STAPHYLOCOCCUS AUREUS

Vancomycin-Intermediate Resistant *Staphylococcus aureus* (VISA);
Vancomycin-Resistant *Staphylococcus aureus* (VRSA)

REPORTING INFORMATION

- **Class B (VISA, VRSA):** Report by the close of the next business day after the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism:
    - The Ohio Disease Reporting System (ODRS) should be used to report lab findings to the Ohio Department of Health (ODH). For healthcare providers without access to ODRS, you may use the Ohio Confidential Reportable Disease form (HEA 3334).
    - In addition to reporting through ODRS, the local health department should call the Ohio Department of Health (ODH) Bureau of Infectious Diseases at 614-995-5599 to report suspected cases of VRSA.
- Key fields for ODRS reporting include: the following in the laboratory section – test name (select "culture" if *S. aureus* is isolated); method (enter "MIC" if antimicrobial MIC testing was performed on the isolate); result (select "positive" indicating the results of the culture); numeric result (enter the numeric MIC results); reference range (enter the reference range for the MIC results [>4 for VISA, >16 for VRSA]); and organism (select "*Staphylococcus aureus*" if the organism was isolated through culture) and in the notes section indicate if the isolate has been submitted to ODH Laboratory/Centers for Disease Control and Prevention (CDC) for confirmation.

AGENT

Staphylococcus aureus (*S. aureus*) is a Gram-positive coccus arranged in grapelike clusters. *S. aureus* is coagulase-positive and is resistant to heat, drying and many chemicals.

CASE DEFINITION

Clinical Description

S. *aureus* can produce a variety of syndromes with clinical manifestations including skin and soft tissue infections, empyema, bloodstream infection, pneumonia, osteomyelitis, septic arthritis, endocarditis, sepsis and meningitis. *S. aureus* may also colonize individuals who remain asymptomatic. The most frequent site of *S. aureus* colonization is the nares.

Laboratory Criteria for Diagnosis

- Isolation of *S. aureus* from any body site, ***and***
- Intermediate resistance or resistance of the *S. aureus* isolate to vancomycin, detected and defined according to the Clinical and Laboratory Standards Institute (CSLI), approved standards and recommendations (minimum inhibitory concentration **[MIC]=4-8 µg/ml for VISA** and **MIC≥16 µg/ml for VRSA**).

Case Classification

Suspected*: A clinically compatible case with presumptive laboratory findings.

Confirmed: A clinically compatible case of vancomycin-intermediate or vancomycin-resistant *Staphylococcus aureus* that is laboratory confirmed with MIC=4-8 µg/ml for VISA and MIC≥16 µg/ml for VRSA.

Not a Case: This status will not generally be used when reporting a case, but may be used to reclassify a report if investigation revealed it was not a case.

* This case classification can be used for initial reporting purposes to ODH as the CDC has not developed a classification.

SIGNS AND SYMPTOMS

Although *S. aureus* is a normal inhabitant of the skin, mucous membranes and respiratory and gastrointestinal tracts, it can invade any organ or system to produce infection, ranging from localized to invasive disease. Localized diseases include furuncles, impetigo, boils and other wound infections. Suppurative and/or invasive infections include septicemia, osteomyelitis, arthritis, endocarditis and pneumonia.

DIAGNOSIS

The organism may be identified in a Gram stain of the infected site. Isolation of the organism from a culture of the infected site is considered diagnostic confirmation. CDC definitions for classifying isolates of *S. aureus* with reduced susceptibility to vancomycin are based on the laboratory breakpoints established by CLSI. Antibiotic sensitivities should be performed on isolates to detect any resistance patterns. NOTE: The breakpoints for *S. aureus* and vancomycin differ from those for other *Staphylococcus* species (2015 CLSI M100-S25).

- **Vancomycin-intermediate resistant *S. aureus*** (VISA)
  Vancomycin MIC = 4-8 µg/ml
  - Vancomycin-intermediate resistant *S. aureus* (VISA) is defined as an isolate for which the minimum inhibitory concentration (MIC) of vancomycin is 4-8 µg/ml. VISA isolates are not detected by disk diffusion. Methods that typically detect VISA are non-automated MIC methods including reference broth microdilution, agar dilution, and Etest® using a 0.5 McFarland standard to prepare inoculum. Automated methods and vancomycin screen agar plates usually detect VISA for which the vancomycin MICs are 8 µg/ml, but further studies are needed to define the level of sensitivity of these methods for *S. aureus* for which the vancomycin MICs are 4 µg/ml.

- **Vancomycin-resistant *S. aureus*** (VRSA)
  Vancomycin MIC $\geq$16 µg/ml
  - Vancomycin-resistant *S. aureus* (VRSA) is defined as an isolate for which the minimum inhibitory concentration (MIC) of vancomycin is $\geq$16µg/ml. Not all susceptibility testing methods detect VRSA isolates. Laboratories should check with manufacturers to determine if their system has U.S. Food and Drug Administration (FDA) clearance for VRSA detection. VRSA are detected by reference broth microdilution, agar dilution, Etest®, MicroScan® overnight and Synergies plus™; BD Phoenix™ system, Vitek2™ system, disk diffusion, and the vancomycin screen agar plate [brain heart infusion (BHI) agar containing 6 µg/ml of vancomycin].

In addition to knowing the appropriate testing methodologies, all laboratories should develop a step-by-step problem-solving procedure or algorithm for detecting VISA/VRSA specifically for their laboratory. A sample algorithm is available at http://www.cdc.gov/HAI/pdfs/visa_vrsa/VRSA_testing_algo2010.pdf.

All *S. aureus* strains for which the vancomycin MIC $\geq$ 4 µg/ml are unusual and should not be discarded until the MICs have been confirmed. In addition to confirming vancomycin susceptibility, laboratories should ensure that the strain is in pure culture and reconfirm the genus and species of the organism; then, repeat the susceptibility test for vancomycin using a validated method. If retesting confirms a vancomycin MIC $\geq$ 4 µg/ml, laboratories should notify infection control. For isolates with a MIC 8 µg/ml, laboratories should notify the local health department so arrangement can be made for the isolate to be shipped to ODH Laboratory

(ODHL) for confirmatory testing at CDC.

EPIDEMIOLOGY

Source and Occurrence

Staphylococci are ubiquitous, living in dust, environmental surfaces and on humans and animals worldwide. Anterior nares and moist body surfaces may be colonized at any given time. *S. aureus* that is capable of withstanding treatment with a particular antibiotic is defined as resistant.

Staphylococcus aureus is one of the most common causes of hospital- and community-acquired infections. Since the recognition of vancomycin-resistant enterococci in 1988, the emergence of vancomycin-resistant *S. aureus* (VRSA) has been anticipated. The transfer of the genetic element containing the *vanA* vancomycin resistance gene from *Enterococcus faecalis* to *S. aureus* was demonstrated in the laboratory in 1992; the first clinical infection with VRSA was reported in July 2002.

VRSA infection continues to be a rare occurrence. A few existing factors seem to predispose case patients to VRSA infection, including:

- Prior MRSA and enterococcal infections or colonization;
- Underlying conditions (such as chronic skin ulcers and diabetes); and
- Previous treatment with vancomycin.

Appropriate antimicrobial prescribing by healthcare providers, adherence to recommended infection control guidelines, and, ultimately, the control of both MRSA and VRE are necessary to prevent further emergence of VRSA strains.

As of May 2015, fourteen VRSA cases have been reported in patients from the United States. While antibiotic therapy is necessary for serious infections, the use of a sensitive agent such as vancomycin for treatment of infections caused by methicillin-resistant *Staphylococcus aureus* should be approached with caution and careful review of antibiograms for alternative antibiotics.

Mode of Transmission

To date, in the United States, VISA strains are characterized by a resistance mechanism that has not transferred to susceptible strains and are usually associated with vancomycin exposure. Therefore, likelihood of transmission to contacts and the maintenance of the VISA phenotype in the absence of vancomycin pressure is presumed to be low. Contact investigations for VISA cases are **not routinely** recommended unless there is suspicion that transmission has occurred.

In contrast, VRSA strains [vancomycin MIC ≥16 µg/ml] are characterized by expression of v*anA* residing on Tn*1546*-like element which was acquired from an *enterococcus* spp; therefore, this resistance is potentially transferrable to susceptible strains or other organisms. Contact investigations and follow-up for VRSA cases **are** recommended.

Incubation Period

Variable, depending upon the site and resistance of the host.

PUBLIC HEALTH MANAGEMENT

Detection of VRSA, given the public health importance, should trigger an investigation that includes a contact investigation regardless of whether transmission is suspected.

- Healthcare facilities should develop a written plan for the management of VISA/VRSA colonized individuals. The plan should include a treatment protocol, follow-up monitoring guidance, and information about work issues.

- Identify and Categorize Contacts:
  - Contacts should be categorized based on their level of interaction (i.e., extensive, moderate, or minimal) with the colonized or infected patient.
  - Priority should be given to identifying contacts who have had extensive interaction with the VISA/VRSA patient during a defined period before the VISA/VRSA culture date
  - Extensive Interaction
    - Patients who share the VISA/VRSA patient's room
    - Nursing or patient-care providers involved in direct patient care
    - Physicians who perform wound dressing, debridement or extensive exams
    - Ancillary staff who have prolonged contact (therapist)
    - Family members who provide primary care or share a room
- Specimen Collection:
  - Clinical laboratories that routinely use polymerase-chain reaction (PCR) assays for detection of MRSA from surveillance swabs, will need to utilize culture-based methods so that vancomycin susceptibilities can be determined:
    - From patients colonized/infected with VISA/VRSA, culture anterior nares, throat, axilla, peri-rectal, wounds, drains, or other clinically relevant sites.
    - From individuals having extensive interactions with colonized/infected persons, culture multiple (e.g., 2 to 3) frequently colonized sites, such as anterior nares, throat, groin, axilla, or peri-rectal area, plus any skin lesions (e.g., abscess or dermatitis, open wounds).
    - Decisions about culturing those with moderate or minimal interactions should be made in consultation with public health authorities. In general, those with minimal interactions do not require screening unless there is substantial transmission among the other groups.
  - Because of exchange of genetic material from vancomycin-resistant enterococci (VRE) to methicillin-resistant *Staphylococcus aureus* (MRSA) in the emergence of VRSA, CDC is asking clinical laboratories, when patients are identified with suspected or confirmed VRSA, to ensure that all VRE, MRSA, and VRSA isolates from these patients are saved.
    - To save isolates, it is best to freeze isolates at -60°C or lower in standard stock culture medium, such as a broth containing 15% glycerol, or in defibrinated sheep blood. However, if a laboratory cannot do this, the isolate should be subcultured to a non-selective agar slant (e.g., trypticase soy agar) and incubated overnight at 35°C. The following day, the caps should be tightened and the slants stored at 2-8°C. Repeated subcultures should be kept to a minimum prior to storage.
- Evaluate Efficacy of Infection Control Precautions:
  - Infection control practices, particularly adherence to hand hygiene and contact precautions, should be assessed at facilities that are caring for VRSA patients. Facilities that might care for the patient (e.g., acute care hospitals if patient is outpatient) should be notified so that they can "flag" the patient's record so that in case of admission appropriate infection control precautions will be put into place. Hospitalized patients with VRSA should be put on standard and contact precautions.

Prevention and Control

CDC has issued specific recommendations intended to reduce the development and transmission of VISA/VRSA. However, these may need to be customized to special healthcare settings. Infection control precautions should remain in place until a defined endpoint (e.g. patient has been culture-negative 3 times over a 3-week period or the patient's infection has healed). This endpoint should be determined in consultation with public health authorities.

- State and/or local health authorities, such as the state antimicrobial resistance program, should notify all healthcare-settings attended by the patient during the potential transmission period of the patient's VRSA colonized/infected status. Below is a checklist of important infection control recommendations. However, these may need to be customized for special healthcare-settings (e.g., dialysis, home healthcare). Infection control precautions should remain in place until a pre-defined endpoint (e.g., patient has been culture-negative 3 times over 3 weeks or the patient's infection has healed). This endpoint should be determined in consultation with public health authorities.

- Acute-Care Settings
  1. Isolate the patient in a private room.
  2. Minimize the number of persons caring for the patient (e.g., assign dedicated staff to care for VRSA patient).
  3. Implement the appropriate infection control precautions during patient care.
     a. Use standard and contact precautions (gown and gloves for room entry).
     b. Per standard precautions, wear facemask and eye protection or face shield if performing procedures likely to generate splash or splatter (e.g., wound manipulation, suctioning) of VRSA contaminated material (e.g., blood, body fluids, secretions, and excretions).
     c. Perform hand-hygiene using appropriate agent (e.g., alcohol-based hand sanitizer or hand washing with plain or antimicrobial soap and water).
     d. Dedicate non-disposable items that cannot be cleaned and disinfected between patients(e.g., adhesive tape, cloth-covered blood pressure cuffs) for use only on the patient with VRSA.
     e. Monitor and strictly enforce compliance with Contact Precautions.
  4. Educate and inform the appropriate healthcare personnel about the presence of a patient with VRSA and the need for contact precautions.
  5. Facilities should flag the patient's chart to indicate infection/colonization with VRSA.
  6. Consult with the local and/or state health department and CDC before transferring the patient or discharging the patient.
  7. Ensure that the patient's VRSA status and required infection control precautions are communicated upon transfer.

- Dialysis Settings
  1. Wear disposable gown and gloves when caring for the patient or touching the patient's equipment at the dialysis station; carefully remove and dispose of gown and gloves and perform hand hygiene when leaving patient station.
  2. If available, use a separate room that is not in use for hepatitis B isolation for patient treatment. If a separate room is not available, dialyze the patient at a station with as few adjacent stations as possible (e.g., at the end or corner of the unit).
  3. Items brought into the dialysis station should be disinfected after use. Items not able to be disinfected should be discarded.
  4. Thoroughly disinfect the dialysis station (e.g., chairs, beds, tables, machines) between patients. Information specific to disinfection in dialysis facilities is available at http://www.cdc.gov/dialysis/PDFs/collaborative/Env_notes_Feb13.pdf and http://www.cdc.gov/dialysis/PDFs/collaborative/Env_checklist-508.pdf.
  5. Educate and inform the appropriate personnel about the presence of a patient with VRSA and the need for contact precautions.
  6. In the event the patient needs to be admitted or referred to another facility, the receiving facility must be notified of the patient's VRSA status.

- Other Outpatient Settings (e.g., primary care, wound clinic)
  1. Healthcare providers in outpatient settings should follow the same VRSA precautions as hospital-based healthcare providers.
     a. Use Standard Precautions with strict adherence to hand hygiene
     b. Use Contact Precautions (gown and gloves) to enter room/care area if extensive contact is anticipated or contact with infected areas is planned (e.g. debridement or dressing of colonized or infected wound)
     c. Per Standard Precautions, wear mask and eye protection or face shield if performing procedures likely to generate splash or splatter (e.g., wound manipulation, suctioning) of VRSA contaminated material (e.g., blood, body fluids, secretions, and excretions).
     d. Perform hand-hygiene using appropriate agent (e.g., alcohol-based hand sanitizer or hand washing with plain or antibacterial soap and water).
     e. Dedicate non-disposable items that cannot be cleaned and disinfected between patients (e.g., adhesive tape, cloth-covered blood pressure cuffs) for use only on the patient with VRSA.
  2. Minimize the number of persons who care for the VRSA colonized/infected patient (e.g., dedicate a single staff person).
  3. Ensure meticulous cleaning of the room/patient care area at the end of each visit.
  4. Educate and inform the appropriate personnel about the presence of a patient with VRSA and the need for contact precautions.
  5. In the event the patient needs to be admitted or referred to another facility, the receiving facility must be notified of the patient's VRSA status.

- Homecare Settings
  1. Home healthcare providers should generally follow the same VRSA precautions as hospital-based healthcare providers.
     a. Wear gown and gloves upon entering the area of house where the patient care will be provided.
     b. Per standard precautions, wear mask and eye protection or face shield if performing procedures likely to generate splash or splatter (e.g., wound manipulation, suctioning) of VRSA contaminated material (e.g., blood, body fluids, secretions, and excretions).
     c. Perform hand-hygiene using appropriate agent (e.g., alcohol-based hand sanitizer or hand washing with plain or antibacterial soap and water).
  2. Minimize the number of persons with access to the VRSA colonized/infected patient (e.g., dedicate a single staff person to care for this patient).
  3. Dedicate non-disposable items that cannot be cleaned and disinfected between patients (e.g., cloth-covered blood pressure cuffs) for use only on a single patient.

  The risk of transmission to household members, even those with extensive contact, is extremely low. Household members should practice good hand hygiene (frequent hand washing with soap and water or use of alcohol-based hand rubs). Additionally, if household members are providing care to the VRSA patient (such as changing the dressing on an infected wound), these persons should follow the same precautions as listed for home health care.

Disease Fact Sheet

Vancomycin-Intermediate Resistant *Staphylococcus aureus* (VISA)
Vancomycin-Resistant *Staphylococcus aureus* (VRSA)

What is VISA/VRSA?

Vancomycin-intermediate *Staphylococcus aureus* (VISA) and vancomycin-resistant *Staphylococcus aureus* (VRSA) are specific types of antimicrobial-resistant bacteria. However, as of October 2010, all VISA and VRSA isolates have been susceptible to other Food and Drug Administration (FDA)-approved drugs.

What is *Staphylococcus aureus*?

Staphylococcus aureus (also called staph) is a bacterium commonly found on the skin and in the nose of about 30% of individuals. Most of the time, staph does not cause any harm. These infections can look like pimples, boils, or other skin conditions and most are able to be treated. Sometimes staph bacteria can get into the bloodstream and cause serious infections which can be fatal, including:

- Bacteremia or sepsis when bacteria spread to the bloodstream usually as a result of using catheters or having surgery.
- Pneumonia which predominantly affects people with underlying lung disease including those on mechanical ventilators.
- Endocarditis (infection of the heart valves) which can be caused by staph bacteria traveling in the bloodstream or put there by direct contact such as following trauma (puncture wound of foot or intravenous [IV] drug abuse).

How do VISA and VRSA get their names?

Staph bacteria are classified as VISA or VRSA based on laboratory tests. Laboratories perform tests to determine if staph bacteria are resistant to antimicrobial agents that might be used for treatment of infections. For vancomycin and other antimicrobial agents, laboratories determine how much of the agent it requires to inhibit the growth of the organism in a test tube. The result of the test is usually expressed as a minimum inhibitory concentration (MIC) or the minimum amount of antimicrobial agent that inhibits bacterial growth in the test tube. Therefore, staph bacteria are classified as VISA if the MIC for vancomycin is 4-8µg/ml, and classified as VRSA if the vancomycin MIC is $\geq$16µg/ml.

Who gets VISA and VRSA infections?

Persons who develop VISA and VRSA infections may have underlying health conditions (such as diabetes and kidney disease), tubes going into their bodies (such as catheters), previous infections with methicillin-resistant *Staphylococcus aureus* (MRSA), and recent exposure to vancomycin and other antimicrobial agents.

What should I do if I think I have a staph, MRSA, VISA, or VRSA infection?

See your healthcare provider.

Are VISA and VRSA infections treatable?

Yes. As of October 2010, all VISA and VRSA isolates have been susceptible to several FDA-approved drugs.

How can the spread of VISA and VRSA be prevented?

Use of appropriate infection control practices (such as wearing gloves before and after contact with infectious body substances and adherence to hand hygiene) by healthcare personnel can reduce the spread of VISA and VRSA.

What should a person do if a family member or close friend has VISA or VRSA?
VISA and VRSA are types of antibiotic-resistant staph bacteria. Therefore, as with all staph bacteria, spread occurs among people having close physical contact with infected patients or contaminated material, such as bandages. Persons having close physical contact with infected patients while they are outside of the healthcare setting should: (1) keep their hands clean by washing thoroughly with soap and water, and (2) avoid contact with other people's wounds or material contaminated from wounds. If they go to the hospital to visit a friend or family member who is infected with VISA or VRSA, they must follow the hospital's recommended precautions.

What is public health doing to address VISA and VRSA?
CDC works with its state and local health partners to ensure that laboratories are using the proper methods to detect VISA and VRSA. In addition, CDC has a Campaign to Prevent Antimicrobial Resistance. The campaign centers around four strategies that clinicians can use to prevent antimicrobial resistance: prevent infections; diagnose and treat infections effectively; use antimicrobials wisely; and prevent transmission. A series of evidence-based steps are described that can reduce the development and spread of resistant organisms such as VISA and VRSA.