

## Letters to the Editor

### Detection of Carriage of Vancomycin-Resistant Enterococci in an Intensive Care Unit in Buenos Aires

#### To the Editor:

Enterococci have been recognized as one of the major causes of nosocomial infections in the United States during the past 2 decades. The prevalence of vancomycin-resistant enterococci (VRE) associated with nosocomial infections in the United States increased from 0.3% in 1989 to 7.9% in 1993.<sup>1</sup> In Argentina, the first infection produced by vancomycin-resistant *Enterococcus faecium* was documented by Marin et al in 1996,<sup>2</sup> and even though other strains of VRE continue to be isolated, they have not been reported in the literature (MEDLINE, 1996-2000). The real prevalence of the intestinal carriage of VRE in Argentina is still unknown.

We conducted a prospective descriptive study on a 12-bed intensive care unit (ICU) during a 7-month period with the aim of assessing the intestinal carriage of VRE in patients at the time of admission to the ICU and during their hospitalization period.

We evaluated 136 patients over a total of 291 admissions in the ICU. Patients admitted in the ICU came either from the community, the general ward of our institution, or another institution. One rectal sample, obtained by swabbing the anal margins, was taken on admission. Those patients hospitalized for more than 7 days had a second sample taken weekly. The swabs were inoculated in Bilis-esculine-azida-agar plates with 6 mg/L of vancomycin and afterwards were suspended in an enriched liquid medium, with 6 mg/L of vancomycin. Standard procedures were followed to achieve final identification. Susceptibility testing was done according to the National Committee for Clinical Laboratory Standards Guidelines, as well as by E-test methodology (AB Biodisk, Solna Sweden), following

the manufacturer's recommendations. Previously reported risk factors for VRE infection or carriage<sup>3</sup> were evaluated on admission and during hospitalization at the ICU.

Two hundred nineteen rectal samples were taken, of which 136 (62%) were taken on admission and 83 (38%) corresponded to weekly samples from the 36 patients who stayed longer than 1 week in the ICU. The presence of vancomycin-resistant *E faecium* was detected in only one patient on admission. This patient was admitted with chest pain for cardiology control and stayed in the hospital for only 3 days. No risk factors for VRE carriage were detected in this patient. *E faecium* isolated showed a high level of vancomycin resistance with the following minimum inhibitory concentrations (MICs): 256 mg/L, 64 µg/mL, and 128 mg/L for vancomycin, teicoplanin, and ampicillin, respectively. It also showed a high level of resistance to aminoglycosides.

Enterococci with low-level glycopeptide resistance was detected in five patients, four *Enterococcus gallinarum* and one *Enterococcus casseliflavus*. MICs (vancomycin) were 8 mg/L and 6 mg/L, respectively. All 5 of these isolates were susceptible to teicoplanin.

While carriage of VRE in Europe among patients from the community has been described clearly,<sup>4</sup> this has not been reported in the United States<sup>5</sup>; on the other hand, nosocomial spread in Europe is not such a serious problem as it is in the United States.<sup>1</sup>

Argentina remained free of this problem until 1996, when the first case was detected. There are no records of VRE prevalence rates as an agent of nosocomial infection, and we also lack data about its prevalence in the community. Our study was designed to detect VRE fecal carriage; none of the patients included acquired this microorganism during hospitalization. It should be noted that no strain of VRE has ever been isolated at our hospital. We detected the presence of vancomycin-resistant *E faecium* in

one patient who was admitted to the ICU from the community with no known risk factors for VRE colonization. We were able to interview the patient again after the isolation of VRE to eliminate previous hospitalization, any kind of contact with the healthcare system, or any of the other risk factors for VRE fecal colonization. The patient had none of the mentioned risk factors. We report herein a case of VRE fecal colonization detected at admission to the ICU that could be assumed to be community-acquired, and such a case has not been reported previously in our country.

Even though the number of patients was not high, we did not detect VRE carriage in patients hospitalized throughout the study period. Our program was useful for obtaining information about the VRE epidemiological situation at our institution.

Development of surveillance programs, adequate use of antibiotics (particularly vancomycin), and continuous education are the three measures we can currently take to prevent the emergence and spread of VRE. We think that further studies, including the investigation of the fecal colonization in animals as a source of VRE, are required to understand the epidemiology of VRE among inpatients and nonhospitalized subjects in Argentina.

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## Nelfinavir in Expanded Postexposure Prophylaxis Causing Acute Hepatitis With Cholestatic Features: Two Case Reports

### To the Editor:

Two medical professionals treated with postexposure prophylaxis (PEP) after exposure to human immunodeficiency virus (HIV) and hepatitis C virus (HCV) developed hepatotoxicity probably related to nelfinavir, one of the three drugs in the regimen. It is unlikely that other infections caused the clinical picture.

The Centers for Disease Control and Prevention (CDC) recommends PEP following percutaneous needlestick injuries.<sup>1</sup> The expanded regimen of three antiretroviral medications, including a protease inhibitor, is indicated after a high-risk exposure.<sup>1,2</sup> Because of good oral absorption and low reported side effects, nelfinavir is one of the recommended protease inhibitors. Commonly reported side effects involve mild abdominal cramps and diarrhea, which usually can be relieved by over-the-counter remedies.<sup>3</sup>

We report here the results of a chart review of all patients treated with PEP expanded regimen over a 12-month period (August 1998-July 1999) at the University of Connecticut Health Center. Fifteen occupational high-risk exposures to HIV occurred during this period. Of those 15, 13 (87%) received triple antiretroviral therapy with a protease inhibitor, and 4 of these 13 (31%) received nelfinavir. Two of these 4 tolerated the regimen without problems, and the other 2

developed liver toxicity with cholestatic features.

The first patient was a 54-year-old gastroenterologist with a history of polycystic kidney disease who was injured while performing a liver biopsy on a patient infected with HIV and HCV. This physician was stuck on his right index finger, through a single glove, by the 20-gauge needle while anesthetizing the abdominal wall. There was no visible blood in the syringe. The puncture wound was moderately deep and bled immediately. The source patient, who had previously received zidovudine and lamivudine, had a viral load of 14,300 HIV copies, as well as a positive HCV-RNA by polymerase chain reaction (PCR) and antibody titer. His hepatitis B serology was negative.

The gastroenterologist was assessed as having had a high-risk percutaneous exposure to HIV and HCV; his baseline blood tests were within normal limits. He was started on an expanded regimen with zidovudine, lamivudine, and nelfinavir. On day 15 of the regimen, he developed fatigue, diarrhea, sweats, myalgias, and nausea. On day 16, his temperature was 103°F, and he developed chills, right upper quadrant abdominal pain, severe diarrhea (12 episodes/day), and weakness. Physical examination demonstrated right upper quadrant abdominal tenderness, no guarding, no rebound, and hepatomegaly, with a 12-cm total liver span. Cultures from blood and urine were negative for aerobic and anaerobic microorganisms; fecal cultures were negative. All three antiviral medications were stopped for 24 hours, and symptoms promptly improved. Zidovudine and lamivudine were restarted on day 17. Ten days after stopping nelfinavir, the physician was feeling better, his liver was 9 cm (total span), and the abdomen was nontender to palpation. He completed a total of 28 days with antiviral medications; from day 17 to day 28, he received only zidovudine and lamivudine. Six weeks from the exposure, his entire laboratory tests, including liver enzymes and HIV and HCV antibodies, were normal. Follow-up evaluations at 3 and 6 months revealed normal laboratory results and negative HIV and HCV antibodies; the 12-month evaluation showed negative HIV and HCV PCRs.

The second case was a 32-year-old surgical resident. He was assist-

ing with the placement of an arteriovenous shunt to prepare an acquired immunodeficiency syndrome patient in renal failure for hemodialysis. During the procedure, another worker passed a bloody #15 scalpel blade and superficially lacerated the resident's arm through the gown.

The source patient had a viral load of 500 viral copies. The source was positive for HCV antibodies and negative for hepatitis B surface antigen. The resident physician was assessed as having had a high-risk exposure. His baseline laboratory tests were within normal range. He was started on zidovudine, lamivudine, and nelfinavir. On day 14 after the exposure, the resident developed fever and chills. On day 15, his temperature was 104°F, and he felt ill with myalgias, anorexia, and nausea. All antiretroviral medications were stopped for 12 hours. Physical examination revealed fever, clear lungs, nontender abdomen, and shoddy enlarged inguinal nodes. On day 16, he remained febrile. After 12 hours without antiretroviral medications, he was rechallenged with zidovudine and lamivudine. On day 17, the physician developed jaundice and abdominal pain, and hepatomegaly was noted. Ultrasonography of liver revealed nonspecific periportal nodes, nonbiliary dilatation, no focal intrahepatic abnormalities, and a thickened gallbladder wall with no stones. On day 21, the resident tested negative for HCV and HIV by PCR. He continued on zidovudine and lamivudine therapy until day 28. On day 34, the liver enzymes were close to the normal range. Follow-up serology at 45 days, 90 days, 6 months, and 12 months after exposure repeatedly documented negative HIV and HCV PCRs.

The possibility of nelfinavir hepatotoxicity is suggested in these two cases. Nelfinavir has been viewed as an ideal antiretroviral medication because of minimal side effects, which usually are relieved by over-the-counter medications, as well as good bioavailability, varying from 20% to 80% after oral administration. Nelfinavir elimination is mostly through the feces (87%), and it does not need dose adjustment for patients with renal failure.<sup>4</sup> In 1998, the CDC incorporated nelfinavir into the expanded PEP regimen for high-risk percutaneous needlestick injuries.

In the two cases reported, the