days to develop, as in this case [7,8]. An IgM antibody directed against ceftriaxone has been one of the processes in third-generation cephalosporin-induced hemolysis [3,8]. The clinical course of our case, with a duration of 10 days between hemolysis and initiation of the ceftriaxone therapy, laboratory results and development of renal failure, suggests that the process was IgM-type immune complex mediated [3].

In all of the reported cases with hemolytic anemia induced by ceftriaxone, the patients were immunocompromised in some way. The majority of the cases were children and had hematologic disorders such as sickle cell anemia. Many of them had been exposed to ceftriaxone previously [1,4] but this patient could not recall any previous cephalosporin therapy. He was apparently immunocompetent. He was hospitalized for the first time in his life, he was completely healthy and he had no recurrent infection or diarrhea.

In this fatal complication of ceftriaxone therapy, no risk factors, such as repeated exposure to ceftriaxone or pre-existing hemolytic anemia, were identified. Although the patient had received amoxycillin–clavulanate immediately prior to receiving ceftriaxone, this is unlikely to have been a contributing factor, as very little of the prescribed dose was taken. Therefore, every patient receiving ceftriaxone, including those with no underlying disease, should be observed carefully. Drug-induced hemolytic anemia should always be considered in the differential diagnosis of intravascular hemolysis in patients receiving ceftriaxone and possibly other third-generation cephalosporins.

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Nosocomial diarrhea caused by *Salmonella derby* infection in two patients on chemotherapy

Clin Microbiol Infect 1999; 5: 586–588

Nosocomial diarrhea, defined as the onset of diarrhea more than 72 h after admission, is most frequently associated with *Clostridium difficile* infection or drug administration. Other enteropathogenic bacteria, although common in community-acquired diarrhea, are rarely involved. Routine stool cultures are therefore generally not required in the investigation of patients with nosocomial diarrhea, and some microbiological laboratories have implemented a rejection policy for such samples [1]. We report on two patients who presented with nosocomial salmonellosis during chemotherapy-induced neutropenia.

Patient A was a 37-year-old woman with a 2-year history of disseminated breast carcinoma, admitted on 2 January 1997 for chemotherapy and peripheral blood stem cell transplantation. She was assigned to a double room with a private lavatory. She had no complaints and reported one or two formed bowel movements per day. There was no history of overseas travel and there were no cases of diarrhea in her family. Her physical examination was unremarkable except for a mastectomy scar. Laboratory data on admission were: hemoglobin 102 g/L, leukocytes 8300/μL, platelets 180 000/μL, and C-reactive protein (CRP) 1 mg/L (normal range <8 mg/L). High-dose chemotherapy with cyclophosphamide (1500 mg/m^2 per day), carboplatin (200 mg/m^2 per day) and thiotepa (125 mg/m^2 per day) was administered from 3 January to 5 January. Supportive therapy included co-trimoxazole (480 mg/day PO), fluconazole (100 mg/day PO), omeprazole (40 mg/day PO) and metoclopramide. Peripheral blood stem cell transplantation was performed on 8 January, and neutropenia developed on the following day. From 7 January to 9 January, she experienced self-limited diarrhea. Stool cultures and ELISAs for *C. difficile* toxin taken on 8 January and 12 January were negative. On 13 January she developed pyrexia, followed the next day by abdominal cramps, watery diarrhea and a rise of CRP. Gram-negative sepsis was suspected and ceftazidime (2 g/8 h IV) given. A set of blood cultures taken on 14 January was negative, as was an ELISA for fecal *C. difficile* toxin. A stool culture grew

Salmonella derby, sensitive to ampicillin, ciprofloxacin, cefotaxime and co-trimoxazole. The patient became afebrile on 15 January, and stool habits reverted to normal on 21 January. Ceftazidime was given for 10 days. Follow-up stool cultures were negative.

Patient B was a 34-year-old woman with a 3-month history of disseminated breast carcinoma, admitted to the same room as patient A on 7 January 1997. She reported one or two formed bowel movements per day and denied overseas travel and recent cases of diarrhea in her family. On physical examination there was a mastectomy scar. Laboratory data on admission were: hemoglobin 108 g/L, leukocytes 2800/μL, platelets 169000/μL, and CRP 1 mg/L. High-dose chemotherapy and supportive therapy (for drugs and dosage, see patient A) were started on 9 January, and peripheral blood stem cell transplantation was performed on 14 January. Watery diarrhea developed on 16 January. The temperature was 37.2°C, and the abdomen was soft and tender. Laboratory investigations revealed neutropenia and a normal level of CRP. Stool cultures from 16, 17 and 18 January grew *S. derby* with the same susceptibility pattern as the strain grown from the stool of patient A. *C. difficile*-toxin was not detected. Ciprofloxacin (200 mg/12 h IV) was started. Follow-up stool cultures on 21 and 26 January were negative. The patient was discharged on 30 January.

All stool examinations were performed in the Institute of Medical Microbiology and Hygiene of the University of Freiburg according to the guidelines of the German Society of Hygiene and Microbiology [2]. Briefly, samples are plated onto Endo agar, Leifson agar, and cefsulodin–irgasan–novobiocin (CIN) agar. Additionally, two enrichment media (Kauffmann broth and selenit broth) are inoculated and subcultivated after 24 h on Endo agar, Rambach agar and brilliant green–phenol red–lactose–saccharose agar. CIN agar plates are incubated at 30°C for 48 h, and all other media are incubated at 37°C for 24 h. From January 1992 to December 1996, *S. derby* was cultured from a total of nine patients, amounting to approximately 0.35% of all *Salmonella* isolates. The most recent isolation of *S. derby* dated back to June 1996, and no further isolates were obtained through August 1998.

We report on two patients who developed nosocomial diarrhea with *S. derby*. Both patients were immunosuppressed due to disseminated malignant disease and chemotherapy-induced neutropenia, and both were on treatment known to decrease the infectious dose for enteropathogens, i.e. antibiotics and acid-suppressive therapy. Of note is the fact that the administration of co-trimoxazole at a dosage aimed at prevention of *Pneumocystis carinii* infection was unable to prevent infection with a susceptible strain of *S. derby*.

Although genetic fingerprinting was not performed, nosocomial transmission of *S. derby* from patient A to B can be assumed on the basis of time course, identity of susceptibility spectra and rarity of human isolates of *S. derby* in our area. Patient A may have acquired *S. derby* through hospital food or staff. However, salmonellosis did not occur in equally immunosuppressed patients exposed to the same food and staff, and neither patient had consumed food from outside the hospital. We therefore consider hospital acquisition to be an unlikely event. The carrier rate for salmonellae in the population served by our laboratory is estimated at 4% [3], and overgrowth of *S. derby* in an asymptomatic carrier triggered by antibacterial and cytotoxic treatment appears to be a plausible explanation.

S. derby is one of the most common serotypes isolated from humans in certain Asian countries [4] but is rarely isolated from humans in Europe [5] and the USA [6]. In the area served by our laboratory, *S. derby* accounts for only 0.35% of all human *Salmonella* isolates. However, this species has been involved in an epidemic of nosocomial infection in the northeastern USA [7] and has previously been found to cause salmonellosis in patients with neoplastic disease with unexpected frequency [8].

Sporadic nosocomial diarrhea in adults is rarely caused by enteropathogenic bacteria other than *C. difficile*. Previously undiagnosed enteropathogens are grown from less than 1% of routine stool cultures taken after the third day of hospitalization [9]. Some laboratories have therefore implemented a '3-day rule', rejecting stool culture requests on patients after the third day of hospitalization except under special circumstances such as suspected nosocomial outbreaks [1] or immunosuppression [9]. However, exempting patients with any degree of immunosuppression from the '3-day rule' would mitigate the effect of such a rule, given the high prevalence of disease- or drug-related immunosuppression in internal medical patients. We feel that exemptions to the '3-day rule' should be defined more precisely. Patients with malignancies undergoing chemotherapy are particularly susceptible to infections with salmonellae and other enteropathogens because of impaired cellular immune mechanisms, frequent antibiotic treatment, gastric acid suppression and mucositis. Salmonellosis in cancer patients is associated with considerable excess mortality [10]. On the basis of our observations and previous reports [7,11,12], we suggest that routine stool cultures, in addition to testing for *C. difficile* toxin, be routinely performed in all neutropenic patients with nosocomial diarrhea. Furthermore, screening for *Salmonella* carriage of patients awaiting high-dose chemotherapy may be appropriate, depending on the local frequency of asymptomatic *Salmonella* carriage.

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Resistance of *Salmonella* and *Shigella* in Turkey

Clin Microbiol Infect 1999; 5: 588–590

Enteric infections caused by *Salmonella* and *Shigella* are endemic in Turkey. Salmonella gastroenteritis is usually self-limiting and does not require antimicrobial therapy, except for some severely ill patients or patients who have underlying diseases [1]. Ampicillin, chloramphenicol and trimethoprim–sulfamethoxazole are the antibiotics of choice for typhoid fever and some bacterial enteritis for which therapy is indicated [2,3]. High resistance rates in non-typhi *Salmonella* and *Shigella* strains against ampicillin, chloramphenicol and trimethoprim–sulfamethoxazole have been reported [4–8]. These long-used antimicrobials are being replaced by quinolones, as they have excellent activity against enteric pathogens, high intestinal luminal concentrations and good intracellular penetration. However, there are alarming reports of reduced susceptibility and even resistance of *Salmonella* strains to quinolones [9,10]. We determined the antimicrobial resistance of *Salmonella* and *Shigella* strains isolated from seven different centers in Turkey.

One hundred and ninety-two *Salmonella* and *Shigella* strains isolated between August 1994 and September 1995 were used in the study. Nineteen *Salmonella typhi* and 82 non-typhi *Salmonella* strains (49 serogroup B, 26 serogroup D, four serogroup A, two serogroup C and one serogroup E) were isolated from blood and stool specimens. *Shigella* strains (53 *Shigella sonnei*, 33 *Shigella flexneri*, four *Shigella boydii* and one *Shigella dysenteriae*) were all stool isolates. There were no duplicate isolates from the same patient. The age of the patients ranged from 12 to 76 years. All of the *Salmonella* and *Shigella* strains were isolated from community-acquired infections. The bacteria from all centers were transported in Mueller–Hinton agar to the study center. The strains were checked for purity and biochemical characteristics and serotyped by using standard type-specific antisera (Difco, Detroit, MI, USA) [11].

In vitro susceptibilities of *Salmonella* and *Shigella* strains against ampicillin, chloramphenicol, ofloxacin, ciprofloxacin and pefloxacin were determined by a broth microdilution method, whereas agar dilution was used for trimethoprim–sulfamethoxazole according to the instructions of the NCCLS [12]. *Escherichia coli* ATCC 25922 was used as the control strain. Minimum inhibitory concentrations (MIC_{90}) of ampicillin, chloramphenicol, ofloxacin, ciprofloxacin, pefloxacin and trimethoprim–sulfamethoxazole for *Salmonella* and *Shigella* strains and the resistance rates are given in Table 1.

Three of 19 (16%) *Salmonella typhi* isolates were resistant to ampicillin, chloramphenicol and trimethoprim–sulfamethoxazole. Ampicillin and chloramphenicol resistance among group B *Salmonella* strains was more striking than that of trimethoprim–sulfamethoxazole. All *Salmonella* isolates were susceptible to the quinolones tested.