



Community-Acquired *Methicillin-Resistant Staphylococcus aureus* (CA-MRSA) on the Rise

Lead author: Narinder M. Duggal, BSc(Pharm), CDE, MD, FRCPC, FASCP

Background

Staphylococcus aureus often referred to simply as "Staph" are bacteria commonly colonizing the skin and the anterior nostrils of healthy people. In fact, 20% to 30% of all individuals are colonized with staphylococci.¹⁻⁴ However, *staphylococcus aureus* has had significant resistance changes over the years and this has important clinical and therapeutic implications. The recent increased recognition of community acquired-MRSA has important clinical and pharmacological implications for the health care provider.

I will start by framing the current issues of resistance. Generally, when a patient has a skin and soft tissue infection the most likely pathogens are gram-positive staph and strep. The clinical evidence of an abscess is usually *Staph. aureus*. The organism involved is usually Methicillin- sensitive *Staph. aureus* (MSSA) and the drugs of choice are beta-lactam antibiotics (penicillin and cephalosporins). The recognition of the first Methicillin- resistant *Staph. aureus* (MRSA) was healthcare acquired (HA-MRSA) and this is a **multi-drug-resistant** (i.e., resistant to beta-lactams and tetracyclines, TMP/sulfamethoxazole and clindamycin) strain that usually requires IV vancomycin. Community-acquired MRSA (CA-MRSA) shares some properties of both but appears to be a distinctly independent resistant strain. The bottom line, clinically, is that this strain is resistant to beta-lactam antibiotics (similar to all MRSA strains) but sensitive to tetracyclines, TMP/sulfamethoxazole and clindamycin, and although sensitive to vancomycin, this is not required as a first line agent.⁵⁻⁷

Staphylococcus aureus has long been responsible for a great deal of human morbidity and mortality throughout history. It causes a variety of skin and soft tissue diseases; most clinically relevant are abscesses, boils, cellulitis, and impetigo.^{1,8-9} It is also responsible for staphylococcus pneumonias and sepsis (bacteremia), which can be fatal.

Historically, *Staph. aureus* has mutated several times. In the 1940's, with the introduction of wide spread penicillin the pathogen was quickly controlled, but this only lasted a few years. Then resistance occurred with the production of beta-lactamase enzymes. The evolution of methicillin, a semi-synthetic penicillin (akin to cloxacillin), was introduced in 1959 and was thought to overcome this resistance but was short lived. In 1968 the first reported case of MRSA occurred in the United States.¹⁻³ In the subsequent 30 years, the prevalence of MRSA has increased. These outbreaks are largely localized to acute and chronic long-term care facilities, with occasional community outbreaks. The community outbreaks are generally assumed to be associated with contemporaneous hospital outbreaks. Healthcare-acquired MRSA (HA-MRSA) is an important pathogen worldwide. However, recent clinical and research data indicates that community-acquired MRSA is a uniquely distinct strain from the HA-MRSA. Every healthcare provider must recognize the difference of these two variants as they have important clinical and therapeutic implications for our patients. John Bartlett, MD-Infectious Disease Specialist notes, "It is a different strain than in the hospital...more dangerous than other staph."¹⁰

Emerging Problem

Widespread reports of CA-MRSA infections now include nearly 13,000 cases.¹¹⁻²¹ The common theme in all reported cases is that the patients appear to have no obvious risk factors. The transmission was associated with minor skin trauma (many cases are misdiagnosed as spider bites), sharing of sports or personal care equipment, and sharing of close quarters. Community-acquired MRSA is associated with younger patients than healthcare-acquired MRSA (median age 23 years vs. 63 years).² Among pediatric patients (age < 18 years) with CA-MRSA, dermatological conditions were the most common underlining medical condition. Among adults (> age 18) with CA-MRSA, the most common underlying medical conditions were smoking, diabetes, and dermatological conditions.² Outbreaks among correctional facilities, athletic teams, and men having sex with men (MSM) have been reported.

Several outbreaks of CA-MRSA have occurred, including in 1997 when four children in Minnesota and North Dakota died of infections.¹² In Alaska in 1996, steam baths were associated with CA-MRSA. In Mississippi between November 1999 and November 2000, an outbreak of MRSA skin and soft tissue infections occurred in state prisons affecting 59 inmates.¹⁸ In Los Angeles County, 928 inmates were diagnosed with CA-MRSA in 2002.¹⁷ In November 2002, CA-MRSA associated with men having sex with men was noted in 35 cases.

Outbreaks were also reported among athletes in several states during 2000/2003. In September/October 2000 in Pennsylvania, an outbreak of MRSA skin and soft tissue infections was reported among ten members of a college football team. In September 2002, two cases of MRSA infections in college football team players were reported in Los Angeles County. In January 2003, two high school wrestlers in Indiana were diagnosed with CA-MRSA.¹⁹ In Colorado, in February 2003 five MRSA infections in members of a fencing club and household contacts were noted.

The recognition that CA-MRSA is a distinctly different pathogen than HA-MRSA is now being more clearly characterized in the literature.

The Distinction between CA-MRSA vs. HA-MRSA^{10, 22-35}

Healthcare-acquired MRSA has the following features:

1. It was initially reported in 1970's and prevalence has increased, especially in hospitalized institution and long-term care facilities.
2. High risk factors include older patients, recent hospitalizations or surgeries, residents in long term care facilities, dialysis, in-dwelling percutaneous medical devices and catheters, prolonged antibiotic treatment, and ICU exposure.
3. It usually involves various types of infection (bacteremia, intravenous lines, pneumonia, skin and soft tissue infection).
4. Transmission is person to person.
5. The growth rate is slow.
6. Microbiological resistance is via SCC-MEC I-III. The virulence factor is unknown and multiple clones exist.
7. Most importantly, HA-MRSA is resistant to multiple antibiotics and usually requires vancomycin, linezolid (*Zyvox*), daptomycin (*Cubicin*), or quinupristin-dalfopristin (*Synercid*).²²⁻²³

Community-acquired MRSA has the following features:

1. Initially reported in the 1990's, it was thought to be secondary to a spillover effect from the burden of HA-MRSA. It is now recognized to be a unique, independent mutating strain of *staph aureus*.
2. Established risk factors have not been identified. Individuals usually appear to be healthy and young with a common association of recurrent close quarters and skin and soft tissue changes.
3. CA-MRSA is usually associated with a dermatological condition, diabetes, smoking, or sharing of close quarters.
4. Transmission is person to person.
5. Growth rate is fast.
6. Microbiological resistance via SCC-MEC IV. The prevalence factor is PVL (panton-valentine leukocidin) and two major clones are identified.
7. Most importantly, all CA-MRSA strains are resistant to beta-lactams (all penicillins and cephalosporins), but susceptible to all antibiotics other than beta-lactam antibiotics.

Clinical Important Take Home Points

Typical treatment of cellulitis, boils, abscesses, and furunculosis have been penicillin and cephalosporins, but it is important to realize that CA-MRSA is a distinct pathogen demographically, microbiologically, and is therapeutically resistant to beta-lactams and cephalosporins.^{22-23, 36-38}

The healthcare provider should suspect CA-MRSA when a skin or soft tissue infection in a patient is not improving after a few days of standard treatment with a beta-lactam or cephalosporin. It is suggested the line of demarcation of erythema or cellulitis be marked at the time of treatment. If the erythema increases or lymphangitic streaking occurs, consider changing antibiotics. An important implication is that the typical first-line beta-lactams and cephalosporins will not cover the cellulitis or abscess if CA-MRSA is involved. Drug therapy will need to be changed. CA-MRSA appears to be sensitive to minocycline, doxycycline, TMP/sulfamethoxazole and clindamycin.²³

The old English proverb "If there is pus about let it out" applies to boils, abscesses and furunculosis. Incision and drainage are of paramount importance and antibiotics are adjunctive.²²⁻²³ It is important to take a swab for culture and sensitivity in order to tailor drug therapy if needed in the future.

Monitor the antibiograms in your community so that you are aware of the change in resistance patterns. In certain geographic areas where CA-MRSA is prevalent, initial therapy will need to be altered appropriately. Over 60% of cases of *Staph* are now resistant to methicillin in parts of Alaska, California, Georgia, Texas, and other states.³⁹⁻⁴⁶

Prevention and Treatment Considerations CA-MRSA

Transmission of CA-MRSA is almost always spread by direct physical contact and not through the air. This may also occur through indirect contact by touching objects (e.g., towels, sheets, wound dressing, clothes, workout areas, and/or sporting equipment) contaminated by the infected skin of the person with *staph* bacteria or MRSA.³⁷⁻³⁸ Prevention strategies involve preventing the direct transmission.

1. Do not share personal items (towels, soaps, etc.)
2. Monitor and treat and dress all open skin abrasions and cuts.
3. Universal infection control procedures and barriers should always be adhered to.
4. Hand hygiene is imperative.
5. Chlorhexidine (*Hibiclens*) baths for extensive skin with soft tissue infection and for recurrent outbreaks is recommended.²³

Recurrent infections

It is important to note that humans are the natural reservoir for *Staph aureus*. The anterior nostrils and skin are the usual sites of MRSA colonization. Approximately 20% to 30% of the population may be colonized with MRSA.² Treatment of recurrent infections is controversial, but since the nostrils are the carrier site, eradications of the carrier state with mupirocin (*Bactroban*) ointment 2% applied to the nares twice daily for five to ten days and applying the anti-infective under the fingernails is suggested.²³ Widespread use of mupirocin is not recommended due to high risk of resistance. It has been suggested to treat household contacts and close contacts if recurrence persists, as it is likely that one or more contacts are asymptomatic carriers of *Staph*.

Treatment of CA-MRSA

CA-MRSA is not susceptible to beta-lactams (all penicillins and cephalosporins are ineffective). Erythromycin is now at least 70% resistant to this strain and is not recommended. Fluoroquinolones are not very effective for *staph* coverage.

Greater than 90% of CA-MRSA is susceptible to TMP/sulfamethoxazole, tetracyclines or clindamycin. Rifampin has excellent CA-MRSA coverage as it has a unique ability to get into the mucosa layer in high concentrations. The problem with rifampin is that it must be used in a combination regimen or resistance quickly emerges. Rifampin is an excellent synergistic adjunct, but it is reserved for refractory, relapsing, or inoperable infections and should NEVER be used as monotherapy for MRSA as rapid resistance will occur.⁴⁷

Tetracycline compounds have a hierarchy rate of effectiveness for CA-MRSA. Minocycline is the most potent and has the highest rate of absorption followed by doxycycline. Other tetracyclines should be avoided. Clindamycin has efficacy for CA-MRSA. Reserve the use of vancomycin, linezolid (*Zyvox*), daptomycin (*Cubicin*), and quinupristin-dalfopristin (*Synercid*) for severe cases. These are not first line agents in CA-MRSA.

Suspected or Proven CA-MRSA^{23,37-39,47}

Treatments of choice (Adult dose):

- Minocycline 100 mg p.o. twice daily x ten days.
- Doxycycline 100 mg p.o. twice daily x ten days.
- Clindamycin 300 mg to 450 mg p.o. four times daily x ten days.
- TMP/sulfamethoxazole DS one-tablet p.o. twice daily x ten days.

Recurrent Infection:

- Add Rifampin to above regimen 300 mg p.o. twice daily x five days.
- Intranasal and under the fingernail treatment with either bacitracin ointment or mupirocin (*Bactroban*) ointment twice daily x five days.
- 5% povidone/iodine cream intranasally four times a day x five days.
- Showers with chlorhexidine (*Hibiclens*) daily x three days and then three times weekly.
- Household and close contact treated (treat by case decisions) with mupirocin ointment to the anterior nostrils twice daily x five days.
- Reserve vancomycin, linezolid (*Zyvox*), daptomycin (*Cubicin*) and quinupristin-dalfopristin (*Synercid*) for severe cases.

Take Home Points

CA-MRSA appears to be a distinctly unique pathogen from HA-MRSA. Typical treatment of skin and soft tissue infections that are usually infected by *staph* and *strep* are

managed by cephalosporins and beta-lactam agents as first line; however, if CA-MRSA is involved, the standard treatment of the beta-lactam or cephalosporin will not be effective. This is the clinical clue that the patient may have CA-MRSA, and regimens of minocycline, doxycycline, clindamycin, or TMP/sulfamethoxazole would be indicated.

References

1. Palavecino E. Community-acquired methicillin-resistant *Staphylococcus aureus* infections. [Clin. Lab Med 2004;24:403-18.](#)
2. Naimi T. et al. Comparison of community and Healthcare-associated methicillin-resistant *Staphylococcus aureus* infection. [JAMA 2003 \(Dec 10\);290:2976-84.](#)
3. Eady E, et al. Staphylococcal resistance revisited: community-acquired methicillin resistant *Staphylococcus aureus* an emerging problem for the management of skin and soft tissue infections. [Curr Opin Infect Dis 2003;16:103-24.](#)
4. Personal Communication Joseph Herman, MD Infectious Disease Specialist, Kitsap County, Washington, October 2004.
5. *Staph* strain infects more healthy people. Associated Press, Oct 1, 2004.
6. Drug resistant bacteria causing infections in healthy people. Public Communications, Inc. (PCI), Sept 2004.
7. Meagan R. "Superbug" - A growing problem outside hospitals http://www.nlm.nih.gov/medlineplus/news/fullstory_20423.html. (Accessed October 6, 2004).
8. Splete H. Community acquired MRSA can be contained <http://www.einternalmedicineneeds.com>. August 15, 2004.
9. Koning S. et al. Treatment of impetigo [BMJ 2004;329:695-6.](#)
10. Bartlett JG. Antibiotic selection for infections involving methicillin-resistant *Staphylococcus aureus*. http://www.medscape.com/viewprogram/3124_pnt. (Accessed October 14, 2004).
11. Browser A. Community-onset MRSA may be less obvious than in the hospital. Medscape Medical News 2004. <http://www.medscape.com/viewarticle/474245>. (Accessed October 14, 2004).
12. Four pediatric deaths from community-acquired methicillin-resistant *Staphylococcus aureus*- Minnesota and North Dakota 1997-1999. [MMWR Morb Mortality Wkly Rep 1999;48:707-10.](#)
13. Groom AV, et al. Community-acquired Methicillin resistant *Staphylococcus aureus* in a rural American Indian community. [JAMA 2001;286:1201-5.](#)
14. Herold BC et al. Community-acquired methicillin -resistant *Staphylococcus aureus* in children with no identified predisposing risk. [JAMA 1998;279:593-8.](#)
15. Purcell K, Fergie E. Exponential increase in community-acquired methicillin-resistant *Staphylococcus aureus* infections in south Texas children. [Pediatr Infect Dis J 2002;21:988-9.](#)
16. Lowy FD. Medical Progress: *Staphylococcus aureus* infections. [N Engl J Med 1998;339:520-32.](#)

17. Outbreaks of community-associated methicillin resistant *Staphylococcus aureus* skin infections - Los Angeles County, California, 2002-2003. *MMWR Morb Mortal Weekly Rep.* 2003;52:88.
18. Methicillin-resistant *Staphylococcus aureus* skin and soft tissue infections in state prison-Mississippi 200. *MMWR Morb Mortal Wkly Rep* 2001;50:919-22.
19. Lindenmayer JM et al. Methicillin-resistant *Staphylococcus aureus* in a high school wrestling team and surrounding community. *Arch Intern Med* 1998;158:895-9.
20. Zinderman CE. et al. Community-acquired methicillin-resistant *Staphylococcus aureus* among military recruits. *Emerg Infect Dis* 2004;10(5):941-4.
21. Johnigan R. Community-acquired methicillin-resistant *Staphylococcus aureus* in children and adolescents. *Arch Otolaryngol Head Neck Surg.* 2003;129:1049-52.
22. Tierney L. et al Ed. Current Medical Diagnosis and Treatment 2004 43rd Edition Lange Publishing.
23. Gilbert D. et al Ed. The Sanford Guide to Antimicrobial Therapy 2004 14th Edition.
24. Marv J. Community associated MRSA differs from healthcare- associated MRSA. Available at: <http://emergency-medicine.jwatch.org>. (Accessed August 27, 2004).
25. Hirschmann J. MRSA in the community <http://dermatology.jwatch.org>. (Accessed August 27, 2004).
26. Weintrub P. Community-acquired resistant *S. aureus*: info for clinical decision making <http://Pediatrics.jwatch.org>. (Accessed August 27, 2004).
27. Zuger A. Community-acquired MRSA: as much mystery as toxicity. <http://general-medicine.jwatch.org>. (Accessed August 27, 2004).
28. Horsburg R. Community-acquired MRSA <http://infectious-diseases.jwatch.org>. (Accessed August 27, 2004).
29. Birnbaumer D. Careful...it may be MRSA. <http://emergency-medicine.jwatch.org>. (Accessed August 27, 2004).
30. Zuger A. Rifampin strengthens oral anti-staph regimens (I=B/C) <http://general-medicine.jwatch.org>. (Accessed August 27, 2004).
31. Weintrub P. Local drugs for local bugs: *Staphylococcus aureus* resistance varies by region. <http://pediatrics.jwatch.org>. (Accessed August 27, 2004).
32. Ampel N. Methicillin resistance contributes to mortality from *S. Aureus* bacteremia <http://infectious-diseases.jwatch.org>. (Accessed August 27, 2004).
33. Ellison R. Vancomycin for *Staph* infections: bactericidal effect essential <http://infectious-diseases.jwatch.org>. (Accessed August 27, 2004).
34. Lede H. Does adequacy of empiric therapy for MRSA bacteremia matter? <http://infectious-diseases.jwatch.org>. (Accessed August 27, 2004).
35. Boyce J. Are the epidemiology and microbiology of methicillin resistant *Staphylococcus aureus* changing? (Editorial) *JAMA* 1998;279(8):623-4.
36. Braunwald E. et al. Ed. Harrison's Principles of Internal Medicine 15th Edition. McGraw-Hill Publishing.
37. CDC DHQP guidelines. MRSA- Information for healthcare personnel Available from <http://www.cdc.gov/ncidod/hip/aresist/mrsafaq.htm>. (Accessed August 27, 2004).

38. CDC DHQP information. Community-associated MRSA frequently asked questions [updated 2003] Available from: <http://www.cdc.gov/ncidod/hip/aresist/mrsafaq.htm>. (Accessed August 27, 2004).
39. Billeter M. Infectious Diseases II - Bacterial Resistance Pharmacotherapy Self Assessment Program, 4th Edition 2004:169-89.
40. Battouli S. et al. Community-acquired methicillin resistant *Staphylococcus Aureus*: An emerging pathogen *Infect Control Hosp. Epidemiology* 2003;24:451-5.
41. Fowler VG Jr., et al. Clinical identifiers of complicated *Staphylococcus aureus* bacteremia. *Arch Intern Med* 2000;163:2066-72.
42. Roghmann M. Predicting methicillin resistance and the effect of inadequate empiric therapy on survival in patients with *Staphylococcus aureus* bacteremia. *Arch Intern Med* 2000;160:1001-4.
43. Osterweil N. MRSA emerges as cause of community-acquired pneumonia. *Medscape Medical News* 2004. <http://www.medscape.com/viewarticle/490516>.
44. Marcinak JF, et al. Treatment of community-acquired methicillin-resistant *Staphylococcus aureus* in children. *Curr Opin Infect Dis* 2003;16:265-9.
45. Johnson BL. Methicillin resistant *Staphylococcus Aureus* as a cause of community acquired pneumonia - a critical review. *Sem Resp Infect* 1994;9(3):199-206.
46. Collins M. et al. Methicillin-resistant *Staphylococcus Aureus* (MRSA) in practice of otolaryngology-an emerging community acquired organism? *Curr Opin Otolaryngael Head Neck Surg* 2003,11:179-183.
47. Dellit T. et al. Interim guideline for evaluation and management of community-associated methicillin resistant *Staphylococcus Aureus* skin and soft tissue infections in outpatient settings. 2004. Infectious Disease Society of Washington, Public Health Seattle and King County, Washington State Department of Health, Tacoma and Pierce County Department of Health.