

# GONORRHOEA AND THE SULPHONAMIDES\*

BY

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After penicillin became available for the treatment of gonorrhœa it was nevertheless decided at the London Lock Hospital to continue to use the sulphonamides for the treatment of acute cases. The decision was made because the proportion of cures achieved by sulphonamide therapy still seemed adequate, and because the danger that penicillin might suppress the signs, or prolong the incubation period of early syphilis, could thus be avoided.

Published reports on the sulphonamide therapy of gonorrhœa in this country showed evidence that its efficiency was declining up to the time that it was replaced by penicillin. The present report is concerned with the position today, and gives evidence to suggest that sulphonamides continue progressively to lose their efficiency in the treatment of the disease.

King (1939) stated that over 90 per cent. of three hundred cases of acute gonorrhœa treated with sulphapyridine had no symptoms and no signs of infection by the third week. The war prevented longer follow up.

Sommerville (1941) treated 300 cases with 2 g. of sulphapyridine daily for seven days, followed by irrigation for two weeks. After nine weeks' observation a cure rate of 92 per cent. was obtained. Complications occurred in only five cases (1.66 per cent.).

Laird (1942) treated 764 cases with sulphapyridine using three schemes of dosage, 6 g. daily for four days, 4 g. daily for six days, or 6 g. daily for three days. The criteria of failure were the persistence of infection for longer than ten days from the start of chemotherapy or the occurrence of a complication. The success rate varied from 81 to 91 per cent. with the different courses of treatment. The proportion of cases followed for three months is not stated.

Jefferiss and McElligott (1943) gave details of 219 cases. They used 18 or 20 g. of sulphathiazole spread over three days, and after three months of observation obtained a cure rate of 90 per cent. Complications appeared in two cases (1 per cent.).

Williams and others (1944) reported on various groups of cases. Among these was one of 540 patients treated for five days with  $4\frac{1}{2}$  g. of sulphapyridine daily. Forty-five per cent. of these were apparently cured by one course alone, a further 30 per cent. being cured by the addition of minor therapy soon after the course was finished. Therefore in 75 per cent. of these cases immediate success was obtained after only one course of sulphonamide. Four hundred of these 540 patients were observed for the full three months, and during that time a relapse occurred in twenty-one cases (5 per cent. of those remaining under observation), and complications in 1 (0.25 per cent.). Results with sulphathiazole were slightly better. This carefully studied series suggested that 25 g. of sulphathiazole in five days was the best course of treatment.

The war-time experience of Campbell (1944) in the North African and Central Mediterranean theatres showed how rapidly sulphonamides could lose their efficacy in the treatment of gonorrhœa.

## The Present Study

This study is based on the treatment and observation of 408 male patients attending at the London Lock Hospital with acute gonococcal urethritis between May 1946 and March 1947. Certain cases had to be excluded, the most important being those in which an attack of gonorrhœa had occurred within the previous six months and those which were treated with penicillin for concomitant syphilis. All were treated as out patients.

## Treatment

Two standard courses of sulphathiazole were used: 28 g. were given in doses of 4 g. daily for seven days, or 25 g. in doses of 5 g. daily for five days. A few patients were given 4 g. daily for ten days to a total of 40 g. The tablets were taken after meals with an alkaline mixture and abundant fluids.

## Tests for Cure

Tests for cure were applied during three months' observation. After the completion of treatment the patient was examined at least once a week for

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three weeks; each patient was instructed to hold the urine for a considerable period, preferably overnight, and any urethral moisture was then examined by smear. When attendance was difficult, smears of morning secretion were made by the patient. After one month of observation prostatic massage was carried out on three separate occasions, at intervals of not less than a week, and the secretions were examined. At the end of three months the patient was given a full clinical examination, his prostatic secretion was examined, he was urethroscopied, and his blood was tested by the Wassermann reaction and complement fixation test for gonorrhœa. The different schemes of dosage gave very similar results.

### Results

Of the 408 patients observed in this series, 181 defaulted before three months and twenty-two were transferred or were presumed to have been reinfected.

The results of treatment can be assessed in the remaining 205. Of these, twenty-nine (14.1 per cent.) completed satisfactory tests after one course of sulphathiazole.

In 176 out of the 205 patients the first course of treatment failed, the evidence of failure being persistence or recurrence of pyuria or the development of complications. Most of these cases were then treated with penicillin, but in seventy cases further sulphonamides were given and in consequence sixteen of these passed tests for cure. In twelve cases sulphonamide therapy was continued for three or more courses with no success.

In most cases failure was soon obvious, and 134 patients had received further treatment by the tenth day, twenty between the eleventh and fifteenth, nine between the sixteenth and twentieth, six on the twenty-first, five on the twenty-eighth, and one on the forty-second.

One hundred and fifty-nine patients eventually received penicillin. In these cases the persistence of a grossly purulent discharge and pyuria was assumed to be due to the gonococcus. For this reason only sixty-four out of the 159 patients receiving penicillin had microscopic tests before re-treatment, the gonococcus being found in 54 (84.4 per cent.). These were the patients in whom the signs of persistent urethritis were minimal.

Nine patients (4.4 per cent.) developed complications of gonorrhœa, six after treatment had been given and three during sulphonamide therapy; of the latter, one developed acute prostatitis the second acute epididymo-orchitis, the third acute prostatitis and epididymo-orchitis. The remaining six were

found to have a gross excess of polymorphonuclear leucocytes in their prostatic secretions.

### Toxic Effects of Sulphonamides

Two patients had severe complications due to sulphonamide therapy. One developed acute toxic œdema, the other severe vomiting and prostration. Neither of these patients had had sulphonamides before. In each case penicillin had to be given.

In addition to the two patients with severe reactions, mild symptoms showed in another fourteen, eleven of whom were on their first course, but all were able to complete the course of tablets. Thus 5.4 per cent. of 205 patients showed slight evidence of intolerance, and 1 per cent. severe reactions to their initial treatment.

These figures do not fully reveal the adverse effects of the sulphonamides. One hundred patients were questioned after their initial sulphonamide therapy and only twelve said that the tablets had no effect on their general well-being.

### Previous Gonorrhœa

A history of one or more previous attacks of gonorrhœa was given by five (17 per cent.) of the group cured with sulphathiazole, also by fifty-three (30 per cent.) of those in which treatment failed, and seventy-two (40 per cent.) of the defaulters. Sulphonamides had been given previously to five (17 per cent.) of the patients cured, to forty-five (26 per cent.) of those in whom the treatment failed, and to fifty-three (29 per cent.) of the defaulters.

### The Defaulters

Of the original 408 patients, no less than 181 defaulted: 122 (67 per cent.) of these had stopped attending by the end of one week. This is an important fact, for it means that the ideal treatment must be short and fully effective within that time.

A detailed analysis of the causes of default would be out of place here. Suffice it to say that the population of Soho is particularly shifting and unstable. It is also known that some defaulting patients went elsewhere for "injections."

### Summary

1. Four hundred and eight male patients with acute gonorrhœa treated with sulphathiazole were studied.

2. Two hundred and five cases were followed for three months with full tests of cure. Twenty-nine (14.1 per cent.) passed these tests.

3. In 176 (85.8 per cent.) of these 205 the treatment failed.

4. Complications of gonorrhœa occurred in nine patients in spite of treatment with sulphonamides.

5. Severe complications of sulphonamide therapy occurred in two (1 per cent.).

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## REFERENCES

- Campbell, D. J. (1944). *Brit. med. J.*, **2**, 44.  
Jefferiss, F. J. G., and McElligott, G. L. M. (1943). *Lancet*, **1**, 65.  
King, A. J. (1939). *Brit. J. vener. Dis.*, **15**, 106.  
Laird, S. M. (1942). *Lancet*, **1**, 463.  
Sommerville, J. (1941). *Brit. med. J.*, **1**, 961.  
Williams, D. I., King, A. J., and Nicol, C. S. (1944). *Brit. J. vener. Dis.*, **20**, 97.