**Correspondence**

**Intestinal side effects of cefoperazone, in perspective**

Sir,

In the article by Carlberg et al. (1982) the authors have expressed concern about an association of the agent with a high incidence of loose stools and diarrhoea, the isolation of *Clostridium difficile*, and the reduction of Simplesin AR values.

We believe that the methodology employed and the criteria for patient inclusion may not necessarily support the authors' conclusions. Cases were selected from two different study protocols without including all patients and without studying control populations. Patients were included who received concomitant medication or had basic disease processes that could have contributed to the diarrhoea and altered Simplesin values. This group of elderly patients included many cases with documented gastrointestinal diseases, diabetes, hepatic disorders, chronic alcoholism, and deficient nutrition.

Cefoperazone has undergone extensive clinical trials for over five years, and is currently being studied by investigators in over 25 countries. In the formal initial development program of 4485 patients, the overall incidence of loose stools and diarrhoea attributed to cefoperazone was only 3-4%. In Japanese studies of 2658 patients the incidence of diarrhoea was 0-9%, and in a large German multicentre study of 2062 patients the incidence was 2-8%. It is recognized that this figure varies somewhat with the study population, however, all patients were carefully monitored for side effects. The agent has been broadly marketed and side effects have not been found to present any significant problems.

D. L. GIBBS
J. L. HAKES
G. ANDO
Medical Department, Pfizer International, Inc.
New York, New York 10017
U.S.A.

**Metronidazole suppositories**

Sir,

In a recent letter (Lane, Pulvertaft & Hewitt, 1981) on the prophylactic efficacy of metronidazole administered rectally, the authors found the use of metronidazole suppositories for this purpose questionable on the grounds that the serum level of the drug was lower than the MIC values of the most common anaerobic pathogens. We were interested in this topic a few years ago, and as a result of *in-vitro* studies a type of suppository was developed containing 1-0 g metronidazole micronized in Massa Estarini 299 (a proprietary suppository base).

The serum levels of metronidazole after the insertion of these suppositories were determined in seven healthy volunteers by the spectrophotometric method. The measured levels and kinetic parameters, on the assumption of a one-compartment open model, are summarized in the table. The serum concentrations of rectally administered metronidazole reach the peak more slowly than in case of oral dosing, $t_{\text{max}}$ being between 4 and 6 h. The average peak concentration is 11-5 mg/l. Thus highly effective serum levels can be attained by means of the suppositories developed by us. Nevertheless, for prophylaxis the insertion of the suppository has to precede the operation by 4-6 h. Besides surgical prophylaxis, we have successfully treated patients suffering from anaerobic infections, in cases when the patients failed to tolerate oral administration.

A. SAMU
Department of Pharmacy
E. LUDWIG
Department of Medicine and Clinical Pharmacology
Hospital Péterfi
Budapest, Hungary

**References**
