Methicillin-Resistant *Staphylococcus aureus*

In January 1998, a 16-month-old girl from rural North Dakota was taken to a local hospital in shock, with a temperature of 105.2°F (40.6°C), seizures, petechial rash and irritability. She was treated with ceftriaxone but developed respiratory failure and cardiac arrest and died within two hours of arriving at the hospital. Methicillin-resistant *Staphylococcus aureus* (MRSA) was cultured from blood and cerebrospinal fluid drawn immediately postmortem. An autopsy revealed multiple small abscesses of the brain, heart, liver and kidneys; autopsy cultures of meninges, blood and lung tissue grew MRSA. Neither the patient nor family members had been associated with common risk factors for MRSA infection.

Another fatal MRSA case in North Dakota followed in February 1999. The patient was a 12-month-old boy who was admitted with a temperature of 105.2°F (40.6°C), bronchiolitis, vomiting, dehydration and petechial rash. The patient developed severe respiratory distress and hypotension the following day and died. These two cases and two additional fatal cases from Minnesota that occurred the same year are described in the Aug. 20, 1999, issue of the MMWR and can be viewed at www.cdc.gov/mmwr/preview/mmwrhtml/mm4832a2.htm.

Staphylococcus aureus (*Figure 1*) is an organism commonly found in the nose and on the skin of healthy people and can cause infection with clinical manifestations ranging from pustules to sepsis and death. Most people are colonized (the presence of *S. aureus* in or on the body without causing illness) with *S. aureus*. Once infected, individuals can remain colonized for prolonged periods of time. These people can become reservoirs for increased transmission to others.

*S. aureus* first acquired resistance to methicillin and other penicillin-based antibiotics in the 1960s in England and emerged in the United States (U.S.) in the mid 1980s. Today, MRSA is resistant to all commonly prescribed beta-lactam antibiotics, including penicillins and cephalosporins.

Known risk factors of MRSA are described in Box 1. MRSA historically has been associated with health-care institutions. In 1999, more than 50 percent of intensive care patients with hospital-acquired *S. aureus*-associated infection had MRSA. This proportion increased to more than 60 percent in 2003. (*Figure 2*)

**Box 1. Risk Factors Associated with MRSA**

- Diabetes mellitus
- IV drug use
- Hemodialysis
- Major surgical procedures
- Immunocompromised conditions
- History of long-term or frequent antibiotic use
- Invasive lines or tubes (IV, urinary catheters)
- Increased age (elderly)
- History of multiple hospitalizations or procedures
- Infections/colonization at other sites
- Morbid obesity
- Orthopedic implant surgery
- Long-term inpatient stay
Figure 2. MRSA prevalence, as a proportion of health-care-acquired *S. aureus* infections among ICU patients, 1989-2003.

Source: [www.cdc.gov/ncidod/hip/ARESIST/mrsa.htm](http://www.cdc.gov/ncidod/hip/ARESIST/mrsa.htm)

**Community-Associated MRSA**

Community-associated MRSA (CA-MRSA) has emerged as a cause of skin infections in the community. CA-MRSA transmission has been associated with previously healthy participants in competitive sports through sharing contaminated items such as athletic equipment, towels, benches and personal items and also in individuals with no known risk factors housed in correctional facilities such as prisons, jails and detention centers.\(^4\),\(^5\) Criteria for determining patients with CA-MRSA are provided in Box 2.

Although community-acquired MRSA infections have emerged as a significant public health problem, it is difficult to determine what the effect of these infections will have on the incidence of MRSA infections among hospitalized patients.

**Box 2. Criteria of people who likely have community-associated MRSA (CA-MRSA) infections.**

- Diagnosis of MRSA was made in the outpatient setting or by a culture positive for MRSA within 48 hours after admission to the hospital.
- The patient has no medical history of MRSA infection or colonization.
- The patient has no medical history in the past year of:
  - Hospitalization.
  - Admission to a nursing home, skilled nursing facility or hospice.
  - Dialysis.
  - Surgery.
- The patient has no permanent indwelling catheters or medical devices that pass through the skin into the body.

**Treatment**

An important consideration for the appropriate treatment of staphylococcal infections is careful evaluation of culture and sensitivity reports. Susceptibility testing always should be conducted prior to initiating treatment. MRSA is usually multi-drug resistant. In addition to most beta-lactams, MRSA is also commonly resistant to erythromycin, clindamycin, aminoglycosides, fluoroquinolones, co-trimoxazole and rifampin. In North Dakota, MRSA isolates commonly display resistance to erythromycin, ciprofloxacin and clindamycin. (Figure 3)

Vancomycin continues to be the drug of choice for treating most MRSA infections caused by multi-drug resistant strains. Clindamycin, co-trimoxazole, fluoroquinolones or minocycline may be useful when patients do not have life-threatening infections caused by strains susceptible to these agents. For serious infections caused by strains that test susceptible to rifampin, adding rifampin to vancomycin or fluoroquinolones may contribute to improved outcomes. Rifampin should not be used alone to treat MRSA infections due to the rapid development of resistance. The two newest antimicrobials, quinupristin-dalfopristin (Synercid) and linezolid (Zyvox), also are effective for MRSA infections, and though routine use is generally discouraged to prevent further resistance to these agents.

Infection also is often confused with colonization and can lead to unnecessary utilization of antimicrobial agents. Consultation with an infectious-disease specialist is recommended for management decisions regarding infection versus colonization.

Basic infection-control measures are critical to preventing transmission of MRSA. However, as demonstrated by the increase of MRSA infections among hospitalized patients, infection control practices have failed to control the spread of these infections in many health-care facilities. Reasons for this lack of control have been due to multiple factors, including (1) the failure to perform active surveillance.

**Figure 3. Percentage of additional drug resistance MRSA isolates, 2001-2003.**

*Antibiotic

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<tr>
<th>Year</th>
<th>Erythromycin</th>
<th>Ciprofloxacin</th>
<th>Clindamycin</th>
<th>Gentamycin</th>
<th>Rifampin</th>
<th>Vancomycin</th>
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<td>2001</td>
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<td>5%</td>
<td>0%</td>
<td>0%</td>
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<tr>
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<td>20%</td>
<td>5%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2003</td>
<td>20%</td>
<td>30%</td>
<td>10%</td>
<td>0%</td>
<td>0%</td>
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</tr>
</tbody>
</table>

*Invasive Isolates Only*
cultures to identify colonized patients, (2) the fact that barrier precaution policies adopted in the 1980s did not address the multiple reservoirs and modes of transmission of MRSA, (3) poor adherence of health-care workers to barrier precaution and hand hygiene policies, and (4) the increasing importation of MRSA by patients admitted from extended-care facilities or other acute care facilities.6

It has been recommended that control of MRSA infections in the hospital must include multiple approaches in addition to standard and contact precautions. These control measures include active surveillance cultures of high-risk patients, the use of contact precautions when caring for colonized or infected patients, hand hygiene using an antimicrobial product, and treatment of health-care workers implicated in transmission.6

Vancomycin-Resistant Staphylococcus aureus (VRSA)
The identification of several cases of Staphylococcus aureus in the United States demonstrating intermediate resistance to vancomycin (VISA) and the first case of Staphylococcus aureus completely resistant to vancomycin (VRSA) in Michigan in June 2002 increased the concern of resistant organisms in North Dakota.7 Such infections are likely to be seen with increasing frequency, particularly among patients who receive prolonged courses of vancomycin or have risk factors for acquiring MRSA. There have been no VISA or VRSA cases reported in North Dakota since it became a reportable condition in 2000.

North Dakota MRSA Statistics
Invasive MRSA infection was made a reportable condition in 2000 and in August 2002, all MRSA infections became a reportable condition.

Reporting was somewhat sporadic until 2003, when increased efforts were conducted to increase reporting. In 2003, 1,329 MRSA infections were reported (Rate = 207/100,000). Of these, 979 (Rate = 152.4/100,000) were classified as noninvasive MRSA infections, while 350 (Rate = 54.5/100,000) were invasive infections. (Figure 4) The greatest percentage of cases was reported among people age 65 and older. In 2003, more than 75 percent of the invasive MRSA and 39 percent of the noninvasive cases were reported among people age 65 years and older. (Figure 5)

VRE (Vancomycin-Resistant Enterococcus)
Enterococci are opportunistic pathogens that are normal inhabitants of human gastrointestinal and genitourinary tracts. Enterococci typically are associated with causing urinary tract infections, intra-abdominal and pelvic sepsis, surgical wound infections and bacteremia. However, they now are emerging as highly resistant organisms and nosocomial pathogens.8

Enterococci have been identified as the third most common cause of nosocomial, hospital-acquired pneumonia. Since its identification in U.S. hospitals in the 1980s, VRE rates have continued to increase and now account for more than 25 percent of ICU enterococci, according to the National Nosocomial Infections Surveillance (NNIS) system. Mortality rates for VRE bacteremia and sepsis have been reported to exceed 30 percent.

Resistant enterococcus can be isolated from patients who have been institutionalized for long periods of time.8 Other risk factors for acquiring a resistant enterococcal infection include severity of underlying illness, presence of invasive devices, prolonged antibiotic use and prior colonization. Those at higher risk include immunosuppressed hosts such as renal dialysis, transplant and oncology patients.
Since vancomycin use is a factor that has been linked with the development of VRE, guidelines for use of vancomycin have been established by the Hospital Infection Control Practices Advisory Committee of the Centers for Disease Control and Prevention (CDC). (Box 3)

An important aspect for controlling VRE is strict infection control practices. In addition to infection control policies and procedures, health-care facilities should have guidelines in place to manage actual or suspected cases of VRE in regards to antimicrobial therapy. Guidelines should include:

- A comprehensive antimicrobial utilization plan that includes education of all staff (medical, nursing and other ancillary services).
- Understanding of antimicrobial use for surgical prophylaxis (if pertinent).
- Recommendations for appropriate antibiotic use (as applicable to the institution).

Based on current trends, it appears VRE will continue to increase as a problem not only in acute care settings, but also in long-term care facilities and the community. Treatment options, though limited, are available and newer agents are being studied. Strict adherence to infection control policies and consultation with infectious disease specialists are important.

Although VRE infections are significant public health problems, only 20 VRE infections were reported in North Dakota in 2003; 16 (80%) were age 65 and older. In 2003, 19 VRE cases were reported to the NDDoH; 84 percent occurred in individuals age 65 and older.

**Recommendations for the Prevention and Control of Antibiotic Resistant Organisms (MRSA/VRE) in North Dakota**

Numerous North Dakota providers have expressed concerns about the increase in the number of gram-positive organisms demonstrating resistance to antibiotics commonly used to treat these infections, most notably MRSA and VRE.

As a result, the North Dakota Drug-Resistant Organisms Work Group was organized to address these concerns. The Work Group is comprised of the state health officer, state epidemiologist, Division of Microbiology director, Division of Disease Control staff, Division of Health Facilities staff, representatives of the Association for Professionals in Infection Control and Epidemiology Inc. (APIC) and members of private health-care facilities (acute care, long-term care and clinics). Consultation also has been provided by North Dakota infectious disease physicians.

The Work Group has developed guidelines for health-care facilities, providers and agencies when providing care for patients/clients in various settings to prevent the spread of these resistant organisms. The document also provides educational resources regarding drug-resistant organisms.

The guidelines are in final review and are expected to be available shortly.

**Box 3. Recommendations for Preventing the Spread of Vancomycin Resistance**

**SITUATIONS IN WHICH THE USE OF VANCOMYCIN IS APPROPRIATE**

1. Treatment of serious infections due to beta-lactam resistant gram-positive organisms.
2. Treatment of serious infections due to gram-positive organisms in patients with serious beta-lactam allergies.
3. Treatment of antibiotic-associated colitis (AAC) when treatment with metronidazole has failed or if the AAC is potentially life-threatening.
4. Prophylaxis for endocarditis for certain procedures based on American Heart Association recommendations.
5. Prophylaxis for certain surgical procedures involving implantation of prosthetic materials in hospitals with a high rate of MRSA or MRSE.

**SITUATIONS IN WHICH THE USE OF VANCOMYCIN SHOULD BE DISCOURAGED**

1. Routine surgical prophylaxis unless the patient has a severe allergy to beta-lactam antibiotics.
2. Empirc treatment for febrile neutropenic patients unless a gram-positive infection is suspected and the institution has a high rate of MRSA.
3. Treatment of one positive blood culture for coagulase-negative staphylococcus if other blood cultures drawn at the same time are negative (i.e., likely contamination).
4. Continued empiric use in patients whose cultures are negative for beta-lactam resistant gram-positive organisms.
5. Prophylaxis for infection or colonization of indwelling central or peripheral intravenous catheters.
6. Selective decontamination of the gastrointestinal tract.
7. Eradication of MRSA colonization.
8. Primary treatment of AAC.
9. Routine prophylaxis for infants with very low birth weight.
10. Routine prophylaxis for patients on continuous ambulatory peritoneal dialysis or hemodialysis.
11. Treatment of infection due to beta-lactam sensitive gram-positive microorganisms in patients with renal failure (for ease of dosing schedule).
12. Use of vancomycin solution for topical application or irrigation.
For: Influenza Sentinel Provider

Why: Monitor the impact of influenza in your community and state

When: October 2004 through May 2005

For more information: Contact Melissa Casteel, Influenza Surveillance Coordinator at 1.800.472.2180 or mcasteel@state.nd.us

- An influenza sentinel provider conducts surveillance for influenza-like illness (ILI) in collaboration with the North Dakota Department of Health and the CDC.
- Most physicians report that it takes them less than 30 minutes a week to compile and report their data.
- Sentinel providers can submit specimens from a subset of patients for virus isolation free of charge.
- Providers of any specialty in any type of practice are eligible to be influenza sentinel providers.
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*Provisional data

1 Meningitis caused by *Staphylococcus aureus* and *Streptococcus pneumoniae*.

2 Includes invasive infections caused by streptococcal disease not including those classified as meningitis.

3 Includes invasive infections of streptococcal, Group B, disease in persons ≥ 3 months of age.

4 Includes invasive infections caused by *Streptococcus pneumoniae* in persons ≥ 5 years of age.