Co-trimoxazole and cephalexin in urinary tract infection

Sir,—A plausible explanation is to hand for the superior performance of co-trimoxazole compared with cephalexin 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 shown4 that the sole effect of therapeutically useful concentrations of cephalexin (and the related cephradine and cephaloglycin) is to cause filamentation of enterobacteria by inhibiting the division process. Because of this cephalexin 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 enzyme of ampicillin-sensitive Escherichia coli strains.4 Consequently tests of sensitivity of enterobacteria to cephalosporins are affected by inoculum size; this is particularly marked with ampicillin-resistant strains. This is because co-trimoxazole, which generally contains more than 10^6 bacteria/ml. Concentrations of cephalosporins achievable in urine only transiently suppress such a bacterial population, recovery occurring as the antibiotic is broken down.4 Disk 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.4 Sulphamethoxazole and trimethoprim are also susceptible to inulin effects, but this is unrelated to degradation of the drugs.7 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.7-11 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.7 Tested against ampicillin-resistant strains, the cephalosporins showed superior sensitivity7 on the basis of disc tests, cephalexins exhibited a further reduced capacity to suppress bacterial growth.10 In both these studies cephalexin was the least effective cephalosporin, and co-trimoxazole and trimethoprim were tested in the model their efficiency in clearing infection was rather better than predicted by conventional tests.7

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5. Schaffner, W, et al, Recent Results in Cancer Research, 1974, 47, 42.