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## REFERENCE

1. European Consensus Group on Hepatitis B Immunity. Are booster immunisations needed for lifelong hepatitis B immunity? *Lancet* 2000; 355: 561-565.

## Prevalence of and Risk Factors for Colonization With Vancomycin-Resistant Enterococcus Among Human Immunodeficiency Virus-Positive Outpatients

TO THE EDITOR—Patients infected with human immunodeficiency virus (HIV) are at increased risk for infection with both typical community-acquired pathogens and drug-resistant organisms. HIV-positive patients often receive antibiotic therapy and have frequent contact with the healthcare system, both of which are factors that have been associated with an increased risk of infection with vancomycin-resistant enterococcus (VRE) in other populations.<sup>1,2</sup> One study of hospitalized patients with enterococcal bacteremia showed that they were more likely to be infected with vancomycin-resistant strains if they were HIV positive or had a history of AIDS.<sup>1</sup>

In spite of the clinical importance of colonization as a precursor to infection with drug-resistant pathogens,<sup>2,3</sup> little is known about the frequency with which HIV-positive outpatients are colonized with VRE. Moreover, specific risk factors for carriage have not been elucidated in this population. The present study was performed to determine the prevalence of VRE colonization among HIV-positive patients visiting an ambulatory clinic. The objectives were to assess the overall percentage of VRE carriage, as determined by analysis of perirectal swab specimens, and to characterize patients who may be at increased risk of VRE colonization.

After approval by the Institutional Review Board, the study was performed at the University of Chicago Infectious Diseases Clinic (Chicago, IL). From November 2003 through April 2004, HIV-positive patients seen during routine care at the clinic were considered for inclusion in the study. For patients who provided consent, a perirectal swab specimen was obtained using the Sterile BBL CultureSwab Plus collection system (Becton, Dickinson, and Company). The swab was dipped into sterile water, applied to the anal verge, and placed into transport culture media. Because colonization status was not known prior to collection of the swab specimens, no additional measures beyond standard precautions were followed in the care of these patients. Multiple swab specimens were obtained during a clinic session, and all of

them were transported to the microbiology laboratory together. Swabs were inoculated on enterococcosel plates and were examined daily. Colonies that were morphologically suggestive of enterococcal species underwent biochemical examination to confirm identity, and susceptibility to vancomycin was confirmed by use of Etest (AB Biodisk). Swab results were made available to healthcare providers. Patients were notified of their carriage status at the time of the subsequent clinic visit. VRE isolates were incubated on blood agar plates and were stored at  $-70^{\circ}\text{C}$  in a freezer until genotypic analysis was performed. After subculturing twice to blood agar plates, genomic DNA was extracted, digested using *Sma*I, and subjected to pulsed-field gel electrophoresis.<sup>4,5</sup> Images of band patterns were acquired by use of the GelDoc2000 system (BioRad) and were compared with each other, to ascertain relatedness, by use of the Bionumerics interpretation software package (Applied Maths).

After the swab specimen was obtained, the patient's information (ie, demographic characteristics, dates of recent hospitalization, medication use, and immunologic and virologic status) was extracted from the clinic chart and electronic medical records. Comparison of patient characteristics was performed using the Wilcoxon rank sum test for continuous variables and Fischer's exact test for dichotomous variables.

Eighty-five HIV-positive patients provided consent and were included in this study (Table). Four (4.7%) of the 85 patients studied were found to be colonized with VRE. None of the colonized patients demonstrated signs or symptoms of active infection with VRE. In comparison with VRE-negative control patients, colonized patients were significantly more likely to be receiving trimethoprim-sulfamethoxazole prophylaxis ( $P = .05$ ), to have a lower nadir CD4 cell count (median, 20 vs 166 cells/mm<sup>3</sup>;  $P = .05$ ), to have a lower recent CD4 cell count (median, 136 vs 401 cells/mm<sup>3</sup>;  $P = .02$ ), and to have been hospitalized more recently (median, 68 vs 440 days since last hospitalization;  $P = .02$ ). Results of pulsed-field gel electrophoresis demonstrated that the 4 VRE isolates were not genetically related.

The prevalence of colonization with VRE in the population studied was low but was higher than reported elsewhere among HIV-positive outpatients. In an earlier study of fecal VRE carriage in 89 HIV-positive outpatients, none was found to be colonized with VRE.<sup>6</sup> The prevalence of VRE colonization observed in the present study is comparable to that observed for methicillin-resistant *Staphylococcus aureus* in HIV-positive outpatients in 2 earlier studies.<sup>7,8</sup> In addition, the level of VRE colonization described here is similar to those reported for other high-risk populations, such as patients awaiting solid-organ transplant.<sup>9</sup>

The risk factors for VRE colonization suggested here are also similar to those reported elsewhere for other outpatient groups colonized with drug-resistant pathogens. Carriage of drug-resistant bacteria has been consistently shown to be more likely among patients with extensive exposure to an-

TABLE. Characteristics of Human Immunodeficiency Virus (HIV)-Positive Outpatients, both With and Without Concomitant Vancomycin-Resistant Enterococcus (VRE) Colonization

Characteristic	VRE-Positive Patients (n = 4)	VRE-Negative Patients (n = 81)	P
<b>Demographic</b>			
Female sex	3 (75)	33 (41)	.31
Age, years	39	43	.98
Black race	4 (100)	72 (89)	1.0
Heterosexual HIV acquisition	3 (75)	39 (48)	.36
History of AIDS	4 (100)	46 (57)	.14
<b>Hospitalization</b>			
Time since last hospitalization, days	68	440	.02
Duration of last hospitalization, days	11.5	3	.14
During the previous 90 days	2 (50)	37 (46)	1.0
During the previous 180 days	3 (75)	42 (52)	.62
During the previous year	4 (100)	54 (67)	.30
<b>Antibiotic use</b>			
At the time the swab specimen was obtained			
All antibiotics	3 (75)	27 (33)	.12
Trimethoprim-sulfamethoxazole prophylaxis	3 (75)	18 (22)	.05
During the previous 90 days	3 (75)	30 (37)	.29
During the previous 180 days	3 (75)	33 (41)	.31
Receiving HAART	4 (100)	60 (74)	.57
<b>Immune status</b>			
Recent CD4 cell count, cells/mm <sup>3</sup>	136	401	.02
Nadir CD4 cell count, cells/mm <sup>3</sup>	20	166	.05
<b>Viral status</b>			
Recent viral load, copies/mL	12,953	87	.25
Zenith viral load, copies/mL	44,478	34,949	.90
Sustained viral suppression	0 (0)	35 (44)	.14

NOTE. Data are no. (%) of patients or median value. HAART = highly active antiretroviral therapy.

tibiotics, severe chronic disease, and more-frequent hospitalization or healthcare contacts.<sup>2,3,7-9</sup> Although advanced immune suppression may be independently associated with VRE colonization among HIV-positive outpatients, in the present study, the specific risk attributed to low CD4 cell counts may actually be a function of other risk factors that may have resulted in patients' having more-frequent contact with the healthcare system, thus increasing their risk of acquiring VRE. Because the present study was not designed to follow up colonized patients longitudinally, a prospective study of VRE colonization in a larger group of patients would be required to fully understand carriage of drug-resistant bacteria and associated risk factors among HIV-positive outpatients.

The finding of 4.7% prevalence of VRE carriage in this population of patients raises concerns with regard to infection control in the outpatient setting, even though genotypic analysis did not demonstrate evidence for horizontal transmission in the cohort studied. As the frequency with which drug-resistant pathogens are encountered outside of the hospital increases, a greater emphasis on infection control in the outpatient setting may be needed. Although the use of gowns and gloves has been found to be cost effective in the intensive

care unit,<sup>10</sup> there are, as yet, no data to support such practices in outpatient clinics. Future prospective studies of cohorts of high-risk outpatients are needed to evaluate the potential benefit of various infection control interventions in these populations.

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#### REFERENCES

1. Bhavnani SM, Drake JA, Forrest A, et al. A nationwide, multicenter, case-control study comparing risk factors, treatment and outcome for van-

comycin-resistant and susceptible enterococcal bacteremia. *Diagn Microbiol Infect Dis* 2000; 36:145-158.

- Zaas AK, Song X, Tucker P, Perl TM. Risk factors for development of vancomycin-resistant enterococcal bloodstream infection in patients with cancer who are colonized with vancomycin-resistant enterococci. *Clin Infect Dis* 2002; 35:1139-1146.
- Roghmann MC, Fink JC, Polish L, et al. Colonization with vancomycin-resistant enterococci in chronic hemodialysis patients. *Am J Kidney Dis* 1998; 32:254-257.
- Tenover FC, Arbeit RD, Goering RV, et al. Interpreting chromosomal DNA restriction patterns produced by pulse-field gel electrophoresis: criteria for bacteria strain typing. *J Clin Microbiol* 1995; 33:2233-2239.
- Matushek MG, Bonten MJ, Hayden MK. Rapid preparation of bacterial DNA for pulsed-field gel electrophoresis. *J Clin Microbiol* 1996; 34:2598-2600.
- Dhawan VK, Nachum R, Bhat N, Tolbert L, Agrawal M. Vancomycin-resistant enterococcal colonization in nonhospitalized HIV-infected patients. *West J Med* 1998; 169:276-279.
- McDonald LC, Lauderdale TL, Lo HL, Tsai JJ, Hung CC. Colonization of HIV-infected outpatients in Taiwan with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus*. *Int J STD AIDS* 2003; 14:473-477.
- Villacian JS, Barkham T, Earnest A, Paton NI. Prevalence of and risk factors for nasal colonization with *Staphylococcus aureus* among human immunodeficiency virus-positive outpatients in Singapore. *Infect Control Hosp Epidemiol* 2004; 25:438-440.
- Hagen EA, Lautenbach E, Olthoff K, Blumberg EA. Low prevalence of colonization with vancomycin-resistant enterococcus in patients awaiting liver transplantation. *Am J Transplant* 2003; 3:902-905.
- Puzniak LA, Gillespie KN, Leet T, Kollef M, Mundy LM. A cost-benefit analysis of gown use in controlling vancomycin-resistant *Enterococcus* transmission: is it worth the price? *Infect Control Hosp Epidemiol* 2004; 25:418-424.

## Colonization by Antibiotic-Resistant Gram-Negative Bacteria and Appropriate Empirical Antibiotic Therapy in Intensive Care Unit Patients

TO THE EDITOR—The June 2005 issue of the journal included an article by Blot et al.<sup>1</sup> that described the potential relationship between prior colonization and appropriate empirical antibiotic therapy for infection with some antibiotic-resistant gram-negative bacteria in intensive care unit (ICU) patients. The authors defined prior colonization as “the presence (detected 2 or more days before the onset of bacteremia and during the ICU stay) of the same antibiotic-resistant gram-negative bacteria in colonization and subsequent blood cultures.”<sup>1(p576)</sup>

In light of this definition, we understand that patients who had been previously colonized by an antibiotic-resistant gram-negative bacterium and subsequently had bacteremia caused by a different antibiotic-resistant gram-negative bacterium may have been included in the group without prior colonization by any antibiotic-resistant gram-negative microorganism. If this is the case, then the analysis of the impact

that colonization status had on the rate of appropriate initial antibiotic therapy is not accurate.

On the same page, Blot et al.<sup>1(p576)</sup> defined antibiotic therapy as appropriate when it included “an in vitro effective antibiotic.” It is known that some gram-negative bacteria—such as *Klebsiella* species, *Escherichia coli*, and many others—may be producers of extended-spectrum  $\beta$ -lactamases<sup>2-6</sup> and that this may lead to false-positive findings of in vitro susceptibility to some  $\beta$ -lactams, including cefuroxime or cefepime, both of which were used for empirical antibiotic therapy at the study institution. Therefore, it is possible that some of the patients who had bacteremia caused by any such bacteria may have been improperly classified as having received appropriate initial empirical antibiotic therapy, because of false-positive findings of in vitro susceptibility to a  $\beta$ -lactam eventually prescribed. Again, if this is the case, then the analysis of the impact that colonization status had on the rate of appropriate initial antibiotic therapy is not accurate.

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## REFERENCES

- Blot S, Depuydt P, Vogelaers D, et al. Colonization status and appropriate antibiotic therapy for nosocomial bacteremia caused by antibiotic-resistant gram-negative bacteria in an intensive care unit. *Infect Control Hosp Epidemiol* 2005; 26:575-579.
- Archibald LK. Gram-negative, hospital-acquired infections: a growing problem. *Infect Control Hosp Epidemiol* 2004; 25:809-811.
- Knothe H, Shah P, Kremery V, Antal M, Mitsuhashi S. Transferable resistance to cefotaxime, cefoxitin, cefamandole and cefuroxime in clinical isolates of *Klebsiella pneumoniae* and *Serratia marcescens*. *Infection* 1983; 11:315-317.
- Chanawong A, M'Zali FH, Heritage J, Lulitanond A, Hawkey PM. SHV-12, SHV-5, SHV-2a and VEB-1 extended-spectrum  $\beta$ -lactamases in Gram-negative bacteria isolated in a university hospital in Thailand. *J Antimicrob Chemother* 2001; 48:839-852.
- Quinteros M, Radice M, Gardella N, et al. Extended-spectrum  $\beta$ -lactamases in *Enterobacteriaceae* in Buenos Aires, Argentina, public hospitals. *Antimicrob Agents Chemother* 2003; 47:2864-2867.
- Poirel L, Menuteau O, Agoli N, Cattoen C, Nordmann P. Outbreak of extended-spectrum  $\beta$ -lactamase VEB-1-producing isolates of *Acinetobacter baumannii* in a French hospital. *J Clin Microbiol* 2003; 41:3542-3547.