Community-acquired MRSA infection: An update

Infection often begins on the skin—where it may be mistaken for a spider bite—but MRSA can quickly cause deadly systemic illnesses such as toxic shock syndrome and necrotizing pneumonia.

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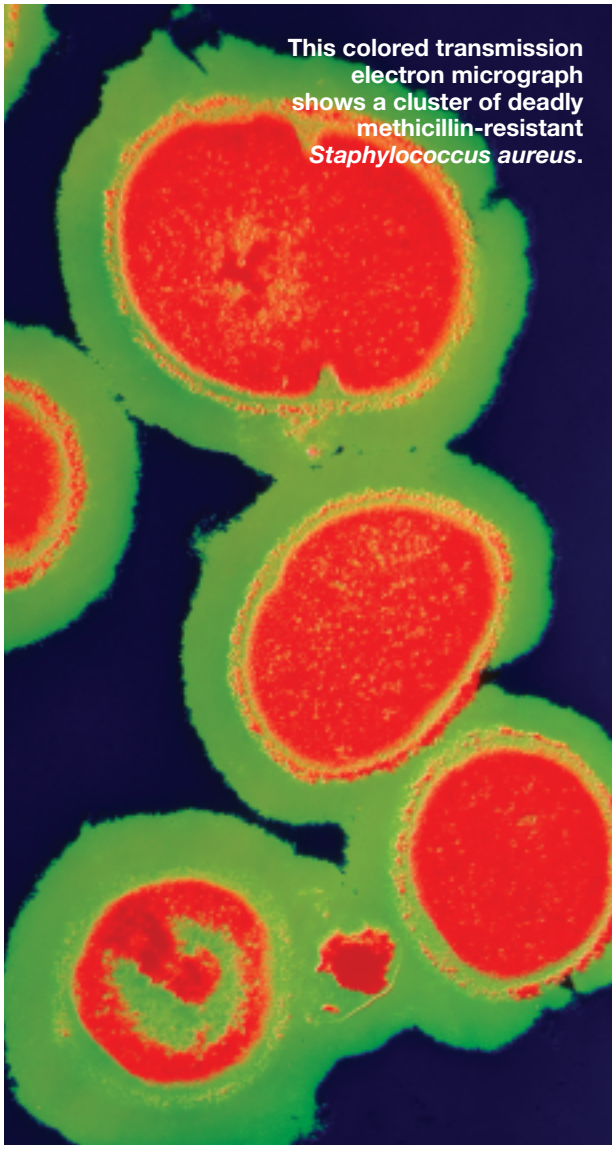

This colored transmission electron micrograph shows a cluster of deadly methicillin-resistant *Staphylococcus aureus*.

Antimicrobial resistance has become such a growing global problem that, according to the Institute of Medicine, it may be a "paramount microbial threat of the twenty-first century."[1] Resistance has produced an increased burden of illness, longer hospitalizations, excess deaths, and greater health care costs.[2-6] Methicillin-resistant *Staphylococcus aureus* (MRSA) is among the most important pathogens in terms of increasing prevalence and impact. MRSA once caused predominantly nosocomial infections in immunocompromised patients. In recent years, however, infectious disease experts have noted an emergence of infections not associated with hospitalization, often referred to as community-acquired (CA) MRSA. The incidence has risen dramatically in the past decade.[7-9] In contrast to hospital- (or health-care-) acquired MRSA (HA-MRSA), CA-MRSA has a number of unique characteristics and may present an even greater threat to public health and a more significant challenge to clinicians.

The clinical presentation of staphylococcal disease

A common bacterium, *S aureus* is frequently present as part of the normal human flora in both children and adults. An estimated 25% to 30% of the population may be colonized, generally harboring the pathogen on their skin or in their noses without evidence of infection.

Despite benign colonization in many people, staphylococcal organisms are frequently pathogenic and a common cause of illnesses ranging from localized skin infection (for example, folliculitis and impetigo) to more serious invasive disease (for instance, arthritis, endo-

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carditis, pneumonia, and septicemia). Staphylococcal bacteria also cause surgical wound and prosthetic implant infections. In some cases, they produce toxins and virulence factors such as superantigens, leading to such unique illnesses as toxic shock syndrome and staphylococcal scarlet fever.

While CA-MRSA primarily causes skin and soft tissue infections, it can cause serious invasive infection (see Table 1, page 26). Patients with skin infections may assume they have a spider bite because of the appearance of the initial lesion, which manifests as a red papule, plaque, or indurated nodule that spreads outward. In one community cohort of 14 patients presenting with necrotizing fasciitis, MRSA, a previously rare cause, was implicated.[10] Concern is also mounting that cases of community-acquired pneumonia associated with influenza and caused by MRSA are on the rise.[9,11]

Methicillin resistance

Although most staphylococcal infections initially responded readily to penicillin G, a strain was soon isolated that produced beta-lactamase (penicillinase). The initial sporadic resistance spread rapidly, and in the early 1960s it led to the development of semisynthetic penicillinase-resistant antimicrobials such as methicillin, nafcillin, oxacillin, and cloxacillin. Methicillin-resistant strains of *S aureus* were identified shortly thereafter.[12] Subsequently, during the 1970s and 1980s, MRSA emerged as one of the greatest challenges in inpatient settings because of its multidrug resistance.

Several classes of antimicrobials—including macrolides, aminoglycosides, fluoroquinolones, tetracyclines, and lincosamide antibiotics such as clindamycin—may be ineffective against HA-MRSA. Vancomycin, a glycopeptide antibiotic, remains the mainstay treatment; however, some strains of HA-MRSA have shown reduced susceptibility to this drug as well.[5,13,14] In contrast, CA-MRSA, which has been surfacing in communities over the past decade, demonstrates a susceptibility pattern more consistent with methicillin-sensitive *S aureus* in that it is typically susceptible to multiple non-beta-lactam antibiotics,[15] including clindamycin, tetracyclines, and trimethoprim-sulfamethoxazole (TMP-SMX).[9]

CA-MRSA has a novel element, SCCmec type IV, not typically found in the nosocomial isolates, and this may account for the transformation of normal staphylococcal flora into MRSA.[16] The genotypes of CA-MRSA also differ, with the most prevalent strain identified as USA 300.[9] The Panton-Valentine leukocidin virulence factor, found in only 2% to 3% of staphylococcal strains,[4] is associated with necrotizing pneumonia and skin and soft-tissue infections and is more likely to be found in CA-MRSA (see Table 2, page 26).[6,9,15,17,18]

Continued on page 26

CME

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Learning objectives

- Describe the colonization and clinical presentation of staphylococcal disease
- Discuss the development of methicillin-resistant *Staphylococcus aureus* (MRSA) and how community-acquired MRSA differs from hospital-acquired MRSA
- Review features of the history, physical examination, and laboratory assessment in patients infected with CA-MRSA
- Outline antibiotic selection for CA-MRSA infection and the crucial role played by patient education and prevention

IN THIS ARTICLE

Key Points

- *Staphylococcus aureus* is a common bacterium, frequently present as part of the normal human flora in both children and adults.
- Despite benign colonization in many persons, staphylococcal organisms are frequently pathogenic and a common cause of illness, ranging from localized skin infection to more serious invasive disease.
- CA-MRSA infections are increasingly being identified in both outpatient and inpatient settings. An estimated 8% to 20% of all MRSA infections are community acquired, a number that is expected to increase significantly over the next decade.
- Culture and susceptibility testing should guide the choice of antibiotics for treating the patient with CA-MRSA infection.

Competencies

Medical knowledge	◆◆◆◆◆
Interpersonal & communication skills	◆
Patient care	◆◆◆
Professionalism	◆
Practice-based learning and improvement	◆◆
Systems-based practice	◆

For an explanation of competencies ratings, see the table of contents.

TABLE 1
Clinical manifestations of CA-MRSA infection

Skin and soft tissue infections*
Abscesses
Cellulitis
Furuncles/carbuncles
Traumatic wound infections
Other infections
Necrotizing fasciitis
Necrotizing pneumonia
Sepsis/bacteremia
Sinusitis
Urinary tract infections

*Typically associated with pus, pain, warmth, and tenderness.

Data from Miller LG et al,[10] Osterweil N,[11] Zetola N et al,[15] and Fridkin SK et al.[19]

TABLE 2
Distinguishing HA-MRSA from CA-MRSA

HA-MRSA	CA-MRSA
SCCmec types* 1, II†, III†	SCCmec type* IV
Genotype: USA 100	Genotype: USA 300
Panton-Valentine leukocidin (PVL) virulence factor rare	PVL common
Multidrug resistance	Selective beta-lactam antibiotic resistance
Multiple infection sites	Primarily skin and soft tissue infection

* Distinguished on the basis of size and genetic composition.

† Associated with multiple drug resistance.

Differentiating HA-MRSA from CA-MRSA: The CDC criteria

Initially a problem in tertiary care centers, MRSA is now endemic in other institutional settings, including community hospitals, nursing homes, and rehabilitation centers. CA-MRSA infections are also increasingly being identified in both outpatient and inpatient settings.[8] An estimated 8% to 20% of all MRSA infections are community acquired,[19] and these percentages are expected to continue to increase significantly over the next decade.

While HA-MRSA and CA-MRSA are epidemiologically and microbiologically different,[20-22] distinguishing between them remains problematic without a consistent case definition. According to the CDC, MRSA infection is considered to be community acquired if

- Diagnosis is made in the outpatient setting or a positive culture result is obtained within 48 hours of hospitalization
- There is no history of MRSA infection or colonization
- There is no history in the past year of hospitalization; admission to a nursing home, skilled nursing facility, or hospice; dialysis; or surgery
- The patient has no permanent indwelling catheters or medical devices that pass through the skin into the body.[23]

In the United States, CA-MRSA was first reported in 1982 in a large, urban Michigan hospital. The infection was found in a cluster of 40 persons, including 24 who were injection-drug users.[5] Subsequent CA-MRSA outbreaks have been reported throughout the United States in children (including those in day care centers),[7,24] military recruits,[25] Alaskan natives,[26,27] Pacific Islanders,[28] athletes including wrestlers, fencers, football players, and others),[29,30] men who have sex with other men,[31] and prison inmates.[32]

Diagnosis

Since CA-MRSA causes a range of illnesses, the clinician should target questions to the area of interest, with consideration of systemic manifestations. To differentiate between CA-MRSA and other etiologies, query all patients about a history of MRSA infection, hospitalization or skilled nursing facility admission within the past year, underlying comorbidities, and the risk factors detailed in Table 3 (page 28).[23] Other clues that may suggest infection with CA-MRSA are failure of a skin infection to respond to a beta-lactam antibiotic, recurrent skin infections, and multiple persons presenting with skin infections at the same time (see Figures 1 and 2, and Figure 3, page 28).

For localized skin and soft tissue infections, a focused physical examination may be sufficient. For more invasive disease, perform a complete physical examination, paying particular attention to signs of bacteremia or systemic disease.

In addition to the history and physical examination, laboratory evaluation of patients with suspected CA-MRSA infection should include culture and susceptibility (C&S) testing. While not routinely indicated, pulsed-field gel electrophoresis can demonstrate characteristic genetic differences among isolates, and polymerase chain reaction amplification can detect virulence and enterotoxin genes.[33]

Treatment

The emergence of CA-MRSA presents several challenges to clinicians.[34] The routine empiric use of beta-lactam antibiotics as first-line treatment for staphylococcal infections is no longer warranted. Rather, knowledge of local epidemiology and C&S results should guide treatment. For localized skin infections caused by CA-MRSA, incision and drainage (I&D) without antibiotic therapy may be effective.

For serious or more complicated infections, antibiotics are the treatment of choice. It is important to monitor therapeutic response; instruct patients to contact you if they do not see improvement within 48 to 72 hours, if the infection progresses, or if fever or other signs of systemic disease develop. Educate patients about the importance of completing the entire course of drug therapy, and remind them to report any significant side effects. Also, instruct them in personal hygiene, appropriate wound care, and the importance of not sharing contaminated items with members of the household.

TMP-SMX is widely used to treat CA-MRSA infections in outpatient settings. Ninety-five percent of isolates are susceptible to this agent, although resistance has been noted in some areas.[7] In cutaneous infections, prompt I&D followed by a course of treatment with TMP-SMX—in combination with rifampin to diminish the likelihood of the development of resistance—is a good choice for patients not allergic to sulfa drugs. Never use rifampin as monotherapy since rapid resistance develops.[5]

Clindamycin is also a good choice for susceptible infections. While many CA-MRSA isolates are susceptible to clindamycin on standard susceptibility testing, concern has arisen that inducible isolates with a greater rate of mutations may result in development of resistance during therapy.[5] A limitation of standard susceptibility testing is that it does not evaluate for this possibility. However, a simple laboratory test, the erythromycin-clindamycin "D-zone" evaluation, can identify strains that are likely to become resistant.[35] This test should be requested at the time of culture.

Fluoroquinolones should be prescribed with caution. Even though many isolates are susceptible to ciprofloxacin,[7] the use of fluoroquinolones in the treatment of MRSA infections is associated with rapid development of resistance. However, the newer fluoroquinolones, such as moxifloxacin and gatifloxacin, may have a role in complicated skin and soft tissue infections in patients who are allergic to penicillin.[5]

Tetracyclines, including minocycline and doxycycline, may also be considered for treatment of mild to moderate skin and soft tissue infections.[15,18] These agents can also be used in conjunction with rifampin.

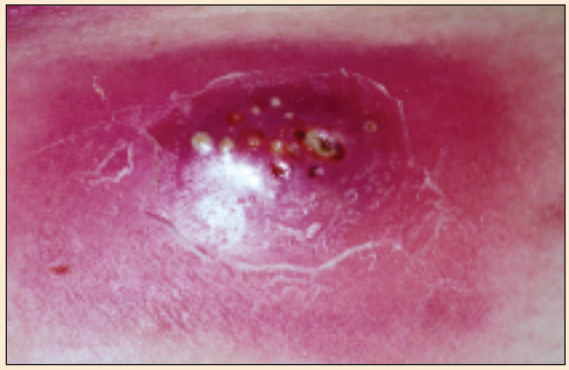
Vancomycin has long been the mainstay therapy for serious MRSA infections, although strains of glycopeptide-intermediate-susceptible *S aureus* and vancomycin-resistant *S aureus* have been identified in a few states. In this case, newer antibiotics such as linezolid, daptomycin, or quinupristin-dalfopristin are indicated.[5,34]

Linezolid was approved for use in 2000. It has demonstrated effectiveness against a number of gram-positive and selected anaerobic infections, including disease caused by MRSA, although there was some resistance. In clinical trials, linezolid was as effective as vancomycin in treating MRSA infections.[36] Indications include the treatment of nosocomial pneumonia caused by MRSA as well as serious skin and skin structure infections.

Daptomycin was approved in 2003 for use in complicated skin and soft tissue infections. It is active

FIGURE 1

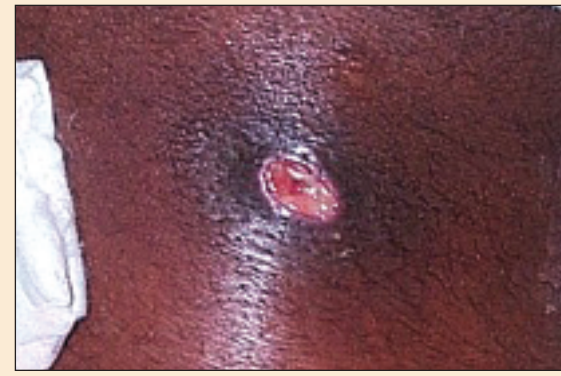
Furuncle



Also known as a carbuncle or boil, a furuncle caused by infection with MRSA often originates in a hair follicle and usually contains pus.

FIGURE 2

Cutaneous abscess



An abscess due to MRSA is seen on the knee of a prison inmate. Transmission of community-acquired MRSA has been reported within prisons.

TABLE 3

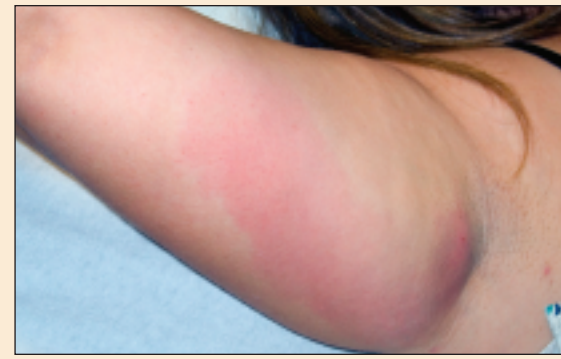
Risk factors for CA-MRSA infection: The five Cs

Contact	Direct skin-to-skin contact, particularly that which is frequent or abrasive
Crowded living conditions	Communal settings such as day care centers, jails, shelters
Compromised skin integrity	Scratches, cuts, abrasions, underlying dermatitis
Contaminated surfaces and items	Objects and surfaces that may transmit infection
Cleanliness	Lack of optimal personal hygiene, inadequate use of soap, inadequate cleaning practices

Data from Methicillin-resistant *Staphylococcus aureus* (MRSA) information for clinicians.[23]

FIGURE 3

Cellulitis



A woman who is chronically infected with MRSA has an infection in her right axilla, with cellulitis extending down her arm and elbow.

against multidrug-resistant gram-positive bacteria, including MRSA. While daptomycin is another option for treatment in selected cases, its role in the routine treatment of CA-MRSA infections has not yet been established.[5]

Quinupristin-dalfopristin is approved for use in serious skin and soft tissue infections and has been used successfully against MRSA.[34] However, its use may be limited by a poor tolerability profile.[5]

Preventing infection

Personal and environmental hygiene measures and judicious, appropriate antibiotic administration are key to controlling the spread of CA-MRSA. Basic personal hygiene, including frequent hand washing—preferably with soap and water or alternatively with an alcohol-based hand sanitizer if obvious contamination is not present—remains a mainstay of infection prevention in both community and institutional settings. Personal items should not be shared; this includes towels, razors, clothing, and uniforms, which may transfer contaminants. Additionally, clothing and linens, particularly those used in sports or other communal activities, should be washed in hot water with laundry soap and dried in a hot dryer, rather than on a line.[37] Patients should observe environmental hygiene, particularly in common areas. They should establish routine cleaning schedules, using commercial disinfectant or bleach (1 tablespoon/quart of water).

For patients with an underlying dermatitis, encourage frequent visual inspection to identify early onset of infection in order to obtain prompt clinical care. All cuts, scrapes, and open wounds should be covered, and patients should discard used bandages appropriately.

Patients who present for admission to a hospital or inpatient health care setting should be screened for potential CA-MRSA infection, which may include evaluation for colonization. For those who are infected, isolation is indicated to curtail nosocomial spread and reduce the incidence of CA-MRSA.[38] Additionally, colonized patients scheduled for elective orthopedic procedures or prosthetic implants may need to be decolonized before surgery to decrease the incidence of postoperative infections.[39]

Conclusion

Antimicrobial resistance is a significant problem. The number of CA-MRSA infections, particularly those not associated with the typical risk factors of nosocomial transmission, has risen dramatically in the past decade, and these infections are likely to present a continuing challenge to clinicians. Prompt recognition of CA-MRSA infection, appropriate use of antibiotics, and institution of consistent prevention measures are essential to curtailing the spread of this disease. □

REFERENCES

1. Weber JT, Courvalin P. An emptying quiver: antimicrobial drugs and resistance. *Emerg Infect Dis*. 2005;11(6):791-793.
2. Reed SD, Friedman JY, Engemann JJ, et al. Costs and outcomes among hemodialysis-dependent patients with methicillin-resistant or methicillin-susceptible *Staphylococcus aureus* bacteremia. *Infect Control Hosp Epidemiol*. 2005;26(2):175-183.
3. Chang FY, MacDonald BB, Peacock JE Jr, et al. A prospective multicenter study of *Staphylococcus aureus* bacteremia. Incidence of endocarditis, risk factors for mortality, and clinical impact of methicillin resistance. *Medicine* (Baltimore). 2003;82(5):322-332.
4. Said-Salim B, Mathema B, Kreiswirth BN. Community-acquired methicillin-resistant *Staphylococcus aureus*: an emerging pathogen. *Infect Control Hosp Epidemiol*. 2003;24(6):451-455.
5. Rybak MJ, LaPlante KL. Community-associated methicillin-resistant *Staphylococcus aureus*: a review. *Pharmacotherapy*. 2005;25(1):74-85.
6. Stratton C. New insights on the emergence of resistance in the community. Available at: http://www.medscape.com/viewarticle/419287?src=search. Accessed February 28, 2006.
7. Johnson LB, Saravolatz LD. Community-acquired MRSA: current epidemiology and management issues. Available at: http://www.medscape.com/viewarticle/498770. Accessed February 28, 2006.

8. Chambers HF. The changing epidemiology of *Staphylococcus aureus*. Available at: http://www.medscape.com/viewarticle/414383. Accessed February 28, 2006.
9. Bartlett JG. Community-acquired methicillin-resistant *Staphylococcus aureus* and other drug-resistant pathogens. Available at: http://www.medscape.com/viewarticle/499462. Accessed February 28, 2006.
10. Miller LG, Perdreau-Remington F, Rieg G, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles. *N Engl J Med*. 2005;352(14):1445-1453.
11. Osterweil N. MRSA emerges as cause of community-acquired pneumonia. Available at: http://www.medscape.com/viewarticle/490516?src=search. Accessed February 28, 2006.
12. Hammerschlag MR. Community-acquired MRSA: a new twist for an old bug. Available at: http://www.medscape.com/viewarticle/448697?src=search%20. Accessed February 28, 2006.
13 CDC. *Staphylococcus aureus* with reduced susceptibility to vancomycin—Illinois, 1999. *MMWR Morb Mortal Wkly Rep*. 2000;48(51-52):1165-1167.
14. Kuehnert MJ, Hill HA, Kupronis BA, et al. Methicillin-resistant *Staphylococcus aureus* hospitalizations, United States. Available at: http://www.medscape.com/viewarticle/505669_print. Accessed February 28, 2006.
15. Zetola N, Francis JS, Nuermberger EL, Bishai WR. Community-acquired methicillin-resistant *Staphylococcus aureus*: an emerging threat. *Lancet Infect Dis*. 2005;5(5):275-286.
16. Hiramatsu K, Cui L, Kuroda M, Ito T. The emergence and evolution of methicillin-resistant *Staphylococcus aureus*. *Trends Microbiol*. 2001;9(10):486-493.
17. Diep BA, Sensabaugh GF, Somboona NS, et al. Widespread skin and soft-tissue infections due to two methicillin-resistant *Staphylococcus aureus* strains harboring the genes for Panton-Valentine leukocidin. *J Clin Microbiol*. 2004;42(5):2080-2084.
18. Bartlett JG. Update on community-acquired MRSA. Available at: http://www.medscape.com/viewarticle/493097?src=search. Accessed February 28, 2006.
19. Fridkin SK, Hageman JC, Morrison M, et al. Methicillin-resistant *Staphylococcus aureus* disease in three communities. *N Engl J Med*. 2005;352(14):1436-1444.
20. Naimi TS, LeDell KH, Como-Sabetti K, et al. Comparison of community- and health care-associated methicillin-resistant *Staphylococcus aureus* infection. *JAMA*. 2003; 290(22):2976-2984.
21. Carleton HA, Diep BA, Charlebois ED, et al. Community-adapted methicillin-resistant *Staphylococcus aureus* (MRSA): population dynamics of an expanding community reservoir of MRSA. *J Infect Dis*. 2004;190(10):1730-1738.
22. Naimi TS, LeDell KH, Boxrud DJ, et al. Epidemiology and clonality of community-acquired methicillin-resistant *Staphylococcus aureus* in Minnesota, 1996-1998. *Clin Infect Dis*. 2001;33(7):990-996.
23. CDC. Methicillin-resistant *Staphylococcus aureus* (MRSA) information for clinicians. 2005. Available at: http://www.cdc.gov/ncidod/dhqp/ar_mrsa_ca_clinicians.html. Accessed February 28, 2006.
24. Cookson BD. Methicillin-resistant *Staphylococcus aureus* in the community: new battlefronts or are the battles lost? *Infect Control Hosp Epidemiol*. 2000;21(6):398-403.
25. Zinderman CE, Conner B, Malakooti MA, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* among military recruits. *Emerg Infect Dis*. 2004;10(5):941-944.
26. Baggett HC, Hennessy TW, Leman R, et al. An outbreak of community-onset methicillin-resistant *Staphylococcus aureus* skin infections in southwestern Alaska. *Infect Control Hosp Epidemiol*. 2003;24(6):397-402.
27. Baggett HC, Hennessy TW, Rudolph K, et al. Community-onset methicillin-resistant *Staphylococcus aureus* associated with antibiotic use and the cytotoxin Panton-Valentine leukocidin during a furunculosis outbreak in rural Alaska. *J Infect Dis*. 2004; 189(9):1565-1573.
28. CDC. Community-associated methicillin-resistant *Staphylococcus aureus* infections in Pacific Islanders—Hawaii. *MMWR Morb Mortal Wkly Rep*. 2004;53(33):767-770.
29. CDC. Methicillin-resistant *Staphylococcus aureus* infections among competitive sports participants—Colorado, Indiana, Pennsylvania, and Los Angeles County, 2000-2003. *MMWR Morb Mortal Wkly Rep*. 2003;52(33):793-795.
30. Nguyen DM, Mascola L, Bancroft E. Recurring methicillin-resistant staphylococcus infections in a football team. *Emerg Infect Dis*. 2005;11:526-532.
31. CDC. Public Health Dispatch: Outbreaks of community-associated methicillin-resistant *Staphylococcus aureus* skin infections—Los Angeles County, California, 2002-2003. *MMWR Morb Mortal Wkly Rep*. 2003. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5205a4.htm. Accessed February 28, 2006.
32. CDC. Methicillin-resistant *Staphylococcus aureus* or soft tissue infections in a state prison—Mississippi, 2000. *MMWR Morb Mortal Wkly Rep*. 2001;50(42):919-922.
33. Hartstein AI, Lemonte AM, Iwamoto PK. DNA typing and control of methicillin-resistant *Staphylococcus aureus* at two affiliated hospitals. *Infect Control Hosp Epidemiol*. 1997;18(1):42-48.
34. Bartlett JG. Antibiotic selection for infections involving methicillin-resistant *Staphylococcus aureus*. Available at: http://www.medscape.com/viewprogram/3124/pnt. Accessed February 28, 2006.
35. Lewis JS 2nd, Jorgensen JH. Inducible clindamycin resistance in staphylococci: should clinicians and microbiologists be concerned? *Clin Infect Dis*. 2005;40(2):280-285.
36. Perry CM, Jarvis B. Linezolid: a review of its use in the management of serious gram-positive infections. *Drugs*. 2001;61(4):525-551.
37. CDC. Community-associated MRSA: information for the public. 2005. Available at: http://www.cdc.gov/ncidod/dhqp/ar_mrsa_ca_public.html#8. Accessed February 28, 2006.
38. Warshawsky B, Hussain Z, Gregson DB, et al. Hospital- and community-based surveillance of methicillin-resistant *Staphylococcus aureus*: previous hospitalization is the major risk factor. *Infect Control Hosp Epidemiol*. 2000;21(11):724-727.
39. Shams WE, Rapp RP. Methicillin-resistant staphylococcal infections: an important consideration for orthopedic surgeons. *Orthopedics*. 2004;27(6):565-568.