



THE CITY OF NEW YORK

DEPARTMENT OF HEALTH AND MENTAL HYGIENE

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nyc.gov/health

2007 Alert # 31: Surveillance for Vancomycin Resistance in *Staphylococcus aureus*

- Six cases of vancomycin-intermediate *Staphylococcus aureus* infections have occurred in NYC since February 2007; the case fatality rate was 67%.
- Infections caused by vancomycin-intermediate (VISA) and -resistant (VRSA) *Staphylococcus aureus* infections are reportable in NYC
- Please submit all *S. aureus* isolates with a vancomycin MIC > 2.0 µg/ml to the Public Health Laboratory for confirmatory testing and molecular characterization

Please Distribute to All Clinical Staff in Internal Medicine, Surgery, Pediatrics, Infectious Diseases, Emergency Medicine, Family Medicine, Laboratory Medicine and Infection Control Staff

October 3, 2007

Dear Colleagues,

There have been six cases of vancomycin-intermediate *Staphylococcus aureus* (VISA) in New York City (NYC) in 2007. These are the first confirmed VISA infections in NYC; to date, there have been no reports of vancomycin-resistant *Staphylococcus aureus* (VRSA). The recent revised susceptibility testing guidelines lowering the minimum inhibitory concentration (MIC) breakpoint for VISA determination has had the expected effect of increasing the number of isolates classified as VISA (see laboratory section below). The Health Department wishes to remind the health care and laboratory community to be alert for infections due to *S. aureus* isolates with reduced susceptibility to vancomycin and to ensure that appropriate susceptibility testing is performed. VISA and VRSA are reportable in NYC. Please submit all suspect isolates to the Public Health Laboratory (PHL) for confirmation. PHL will forward confirmed isolates to the New York State Department of Health Wadsworth Center for *vanA* gene testing.

Until 1997, when the first clinical isolate of *Staphylococcus aureus* with reduced susceptibility to vancomycin was reported in the United States, vancomycin was the only uniformly effective treatment for staphylococcal infections. While VISA and VRSA infections are rare, they can be serious and difficult to treat. According to the Centers for Disease Control and Prevention (CDC), sixteen cases of VISA (through January 2006) and seven cases of VRSA (through September 2007) have been reported in the US. These infections are usually spread by skin-to-skin contact or by contact with contaminated bandages or body fluids. Persons who develop these infections usually have multiple underlying health conditions such as previous infections with MRSA, recent hospitalizations, intravenous catheters, major surgery, hemodialysis and recent exposure to vancomycin.

Case summaries for NYC VISA isolates

Six VISA cases were reported to the Health Department, all since February 2007, including three cases that were diagnosed in August 2007. Vancomycin MICs on all isolates were between 3.0 - 6.0 µg/ml and were confirmed by the NYC PHL. Three case-patients were aged younger than 60 years and three were over 70 years old. All case-patients had a history of MRSA infection and prior treatment with vancomycin. Co-morbidities included: diabetes, heart disease, end-stage renal disease and chronic obstructive pulmonary disease. Resistance to daptomycin was

present in 3 isolates. Five case-patients were either hospitalized or resided in a nursing home at the time of their diagnosis. Four case-patients died. No secondary spread within healthcare institutions has been observed. All isolates tested negative for the *vanA* gene at the New York State Wadsworth Laboratory.

NYC VISA Case Summary, 2007

	Diagnosis Date	Sex	Age	Borough	Source	Daptomycin resistance
1	2/23/2007	F	55	Brooklyn	Blood	Not tested
2	6/4/2007	F	75	Brooklyn	Blood	Not tested
3	8/8/2007	M	57	Queens	Blood	Not tested
4	8/24/2007	M	46	Bronx	Joint	Yes
5	8/28/2007	M	83	Queens	Blood	Yes
6	9/6/2007	F	77	Manhattan	Wound	Yes

Laboratory Detection of Vancomycin Resistance

In 2006, after reviewing data regarding treatment failure of vancomycin against *S. aureus*, the Clinical and Laboratory Standards Institute (CLSI) revised the vancomycin MIC breakpoints for *S. aureus*. Susceptibility was redefined as MIC \leq 2.0 $\mu\text{g/ml}$ (lowered from \leq 4.0 $\mu\text{g/ml}$); intermediate resistance as 4.0-8.0 $\mu\text{g/ml}$ (lowered from 8.0-16.0 $\mu\text{g/ml}$) and resistance as \geq 16.0 $\mu\text{g/ml}$ (lowered from \geq 32.0 $\mu\text{g/ml}$). Based on these changes the CDC revised its VISA and VRSA testing algorithm, which can be found at:

<http://www.cdc.gov/ncidod/dhqp/images/VAalgoApril06v7.gif>.

S. aureus isolates with an MIC of $>$ 2.0 $\mu\text{g/ml}$ should be reported to the Health Department and require confirmatory testing at the PHL (contact information for reporting and arranging testing is included at the end of this alert). Isolates with MIC=2 $\mu\text{g/ml}$ may require further testing if there are clinical indications that vancomycin treatment is failing. In most VISA cases, resistance increases during vancomycin therapy and it has been shown that MIC values are not always stable throughout the course of treatment. Most MRSA isolates remain susceptible to vancomycin; however, MIC levels have been slowly rising over the past several years.

To confirm VISA, non-automated MIC methods are recommended. Reference broth microdilution, agar dilution and Etest[®] are suggested options as automated systems and disk diffusion may not accurately detect intermediate susceptibility results. Reduced susceptibility to vancomycin of *S. aureus* can occur by one of two identified mechanisms: 1) acquisition of the *vanA* gene which confers resistance in vancomycin-resistant enterococcus; or 2) increased cell wall thickness inhibiting drug entry. For *vanA* negative *S. aureus* isolates, resistance is believed to be secondary to cell wall changes due to prolonged exposure to vancomycin, and not via the more worrisome mechanism of acquiring the resistant *vanA* gene. Resistance to vancomycin in *S. aureus* due to changes in cell wall permeability is non-transferable and reversible, whereas resistance due to the *vanA* gene is transferable and likely irreversible.

Heterogeneous VISA (hVISA) is also a growing concern and has been identified in patients with MRSA who fail to improve on vancomycin treatment. The vancomycin MIC value for hVISA isolates is \leq 2.0 $\mu\text{g/ml}$ but there is a subpopulation of bacteria that are able to survive at higher concentrations of vancomycin. The exact clinical implications of hVISA are unknown, but hVISAs could be precursors to VISA.

Conventional susceptibility testing does not identify hVISA. Although not yet approved by the FDA, Etest[®] GRD (Glycopeptide Resistance Detection) vancomycin and teicoplanin double strips with a 2.0 McFarland on Mueller-

Hinton agar with 5% blood is a suggested method to test for hVISA¹. Alert the treating clinician that patients with hVISA should be watched closely for treatment failure and antimicrobial therapy may need to be adjusted as appropriate.

Laboratory screening of all *S. aureus* isolates for hVISA is not cost-effective and is currently unnecessary. To date, nearly all VISA and hVISA cases have been MRSA and the decision to test for hVISA should be made on clinical grounds.

Susceptibilities for daptomycin and linezolid are not routinely performed by most microbiology laboratories. Clinicians should consider requesting these susceptibility tests as resistance to daptomycin has been reported and was found in three NYC VISA case-patients in 2007.

Hospital Guidelines

Although the spread of VISA in NYC hospital and long-term care settings has not been documented, the potential risk of nosocomial transmission demands heightened vigilance with strict adherence to infection control precautions for all patients with VISA infection or colonization:

- Isolate patient in a private room
- Minimize the number of staff that enter the room
- In addition to Standard precautions, institute Direct and Indirect Contact precautions:
 - Prior to entering the room, and prior to contact with the patient or with items that have been in contact with the patient, don gown and gloves;
 - Carefully discard gown and gloves prior to exiting room as outlined in the CDC Sequence for Donning and Removing Personal Protective Equipment (<http://www.cdc.gov/ncidod/dhqp/ppe.html>).
 - Additionally, masks and eye protection should be worn whenever performing procedures that could disseminate infectious particles (e.g., wound debridement, dressing changes and suctioning)
 - Use disposable equipment whenever possible and when not possible, use dedicated equipment.
 - Equipment that cannot be dedicated to a single patient must be disinfected with an EPA-registered hospital disinfectant following the manufacturer's instructions.
 - Patient care items that cannot be adequately disinfected (e.g., rolls of adhesive tape) should be disposed of after use according to hospital policies regarding regulated medical waste.
 - Enforce rigorous hand hygiene with an appropriate agent (either antimicrobial soap and water or alcohol-based hand sanitizers)
- Disinfect surfaces regularly. Review environmental cleaning protocols and practices to assure adequate cleaning of high-contact surfaces (e.g., doorknobs) and patient care equipment
- Actively monitor staff and visitor compliance with infection control precautions
- Educate personnel caring for these patients about VISA and VRSA

Contact investigations for VISA are not routinely recommended unless there is a concern that transmission may have occurred. Contact investigations for suspected or confirmed VRSA should be performed as per CDC guidelines below, and in consultation with the New York City and New York State Health Departments.

Additional information can be found in the following CDC guidance documents on VISA/VRSA available on the internet:

¹ Personal communication from Dr. Vincent LaBombardi, Chief of Microbiology at St. Vincent's Hospital & Medical Ctr., NY, NY

Guide to the Management of Multi-drug Resistant Organisms in Healthcare Settings, 2006.
<http://www.cdc.gov/ncidod/dhqp/pdf/ar/mdroGuideline2006.pdf>

Investigation and Control of Vancomycin-Intermediate and -Resistant *Staphylococcus aureus* (VISA / VRSA): A Guide for Health Departments and Infection Control Practitioners
http://www.cdc.gov/ncidod/dhqp/pdf/ar/visa_vrsa_guide.pdf

Treatment

Currently there are no published treatment recommendations for VISA. Anecdotal reports suggest that combination therapy and high-dose vancomycin are effective but there have been no published clinical trials on these regimens. Use of newer antibiotics such as linezolid and daptomycin should be based whenever possible on susceptibility testing demonstrating activity of these agents against the patient's isolate. As found with three NYC patients, resistance to daptomycin has been associated with VISA with vancomycin MIC ≥ 4.0 $\mu\text{g/ml}$. As newer agents become available, extreme care must be taken to use them judiciously in order to preserve their activity against VISA and VRSA (see Micek ST, Alternatives to vancomycin for the treatment of methicillin resistant *Staphylococcus aureus* infections. CID 2007; 45: S184-90).

To report a suspect or confirmed VISA or VRSA case, consult on infection control practices, or to obtain additional information, please contact the Antibiotic Resistance Unit of the Bureau of Communicable Disease at:

During business hours: 212-788-9830
After hours, contact the Poison Control Center: 212-764-7667 or 1-800-222-1222 and ask for the Doctor on Call

Submit VISA, VRSA and concerning MRSA isolates for antibiotic susceptibility testing and molecular characterization to:

NYC DOHM Public Health Laboratory
Specimen Receiving, Room 136
Attn: Microbiology Laboratory
455 First Avenue
New York, NY 10016
(212) 447-6966

We appreciate your assistance in tracking vancomycin resistance among *Staphylococcus aureus* isolates in New York City.

Sincerely,

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