Co-trimoxazole and cephalixin in urinary tract infection

Sir,—A plausible explanation is to hand for the superior performance of co-trimoxazole compared with cephalixin in the urinary tract infection trial of Drs P E Gower and R W Tasker (20 March, p 684).

Contrary to their statement that "cephalexin readily induces spheroplast formation,"* it has repeatedly been shown that the sole effect of therapeutically useful concentrations of cephalixin (and the related cephadine and cephaloglycin) is to cause filamentation of enterobacteria by inhibiting the division process. Because of this cephalixin is more slowly bactericidal than other β-lactam antibiotics and more bacteria are likely to survive in the urine, where, as Drs Gower and Tasker rightly point out, a twice-daily dosage may achieve only transient high levels.

In addition, all cephalosporins now available are somewhat susceptible to enterobacterial β-lactamases, including a slow-acting extension of ampicillin-sensitive Escherichia coli strains.* Consequently tests of sensitivity of enterobacteria to cephalosporins are affected by inoculum size; this is particularly marked with ampicillin-resistant strains which frequently contain more than 10⁷ bacteria/ml. Concentrations of cephalosporins achievable in urine only transiently suppress such a bacterial population, recovery occurring as the antibiotic is broken down.† Disc sensitivity tests may give an over-optimistic view of the sensitivity of such strains to cephalosporins, even when conventional "high inocula" are used, as in the Bauer-Kirby test.‡

Sulphadiazine and trimethoprim are also susceptible to inulinom effects, but this is unrelated to degradation of the drugs.§ In contrast to β-lactam antibiotics, the components of co-trimoxazole are excreted into the urine slowly and the antibacterial activity is maintained in support of intrinsic clearance mechanisms.

Evidence for the validity of these considerations has been provided by experiments employing an in-vitro model in which some important aspects of the treatment of bacterial cystitis can be simulated.⁷-¹⁺ Such studies have shown that cephalosporins perform less well than penicillins (including benzyl- and phenoxymethyl-penicillin) in the dynamic conditions of the urinary bladder, using an initially dense, but ostensibly sensitive, bacterial population.⁸ Tested against ampicillin-resistant strains, judiciously chosen cephalosporins were also sensitive on the basis of disc tests, cephalosporins exhibited a further reduced capacity to suppress bacterial growth.⁹ In both these studies cephalixin was the least effective cephalosporin. Cephalosporina-zole and trimethoprin were tested in the model their efficiency in clearing infection was rather better than predicted by conventional tests.⁷

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Rheumatoid arthritis and ankylosing spondylitis occurring together

Sir,—The paper by Professor G H Fallet and others (3 April, p 804) documents a series of cases of rheumatoid arthritis occurring in patients with ankylosing spondylitis. They describe as extremely unlikely the possibility that these patients represent the random occurrence of two separate disease entities. Critical examination of the argument shows that coincidental occurrence is certainly not ruled out.

An accurate estimate of the real prevalence of ankylosing spondylitis is not available. The study of West and co-workers (29 October, p 995) suggests that ankylosing spondylitis may be as common as rheumatoid arthritis in certain parts of the country. In certain areas there are families of probands without spondylitis. The data of Lawrence⁴ offer the best available estimate of the prevalence of ankylosing spondylitis in the UK; in these controls there were no cases of rheumatoid arthritis. However, there are methodological problems which suggest that his prevalence figures are only an approximation and probably an underestimate. The figure given by the authors for the prior probability of a patient aged 40 with both severe rheumatoid arthritis and ankylosing spondylitis is unreliable and probably too