

## PAPERS AND ORIGINALS

## Duration of Treatment for Urinary Tract Infections in Children

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### Summary

**In a double-blind trial 45 children aged 6 months to 14 years with *Escherichia coli* infections of the urinary tract were given co-trimoxazole for two weeks and then allotted at random to one of two treatment groups for the remainder of six months; one continued with the active drug and the other with dummy tablets of identical appearance. Of the 24 children who took co-trimoxazole for two weeks and the 21 who took it for six months, 11 and 10, respectively, remained without further infections for at least a year. Over 90% of the reinfections occurred within five months of stopping the antibiotics, and the longer treatment did not cause any delay in their appearance. Thus probably a six-month course of treatment is no more likely to achieve a cure than a two-week course; nevertheless, no infection occurred during treatment, and there may be an advantage in continuing with antibiotics in small dosage.**

### Introduction

Opinions on the optimum duration of treatment with antibiotics for urinary tract infections in adults and children vary from a week<sup>1-3</sup> to a year or more.<sup>4-6</sup> Most workers agree that a short course will get rid of the infection, and also that reinfection is prevented while antibiotics are continued. Whether further infection is less likely after a long course than after a short one is not known.

De Luca *et al.*<sup>7</sup> studied children with uncomplicated urinary infections and compared 597 who were treated for up to a month with 412 treated for six months. They considered the six months of treatment to be the better, but their follow-up observations were incomplete and there were many non-

attenders. Kincaid-Smith and Fairley<sup>2</sup> studied adults with recurrent urinary infections who were given ampicillin or nitrofurantoin for either two or six weeks. One and six weeks later similar numbers of urines were infected. Bergström *et al.*,<sup>8</sup> in a trial on 279 girls with first- or second-time urinary tract infections, found that sulphafurazole given for 60 days was no better than when given for only 10 days in preventing reinfection the following year. Unfortunately, most of the organisms causing fresh infections both during and after treatment were sulphonamide-resistant, so that the sulphafurazole did not seem satisfactory however long it was given.

### Present Trial

Most strains of *Escherichia coli* are sensitive to co-trimoxazole and rarely acquire resistance. When this drug combination became available I undertook a further comparative trial of different lengths of treatment since the same drug could be used for all cases with a reasonable chance that it would remain effective throughout. The trial was started in 1969 with the aim of comparing two weeks with six months of treatment. I hoped that with such extremes any difference in reinfection rate would be apparent. All the patients were children with active urinary tract infections, either first attacks or reinfections. Neonates were excluded, as were children with impaired drainage due to obstruction or bladder paralysis. On the other hand, children with vesicoureteric reflux, mild kidney scarring, or duplications were included in the trial. In each case before the trial I obtained the agreement of the family doctor and asked him not to prescribe other antibiotics during the trial. Criteria for inclusion were thus: age 6 months to 14 years; active urinary tract infections proved by two or more consecutive, significant, and consistent urine cultures accompanied by pyuria; *E. coli* infections sensitive to co-trimoxazole; unimpaired drainage of the urinary tract; and willingness of parents and general practitioner to allow the child to participate.

The trial was double-blind. All patients were given co-trimoxazole for two weeks and then allotted at random to one of two groups according to a key held in the pharmacy. At the end of the two weeks one group continued with the active drug for the remainder of six months and the other with dummy tablets of identical appearance. The children were seen at intervals of one or two months, both when taking the tablets and for at least a year after stopping them. At each visit they were asked about symptoms and whether there had been any other illness or treatment at home. Samples of urine were also cultured and examined for leucocytes. Tablets were supplied from hospital, the exact number being given to last until the next outpatient visit, when mother and child were asked if they had any left.

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## Results

The trial was stopped after 50 cases had been collected, when it was found that one patient had been wrongly included because the *E. coli* were resistant to co-trimoxazole, while four others had either defaulted or been given antibiotics for other infections. Of the remaining 45 patients 24 had been given two weeks of treatment and 21 six months of treatment. The two groups seemed comparable (table I), the only appreciable differences being the inclusion of all three boys in the group treated for six months and a greater number with vesicoureteric reflux in the group treated for two weeks. Blood values including white cell count, haemoglobin, urea, and creatinine were similar.

TABLE I—Comparison of Groups Treated for Two Weeks and Six Months

	2 Weeks	6 Months
Total No. of cases	24	21
No. of boys	0	3
Average age at onset (years)	3.75	4.0
Average age when entered trial (years)	8.0	7.9
Length of history:		
Under 1 week	1	2
From 1 week to 1 month	4	2
From 1 month to 1 year	4	6
Over a year	13	9
Unknown	2	2
Previous urinary infections:		
None	8	7
Average for cases known	1.4	1.6
Range	0-8	0-6
Unknown	3	3
Vesicoureteric reflux:		
None	13	16
Unilateral	6	1
Bilateral	4	2
Unknown	1	2

"Cure" was taken as the absence of any further infection in the year after active treatment was stopped. Table II gives the numbers regarded as cured in the two groups subdivided according to length of history. Of the patients with symptoms for less than a month four out of five were cured with two weeks of treatment and four out of four with six months of treatment. Of those with a history longer than a month or of unknown duration 7 out of 19 (37%) were cured with two weeks of treatment and 6 out of 17 (35%) with six months of treatment. Overall the cure rates were 46% and 48% for two weeks and six months of treatment, respectively. Thus there was little difference between the groups, and this was still so when "cure" was taken as freedom from infection for any shorter period than a year.

TABLE II—No. of Cases without Further Infection in Year after Stopping Treatment Related to Length of History and Duration of Treatment

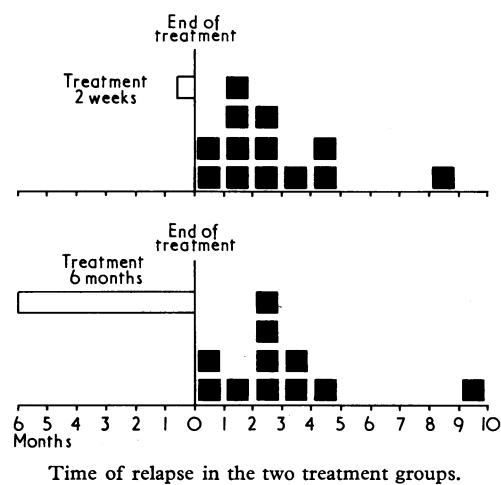
Length of history:	<1 Month	≥1 Month	Not Known	Total
Treated for 2 weeks	4	5	2	11
Treated for 6 months	4	4	2	10

Since the differences in sex and vesicoureteric reflux distribution between the two groups might have biased the results, the data were re-analysed, first omitting the boys and then those with reflux. All three boys had six months of treatment and all were cured, so that their removal made the two-week results relatively better. Similarly, removal of the refluxing cases also favoured the short-treatment group, since all three cases treated for six months were cured compared with only four of the 10 treated for two weeks.

Further infections were frequent in both groups. In all, apart from one after a fortnight's treatment, the organisms were still sensitive to co-trimoxazole. Over 90% of the reinfections occurred within five months of stopping co-trimoxazole, and it could not be shown that the longer treatment caused any delay in their appearance (see fig.).

## Discussion

These observations suggest that a six-month course of treatment is no more likely to achieve a cure than a two-week course. This does not necessarily mean that prolonged treatment is of no value, for infections did not occur while it was being given (see fig.). Such antibiotic protection, which may be achieved with remarkably small doses, is likely to benefit patients who are subject to repeated urinary infections or who, because of vesicoureteric reflux, have kidneys especially vulnerable to ascending infection. The prevention of reinfection may also help in management. It avoids discouraging parents, who are apt to lose heart when new infections occur often. The child is more likely to be brought for follow-up if she is still having treatment; moreover, the visits need be less frequent. A reasonable practice might be to treat first and second infections with antibiotics for one or two weeks only but, for any subsequent infection, to continue, after initial control, with small doses of



antibiotic as a preventative measure for six months or more. In all cases it is essential to keep a close watch for further evidence of infection, particularly in the first five months after stopping treatment.

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