

## NON-SPECIFIC URETHRITIS\*

A PROBLEM OF MANAGEMENT RATHER THAN OF REPEATED ANTIBIOTICS

BY

Captain P. S. KERSHAW  
*Royal Army Medical Corps*

AND

Lieutenant J. G. LINDSAY  
*Royal Army Medical Corps*  
*Special Treatment Centre, Britcom General Hospital, Japan*

### INTRODUCTION

NON-SPECIFIC urethritis is a disease of uncertain aetiology, which is difficult to treat and often relapses. As many antibiotics have been used in its treatment as pathogens have been blamed for its causation. Our experience in this Centre leads us to believe that a further reduction in the relapse rate can be achieved by skilful man-management.

### METHOD

The relapse rate and its causation have been studied in 378 fresh cases of non-specific urethritis. None of these cases had had treatment for the condition prior to attending this Centre.

The diagnosis was established by finding, within seven to twenty-one days of exposure, a hazy urine with numerous pus threads and a mucopurulent discharge which on staining by Gram's method showed numerous pus cells, occasional epithelial cells and organisms other than gonococci—*e.g.* diphtheroids, straphylococci, streptococci, coliforms and mouth commensals.

Non-specific urethritis was differentiated from traumatic urethritis produced by excessive sexual activity or "milking down" of the urethra, and from chemical urethritis produced by the intra-urethral use of strong antiseptics. These conditions cause a sparse discharge in which epithelial cells greatly outnumber pus cells. All cases were treated as follows :

- (a) Streptomycin 1 gram *stat.*
- (b) Sulphadiazine 2 grams *stat.*, followed by 1 gram every four hours to a total of 32 grams.
- (c) *Mist. sod. cit.*  $\frac{1}{2}$  fl. oz. *q.d.s.* and fluids to 7 pints daily throughout the course of treatment.

In addition it was strongly stressed to the patient that he should abstain for

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six weeks from all forms of alcohol, coca-cola, coffee (the latter two contain caffeine), further sexual exposure and all manual interference.

Routine surveillance was a clinical check of urine and discharge (if present) at seven and fourteen days. Final test of cure at three months was a clinical examination of urine, discharge (if present) and prostate.

Serological tests for syphilis were negative in all cases.

Table 1. *Results of treatment*

| Follow-up           | Fresh Cases |          |         | After Gonorrhœa |          |         | Combined Relapse Rate |
|---------------------|-------------|----------|---------|-----------------|----------|---------|-----------------------|
|                     | Followed    | Relapsed | Relapse | Followed        | Relapsed | Relapse |                       |
| 1-7 days            | 329         | 27       | 8.2%    | 49              | 2        | 4.1%    | 7.7%                  |
| 8-14 days           | 329         | 25       | 7.6%    | 49              | 6        | 12.2%   | 8.2%                  |
| 15-28 days          | 329         | 8        | 2.4%    | 49              | —        | —       | 2.1%                  |
| 28 days to 3 months | 329         | 2        | 0.6%    | 49              | —        | 0       | 0.5%                  |

In 378 cases, 70 relapses. Total Relapse Rate 18.5%.

Table 2. *Details of relapses*

| Follow-up             | Fresh Cases |               |                |         | After Gonorrhœa |               |                |         |
|-----------------------|-------------|---------------|----------------|---------|-----------------|---------------|----------------|---------|
|                       | Alcohol     | Manual trauma | Fresh exposure | Unknown | Alcohol         | Manual trauma | Fresh exposure | Unknown |
| 1-7 days              | 2           | 5             | 1              | 19      | 1               | 0             | 0              | 1       |
| 8-14 days             | 12*         | 6             | 2              | 5       | 4               | 1             | 0              | 1       |
| 15-28 days            | 3           | 1             | 0              | 4       | —               | —             | —              | —       |
| 28 days to 3 months   | 0           | 0             | 0              | 2       | —               | —             | —              | —       |
| Total Relapses due to | 17          | 12            | 3              | 30      | 5               | 1             | 0              | 2       |

\* Two cases classified under alcohol were actually anæsthetic relapses. Both cases had ether.

Table 3. *Relapses due to unknown causes (i.e., true treatment failure) compared with known causes*

| Follow-up   | Fresh Cases (329) |     |         |     | After Gonorrhœa (49) |      |         |     | Combined (378) |      |         |     |
|-------------|-------------------|-----|---------|-----|----------------------|------|---------|-----|----------------|------|---------|-----|
|             | Known             |     | Unknown |     | Known                |      | Unknown |     | Known          |      | Unknown |     |
|             | No.               | %   | No.     | %   | No.                  | %    | No.     | %   | No.            | %    | No.     | %   |
| At 3 months | 32                | 9.7 | 30      | 9.1 | 6                    | 12.2 | 2       | 4.1 | 38             | 10.1 | 32      | 8.5 |

## RESULTS

Table 1 shows that of 378 cases treated during the period, 70 relapsed, giving a relapse rate of 18.5 per cent., and that there was no significant difference in the relapse rate between fresh cases and cases occurring after gonorrhœa.

Table 2 shows that of the 70 cases which relapsed, 22 were due to indulgence in alcohol, 13 to manual trauma, 3 to fresh exposure, and 32 to unknown causes.

Table 3 shows that the true relapse rate due to failure of treatment was 8.5 per cent.

To determine the effect of other antibiotics on the relapse rate a further 75 cases of previously untreated non-specific urethritis were divided into three groups of 25 cases each.

The first group was treated with the routine method of 1 gram streptomycin and 32 grams sulphadiazine, and had a relapse rate of 19 per cent.

The second group was treated with a course of terramycin, 500 mg. *stat.* and 250 mg. every six hours to a total of 5.5 g. This group had a relapse rate of 36 per cent.

The third group was treated with a course of aureomycin 500 mg. *stat.* and 250 mg. every four hours to a total of 8.5 g. This group had a relapse rate of 25 per cent.

The number of cases in this trial was small. Nevertheless the trial indicates that the tetracycline group of antibiotics hold no dramatic therapeutic advantages over the current method of treatment using streptomycin and sulphadiazine.

#### *Mechanism of Relapse*

The one common factor in the relapses due to known causes is excessive production of mucus by the glands surrounding the urethra. This can be caused by alcohol, anæsthetic gases (especially ether), trauma (either manual interference or sexual intercourse) and caffeine. No adequate explanation has been discovered for the relapses not due to the agents listed above, and it must be surmised that they are due to failure of the treatment given.

#### *Treatment of Relapses*

Treatment of the first relapse was a course of streptomycin 1 gram daily for six days and *mist. sod. cit.*  $\frac{1}{2}$  fl. oz. *q.d.s.* for seven days. Treatment of the second relapse was a course of aureomycin 500 mg. *stat.* and 250 mg. four-hourly to a total of 8 g. Fluids during this course were restricted to 3 pints per day.

Of the 22 relapses due to alcohol, 17 responded to streptomycin and 3 responded to streptomycin followed by aureomycin. The remaining 2 had developed prostatitis despite courses of streptomycin and aureomycin, and finally responded to irrigations of potassium permanganate, 1/10,000.

Of the 13 traumatic relapses, 10 responded to streptomycin and the other 3 to a course of streptomycin followed by aureomycin. All the relapses due to fresh exposure responded to a further course of streptomycin.

Of the 32 relapses due to unknown causes, 8 responded to streptomycin and 14 responded to streptomycin followed by aureomycin. The remaining 10 developed prostatitis; 8 responded to irrigations (after courses of streptomycin and aureomycin) and 2 responded to intravenous T.A.B. therapy after courses of streptomycin, aureomycin and irrigations.

The 70 relapses were followed for a further three months and were all

clear at that time, when prostatic examination revealed normal prostates in every case.

It should be noted that the relapses due to known causes responded much more readily to treatment and developed fewer complications.

An interesting case which illustrates our point for the necessity of management is the following. A warrant officer who contracted non-specific urethritis was treated at a clinic outside our jurisdiction. Over a period of six weeks he received sulphadiazine (32 g.), streptomycin 8 g., penicillin 1 mega unit, chloromycetin 7.5 g., aureomycin 8 g. and terramycin 6.5 g. His discharge persisted in spite of the sustained antibiotic medication, and when he attended this Centre he presented with a typical non-specific urethritis. On questioning it became obvious he had received inadequate instruction on the conduct necessary whilst undergoing treatment and surveillance. He had not only made a habit of "milking down" his urethra twice daily to ascertain if his discharge persisted, but also had been consuming alcohol at regular intervals during his treatment. The position was explained to him and he was given a course of streptomycin 1 gm. daily for six days, sulphadiazine 1 g. four-hourly to a total of 32 g., *mist. sod. cit.*,  $\frac{1}{2}$  fl. oz. *q.d.s.*, and fluids to 7 pints. He was clinically clear for the first time at seven days and remained so until his final test of cure.

### CONCLUSIONS

We consider that the treatment for non-specific urethritis is much more than merely the administration of antibiotics. Very little has been said in the existing publications about the necessity for the patient's co-operation whilst undergoing the appropriate drug therapy. We believe that drug therapy alone is never sufficient; this is brought out when the low relapse rate (8.5 per cent.) due to unknown causes is considered.

The clinical trial involving 75 cases revealed that streptomycin and sulphadiazine are the most effective therapeutic agents in the treatment of this condition, bearing in mind that the co-operation of the patient is essential, and that aureomycin appears more efficacious after a course of streptomycin and sulphadiazine. Aureomycin given from the onset appears to give slightly better results than terramycin.

### SUMMARY

Some 378 previously untreated cases of non-specific urethritis were treated with streptomycin and sulphadiazine. The total relapse rate after three months was 18.5 per cent., but if relapses due to known and avoidable causes were subtracted the relapse rate was 8.4 per cent.

The importance of avoiding known causes of relapse by management of the patient is emphasized.

The mechanism of relapse and treatment of relapse are discussed, and an

illustration of a mismanaged case given. The incidence of complications related to the cause of the relapse is noted.

From a small clinical trial involving a further 75 fresh cases of non-specific urethritis it was found that treatment using streptomycin combined with sulphadiazine gave the best results, and that aureomycin gave slightly better results than terramycin.

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