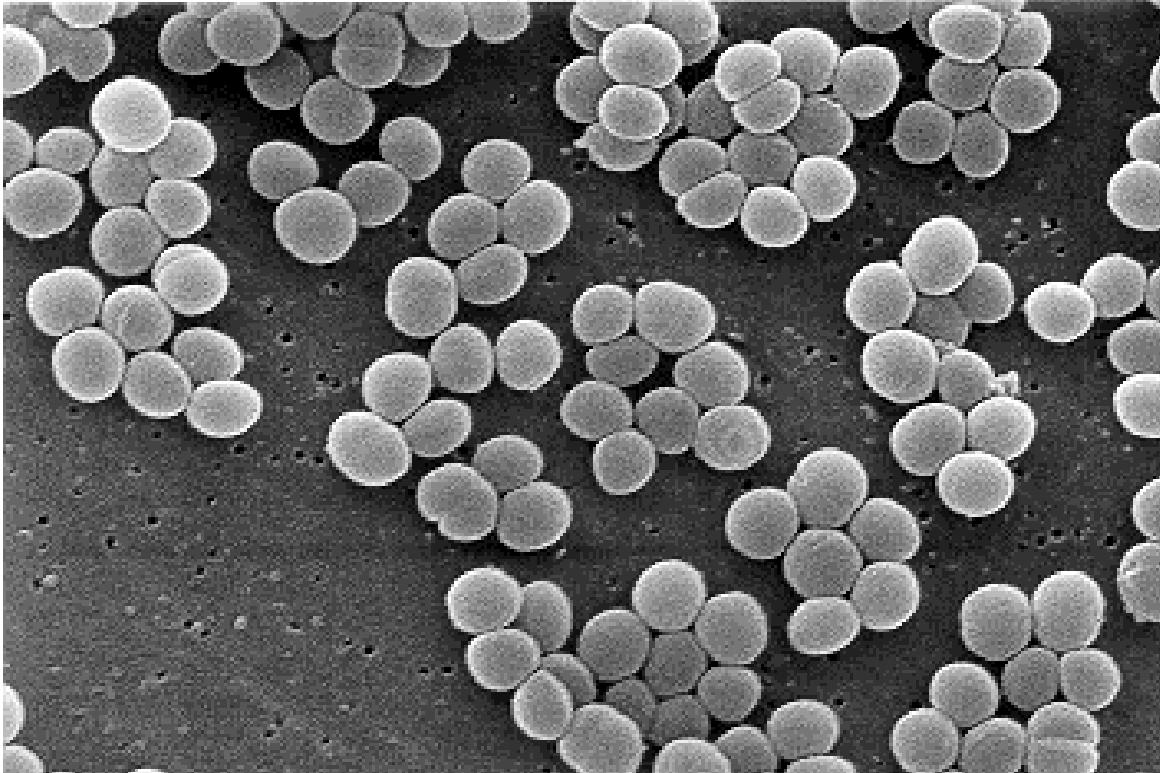




Investigation and Control of Vancomycin-
Intermediate and -Resistant
Staphylococcus aureus (VISA/VRSA)
A Guide for Health Departments and Infection Control Personnel



Vancomycin-Intermediate *S. aureus* magnified 10000x by scanning electron microscopy

Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention
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DEPARTMENT OF HEALTH AND HUMAN SERVICES
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Prepared by:
Jeffrey C Hageman, M.H.S.
Jean Patel, Ph.D.
Roberta Carey, Ph.D.
Fred C. Tenover, Ph.D.
L. Clifford McDonald, M.D.

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Resources:

Division of Healthcare Quality Promotion: www.cdc.gov/ncidod/dhqp/index.html
VISA/VRSA webpage: www.cdc.gov/ncidod/dhqp/ar_visavrsa.html
Centers for Disease Control and Prevention: www.cdc.gov
MASTER-laboratory training: www.phppo.cdc.gov/dls/master/default.asp

Reporting and Confirmatory Testing

To report or request testing of suspected VISA/VRSA, send an email to SEARCH@cdc.gov with your contact information (i.e., name, facility or laboratory name, telephone number, and test results).

Overview

This document provides guidance in conducting a public health evaluation of patients from whom vancomycin-intermediate *Staphylococcus aureus* (VISA; minimum inhibitory concentration [MIC] = 4-8 µg/ml) and vancomycin-resistant *S. aureus* (VRSA, vancomycin MIC \geq 16 µg/ml) has been isolated or is suspected. The information reflects the experience gained from several field investigations and consultations for addressing issues pertaining to VISA/VRSA.

S. aureus is an important cause of healthcare- and community-associated infections. The diseases associated with this organism range from mild skin and soft-tissue infections to potentially fatal systemic illnesses such as endocarditis and toxic-shock syndrome. *S. aureus* is a common pathogen that affects individuals across the age spectrum.

At the time of the introduction of penicillin in the early 1940s, *S. aureus* was uniformly susceptible to this drug. However, during the 1950s widespread resistance to penicillin developed, followed in the 1970s by increasing resistance to the new semisynthetic penicillinase-resistant antimicrobial agents (i.e., methicillin, oxacillin, nafcillin). By the 1990s, resistance to the semisynthetic penicillins had spread throughout the world, compromising the use of these drugs for empiric therapy for staphylococcal infections in a number of regions. This has led to increased reliance on vancomycin for treatment of documented methicillin-resistant *S. aureus* (MRSA) infections, as well as for empiric therapy of infections in populations where the prevalence of MRSA is high.

Reports in the 1990s suggested that the susceptibility of *S. aureus* to vancomycin was changing. In May 1996, the first documented infection with VISA was reported in a patient in Japan. Subsequently, infections with VISA strains have been reported in patients from the United States, Europe, and Asia. Although healthcare-associated spread of VISA strains has not been observed in U.S. hospitals, reports from France and Denmark suggest that transmission has occurred in a hospital, and transmission of hetero-resistant *S. aureus* strains (i.e., vancomycin susceptible strains that contain vancomycin nonsusceptible subpopulations) has occurred in Japan, Hong Kong, and elsewhere. As of September 2006, six VRSA infections have been reported in patients from the United States. All VRSA isolates contained the vancomycin resistance gene, *vanA*, commonly found in vancomycin-resistant enterococci.

Vancomycin is ineffective for treatment of VRSA infections. Published data indicate that infections due to *S. aureus* strains for which the vancomycin MICs are \geq 4 µg/ml are refractory to vancomycin therapy. Patients infected with these strains may fail to improve clinically on vancomycin therapy, particularly when the patients have indwelling catheters or an unrecognized focus of infection.

Definitions

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 January 2006.

Vancomycin-susceptible *S. aureus* (VSSA)

- Vancomycin MIC ≤ 2 $\mu\text{g/ml}$

Vancomycin-intermediate *S. aureus* (VISA)

- Vancomycin MIC =4-8 $\mu\text{g/ml}$.

Vancomycin-resistant *S. aureus* (VRSA)

- Vancomycin MIC ≥ 16 $\mu\text{g/ml}$.

*Note: The breakpoints for coagulase-negative staphylococci and vancomycin were not modified and now differ from those for *S. aureus*.*

The acronyms VRSA, VISA, and GISA (glycopeptide-intermediate *S. aureus*, the glycopeptide class of antimicrobial agents include both vancomycin and teicoplanin) all have been used to indicate *S. aureus* strains with reduced susceptibility to vancomycin. The term VRSA has been used in the literature by Japanese and European investigators to denote strains of *S. aureus* for which the vancomycin MICs are 8 $\mu\text{g/ml}$ that have been associated with apparent treatment failures. In the U.S., the term VRSA is reserved for *S. aureus* strains for which the vancomycin MICs ≥ 16 $\mu\text{g/ml}$. The acronyms VISA and GISA come from interpretive criteria published by the CLSI. While the term GISA may be more specific for strains intermediate to both vancomycin and teicoplanin, not all VISA strains are intermediate to teicoplanin; therefore, VISA is the more accurate and widely used term.

Laboratory Surveillance and Diagnosis Issues

Testing Difficulties

Detecting emerging antimicrobial resistance in bacterial isolates is an increasing problem in clinical microbiology laboratories. In the following section, we describe some steps laboratories may take to improve their ability to detect emerging vancomycin resistance in *S. aureus*.

Additional laboratory testing information may be found at:

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

Testing Recommendations

Not all susceptibility testing methods detect VRSA isolates. Three out of six confirmed VRSA isolates were not reliably detected by automated testing systems. Subsequently, some manufacturers have optimized their systems for VRSA detection; so, laboratories should check with manufacturers to determine if their system has FDA clearance for VRSA detection. VRSA isolates are detected by reference broth microdilution, agar dilution, Etest[®], MicroScan[®] overnight and Synergies plus[™], BD Phoenix[™] system, TREK Sensititre MIC plate, disk diffusion, VRSA screen test for VITEK[®] 2, and vancomycin screen agar plates [brain heart infusion (BHI) agar containing 6 µg/ml of vancomycin].

For disk diffusion, VRSA strains may produce only subtle growth around vancomycin disk.

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. VISA isolates are not detected by disk diffusion. 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.

*Disk diffusion **will not** differentiate VISA strains from VSSA strains.*

Laboratories that use automated methods not validated for VRSA detection should also include a vancomycin screen agar plate (see page 7) for enhanced detection of VRSA. If possible, laboratories should incorporate the vancomycin agar screen plate for testing all *S. aureus*. Alternatively, the screening may be limited to MRSA isolates, since nearly all VISA and all VRSA reported to date (i.e., June 2006) were also MRSA. Laboratories using disk diffusion to determine vancomycin susceptibility should consider adding a second method for VISA detection. The vancomycin screen plate is useful for detecting some VISA isolates (MIC 4-8 µg/ml). Reliable detection of other VISA (MIC = 4 µg/ml) may require a non-automated MIC method.

Testing Algorithm

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 ≥ 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 ≥ 4 $\mu\text{g/ml}$, laboratories should notify infection control; the local and/or state health department; and the Division of Healthcare Quality Promotion, CDC, by sending an email to SEARCH@cdc.gov. The isolate should be sent to the health department and/or CDC for confirmatory testing. If the isolate is confirmed to have reduced susceptibility to vancomycin (MIC ≥ 4 $\mu\text{g/ml}$), CDC will work with the public health department and infection control personnel to address any local infection control issues, and the health department to address broader public health implications.

Using Vancomycin Agar Screen Plates

The vancomycin agar screen test uses **commercially prepared** plates to screen pure cultures of bacteria for vancomycin resistance. These plates contain brain heart infusion (BHI) agar and 6 $\mu\text{g/ml}$ of vancomycin. In studies conducted at CDC, some lots of vancomycin-containing BHI agar prepared in-house were less specific than those plates prepared commercially and allowed growth of the susceptible quality control strains.

Commercially-prepared plates that contain BHI agar and 6 $\mu\text{g/ml}$ of vancomycin may be used for screening.

Thus, adequate quality control of the agar test medium is critical. A 10 μl inoculum of a 0.5 McFarland suspension should be spotted on the agar using a micropipette (final concentration 10^6 colony-forming units [CFUs]/ml). Alternatively, a swab may be dipped in the McFarland suspension, the excess liquid expressed, and used to inoculate the vancomycin agar plate. For quality control, laboratories should use *Enterococcus faecalis* ATCC 29212 as the susceptible control and *E. faecalis* ATCC 51299 as the resistant control. Up to eight isolates can be tested per plate; quality control should be performed each day of testing. Growth of more than one colony is considered a positive result. All of the isolates for which the vancomycin MIC ≥ 8 $\mu\text{g/ml}$ grow on these plates and some isolates for which the vancomycin MIC=4 $\mu\text{g/ml}$ will also grow. Ultimately, all staphylococci that grow on these plates should be inspected for purity, and the original clinical isolates should be tested using an FDA-cleared MIC method for confirmation. Plates prepared in-house using various lots of media performed inconsistently and were inferior to those obtained commercially (CDC unpublished data); therefore, commercially-prepared plates are preferred. Performance of commercially-prepared plates varies by individual manufacturer.

Confirmatory Testing Methods Used by CDC

CDC defines *S. aureus* strains as a VISA or VRSA based on the MIC for vancomycin obtained by reference broth microdilution. Additionally, CDC tests all presumptive VISA/VRSA isolates by Etest[®] and vancomycin agar screen. Email SEARCH@cdc.gov for information on how to send isolates to CDC for testing.

Technique	VRSA Results	VISA Results	Comment
Reference Broth Microdilution	VA* MIC \geq 16 μ g/ml in Mueller-Hinton broth	VA MIC = 4-8 μ g/ml in Mueller-Hinton broth	Hold test for full 24 hrs.
Brain Heart Infusion Agar containing 6 μg/ml of vancomycin obtained from a commercial source	Growth of >1 colony in 24 hrs.	Growth of >1 colony in 24 hrs.	Two or more colonies is a positive result; For QC* use <i>Enterococcus faecalis</i> ATCC 29212 as susceptible control and <i>E. faecalis</i> ATCC 51299 as resistant control
Etest[®]	VA MIC \geq 16 μ g/ml on Mueller-Hinton agar	VA MIC \geq 4 μ g/ml on Mueller-Hinton agar	Use a 0.5 McFarland standard to prepare the inoculum suspension. Hold test for full 24 hrs.

*VA, vancomycin; QC, quality control

Contact Investigation

Contact investigations to identify potential transmission may be warranted on a case-by-case basis after consultation between healthcare providers, local and state health departments, and CDC.

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. Therefore, the 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 *vanA* residing on Tn1546-like element which was acquired from an *Enterococcus* spp; therefore, this resistance is potentially transferable to susceptible strains or other organisms. Contact investigations and follow-up for VRSA cases are recommended.

This section discusses how and where to obtain specimens from healthcare workers, patient roommates, and others having had contact with a patient infected or colonized with VISA or VRSA. This plan should be determined in consultation with public health authorities as activities may need to extend beyond the facility where the VISA/VRSA was identified.

Step 1: Develop a written plan for VISA/VRSA colonized individuals

Before any culturing is performed, a plan should be developed outlining how VISA/VRSA colonized individuals will be handled **including at a minimum**: treatment protocol (e.g., will decolonization be attempted and how), follow-up (e.g., will follow-up cultures be obtained), when will the individual be considered free of colonization (e.g., 3 negative cultures over 3 weeks post therapy), and work issues (e.g., if a healthcare worker is positive for MRSA, VISA, or VRSA will they be removed from patient-care activities and, if yes, under what circumstances and when can they return to work).

Step 2: 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. The

*First, identify contacts who have had **extensive interaction** with the VISA/VRSA patient.*

length of this period depends on recent culture results, setting the patient is receiving healthcare, and the clinical assessment. Examples of persons having extensive, moderate, and minimal interactions are displayed on page 10.

Extensive Interaction

A. Patients who:

- Share the VISA/VRSA patient's room

B. Nursing or patient-care providers involved in direct patient care who:

- clean/bathe/rotate/ambulate the patient
- change dressings
- make frequent visits (>3 visits per day including nurses assigned to the patient)
- handle secretions and body fluids, including respiratory secretions
- manipulate intravenous lines

C. Physicians who:

- care for wound dressings or perform debridement
- conduct physical exams on the VISA/VRSA patient

D. Ancillary staff who:

- have documented prolonged patient contact, including physical therapy or rehabilitation personnel and dialysis or respiratory technicians.

E. Family members or household contacts who:

- provide primary care
- had/have close contact with patient (e.g., sleep in the same bed, or same room)

Moderate interaction

A. Nursing or patient-care providers who:

- deliver medications
- cross-cover patient only

B. Physicians who:

- see patient on daily rounds, without conducting extensive exams
- perform surgical or invasive procedures where sterile barriers or aseptic techniques are used

C. Ancillary staff who:

- monitor patient-care equipment without handling secretions
- have limited interactions (e.g., radiology technicians)

Minimal interaction

A. Nursing or patient-care providers who:

- work on the same floor without formal cross-coverage of patient
- perform predominately administrative duties

B. Physicians who:

- consult without extensive exam
- visit during teaching rounds only

C. Ancillary staff who:

- provide dietary or maintenance services that do not interact directly with the patient

Step 3: Specimen Collection

Clinical laboratories that routinely use rapid 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 or infected with VISA or VRSA:

- Culture anterior nares, wounds, drains, other clinically relevant sites (e.g., catheter exit site).
- For VRSA-infected patients, consider collecting specimens (e.g., rectal, perirectal) to determine vancomycin-resistant enterococci (VRE) carriage status.

From persons having EXTENSIVE INTERACTION with colonized/infected patient:

- Culture anterior nares and skin lesions (e.g., abscess or dermatitis, open wounds)
- If no contacts among this group are identified as being VISA or VRSA positive, no additional groups should be cultured. Ultimately, the decision to culture those with less interaction should be made in consultation with public health authorities.

From persons with moderate or minimal interaction:

- Only culture if “Extensive Interaction” contacts have positive results
- Culture anterior nares and skin lesions (e.g., abscess or dermatitis, open wounds)

If contacts are identified as MRSA carriers but not VISA/VRSA carriers, the MRSA isolates may still be of laboratory interest and should be saved for further testing.

Step 4: 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. Placing a log book at the entrance of the patient’s room would help identify and track these VISA/VRSA patient contacts during the evaluation period. The duration of evaluation and the decision to prospectively culture those with less interaction should be made in consultation with public health authorities.

Procedure for Culturing Anterior Nares

Anterior nares specimens should be obtained with a commercially prepared sterile swab. Although various methods (e.g., swabbing 1 nostril vs. both, pre-moistening swabs vs. dry) have been used to obtain nasal swab specimens for *S. aureus* and MRSA, data are lacking to recommend one method. However, if obtaining swabs from multiple individuals, pre-moistening by dipping the swab into a common container of sterile saline might increase the chance of cross contamination if an appropriate aseptic technique is not followed. Below is an example of a method that could be used.

1. Label swab container with either the patient name or patient code.
2. Obtain informed consent from participants. Explain to the participants that you will only be touching the inside of the nostril (1-2 cm or the length of fingernail from cuticle to tip of finger). Inform them that it may make their nose itch, eyes water, or sneeze, but it shouldn't hurt.
3. Have participant tilt head back.
4. Carefully remove swab from plastic packaging making sure not to touch any object with the swab.
5. Insert swab into one nostril (about 2 cm on an adult) without touching anything but the inside or anterior part of the nostril.
6. Lightly rotate swab on all surfaces of the anterior, or forward, internal part of the nasal mucosa for about 3 seconds and remove.
7. Immediately return swab into its plastic transport container, taking care not to touch anything else with it; tighten the cap of the swab container and ensure that the swab is firmly secured in the transport container and properly labeled; invert the swab, and then activate the ampule of transport medium if present (e.g., squeeze bottom bulb until you feel the bulb with transport medium break).
8. Package swabs according to testing laboratory's instructions (e.g., sealed in biohazard plastic bags, properly labeled, in a suitable container with or without ice packs) and send swabs to the laboratory for processing.

Laboratory Processing of Specimens

Step 1: Processing nares and hand cultures for *Staphylococcus aureus*

- Anterior nares specimens should be obtained with a commercially prepared sterile swab (e.g., Culturette II, Becton Dickinson, Sparks MD). One method for swab processing includes inoculating the swab onto mannitol salt agar (MSA) (i.e., swabbed over the first quadrant while rotating the swab, then streaked for isolation) and incubated at 35°C. The MSA plate should be examined daily for *S. aureus* for 72 hr. After incubation, colonies should be identified as *S. aureus* using standard laboratory methodology. Alternatively, screening plates designed to isolate only MRSA may be used, but definitive identification of isolates as *S. aureus* is still recommended. After specimen identification is complete, proceed to step 2.
- Hand cultures may be obtained by many different methods. One method, which is relatively simple and well-accepted by healthcare personnel, is the wipe-rinse technique. Supplies needed include 0.02% aqueous solution of Tween 80, Handi-Wipe® cleaning cloth, and sterile leak proof specimen containers. First cut the Handi-Wipe® into 8 sections of equal size and moisten with 10 ml 0.02% Tween 80 solution. Wrap each wipe in aluminum foil and sterilize in an autoclave (refrigerate wipes until use). Have the subject open and remove the wipe and rub both hands carefully. Make sure to get between the fingers and up to the wrists. Have the subject place the wipe in a sterile specimen container and cap tightly. Label each container and send to the laboratory. Samples can be refrigerated overnight if they cannot be sent directly to the lab. Samples should be assayed within 48 hours. To assay, place approximately 100 ml sterile 0.02% Tween 80 into each specimen container with the Handi-Wipe. Place the container on a shaker for 15-30 minutes. Split the 100 ml sample into two 50 ml samples. Filter the broth from the two samples separately to collect bacteria using the membrane filtration technique and 0.45 µ filters. Place one membrane filter on Columbia Blood Agar plate with colistin and naladixic acid (CNA agar) and one filter on an MSA plate. Hand cultures should be incubated for up to 72 hours at 35°C. Isolates should be identified as *S. aureus* using standard laboratory methodology.

Step 2: Detecting VISA/VRSA

- After identification of isolates as *S. aureus* or MRSA, laboratories should perform susceptibility testing using a validated MIC method or vancomycin screen plates if a large number of isolates are being processed (see page 7).
- If after conducting susceptibility testing or screening, the *S. aureus* isolates show reduced susceptibility to vancomycin (MIC \geq 4 µg/ml), health departments should be notified where such isolates are reportable. The CDC may be contacted for confirmatory and susceptibility testing of these isolates by sending an email to SEARCH@cdc.gov.

Decolonization in MRSA, VISA, or VRSA Carriers

Some patients, healthcare workers, or family members may be identified as colonized or as carriers of MRSA, VISA, or VRSA during a contact investigation. Colonization refers to the presence of microorganisms in or on a person who has not clinical signs or symptoms of infection. Decolonization refers to reducing the 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; 3) the risk of transmission to others. In general, CDC does not recommend decolonization of carriers unless they are implicated in transmission organisms during an outbreak.

Decolonization Decision making for:

1. **VISA- or VRSA-infected patients colonized with MRSA, VISA, or VRSA:**

The decision to decolonize is made by the patient's primary physician in consultation with the infection control team and public health authorities (e.g., local and/or state health department).

2. **Healthcare workers colonized with MRSA, VISA, or VRSA:**

The decision to decolonize is made by occupational health services, the infection control team, the healthcare worker, and the workers personal physician. For those colonized with VISA/VRSA, public health authorities (e.g., local/state health departments) should be included.

3. **VISA patient contacts colonized with MRSA, VISA, or VRSA:**

The decision to decolonize contacts who are not healthcare workers is made by the contact, their primary care physician, and public health authorities (e.g., local and/or state health departments).

Overview of nasal decolonization treatment:

Regimens to eliminate *S. aureus* colonization have been used in healthcare settings in an effort to prevent autoinfection among colonized patients and control MRSA. However, a limited number of antimicrobial agents are available for the eradication of *S. aureus* colonization. These regimens have included various combinations of topical and systemic antimicrobial agents and antiseptic body washes and have typically been used as part of multi-faceted infection control interventions, making it difficult to evaluate the effectiveness of any individual component. Mupirocin, a topical antimicrobial with antistaphylococcal activity, is usually the agent of choice for eradication of staphylococcal nasal colonization in patients and healthcare workers during localized MRSA outbreaks. Data from healthcare settings indicate that intranasal mupirocin can be effective at eliminating *S. aureus* colonization in the short term; however, recolonization is common.

Before the decision is made to use mupirocin, several limitations of the agent must be considered. First, elimination of colonization may be transient. In settings where MRSA is endemic, persons may be recolonized from external sources. Second, *S. aureus* can develop resistance to mupirocin during therapy, and resistance has been attributed to widespread application of intranasal mupirocin ointment for hospitalized patients. Finally, in most studies of its use to eliminate MRSA carriage in outbreak situations, mupirocin was administered in conjunction with multiple infection control measures. Therefore, it is difficult in these studies to attribute eradication of MRSA colonization to the use of mupirocin alone.

Infection Control Issues

CDC has issued specific recommendations intended to reduce the development and transmission of VISA/VRSA. Below is a checklist of important infection control recommendations. However, these may need to be customized to special healthcare-settings (e.g., dialysis, home healthcare; see page 16). Infection control precautions should remain in place until a 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.

For assistance contact CDC's Division of Healthcare Quality Promotion by telephone 800-893-0485 or send an email to SEARCH@cdc.gov.

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 VISA/VRSA patient).
3. Implement the appropriate infection control precautions during patient care.
 - a. Use contact precautions (gown and gloves for room entry).
 - b. Wear mask/eye protection or face shield if performing procedures likely to generate splash or splatter (e.g., wound manipulation, suctioning) of VISA/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 VISA/VRSA.
 - e. Monitor and strictly enforce compliance with contact precautions.
4. Educate and inform the appropriate personnel about the presence of a patient with VISA/VRSA and the need for contact precautions:
 - a. Patient's physicians
 - b. Admitting or emergency room personnel
 - c. Personnel admitting patients to unit
 - d. Personnel transporting patients between institutions
5. Consult with the local and/or state health department and CDC before transferring the patient (for emergencies only) or discharging the patient.

Dialysis Settings

Infection control precautions recommended for all hemodialysis patients are adequate to prevent transmission from most patients infected/colonized with VISA/VRSA.

1. Wear disposable gloves when caring for the patient or touching the patient's equipment at the dialysis station; remove gloves and wash hands between each patient or station.
2. Nondisposable items that cannot be cleaned and disinfected (e.g., adhesive tape, cloth-covered blood pressure cuffs) should be dedicated for use only on a single patient.
3. Unused medications (including multiple dose vials containing diluents) or supplies (e.g., syringes, alcohol swabs) taken to the patient's station should be used only for that patient and should not be returned to a common clean area or used on other patients.
4. When multiple dose medications vials are used (including vials containing diluents), prepare

- individual patient doses in a clean (centralized) area away from dialysis stations and deliver separately to each patient. Do not carry multiple dose medication vials from station to station.
5. Do not use common medication carts to deliver medications to patients. Do not carry vials, syringes, alcohol swabs, or supplies in pockets. If trays are used to deliver medications to individual patients, they must be cleaned between patients.
 6. Clean areas should be clearly designated for the preparation, handling, and storage of medications and unused supplies and equipment.
 7. Use external venous and arterial pressure transducer filters/protectors for each patient treatment to prevent blood contamination of the dialysis machines' pressure monitors. Change filter/protectors between each patient treatment, and do not reuse them. Internal transducer filters do not need to be changed routinely between patients.
 8. Clean and disinfect the dialysis station (e.g., chairs, beds, tables, machines) between patients.
 9. For dialyzers and blood tubing that will be reprocessed, cap dialyzer ports and clamp tubing. Place all used dialyzers and tubing in leakproof containers for transport from station to reprocessing or disposal area.

Additional infection control precautions should be considered for treatment of patients who might be at increased risk for transmitting pathogenic bacteria. For these patients, consider adding the following precautions:

1. Staff members treating the patient should wear a separate gown over their clothing and remove the gown when finished caring for the patient
2. Dialyze the patient at a station with as few adjacent stations as possible (e.g., at the end or corner of the unit).

Home Healthcare Settings

1. Home healthcare providers should follow the same VISA/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. Wear mask and eye protection or face shield if performing procedures likely to generate splash or splatter (e.g., wound manipulation, suctioning) of VISA/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).
 - d. Develop systems to monitor and strictly enforce compliance with contact precautions in the home by healthcare workers.
2. Minimize the number of persons with access to the VISA/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.

References

Infection Control

1. CDC. Interim guidelines for prevention and control of staphylococcal infections associated with reduced susceptibility to vancomycin. MMWR 1997;46:626-8,635.
2. CDC. Guideline for hand hygiene in health-care settings: recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. MMWR 2002;51(No. RR-16).
3. CDC. Recommendations for preventing transmission of infections among hemodialysis patients. MMWR. 2001;50:2-32.
4. Fridkin S.K. Vancomycin-Intermediate and -Resistant *Staphylococcus aureus*: What the Infectious Disease Specialist Needs to Know. Clinical Infectious Diseases. 2001;32:108-115.
5. McDonald LC, Hageman JC. Vancomycin intermediate and resistant *Staphylococcus aureus*. What the nephrologist needs to know. Nephrol News Issues. 2004;8(11):63-4, 66-7, 71-2.
6. Edmond MB, Wenzel RP, Pasculle AW. Vancomycin-resistant *Staphylococcus aureus*: perspectives on measures needed for control. Ann Intern Med. 1996;124(3):329-34.

Case Reports and Epidemiology

1. CDC. Reduced susceptibility of *Staphylococcus aureus* to vancomycin, Japan, 1996. MMWR 1997;46:624-4.
2. Smith TL, Pearson ML, Wilcox KR, Cruz C, Lancaster MV, Robinson-Dunn B, Tenover FC, Zervos MJ, Band JD, White E, Jarvis WR. Emergence of vancomycin resistance in *Staphylococcus aureus*. N Engl J Med. 1999;340(7):493-501.
3. CDC. *Staphylococcus aureus* with reduced susceptibility to vancomycin--Illinois, 1999. MMWR. 2000;48(51-52):1165-7.
4. Hageman JC, Pegues DA, Jepson C, Bell RL, Guinan M, Ward KW, Cohen MD, Hindler JA, Tenover FC, McAllister SK, Kellum ME, Fridkin SK. Vancomycin-intermediate *Staphylococcus aureus* in a home health-care patient. Emerg Infect Dis. 2001;7(6):1023-5.
5. Naimi TS, Anderson D, O'Boyle C, Boxrud DJ, Johnson SK, Tenover FC, Lynfield R. Vancomycin-intermediate *Staphylococcus aureus* with phenotypic susceptibility to methicillin in a patient with recurrent bacteremia. Clin Infect Dis. 2003;36(12):1609-12.
6. Fridkin SK, Hageman J, McDougal LK, Mohammed J, Jarvis WR, Perl TM, Tenover FC; Vancomycin-Intermediate *Staphylococcus aureus* Epidemiology Study Group. Epidemiological and microbiological characterization of infections caused by *Staphylococcus aureus* with reduced susceptibility to vancomycin, United States, 1997-2001. Clin Infect Dis. 2003;36(4):429-39.
7. CDC. *Staphylococcus aureus* Resistant to Vancomycin-United States, 2002. MMWR 2002;51:565-7.
8. Chang S, Sievert DM, Hageman JC, Boulton ML, Tenover FC, Downes FP, Shah S, Rudrik JT, Pupp GR, Brown WJ, Cardo D, Fridkin SK; Vancomycin-Resistant *Staphylococcus aureus* Investigative Team. Infection with vancomycin-resistant *Staphylococcus aureus* containing the vanA resistance gene. N Engl J Med. 2003;348(14):1342-7.
9. CDC. Vancomycin-resistant *Staphylococcus aureus*--Pennsylvania, 2002. MMWR. 2002;51:902
10. Whitener CJ, Park SY, Browne FA, et al. Vancomycin-resistant *Staphylococcus aureus* in the absence of vancomycin exposure. Clin Infect Dis 2004;38:1049-55
11. CDC. Brief Report: Vancomycin-Resistant *Staphylococcus aureus* --- New York, 2004. MMWR. 2004;53:322

12. Kacica M, Scott C, Kurpiel P, Johnson G, Kohler-Schmidt D, Musser K, Bopp D, Mitchell E, Ginocchio C, Patel J, Hageman JC, McDonald LC. Vancomycin-resistant *Staphylococcus aureus* in a resident of a long-term care facility. 42nd Annual Meeting of the Infectious Diseases Society of America, Boston, MA, 2004.
13. Madhavan T, D. Sievert, J. Torresan, J. Rudrik. VRSA Infection of a Gangrenous Toe in a Community Hospital. 43rd Annual Meeting of the Infectious Diseases Society of America, San Francisco, CA 2005.
14. Sievert D, Dyke TL, Bies S, Robinson-Dunn B, Hageman JC, Patel J, McDonald LC, Rudrik J. Fifth Case of Vancomycin-Resistant *Staphylococcus aureus* in United States and Third for Michigan. 16th Annual Meeting of the Society for Healthcare Epidemiology of America, Chicago, IL 2006.
15. Kluytmans J, van Belkum A, Verbrugh H. Nasal Carriage of *Staphylococcus aureus*: Epidemiology, Underlying Mechanisms, and Associated Risks. *Clin Microb Rev.* 1997;10:505-520.
16. Boyce J. Preventing Staphylococcal Infections by Eradicating Nasal Carriage of *Staphylococcus aureus*: Proceeding with Caution. *Infection Control and Hospital Epidemiology.* 1996;17:775-779.
17. Harbarth S, Dharan S, Liassine N, Herrault P, Auckenthaler R, Pittet D. Randomized, Placebo-Controlled, Double-Blind Trial to Evaluate the Efficacy of Mupirocin for Eradicating Carriage of Methicillin-Resistant *Staphylococcus aureus*. *Antimicrobial Agents and Chemotherapy.* 1999;43:1412-1416.
18. Laupland KB, Conly JM. Treatment of *Staphylococcus aureus* colonization and prophylaxis for infection with topical intranasal mupirocin: an evidence-based review. *Clin Infect Dis.* 2003;37(7):933-938.
19. Loeb M, Main C, Walker-Dilks C, Eady A. Antimicrobial drugs for treating methicillin-resistant *Staphylococcus aureus* colonization. *Cochrane Database Syst Rev.* 2003(4):CD003340.
20. Franchi D, Climo MW, Wong AH, Edmond MB, Wenzel RP. Seeking vancomycin resistant *Staphylococcus aureus* among patients with vancomycin-resistant enterococci. *Clin Infect Dis.* 1999 Dec;29(6):1566-8.

Laboratory Testing Methodology and Research

1. Tenover FC, Lancaster MV, Hill BC, et al. Characterization of staphylococci with reduced susceptibilities to vancomycin and other glycopeptides. *J Clin Microbiol* 1998;36:1020-7. [Erratum, *J Clin Microbiol*;36:2167.]
2. Hubert SK, Mohammed JM, Fridkin SK, Gaynes RP, McGowan JE Jr, Tenover FC. Glycopeptide-intermediate *Staphylococcus aureus*: evaluation of a novel screening method and results of a survey of selected U.S. hospitals. *J Clin Microbiol.* 1999;37(11):3590-3.
3. Clinical and Laboratory Standards Institute/NCCLS. *Performance Standards for Antimicrobial Susceptibility Testing.* Sixteenth informational supplement. M100-S16. Wayne, PA: CLSI, 2006.
4. Peterson NJ, Collins DE, Marshall JH. A microbiological assay technique for hands. *Health Lab Sci* 1973;10:18-22.
5. Peterson NJ, Collins DE, Marshall JH. Evaluation of skin cleansing procedures using the wipe-rinse technique. *Health Lab Sci* 1974;11:182-87.
6. CDC. Laboratory capacity to detect antimicrobial resistance, 1998. *MMWR* 2000;48(51):1167-71.
7. Weigel LM, Clewell DB, Gill SR, et al. Genetic analysis of a high-level vancomycin-resistant isolate of *Staphylococcus aureus*. *Science* 2003;302:1569-71

8. Tenover FC, Weigel LM, Appelbaum PC, et al. Vancomycin-resistant *Staphylococcus aureus* isolate from a patient in Pennsylvania. *Antimicrob Agents Chemother* 2004;48:275-80
9. Boyle-Vavra S, Berke SK, Lee JC, Daum RS. Reversion of the glycopeptide resistance phenotype in *Staphylococcus aureus* clinical isolates. *Antimicrob Agents Chemother*. 2000;44(2):272-7.
10. Sakoulas G, Eliopoulos GM, Moellering RC Jr, Wennersten C, Venkataraman L, Novick RP, Gold HS. Accessory gene regulator (agr) locus in geographically diverse *Staphylococcus aureus* isolates with reduced susceptibility to vancomycin. *Antimicrob Agents Chemother*. 2002;46(5):1492-502.
11. Sieradzki K, Leski T, Dick J, Borio L, Tomasz A. Evolution of a vancomycin-intermediate *Staphylococcus aureus* strain in vivo: multiple changes in the antibiotic resistance phenotypes of a single lineage of methicillin-resistant *S. aureus* under the impact of antibiotics administered for chemotherapy. *J Clin Microbiol*. 2003;41(4):1687-93.
12. Cui L, Ma X, Sato K, Okuma K, Tenover FC, Mamizuka EM, Gemmell CG, Kim MN, Ploy MC, El-Solh N, Ferraz V, Hiramatsu K. Cell wall thickening is a common feature of vancomycin resistance in *Staphylococcus aureus*. *J Clin Microbiol*. 2003;41(1):5-14.
13. Cui L, Iwamoto A, Lian JQ, Neoh HM, Maruyama T, Horikawa Y, Hiramatsu K. Novel mechanism of antibiotic resistance originating in vancomycin-intermediate *Staphylococcus aureus*. *Antimicrob Agents Chemother*. 2006;50(2):428-38.
14. McAleese F, Wu SW, Sieradzki K, Dunman P, Murphy E, Projan S, Tomasz A. Overexpression of genes of the cell wall stimulon in clinical isolates of *Staphylococcus aureus* exhibiting vancomycin-intermediate- *S. aureus*-type resistance to vancomycin. *J Bacteriol*. 2006;188(3):1120-33.