Staphylococcus aureus, Vancomycin Non-Susceptible 

PROTOCOL CHECKLIST

- ☐ IMMEDIATELY notify Florida Department of Health (DOH) Bureau of Epidemiology (BOE) and assure that the healthcare facility's infection control practitioner is aware of the report
- ☐ Enter available information into Merlin upon receipt of initial report
- ☐ Obtain the following information on the patient from the submitting laboratory:
  - ☐ Verify the MIC and request a copy of the susceptibility pattern
  - ☐ Verify the specific test used to obtain the MIC (e.g., E-test, Vitek/Microscan)
  - ☐ Note if the test was repeated
- ☐ If the only laboratory test result is based on an automated testing method (e.g. Vitek/Microscan), ask the laboratory to repeat the test using a manual method (e.g. E-test).
- ☐ If the isolate is determined to be vancomycin susceptible upon repeat testing, mark the case for deletion
- ☐ If the isolate is still determined to be vancomycin non-susceptible after repeat testing, coordinate the shipment of specimen to the DOH Bureau of Public Health Laboratories (BPHL) Jacksonville for confirmation. The specimen should be obtained from an original pure culture and not a vancomycin screening plate.
  - ☐ DOH BPHL will either rule out the case as VISA/VRSA or isolate will be sent to CDC for further testing
- ☐ **For VRSA** → One confirmed case of VRSA is a sentinel event requiring detailed investigation. The BOE should be notified immediately. Contact investigation is required. Work with hospital infection control, the BOE, and/or CDC as indicated to assure adequate infection control measures are being taken
- ☐ **For VISA** → Contact investigation is <u>not required</u> unless transmission is suspected. Communicate with hospital infection control staff to ensure adequate infection control measures are being taken.
- ☐ Enter additional data obtained into Merlin

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1. DISEASE REPORTING

A. Purpose of reporting and surveillance

To assess the risk of the patient transmitting infection to others, and to prevent such transmission. Additionally, to track the emergence of a relatively new and rare, clinically important organism.

B. Legal reporting requirements

Laboratories and physicians are required to report immediately, 24 hours a day, 7 days a week (24/7), by phone upon diagnosis to the county health department (CHD). Isolates are required to be submitted to the FDOH Bureau of Public Health Laboratories (BPHL), per Chapter 64D-3 Florida Administrative Code.

C. County health department investigation responsibilities

1. Begin investigation immediately upon report from a provider.
2. Administer appropriate measures to control further spread.
3. Report all confirmed infections in Merlin.
4. Ensure isolates are submitted to the BPHL for confirmation.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic agent

Vancomycin-intermediate *Staphylococcus aureus* (VISA) and vancomycin-resistant *S. aureus* (VRSA) are strains of the bacteria *Staphylococcus aureus* that have acquired intermediate or complete resistance to the glycopeptide antibiotics vancomycin or teicoplanin. If an isolate of *S. aureus* is resistant to either of these antibiotics it is classified as glycopeptides-intermediate or –resistant *S. aureus* (GISA/GRSA). Methicillin-resistant *S. aureus* (MRSA) is typically resistant to many antibiotics. Consequently, physicians rely heavily on vancomycin as the primary antibiotic for treating patients with serious MRSA infections.

VISA emerges when a patient with preexisting MRSA infection or colonization is exposed to repeated vancomycin use and the *S. aureus* strain develops a thicker cell wall. This resistance mechanism is not transferrable to susceptible strains.

The emergence of VISA in response to vancomycin exposure is in contrast to the emergence of VRSA, which results from the acquisition of the *vanA* gene from a vancomycin-resistant *Enterococcus* (VRE) organism.

To date, VISA strains (vancomycin MIC = 4-8 µg/ml) are characterized by a resistance mechanism that is not transferable to susceptible strains and is usually associated with vancomycin exposure. VISA organisms have a thicker cell wall that makes it more difficult for the vancomycin to bind to its cell membrane and take action. The likelihood of transmission to contacts and the maintenance of the VISA phenotype in the absence of vancomycin pressure is assumed to be low.

So far, all VRSA strains (vancomycin MIC ≥16 µg/ml) have contained the vancomycin resistance gene *vanA*, which is usually found in vancomycin-resistant *Enterococcus* spp. Therefore, this resistance **is** potentially transferrable to susceptible strains or other organisms.

B. Description of illness

S. aureus can cause a variety of skin and soft tissue infections, as well as invasive disease including bacteremia, endocarditis, and toxic shock syndrome. *S. aureus* is also an important cause of healthcare associated infection, especially among chronically ill patients who have recently had invasive procedures or who have indwelling medical devices.

C. Reservoirs

S. aureus commonly colonizes the skin and mucosal surfaces. About 20% of the population is long-term carriers of *S. aureus* and over 60% may carry it intermittently.

D. Modes of transmission

Transmission is from person-to-person by direct contact. The main ways *S. aureus* is spread is via hands, especially among healthcare workers, which may become contaminated by contact with colonized or infected patients, colonized or infected body sites of the healthcare workers themselves, or devices, items, or other environmental surfaces contaminated with body fluids containing *S. aureus*.

E. Incubation period

Not applicable.

F. Period of communicability

This infection is communicable as long as the bacteria are present on the host. Long term colonization is common with *S. aureus*, therefore the period of communicability may be prolonged.

The likelihood of transmission to contacts and the maintenance of the VISA phenotype in the absence of vancomycin pressure is assumed to be low.

Cases of VRSA require long term contact precautions while receiving healthcare.

G. Treatment

To date, all cases of VISA and VRSA have been susceptible to other licensed antibiotics. There is concern, however, that an extremely-resistant bacteria could emerge from a case of VISA/VRSA that would not be susceptible to therapy. Treatment recommendations for infections with multidrug resistant organisms, including VISA or VRSA, should be made on a case-by-case basis, determined by the results of the antimicrobial susceptibility testing of the organism performed by a microbiology lab and the clinical evaluation by the patient's physician.

The decision to decolonize carriers should be made by the primary care physician in conjunction with hospital infection control and public health.

H. Prophylaxis

None indicated. See the discussion on decolonization in section 6H of this document.

J. Epidemiology

The first documented infection with VISA was in a patient in Japan in May 1996. The first documented infection with VISA in the U.S. was reported in 1997. Although healthcare-associated spread of VISA strains has not yet been observed in U.S. hospitals, other countries have reported suspected hospital transmission. The first VISA isolate was reported in Florida in 2007. There were 3 VISA cases reported in 2008, 6 in 2009, 1 in 2010 and 4 in 2011. Nationally, 65 VISA cases were reported in 2011.

The first clinical isolate of VRSA was reported in 2002 in Michigan. From 2002 through 2010, only 11 VRSA isolates were reported in the United States; 8 from Michigan, 1 each from Delaware, New York, and Pennsylvania. Most case patients had a history of previous MRSA and enterococcal infections or colonization. Most had several underlying conditions. History of vancomycin therapy is a risk factor for developing VRSA. To date, VRSA has not been found in Florida. All previous reports of VRSA to the Florida DOH were not confirmed upon repeat testing. Nationally, only 2 cases of VRSA were reported in 2010 and none were reported in 2011.

3. CASE DEFINITION

A. 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.

B. Laboratory criteria for diagnosis

Intermediate Resistance (GISA/VISA):

- Isolation of *Staphylococcus aureus* from a clinical specimen with an MIC 4-8 µg/ml to Vancomycin

Resistance (GRSA/VRSA):

- Isolation of *Staphylococcus aureus* from a clinical specimen with an MIC ≥16 µg/ml to Vancomycin

C. Case classification

Confirmed: a clinically compatible case that is laboratory confirmed

D. Comment

Isolates from all cases must be submitted to the Bureau of Laboratories for confirmation

4. LABORATORY TESTING

A. Criteria for diagnosis

Automated testing methods commonly used by laboratories may not reliably characterize vancomycin resistance in *S. aureus*.

If an initial automated test indicates vancomycin non-susceptibility, the test must be repeated using a manual method, such as an E-test.

If the isolate is still found to be vancomycin non-susceptible upon retesting with a manual method, the specimen must be sent to the BPHL Jacksonville for further testing.

All isolates with a vancomycin MIC ≥4 µg/ml are unusual and should not be discarded until the MICs have been confirmed.

More information on laboratory detection of VISA/VRSA can be found at:
http://www.cdc.gov/HAI/settings/lab/visa_vrsa_lab_detection.html

A testing algorithm is available at:
http://www.cdc.gov/HAI/settings/lab/visa_vrsa_algorithm.html

B. Testing requests

1. Suspected VISA/VRSA isolates must be sent to the BPHL, according to 64D-3, for confirmation of vancomycin non-susceptibility.
   a. All submissions should be accompanied by a Clinical Lab Submission Form: http://www.doh.state.fl.us/lab/PDF_Files/DOH_Form_DH1847_1009_v12152010.pdf
   b. Include a note in the comments section on the form that a copy of the results should be faxed to the Bureau of Epidemiology on the confidential fax: 850-414-6894.
2. Packaging and shipping information:
   a. The majority of requests for *Staphylococcus aureus* involve submitting pure isolates on chocolate agar slants for confirmation of the identification as well as determining resistance. Be sure to write "*Staphylococcus aureus VISA/VRSA* confirmation" in the comment section of the 1847 form or ELO.
   Please place the form 1847 in a plastic ziplock between the inner and outer container. Package according to IATA regulations, labeling the outer shipping container: *UN3373, Biological Substance Category B.*
   b. http://www.doh.state.fl.us/lab/PDF_Files/Packaging_Flowchart_0422051.pdf
   c. http://www.doh.state.fl.us/lab/PDF_Files/Packaging_Flowchart_notes_0422051.pdf
3. Contact the regional laboratory with questions:
   http://www.doh.state.fl.us/lab/addpages/BOL_Contacts.html.

5. CASE INVESTIGATION

A. Ensure the patient is in contact isolation

Vancomycin resistance has not spread person-to-person from patients infected or colonized with VISA. However, as VISA arises typically from a MRSA infection, MRSA infection control procedures should be followed. VRSA is transmissible from person-to-person and contact precautions are extremely important.

The application of contact precautions for patients infected or colonized with multi-drug resistant organisms (MDROs) is described in the HICPAC/CDC MDRO guidelines found at: http://www.cdc.gov/hicpac/mdro/mdro_4.html

For patients who are not hospitalized, family members, care takers, and healthcare providers should be advised on how to prevent transmission of infection or colonization. Persons having close contact with infected patients or contaminated material, such as bandages, should:

- Keep their hands clean by washing thoroughly with soap and water
- Avoid contact with other people's wounds or material contaminated by their wounds

B. Check the laboratory report

Automated testing methods commonly used by laboratories may not reliably detect this organism. Ask the laboratory to confirm any results obtained with automated testing methods by using a manual testing method.

C. Send specimen to the DOH Bureau of Laboratories

If the specimen is vancomycin susceptible upon retesting, mark the case for deletion. If the specimen continues to test vancomycin non-susceptible, the specimen must be sent to the BPHL Jacksonville, according to 64D-3, for confirmation. The BPHL form should be attached with a request to test for VISA/VRSA. In the comments section on the form, include a note that a copy of the results should be faxed to the BOE (confidential fax: 850-414-6894).
The BPHL form can be found at:
http://www.doh.state.fl.us/lab/PDF_Files/DOH_Form_DH1847_1009_v12152010.pdf

D. Medical records review

If a VISA case is identified, a medical records review should be done to identify relevant risk factors, including: history of MRSA, history of vancomycin use, and pertinent medical history.

If a VRSA case is identified, intensive investigation will be undertaken in cooperation with the Bureau of Epidemiology and/or the CDC. The investigation will include a medical records review to identify relevant risk factors in the patient's medical history, including: prior hospitalizations, intravenous catheters, history of MRSA infection or colonization (include dates of positive and negative cultures), history of VRE infection or colonization (include dates of positive and negative cultures), prior treatment with vancomycin (include does and duration), and underlying health conditions (e.g., diabetes, kidney disease).

E. Merlin data entry

Create a case in Merlin under disease code STAPHYLOCOCCUS AUREUS (GISA/VISA) – 38100 or STAPHYLOCOCCUS AUREUS (VRSA/VRSA) – 38101. Enter the data collected into Merlin, being sure to include all required fields on the Basic Data screen, complete the Case Symptoms screen, describe the relevant medical history in the case notes, and attach all relevant labs. There is no case report form for VISA or VRSA.

6. CONTROLLING FURTHER SPREAD

A. VISA versus VRSA

To date, VISA strains (vancomycin MIC 4-8 µg/ml) are characterized by a mechanism that is not transferrable to susceptible strains and is usually associated with vancomycin exposure. Therefore, both the likelihood of transmission to contacts and the maintenance of the VISA phenotype in the absence of vancomycin pressure are 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 the *vanA* gene, which was acquired from an *Enterococcus* spp. Therefore, this resistance is potentially transferrable to susceptible strains and other organisms. Contact investigations and follow-up for VRSA cases are required.

B. Isolation of cases

Isolation of case patients is crucial for controlling further spread, regardless of whether the patient has VISA (VISA patients are typically already under contact isolation to control the spread of MRSA) or VRSA. Key to the success of contact precautions is ensuring they are strictly followed by anyone that may interact with the patient.

THE FOLLOWING CONTROL MEASURES ARE ONLY ROUTINELY RECOMMENDED FOR VRSA. It is expected that the following control measures would be undertaken in cooperation with the BOE and/or the CDC as indicated. More specific details on each of the following steps are available elsewhere.[1]

C. Develop a written plan with hospital infection control to assure appropriate infection control actions are taken

The plan must include, at a minimum:

1. Treatment protocols (e.g., will decolonization be attempted and how?)
2. Follow-up cultures (e.g., will follow-up cultures be obtained and how often?)
3. When carriers or infected individuals will be considered free of colonization (e.g., 3 negative cultures over 3 weeks post-therapy)
4. Isolation protocols for carriers

[1] Hageman JC, Patel JB, Carey RC, Tenover FC, and Mcdonald LC. Investigation and Control of Vancomycin-Intermediate and -Resistant Staphylococcus aureus: A Guide for Health Departments and Infection Control Personnel, Atlanta GA, 2006. http://www.cdc.gov/ncidod/dhqp/pdf/ar/visa_vrsa_guide.pdf

5. Work issues (e.g., if a healthcare worker is positive for MRSA, VISA, or VRSA, will they be removed from patient-care activities and under what circumstances and when can they return to work?)

D. Identification and management of contacts

All contacts should be identified and categorized as extensive, moderate, or minimal, according to their level of interaction with the colonized or infected patient.

E. Specimen collection

Collect surveillance cultures from contacts identified as having had extensive interaction with the patient.

Collect surveillance cultures from patients from the nares, axilla, wounds, drains, or other clinically relevant sites. Consider rectal and/or perirectal specimens for VRSA-colonized patients to determine VRE carriage status. Collect surveillance cultures from healthcare providers and staff from nares and all skin lesions/wounds.

If no one in the "extensive interaction" group is identified as colonized with VISA/VRSA, then do not continue with surveillance cultures for individuals with moderate or minimal interaction.

F. Evaluate efficacy of infection control precautions

To assess the efficacy of infection control precautions, identify and track individuals having contact with the patient. Additionally, culture the nares of contacts with extensive interaction with VISA/VRSA colonized patients weekly until the case is no longer colonized or infected.

G. Decolonization of MRSA, VISA, or VRSA carriers

Colonized individuals (patients, healthcare workers, or family members) may be identified during a contact investigation. Colonization refers to the presence of microorganisms in or on a person who has not had clinical signs or symptoms of infection. Decolonization refers to the reduction of organism burden on the colonized person with the goal of eradicating the organism. The rationale is that by decreasing the reservoir of MRSA, VISA, or VRSA, the risks of infection and of transmission of the organism are reduced. The decision to attempt decolonization therapy is based upon a number of considerations, including: 1) the individual's underlying disease and/or immune status; 2) the ability of the individual to tolerate the recommended regimen; and 3) the risk of transmission to others. *In general, CDC does not recommend decolonization of carriers unless they are implicated in transmission of organisms during an outbreak*.

If decolonization is attempted, criteria should be included in the infection control plan for when the individual will be considered free of colonization (e.g., after three negative cultures over three weeks post-therapy).

7. REFERENCES

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D. Principles and Practice of Infectious Disease (6th Edition), Gerald L. Mandell, John E. Bennett, and Raphael Dolin Eds; 2005.

E. CDC's Vancomycin-Intermediate/Resistant *Staphylococcus* (VISA/VRSA) in Healthcare Settings homepage: http://www.cdc.gov/hai/organisms/visa_vrsa/visa_vrsa.html

F. CDC's Laboratory Detection of Vancomycin-Intermediate/Resistant *Staphylococcus aureus* (VISA/VRSA) webpage: http://www.cdc.gov/HAI/settings/lab/visa_vrsa_lab_detection.html

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