In 1948 John Woodward successfully used chloramphenicol to treat patients with typhoid fever (TF) [1]. After this accomplishment, the first choice for the therapy of TF was chloramphenicol until the 1970s, when the first outbreaks of infection by antibiotic-resistant bacteria appeared. The loss of sensitivity by Salmonella typhi to the antibiotics used for the treatment of typhoid fever was noted in the years following the beginning of antimicrobial therapy. Resistance strains frequently are resistant to chloramphenicol, trimethoprim-sulfamethoxasole and ampicillin. Resistance to these drugs is called multi-drug resistance (MDR). In places with high incidence of MDR strains of Salmonella typhi, quinolones like ciprofloxacin are the chosen agents for the treatment of TF. Recently, some countries have reported an increased resistance to these antibiotics.[2] Unfortunately, quinolones are contraindicated in pediatric patients and pregnant woman due to the potential damage to the articular cartilage. Additionally, the wide use of quinolones in the treatment and prophylaxis of different diseases contribute to the appearance of S. typhi resistant to ciprofloxacin [3,4]. In the search for alternative antibiotics for the treatment of typhoid fever, the third generation cephalosporins have shown good activity against S. typhi [5]. However, only cefixime and cefpodoxime proxetil allow oral administration for use in ambulatory patients. Cefixime is a third generation cephalosporin, for oral use in children and adults, administered once or twice daily with good antimicrobial activity against S. typhi. Due the emergence of MDR S. typhi in endemic countries, alternative drugs for the treatment of typhoid fever are required. We conducted this study to assess the efficacy of cefixime in the treatment of TF.

**PATIENTS AND METHODS:** We performed an open and non-randomized trial to assess the efficacy of cefixime in the antibiotic treatment of TF. The study was carried out at the University General Hospital, a secondary care facility in San Luis Potosí City, Mexico, from March 1997 to September 1999. We enrolled adult and pediatric (<15 years old) out-patients, both sexes, formerly healthy, with functional gastrointestinal tract, and without intestinal complications as perforation or extraintestinal complications like lymphadenitis, arthritis, multifocal osteomyelitis, brain abscesses, pneumonia or sepsis. Subjects with history of hypersensitivity to penicillins or cephalosporins were rejected. Typhoid fever was defined by fever >38.5°C for longer than three days and the isolation of S. typhi from blood or bone marrow culture. Culture specimens were processed in an automatic device (BacT Alert System, Organon Teknika Corp., Durham, NC). Identification of S. typhi was made by growth in Salmonella-Shigella agar and subsequently by biochemical tests. Patients were included after medical history and cultures were taken (day 0). All pediatric patients received doses of 5 mg/kg of cefixime po, twice-daily. Adult patients received a dose of 200 mg po, twice-daily. Subjects were evaluated on day 0 (start of study), day 5, and day 10. The primary criteria of efficacy were clinical cure (defined as absence of symptoms and signs of infection at day 10 of treatment) and bacteriological cure (defined as a negative culture to S. typhi at day 10 of treatment). Antimicrobial susceptibilities were performed in all isolates for a reference method: agar dilution. Agar dilution method was carried out on Mueller-Hinton agar. Results for each antimicrobial agent were interpreted as indicating susceptibility, intermediate susceptibility, or resistance according to current guidelines of the National Committee for Clinical Laboratory Standards (NCCLS). The hospital ethics committee approved the study, and all subjects or parents gave informed consent.

**RESULTS:** The study included 24 adult and pediatric patients. The demographic characteristics of the subjects enrolled in the study are summarized in Table 1. All patients showed improvement of symptoms and signs, particularly fever abatement, which was observed on the average at day 4 after start of treatment. At the end of the study, 23 (96%) patients, showed clinical cure. Clinical relapse was observed in one case (4%) at day 8 after start.
of treatment, with isolation of *S. typhi* from stools. This case was successfully treated with ceftriaxone (1 g iv twice daily). Bacteriological cure was observed in the remaining 23 patients with blood, stool and urine cultures negatives after therapy (day 10).

**Results of susceptibility test.** From 24 isolates, 22 (87%) were sensitive to ampicillin, and 96% were sensitive to chloramphenicol, and trimethoprim-sulfamethoxasole. All strains were sensitive to cefixime (Figure 1). We found no cases of multi-drug resistance.

Figure 1. Antibiotic susceptibility of 24 isolates of *Salmonella typhi*.

**DISCUSSION:** Traditionally, chloramphenicol has been the antibiotic of choice for the treatment of typhoid fever particularly in developing countries, with ampicillin and trimethoprim-sulfamethoxasole as alternative drugs. Due to a high rate of relapses, the unacceptable risk for inducing aplastic anemia of chloramphenicol and the emergence of multi-drug resistance, its necessary to search drugs that, prevent relapses and chronic carrier state, produce quick remission of the fever, sterilize infected tissues, and can be administered orally with the smallest number of daily doses.

To date, the fluoroquinolones are the agents of choice for the treatment of MDR typhoid fever. However, the role of these agents in the pediatric population is controversial, as they can cause damage to the articular cartilage [6]. In this setting, cefixime accomplishes the desired characteristics of an antibiotic and may be the treatment of choice of MDR and non-MDR typhoid fever, particularly in children from endemic areas with high prevalence of MDR typhoid fever. In our study, cefixime showed clinical efficacy around 100%, with low-rate of relapses. All strains isolated were sensitive to cefixime.

**REFERENCES**