 50 days or more.

Results.—(see Table) Ten were completely successful, but one received additional treatment in the form of local applications of 'Negatol' to the cervix, and one other was given penicillin for other reasons but only after one satisfactory post-treatment test had been obtained. Two cases, also showing negative post-treatment tests, received other treatment for non-specific conditions. One was given sulphadiazine for persistent cervicitis at 53 days, and another the same drug at 20 days for salpingitic pains which had been in existence for some months.

The one woman who had already failed to respond to penicillin had satisfactory post-treatment tests at from 7 to 21 days, after which time she defaulted. She was next seen at 119 days, having contracted a re-infection from a seaman two weeks before. There was one possible failure, in whom a few suspect intra-cellular pairs were observed nine days after treatment but which were not confirmed either by culture or by a second smear examination. She was, however, re-treated with penicillin for safety.

Male Cases (47).—These included four Negroes and 43 Europeans, and were aged from 18 to 51 years (average 27.9). Thirteen patients admitted to sixteen previous attacks of gonorrhoea, two to syphilis, and

one to non-specific urethritis. With the exception of one patient, whose discharge has been in existence for 77 days before treatment, the average duration of the urethritis was 2½ days. Gonococci were recovered without difficulty from the urethral smears in each case. The Wassermann reaction and Kahn test were negative in all except one Nigerian, who was suspected of having had yaws in the past. Only four patients had a positive gonococcal complement-fixation test. The disease was uncomplicated in all but one Negro patient with left Cowperitis and a history of an abscess in this situation during a previous attack.

Therapy.—Treatment consisted of a single injection of 0.2 to 1.0 g. streptomycin. Three patients received 0.2 g., one 0.3 g., one 0.4 g., one 0.6 g., thirteen 0.5 g., and twenty-eight 1.0 g. No toxic effects were noted except in one who developed a generalized macular rash the day after treatment which faded the same evening; a possible Herxheimer reaction was suspected but the Wassermann reaction and Kahn test were both negative.

Results (see Table, overleaf)

DOSE OF 0.2 TO 0.6 G. (NINETEEN CASES).—Three patients defaulted at once but the remaining sixteen attended for 48 (average three) post-treatment tests from 1 to 330 days (average 71 days) after treatment. Eight patients attended for fifty days or more.

Ten were unqualified successes while they were observed. Two were treated with sulphadiazine for subacute urethritis at 36 and 105 days respectively, no gonococci being found in the smears. These two cases were regarded as having concomitant non-specific urethritis. Two other patients, found to have fresh profuse urethral discharges containing gonococci at 196 and 330 days after treatment respectively, were classified as re-infections. There were only two failures: one was the Negro with Cowperitis who, having been given a single injection of only 0.2 g., not surprisingly relapsed three days later, and was re-treated with penicillin and aspiration of the abscess; the other was a man given 0.6 g., whose infected wife was at that time untreated, who relapsed three days later although he denied re-exposure. He was successfully re-treated, and his wife also was successfully treated with a single dose of 0.6 g.; both remained well during the subsequent eight weeks' observation.

DOSE OF 1.0 G. (28 CASES).—Six cases in this group defaulted immediately. The remaining 22 cases had 65 (average 3) post-treatment tests for from 3 to 340 (average 72) days. There were thirteen unqualified successes, eight of which were observed for more than 50 days. Four developed non-specific discharges in which gonococci could not be isolated; one noted at nine days was treated with penicillin, one originally complicated by paraphimosis had a mucoid discharge at eleven days and was treated with sulphadiazine, and one who showed pus in the prostatic bead at 72 days was also given sulphadiazine. The fourth and most severe case in this group was that of a man who, seven days after treatment, had a slight mucoid discharge containing only a trace of pus; the urine was

TABLE
SUMMARY OF RESULTS

Dose (g.)	Patients		Treated	Observed	Success	Non-Specific Infection	Re-infection	Proved Failure	
	M	F						No.	%
0.2-0.6	19	1	20	17	11	2	2	2	11.7
1.0	28	14	42	35	22	6	4	3	8.5
Total	47	15	62	52	33	8	6	5	9.6

clear with threads. He was given a further injection of 1.0 g. streptomycin but his condition had not improved two days later when more pus was noted in the smear, but no gonococci. He defaulted for 19 days after being given a third injection of 1.0 g. On his return he complained of left-sided epididymitis of one week's duration and his urine was hazy with threads. There was no improvement two days after yet another injection of 1.0 g. streptomycin, and he was then given three injections of 2.4 million units each of procaine penicillin G with 2 per cent. aluminium monostearate, over a period of one week, during which time he markedly improved.

There were three re-infections, who all admitted fresh exposure, one at 90 days, one at 33 days, and another, whose consort was known to be under treatment for Bartholinitis, at 21 days. There were only two proved failures confirmed by smear examination at 3 and 12 days respectively.

Summary and Conclusions

Sixty-two persons with gonorrhoea, 47 males and fifteen females, only one of whom had a complicated infection, were treated with streptomycin. Twenty received a single injection of 0.2 to 0.6 g. and 42 1.0 g. Of 52 who attended for post-treatment examination, eight developed non-gonococcal discharges, thought to be due to concomitantly acquired non-specific urethritis, six had re-infections, and five (9.6 per cent.) were failures.

The failure rate of those receiving a single

injection of 1.0 g. (8.5 per cent.) was only slightly higher than that of penicillin at its best. Taking all unsatisfactory results into consideration, these results with streptomycin are not inferior to those of penicillin at its worst, as reported by King and others (1950) from a large series of cases.

A single dose of 0.5 g. streptomycin probably represents the best treatment for uncomplicated gonococcal infection in patients in whom, pending its exclusion, the risk of syphilis is above average.

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