patients pefloxacin dramatically shortened the duration of both fever and diarrhea after clinical failure of the initial therapy regimen. The initial antibiotic was active against the pathogen in vitro in all cases and the failure of this treatment, which was not explained by immunodeficiency, sickle-cell disease or gall bladder abnormality, was probably related to low intracellular penetration of the antibiotic. Children with enteric fever or invasive salmonellosis given the usual antibiotics such as ampicillin or cotrimoxazole can be expected to become afebrile in four to five days (4).

These seven patients remained febrile with severe bloody diarrhea for 4 to 8 days despite antibiotic therapy. The decrease in clinical signs and symptoms was significantly earlier when they were treated with pefloxacin, as shown in Table 2. There was no difference in the clinical presentation of the salmonellosis between patients in whom conventional treatment with ampicillin or amoxicillin was effective and patients in whom this treatment failed. Sensitivity of the bacteria to the antibiotics in vitro was the same in the two groups, but the clinical efficacy of amoxicillin, ampicillin or cotrimoxazole differed. Furthermore, six of nine patients successfully treated with beta-lactams became chronic asymptomatic carriers of salmonella, compared to only one of seven in the pefloxacin group.

The main potential side effect of the use of fluoroquinolones in children is toxicity for proliferating and articular cartilages, as described in some animals models. No analogous effects have been observed in humans of any age group after many years of use of the parent compound nalidixic acid (5). In children with cystic fibrosis treated with ciprofloxacin for three months, no evidence of arthropathogenicity of the drug has been found in clinical, radiologic and resonance imaging studies (6). Joint pains or stiffness are sometimes described with high doses of fluoroquinolones during prolonged treatment, but were not observed in our patients. Further studies on the safety of quinolones in the treatment of salmonellosis in children are needed (7). However, short-term treatment with pefloxacin could be useful in children with severe invasive salmonellosis after failure of conventional therapy, resolution of signs and symptoms being rapidly obtained.

References

Cefotiam hexetil is an ester prodrug of the cephalosporin cefotiam. Following oral administration of cefotiam hexetil, the drug is metabolized mainly into cefotiam and 1,2-cyclohexanediol (1). Compared to intravenous cefotiam, the bioavailability of cefotiam hexetil given per os is 68 % (1). Meals delay absorption but do not lower bioavailability (2). Cefotiam hexetil kinetics are linear at least in the 200-400 mg range and show no time dependency (1). The drug has been shown to be effective in the treatment of respiratory and urinary tract infections (2–4) and infections in the fields of surgery (5), dermatology (6) and otorhinolaryngology (7). In the last case, cefotiam concentrations have only been determined in rhinorrhea and otorrhea after oral administration of cefotiam hexetil (8); cefotiam penetration into sinus mucosa has been studied after intravenous (9) or intramuscular (10) administration of cefotiam. Because high tissue concentrations of the drug may be relevant to efficacy, in this study cefotiam concentrations were determined in secretions obtained from patients with chronic sinusitis by sinus puncture after administration of cefotiam hexetil.

Materials and Methods. Eighteen patients (10 men, 8 women) suffering from an acute infectious exacerbation of chronic maxillary sinusitis gave their informed consent to participate in the study, which was approved by the Ethics Committee of La Roseraie Clinic. The diagnosis was based on clinical criteria (relapsing infection) and x-ray findings, but no biopsy was performed. The mean age with standard deviation of the patients was 39.3 ± 13.0 years and their mean weight with standard deviation was 66.2 ± 9.8 kg. All participants were in good overall health and satisfied the inclusion criteria. Subjects were excluded for the following reasons: evidence of any major disease; presence of factors affecting absorption (e.g. gastrectomy, ulcers); administration of any antimicrobial therapy less than five days prior to sinus puncture; known hypersensitivity to any drug.

All patients were given 400 mg of cefotiam hexetil orally (on an empty stomach) in the form of two 200 mg capsules taken 12 h apart. Patients were divided into four groups according to the time which elapsed between the last dose (i.e. the second dose) and collection of secretion samples. The last dose was administered 2 h (group I), 3 h (group II), 4 h (group III) or 6 h (group IV) before sinus puncture. Aspiration of the fluid sample from the tapped sinus was performed using a syringe with a needle.

Sinus secretions were treated the same as plasma. Viscous or clotted puncture samples were deposited in tubes, accurately weighed and pulverized in liquid nitrogen using a Spex grinder (Spex 6700, Polylabo, France). The powder was then shaken for 15 min in 0.1 M phosphate buffer (pH 7.0), 1 ml/g of tissue. After centrifugation, the supernatant was treated the same as plasma.

Cefotiam concentrations in samples were determined by agar diffusion bioassay (11), using as the test organism a Proteus mirabilis strain isolated by the Microbiology Laboratory of Avicenne Hospital, Bobigny, France. The limit of quantification of the assay was 0.1 mg/l, and the linear range of the assay was 0.1 to 1.0 mg/l, using 50 µl samples. Interassay coefficients of variation were 20 % at 0.15 mg/l and 19 % at 1 mg/l.

Cefotiam concentrations were also measured by high-pressure liquid chromatography (HPLC) with UV detection using the assay described by Kees et al. (12). The limit of quantification was 0.05 mg/l and the calibration was linear until 2 mg/l using 200 µl samples. Interassay coefficients of variation were 6.2 % at 0.25 mg/l and 5.8 % at 1.0 mg/l.

Results and Discussion. Cefotiam concentrations measured in sinus secretions and plasma are summarized in Table 1 and Figure 1. Sinusitis exudate samples were sometimes too small to be assayed by HPLC; in those cases cefotiam concentrations were measured by microbiological bioassay. In a few patients, sinusitis secretions were obtained from both sides. The ratio of the concentrations from both sides ranged from 1.2 to 3.0. The mean of left and right concentrations was used in the calculation of the overall mean concentration of the group to avoid giving excessive weight to these patients in the estimation of the mean. In three patients, the sinus fluid was clotted and cefotiam concentrations had to be expressed in µg/g; these values were used without further transformation for the calculation of the mean (assuming the density of the sample was very