**Staphylococcus aureus With Reduced Susceptibility to Vancomycin—Illinois, 1999**

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**Staphylococcus aureus** is one of the most common causes of hospital- and community-acquired infections. Nosocomial methicillin-resistant *S. aureus* (MRSA) infections have become common, and cases of community-acquired MRSA infections also have occurred.1,2 Since 1996, vancomycin-intermediate *S. aureus* (VISA); vancomycin minimum inhibitory concentration [MIC] = 8-16 µg/mL) has been identified in Europe, Asia, and the United States.3-5 The emergence of reduced vancomycin susceptibility in *S. aureus* increases the possibility that some strains will become fully resistant and that available antimicrobial agents will become ineffective for treating infections caused by such strains. This report describes the fourth case of confirmed VISA from a patient in the United States.

In April 1999, a 63-year-old woman with MRSA bacteremia (MIC <1 µg/mL) was transferred from a long-term-care facility to an Illinois hospital (hospital A). The patient had a history of frequent hospitalizations for complications of hemodialysis-dependent, end-stage renal disease, and intravascular access, including two failed arteriovenous grafts, multiple central venous catheter-associated infections, and intermittent receipt of vancomycin therapy through June 1998. Thirteen days after hospital admission and 25 days after initiating vancomycin therapy (median vancomycin serum concentration = 12.7 µg/mL; range: 12.1 µg/mL-20.9 µg/mL), a culture from her blood grew *S. aureus* with an MIC of 4 µg/mL; the blood culture was tested using the Vitek® system (bioMerieux; Hazelwood, Missouri).3 Three subsequent blood specimens drawn within the next 3 days grew *S. aureus* with MICs of 8-16 µg/mL on confirmatory testing. The isolates, identical by pulsed-field gel electrophoresis, were resistant to penicillin, oxacillin, clindamycin, erythromycin, ciprofloxacin, and rifampin but susceptible to trimethoprim-sulfamethoxazole, tetracycline, gentamicin, and had intermediate susceptibility to chloramphenicol. No VISA strains were recovered from other body sites. An echocardiogram demonstrated a mitral valve vegetation but the patient declined surgical intervention. Despite treatment with intravenous vancomycin, rifampin, and tobramycin, the patient died 10 days after the first VISA blood specimen was drawn; the cause of death was endocarditis.

The VISA isolate was interpreted as "susceptible" at 4 µg/mL by the Vitek system. Because of the increased awareness of VISA strain emergence, according to laboratory protocol at hospital A, confirmatory testing was performed on all strains of *S. aureus* with Vitek (MIC ≥4 µg/mL) using three additional independent methods: the Pasco Gram Positive Microtiter Panel (Pasco Laboratories, Wheatridge, Colorado), MIC = 8 µg/mL; the Etest (AB Biodisk, North America, Inc., Piscataway, New Jersey), MIC = 6 µg/mL; and inoculation into brain heart infusion (Remel, Lenexa, Kansas) agar with 6 µg/mL of vancomycin (e.g., a vancomycin screen plate indicated growth). Susceptibility results were confirmed by CDC.

After identifying the VISA isolate, hospital A’s infection-control department implemented CDC’s Interim Guidelines for Prevention and Control of Staphylococcal Infection Associated with Reduced Susceptibility to Vancomycin and began an epidemiologic investigation to evaluate potential transmission. None of 10 family members or 171 health-care workers screened by nares culture was colonized with VISA. No other VISA isolates were identified in other hospitalized patients.

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**CDC Editorial Note:** Since the emergence of nosocomial MRSA infections in the 1980s, and more recently the emergence of community-acquired MRSA infections, vancomycin is being used increasingly as therapy for treating suspected *S. aureus* infections. Because few therapies are available to treat MRSA, the confirmed reports of VISA strains demonstrating reduced susceptibility to vancomycin, which has been the drug of last resort to treat MRSA, is of concern.

The acronyms “VISA” and “GISA” (glycopeptide-intermediate *S. aureus*) have been used in the United States to describe *S. aureus* isolates with reduced susceptibility to vancomycin. The National Committee for Clinical Laboratory Standards published interpretive criteria defining both.7 The term “GISA” is a technically more accurate description of VISA strains, because all isolates have shown intermediate level MICs to the glycopeptide drugs, vancomycin and teicoplanin. However, clinicians may not recognize the term glycopeptide, and the acronym VISA is used more frequently.

Laboratorians may not be aware of proper methods for accurately identifying VISA.8 Hospital A’s laboratory described in this report properly identified this VISA-infected patient by using a confirmatory testing protocol consistent with CDC’s interim guidelines.6 This protocol included an algorithm to identify candidate strains (i.e., vancomycin MIC ≥4 µg/mL) for confirmatory testing. At hospital A’s labora-

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tory, the Vitek system is not used only to detect intermediate resistance of *S. aureus* isolates but also to detect candidate strains for confirmatory susceptibility testing. Correct and prompt identification of VISA is critical in preventing transmission.

If candidate strains are detected, CDC is available to perform expedited confirmatory susceptibility testing. CDC is seeking laboratory reports of confirmed cases of VISA infection for an ongoing nationwide epidemiologic study. Information on confirmatory testing, investigation therapy, and infection-control guidelines can be obtained from CDC’s Hospital Infections Program, National Center for Infectious Diseases, telephone (404) 639-6413; World-Wide Web site, http://www.cdc.gov/ncidod hip/vanco/vanco.htm, or e-mail SEARCH@cdc.gov. The recovery of *S. aureus* with reduced susceptibility to vancomycin (e.g., MIC ≥4 µg/mL) should be reported promptly to local and state health departments and to CDC, infection-control precautions should be implemented, and an epidemiologic investigation should be conducted.

### Alcohol Involvement in Fatal Motor-Vehicle Crashes—United States, 1997-1998

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The following table compares alcohol involvement in fatal motor-vehicle crashes by age group and blood alcohol concentration (BAC) levels for 1997 and 1998. A fatal crash is considered alcohol-related by the National Highway Traffic Safety Administration (NHTSA) if either a driver or nonoccupant (e.g., pedestrian) had a BAC of ≥0.01 g/dL in a police-reported traffic crash. Because BACs are not available for all persons in fatal crashes, NHTSA estimates the number of alcohol-related traffic fatalities on the basis of a discriminant analysis of information from all cases for which driver or nonoccupant BAC data are available.1

Overall, the percentage of traffic fatalities that were alcohol related remained constant at 38.4% in 1998 and 38.5% in 1997. From 1997 to 1998, the number of alcohol-related traffic fatalities decreased 1.6% (95% confidence interval = -3.7%–0.6%), with a decrease of 2.0% for BACs ≥0.10 g/dL (the legal limit of intoxication in most states) and no percentage change (but one less death) for BACs of 0.01-0.09 g/dL.

A decrease of 5.8% in the number of alcohol-related traffic fatalities is needed to achieve the national health objective for 2000. Effective strategies for reducing alcohol impaired driving include strict enforcement of impaired

<table>
<thead>
<tr>
<th>Age group (yrs)</th>
<th>1997</th>
<th>1998</th>
<th>Percentage change in fatalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>2,111</td>
<td>2,029</td>
<td>-4.2%</td>
</tr>
<tr>
<td>15-20</td>
<td>4,078</td>
<td>3,958</td>
<td>-3.0%</td>
</tr>
<tr>
<td>21-24</td>
<td>1,729</td>
<td>1,643</td>
<td>-5.1%</td>
</tr>
<tr>
<td>25-34</td>
<td>3,354</td>
<td>3,224</td>
<td>-4.2%</td>
</tr>
<tr>
<td>35-64</td>
<td>8,153</td>
<td>8,357</td>
<td>+2.5%</td>
</tr>
<tr>
<td>&gt;65</td>
<td>6,336</td>
<td>6,229</td>
<td>-1.7%</td>
</tr>
<tr>
<td>Total</td>
<td>25,824</td>
<td>25,536</td>
<td>-1.1%</td>
</tr>
</tbody>
</table>

**Changes in the estimated number and percentage of traffic fatalities (including drivers, occupants, and nonoccupants), by age group* and highest blood alcohol concentration (BAC)† of drivers or nonoccupants in crashes—United States, January 1–December 31, 1997, compared with January 1–December 31, 1998**

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**REFERENCES**


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*Age of decedent was unknown for 109 traffic fatalities in 1997 and 105 in 1998. Decedents of vehicle crash on a public roadway. Fatalities include all occupants and nonoccupants who died within 30 days after a motor-vehicle crash. No percentage change (but one less death) for BACs of 0.01-0.09 g/dL.

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*Driver may or may not have been killed.

†BAC distributions are estimates for drivers and nonoccupants involved in fatal crashes. Fatalities include all occupants and nonoccupants who died within 30 days after a motor-vehicle crash on a public roadway.

‡Driver may or may not have been killed.

§Driver may or may not have been killed.

¶ the number of fatalities for each BAC category is rounded to the nearest whole number.

*Percentage change statistically significant at p<0.05.

Laboratory Capacity to Detect Antimicrobial Resistance, 1998

EMERGING MECHANISMS OF ANTIMICROBIAL RESISTANCE HAVE CLINICAL, MICROBIOLOGIC, AND INFECTION-CONTROL IMPLICATIONS FOR HEALTH-CARE PROVIDERS. Antimicrobial resistant organisms include Staphylococcus aureus with reduced susceptibility to vancomycin (minimum inhibitory concentration [MIC] ≥4 µg/mL), including vancomycin intermediate S. aureus (VISA; vancomycin MIC = 8-16 µg/mL)\(^1\,^2\) and Enterobacteriaceae that produce extended spectrum β-lactamases (ESBLS), which result in resistance to a broad range of β-lactam antibiotics.\(^3\) Detecting VISA and ESBLS-producing gram-negative pathogens can be difficult for clinical microbiology laboratories. Although CDC\(^1\,^3\,^6\) and the National Committee for Clinical Laboratory Standards (NCCLS)\(^7\,^8\) have published screening and confirmatory methods for these pathogens, the extent of use of these methods is unknown. This report summarizes results from a survey of microbiology laboratories that participate in the Active Bacterial Core Surveillance (ABCS)/Emerging Infections Program (EIP) Network to assess the capacity of clinical microbiology laboratories to detect VISA and ESBL-producing pathogens; findings indicate that despite adequate capacity for proper testing, many laboratories do not have appropriate methodology to detect these resistant pathogens.

A survey of laboratory practices was sent to the primary contact for participating ABCS/EIP Network laboratories during August-September 1998. Follow-up was conducted by site coordinators.

As of June 1999, 416 (93%) of 447 ABCS/EIP Network laboratories from eight states (California, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee) had responded to the survey. Of the 416 respondents, 369 (89%) performed clinical microbiologic services (i.e., “study laboratories”). Of the 369 study laboratories, 44 (12%) were from referral laboratories. The other 325 (88%) served health-care facilities that had a median of 121 (range: 5-2306) licensed beds. Seventy-six (36%) of the laboratories served health-care facilities that were part of a health-maintenance organization.

In reviewing the susceptibility testing methods for S. aureus, 278 (84%) of 329 laboratories used methods that allowed them to detect an isolate with reduced susceptibility to vancomycin. Fifty-two (16%) laboratory used methods that would not identify these isolates, such as disk diffusion with no additional method (n = 13), Microscan® Walkaway Rapid™ panels (which provides <24 hours incubation) (n = four), and Vitek systems (bioMerieux, Hazelwood, Missouri) with a vancomycin MIC of ≥8 µg/mL as the indicator for additional testing (Vitek software typically did not report isolates of S. aureus with an MIC >4 µg/mL) (n = 25). Of 369 study laboratories, 216 (59%) reported performing confirmatory testing of suspected isolates that were possibly VISA (candidate strains). Of the 204 study laboratories who reported criteria for selecting strains of S. aureus as candidates for confirmatory susceptibility testing to vancomycin, 173 (85%) used recommended criteria. Of the 201 study laboratories who reported methodology for confirming S. aureus with reduced susceptibility to vancomycin, 135 (67%) used an acceptable methodology.

Of the 369 study laboratories, 117 (32%) reported performing tests to identify ESBL-producing organisms. Of the 112 laboratories who described their methods, 93 (83%) used adequate methods for ESBL screening, and 19 (17%) reported performing definitive confirmatory tests for ESBL production (i.e., E-Test, MIC susceptibility testing of
ceftazidime, alone and in combination with clavulanic acid). One hundred eight laboratorians commented on interpretation and clinical reporting of extended-spectrum cephalosporin and other susceptibility to β-lactam agents: 76 (70%) reported isolates identified as ESBL-producers as resistant to all extended-spectrum cephalosporins; 57 (53%) reported that these isolates also were resistant to aztreonam.

Variability in practices occurred based on demographics and characteristics of laboratories. Within the ABCs/EIP Network, the percentage of study laboratories confirming S. aureus with reduced susceptibility to vancomycin or testing for ESBL-producing organisms varied from 39% to 100% and 18% to 84%, respectively. Laboratories performing services for hospitals with > 200 beds were significantly more likely to confirm S. aureus with reduced susceptibility to vancomycin (odds ratio [OR] = 8.2; p = 0.0001) or test for ESBL-producing organisms (OR = 2.1; p = 0.002) than were other laboratories surveyed. Managed-care-based laboratories were significantly less likely to confirm S. aureus with reduced susceptibility to vancomycin than were laboratories that were not part of a managed-care organization (OR = 0.3; 95% confidence interval = 0.2-0.6).

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CDC Editorial Note: The findings in this report indicate that most ABCs/EIP Network laboratories were using routine methods that would allow detection of VISA or ESBL-producing pathogens; however, approximately 40% of the laboratories were not performing confirmatory testing of S. aureus for reduced susceptibility to vancomycin and even fewer laboratories tested Enterobacteriaceae for ESBL production. Smaller hospital-based laboratories, managed-care-based laboratories, and laboratories from specific ABCs/EIP state locations did not report testing for these resistant pathogens.

Recent reports of S. aureus with reduced susceptibility to vancomycin underscore the importance of increasing awareness of clinical microbiology laboratory personnel on proper testing methods.

The testing of isolates of S. aureus for reduced susceptibility to vancomycin requires that laboratorians know the appropriate susceptibility testing methods and strategies for selecting candidate strains. Despite the national recommendations for testing, many laboratorians may not be aware of the need to perform confirmatory testing on candidate VISA strains. Manufacturers should be aware of the difficulties in resistance identification. For example, Vitek systems software typically did not report MICs > 4 µg/mL for S. aureus isolates. Therefore, a laboratory that used this system and the criteria for additional testing of 8 µg/mL may not have reliably detected isolates. In November 1999, Vitek upgraded its software to improve detection and reporting of S. aureus isolates with reduced susceptibility to vancomycin.

The recommendations and guidelines for testing for ESBL-producers have evolved over several years, and this may explain the variations in practices among ABCs/EIP laboratories. In January 1999, NCCLS attempted to clarify this topic by publishing new recommendations, including methods to confirm ESBL production.

The findings in this report are subject to at least two limitations. First, the data were self-reported. The degree of correlation between actual practice and such reports is unknown. Second, the sample was not random and results may not be representative of other facilities. Despite these limitations, the survey indicates a need to increase awareness among clinical microbiology laboratory and related personnel about evolving practices of susceptibility testing for antimicrobial resistant bacteria.

Additional information about survey results or resistance testing is available from CDC’s Hospital Infections Program. Telephone (404) 639-6413. In addition, information about testing for these resistant organisms is available on CDC’s National Center for Infectious Diseases, Hospital Infections Program World-Wide Web site, http://www.cdc.gov/ncidod/hip.htm, click on “Laboratory.”

REFERENCES