STAPHYLOCOCCUS AUREUS

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

REPORTING INFORMATION

- **Class B1 (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: Ohio Confidential Reportable Disease form (HEA 3334, rev. 1/09), Positive Laboratory Findings for Reportable Disease form (HEA 3333, rev. 8/05), the local health department via the Ohio Disease Reporting System (ODRS), or telephone.
- In addition to reporting through ODRS, the local health department should call the Ohio Department of Health (ODH) Outbreak Response and Bioterrorism Investigation Team (ORBIT) at 614-995-5599 to report suspected cases of VISA/VRSA.

AGENT

Staphylococcus 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, formerly NCCLS) approved standards and recommendations (Minimum inhibitory Concentration **[MIC]=4-8 µg/ml for VISA** and **MIC≥16 µg/ml for VRSA**).

Case Classification

Suspect*: 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 Centers for Disease Control and Prevention (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 Clinical and Laboratory Standards Institute (CLSI). The CLSI breakpoints for *S. aureus* and vancomycin were modified in March 2006. Antibiotic sensitivities should be performed on isolates to detect any resistance patterns.

- **Vancomycin-intermediate *S. aureus*** (VISA)
  Vancomycin MIC = 4-8 µg/ml
- **Vancomycin-resistant *S. aureus*** (VRSA)
  Vancomycin MIC $\geq$16 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. Methods that typically detect VISA are non-automated MIC methods including reference broth microdilution, agar dilution, and Etest (registered) using a 0.5 McFarland standard to prepare inoculum. Disk diffusion will not differentiate VISA strains from strains sensitive to vancomycin.

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.

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 www.cdc.gov/ncidod/dhqp/ar_visavrsa_algo.html.

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 and the local health department so arrangement can be made for the isolate to be shipped to ODH Laboratory (ODHL) for confirmatory testing at the 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.

The emergence of VISA in the United States predicted that *S. aureus* strains with full resistance to vancomycin would eventually emerge. As of October 2008, nine 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
Contact investigations to identify potential transmission may be warranted on a case by case basis after consultation between healthcare providers, the local health department(s), ODH and CDC.

- 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 or debridement
        - 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, wounds, drains, other clinically relevant sites.
    - From individuals having **extensive interactions** with colonized/infected persons, culture anterior nares and skin lesions.
    - If there are no positive results from the contact group (i.e. individuals having extensive interactions with colonized/infected persons), no additional groups should be cultured. Ultimately, the decision to culture those with less interaction should be made in consultation with public health authorities
- Evaluate Efficacy of Infection Control Precautions:
    - If VISA/VRSA colonization of contacts is identified or until the case-patient is no longer colonized or infected, culturing the anterior nares of contacts with **extensive interaction** could be performed on a regular (e.g. weekly) basis to assess the efficacy of infection control precautions.
    - The duration of evaluation and the decision to prospectively culture those with less interaction should be made in consultation with public health authorities.

Prevention and Control

The 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.

- Acute-Care Settings:
    - Isolate the patient in a private room.
    - Minimize the number of persons caring for the patient.
    - Implement **Contact Precautions.**
- Dialysis Settings:
    - Infection control precautions recommended for all hemodialysis patients are adequate to prevent transmission from most patients infected/colonized with VISA/VRSA.
- Homecare Settings:
    - Home healthcare providers should follow the same VISA/VRSA **Contact Precautions** as hospital-based healthcare providers

Disease Fact Sheet **Vancomycin Intermediate Resistant *Staphylococcus aureus* Vancomycin Resistant *Staphylococcus aureus* (VISA/VRSA)**

What is VISA/VRSA?

Vancomycin-intermediate *Staphylococcus aureus* (also called VISA) and Vancomycin-resistant *Staphylococcus aureus* (also called 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.