

Have you been diagnosed with a *Staphylococcus aureus* or MRSA infection?

Below are answers to some common questions...

What is *Staphylococcus aureus* or Staph?

Staph is a type of bacteria. It may cause skin infections that look like pimples or boils. Skin infections caused by Staph may be red, swollen, painful, or have pus or other drainage. Some Staph (known as Methicillin-Resistant *Staphylococcus aureus* or MRSA) are resistant to certain antibiotics, making it harder to treat. The information on this page applies to both Staph and MRSA.

Who gets Staph infections?

Anyone can get a Staph infection. People are more likely to get a Staph infection if they have:

- Skin-to-skin contact with someone who has a Staph infection
- Contact with items and surfaces that have Staph on them
- Openings in their skin such as cuts or scrapes
- Crowded living conditions
- Poor hygiene

How serious are Staph infections?

Most Staph skin infections are minor and may be easily treated. Staph also may cause more serious infections, such as infections of the bloodstream, surgical sites, or pneumonia. Sometimes, a Staph infection that starts as a skin infection may worsen. It is important to contact your doctor if your infection does not get better.

How are Staph infections treated?

Treatment for a Staph skin infection may include taking an antibiotic or having a doctor drain the infection. If you are given an antibiotic, be sure to take all of the doses, even if the infection is getting better, unless your doctor tells you to stop taking it. Do not share antibiotics with other people or save them to use later.

How do I keep Staph infections from spreading?

- Wash your hands often or use an alcohol-based hand sanitizer
- Keep your cuts and scrapes clean and cover them with bandages
- Do not touch other people's cuts or bandages
- Do not share personal items like towels or razors

If you have any questions about your condition, please ask your doctor.
For more information, please visit: http://www.cdc.gov/ncidod/dhqp/ar_mrsa.html.



Methicillin-Resistant *Staphylococcus aureus* (MRSA) in the News Again

—**PATIENT INFORMATION** about staph and MRSA is available at
<http://www.cdc.gov/ncidod/dhqp/pdf/ar/MRSAPatientInfoSheet.pdf>—

[Methicillin-resistant staph aureus (MRSA) is making headlines again. The recent death of a high school student and school closures in Virginia are the cause of the renewed media coverage. This coincides with the recently published article in *JAMA* concerning the rates of MRSA infections in the U.S.

For more information about CA-MRSA, including treatment, see our *Pharmacist's Letter/Prescriber's Letter Detail-Document #221008*, "Community-acquired Methicillin-resistant *Staphylococcus aureus* (CA-MRSA): an Update.]

Methicillin-resistant staph aureus (MRSA) caused more than 94,000 life-threatening infections and nearly 19,000 deaths in the United States in 2005. Most of them were associated with healthcare settings, according to the most thorough study of life-threatening infections caused by these bacteria, experts with the Centers for Disease Control and Prevention (CDC) report.

The study in the October 17, 2007 edition of the *Journal of the American Medical Association (JAMA)* establishes the first national baseline by which to assess future trends in invasive MRSA infections. MRSA infections can range from mild skin infections to more severe infections of the bloodstream, lungs, and at surgical sites.

The study found about 85% of all invasive MRSA infections were associated with healthcare settings, of which two-thirds surfaced in the community among people who were hospitalized, underwent a medical procedure, or resided in a long-term care facility within the previous year. In contrast, about 15% of reported infections were considered to be community-associated, which means that the infection occurred in people without documented health care risk factors.

The 2005 rates of invasive infection were highest among people 65 years of age or older.

Black people were affected at twice the rate of whites, which could be due to higher rates of chronic illness among blacks.

Experts arrived at the new national estimate by projecting from the number of invasive MRSA cases from nine U.S. sites. The sites included the state of Connecticut; the Atlanta metropolitan area; the San Francisco Bay area; the Denver metropolitan area; the Portland, Ore., metropolitan area; Monroe County, N.Y.; Baltimore City, Md.; Davidson County, Tenn.; and Ramsey County, Minn. All the sites were part of CDC's Active Bacterial Core surveillance program, which actively tracks a number of pathogens in the U.S. representing a population of 38 million Americans.

In healthcare settings, MRSA occurs most frequently among patients who undergo invasive medical procedures or who have weakened immune systems and are being treated in hospitals and health care facilities such as nursing homes and dialysis centers.

For more information on MRSA, please visit http://www.cdc.gov/ncidod/diseases/submenus/sub_mrsa.htm. For more information on CDC's guidelines for the prevention of MRSA in healthcare settings, visit http://www.cdc.gov/ncidod/dhqp/ar_mrsa_prevention.html.

The above excerpts are reprinted from the CDC's October 16, 2007 release concerning the rates of MRSA. <http://www.cdc.gov/od/oc/media/pressrel/2007/r071016.htm>.

Users of this document are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and Internet links in this article were current as of the date of publication.

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Community-Acquired *Methicillin-Resistant Staphylococcus aureus* (CA-MRSA): An Update

Background

Staphylococcus aureus often referred to simply as “staph” are gram-positive 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 *S. 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 healthcare provider.

Generally, when a patient has a skin and soft-tissue infection the most likely pathogens are staph and strep. The clinical evidence of an abscess is usually *S. aureus*. The organism involved may be methicillin-sensitive *S. aureus* (MSSA) and the drugs of choice are beta-lactam antibiotics (penicillins and cephalosporins). The recognition of the first methicillin-resistant *S. aureus* (MRSA) was healthcare acquired (HA-MRSA) and this is a **multi-drug-resistant** (i.e., resistant to beta-lactams, tetracyclines, TMP/SMX, 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 TMP/SMX, tetracyclines, and clindamycin, and although sensitive to vancomycin, this is not required as a first-line agent.⁵⁻⁷ CA-MRSA accounts for more than half of *S. aureus* isolates in skin and soft-tissue infections.^{8,9}

S. 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.^{1,10,11} It is also responsible for *Staphylococcus* pneumonias and sepsis (bacteremia), which can be fatal.

Historically, *S. aureus* has mutated several times. In the 1940s, with the introduction of widespread penicillin use, 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 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. HA-MRSA is an important pathogen worldwide. However, recent clinical and research data indicate that CA-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.”¹²

Emerging Problem

Widespread reports of CA-MRSA infections now include nearly 13,000 cases.¹³⁻²³ CA-MRSA can cause a spectrum of infections similar to methicillin-sensitive *S. aureus*.²⁴ In patients with skin and soft-tissue infections, prevalence of CA-MRSA may reach nearly 75%.⁹ A common theme in all reported cases is that the patients appear to have no obvious risk factors. Transmission is associated with minor skin trauma (patients may mistake for a “spider bite”), sharing of sports or personal care equipment, and sharing of close quarters. CA-MRSA is associated with younger patients more than HA-MRSA (median age 23

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years vs. 63 years).² Among pediatric patients (age < 18 years) with CA-MRSA, dermatological conditions were the most common underlying 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 who have sex with men (MSM) have been reported. In addition, among patients with skin and soft-tissue infections, a positive correlation has been shown between Black race, female gender, and use of an antibiotic within the past month and CA-MRSA infection.^{8,9}

Several outbreaks of CA-MRSA have occurred, including in 1997, when four children in Minnesota and North Dakota died of infections.¹⁴ 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.²⁰ In Los Angeles County, 928 inmates were diagnosed with CA-MRSA in 2002.¹⁹ In November 2002, CA-MRSA associated with men who have sex with men was noted in 35 cases. The first outbreak of CA-MRSA in Canada was in the Calgary Health Region in 2004, where up to 40 cases were reported, mostly skin and soft-tissue infections.⁵³

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.²⁰ 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^{12,25-38}

Healthcare-acquired MRSA has the following features:

1. It was initially reported in the 1970s 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*), quinupristin-dalfopristin (*Synercid*), or tigecycline (*Tygacil*).^{25,26}

Community-acquired MRSA has the following features:

1. Initially reported in the 1990s, 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 *S. 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 is via SCC-MEC IV. The prevalence factor is PVL (Panton-Valentine leukocidin) and two major clones are identified (USA 300 and USA 400).⁸
7. Most importantly, all CA-MRSA strains are resistant to beta-lactams (all

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penicillins and cephalosporins), but susceptible to antibiotics such as TMP/SMX, tetracyclines, and clindamycin.

Clinical Important Take Home Points

Typical treatment of cellulitis, boils, abscesses, and furunculosis have been penicillins and cephalosporins, but it is important to realize that CA-MRSA is a distinct pathogen demographically, microbiologically, and is therapeutically resistant to beta-lactams.^{25,26,39-41}

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. Over half of CA-MRSA skin and skin structure infections may be empirically treated with the wrong antibiotics.⁹

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 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 TMP/SMX, minocycline, doxycycline, and clindamycin.²⁶

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.^{25,26} It is important to take a swab for culture and sensitivity in order to tailor drug therapy if needed in the future, especially for purulent skin lesions.²⁴ As one study showed no difference in outcome for patients who were and were not treated with appropriate antibiotics, drainage of a wound may be adequate treatment for less severe infections.^{9,24}

Monitor the antibiograms in your community so that you are aware of the change in resistance patterns. In geographic areas where CA-MRSA is prevalent, initial therapy will need to be altered appropriately. Over 60% of cases of *S. aureus* are now resistant to methicillin in parts of Alaska, California, Georgia, Texas, and other states.⁴²⁻⁴⁹

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 skin of the infected person.^{40,41} Prevention strategies involve preventing 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.²⁶
6. Consider contact precautions in all patients with purulent skin and soft tissue infections in areas where prevalence of MRSA is high.⁹

Recurrent Infections

It is important to note that humans are the natural reservoir for *S. 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.²⁶ 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/SMX, tetracyclines, or clindamycin.⁸ Rifampin has excellent CA-MRSA coverage as it

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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.⁵⁰

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. Tetracyclines should be avoided in pregnant patients.

Clindamycin has efficacy for CA-MRSA, although inducible resistance is possible. D-zone disk diffusion testing can determine this and inducible resistance is indicated when, on an agar plate, the zone of inhibition around clindamycin is blunted by a neighboring erythromycin disk, forming a "D"-shape around the clindamycin disk.⁵¹ Because clindamycin covers Group A strep (GAS), a common pathogen for skin infections, it may be a good choice or empiric treatment. (In contrast to CA-MRSA, GAS may be more likely to cause cellulitis without abscess). In contrast, TMP/SMX lacks efficacy against GAS, so a beta-lactam may be added to ensure adequate coverage of both CA-MRSA and GAS.

Reserve the use of vancomycin, linezolid (Zyvox), daptomycin (Cubicin), quinupristin-dalfopristin (Synercid), and tigecycline (Tygacil) for severe cases. These are not first-line agents for CA-MRSA. Quinupristin-dalfopristin and tigecycline may actually be considered second-line agents due to limited clinical experience.

Suspected or Proven CA-MRSA^{26,40-42,50}

Treatments of choice (Adult dose):

- Minocycline 100 mg p.o. twice daily x ten days (AWP \$6.70 per day).
- Doxycycline 100 mg p.o. twice daily x ten days (AWP \$4.26 per day).
- Clindamycin 300 mg to 450 mg p.o. four times daily x ten days (AWP \$14.29 to \$14.87 per day).
- TMP/SMX DS one to two tablets p.o. two to three times daily x ten days.^{51,52} (AWP \$0.70-\$2.09 per day)

Recurrent Infection:

- Add rifampin to above regimen 300 mg p.o. twice daily x five days (AWP \$3.14 per day).
- 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), quinupristin-dalfopristin (Synercid), and tigecycline (Tygacil) 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 caused by staph and strep are managed by cephalosporins and penicillins first line; however, if CA-MRSA is involved, the standard treatment will not be effective. This is the clinical clue that the patient may have CA-MRSA, and regimens of TMP/SMX, minocycline, doxycycline, or clindamycin would be indicated. If prevalence of CA-MRSA is high, consider empiric treatment with an effective agent.²⁴

Users of this document are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and Internet links in this article were current as of the date of publication.

Project Leaders in preparation of this Detail-Document: Narinder M. Duggal, BSc(Pharm), CDE, MD, FRCPC, FASCP and Stacy A. Hester, RPh, BCPS

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