

Guidelines for Evaluation, Management and Prevention of Community-Associated Methicillin-Resistant *Staphylococcus aureus* Infections in Outpatients

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Introduction

A small task force was convened in June 2005 to review the local epidemiology of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) and to advise the Public Health Department regarding the information and tools needed in the community.

This document was developed by the task force and is intended to provide interim clinical guidance for the evaluation, management and prevention of methicillin-resistant *Staphylococcus aureus* skin and soft tissue infections (SSTI) in outpatients. We are grateful for the work of Seattle-King County¹, the state of Louisiana², and the U.S. Navy³, all of whom developed CA-MRSA guidelines. We used these guidelines as our beginning framework, borrowing some text word for word, and adapting other parts to reflect our local epidemiology and experience. In the setting of increasing levels of CA-MRSA in Santa Clara County, we felt we needed to provide guidelines to our medical community until more definitive guidelines are available from the Centers for Disease Control and Prevention and/or medical professional organizations. These guidelines do not address the general approach to management of skin and soft tissue infections or management of hospitalized patients or patients in skilled nursing facilities with MRSA, for which other references are available.^{4,5}

Glossary of Terms

CA-MRSA – Community-associated methicillin-resistant *Staphylococcus aureus*

HA-MRSA – Healthcare-associated methicillin-resistant *Staphylococcus aureus*

SSTI – Skin and soft tissue infections

I & D – Incision and drainage

Background

Since its recognition in the 1960s, methicillin-resistant *S. aureus* (MRSA) has become a well-known source of infection in hospitals and health care facilities. MRSA are resistant to β -lactam antibiotics, including penicillinase-resistant penicillins (methicillin, oxacillin, nafcillin) and cephalosporins.

In the last few years, MRSA has been reported with increasing frequency as a community-acquired infection.^{6,7} Outbreaks of community-associated MRSA (CA-MRSA) have been reported in a variety of non-hospital related populations including prison inmates,⁸ athletic teams,⁹ men who have sex with men,¹⁰ military members, and children in daycare.¹¹ **These recent outbreaks of CA-MRSA often occur in otherwise healthy people without traditional risk factors.**

Key features of CA-MRSA include:

- Current evidence indicates that these CA-MRSA strains are genetically distinct from hospital-associated MRSA (HA-MRSA), and that several unique community-associated clones emerged simultaneously in different locations in the world.¹²
- CA-MRSA infections occur in otherwise healthy people without traditional risk factors.

- CA-MRSA cause a different spectrum of illness than HA-MRSA, and some CA-MRSA strains may be more virulent. CA-MRSA frequently causes SSTI, however, CA-MRSA also can be associated with severe invasive disease (e.g., bacteremia/sepsis syndrome, pneumonia, pyomyositis, bone and joint infections, endocarditis, necrotizing fasciitis).¹³
- Two genes are unique to CA-MRSA isolates and shared by isolates from three continents: a type IV SCC mec cassette and the PVL locus (Panton-Valentine leukocidin).
- CA-MRSA have different antibiotic susceptibility patterns from HA-MRSA; CA-MRSA are resistant to methicillin but generally are not multi-drug resistant. Many are sensitive to trimethoprim-sulfamethoxazole, clindamycin, aminoglycosides and quinolones.

CA-MRSA can be distinguished from HA-MRSA by using the following criteria:¹⁴

- Diagnosis of MRSA is made in the outpatient setting or by a culture positive for MRSA within 48 hrs of hospital admission, AND
- The patient has no past medical history of MRSA infection or colonization, AND
- The patient has no past medical history in the past 1 year of:
 - Hospitalization
 - Admission to a nursing home, skilled nursing facility, or hospice
 - Dialysis
 - Surgery
 - Permanent indwelling catheters or percutaneous medical devices

Review of surveillance data, scope of problem nationally and locally

An estimated 20-30% of persons are nasal carriers of *Staphylococcus aureus*.¹⁵ A small subset of these persons are colonized with MRSA. As there is no nationwide, systematic community surveillance of MRSA isolates, the actual prevalence of MRSA colonization is unknown. However, several recent studies on this topic have found prevalence rates ranging from 1-5%.^{16,17,18}

MRSA is not a nationally notifiable disease, so there are no national level data on the prevalence of MRSA infection. **In Santa Clara County, however, MRSA has been a reportable condition since 1995.** Rates of reported MRSA infection have been increasing each year since 2000, with the most dramatic increases seen beginning in 2004. Skin and soft tissue infections account for the greatest number of infections, and proportionately more of the total each year (see Figures 1 and 2).

Reporting Requirements

MRSA infections are a reportable condition in Santa Clara County. MRSA should be reported using a Confidential Morbidity Report (CMR) within 1 week of diagnosis. The form can be downloaded at www.sccphd.org under the Disease Prevention and Control Program. These data assist us in tracking the scope and spread of MRSA within our community, information that is critical to tailoring control measures.

A number of outbreaks of CA-MRSA have been reported in Santa Clara County, most notably an outbreak among professional athletes, high school athletic teams, and an outbreak at two county adult correctional facilities where MRSA is now endemic.

We collected data from local hospitals to determine the percentage of all *S. aureus* isolates that are methicillin resistant among emergency department patients and outpatients. These data are incomplete; however, two trends are evident:

- 1) the percentage of *S. aureus* that is MRSA increased from 2004 to 2005 in each institution for which we have data, and
- 2) **the percentage of *S. aureus* that is MRSA now approaches or exceeds 50%.** In two county adult correctional facilities, upwards of 70% of all *S. aureus* isolated is MRSA.

CA-MRSA is now endemic in Santa Clara County, and must be considered even if the patient is healthy and no traditional risk factors for MRSA are present.

Diagnosis

The clinical approach to skin and soft tissue infections is based on the clinical presentation and severity of the infection, and the presence of co-morbidities. Given the high prevalence of MRSA in Santa Clara County and the fact that many infections have occurred among previously healthy persons with no identifiable risk factors^{*}, it may be wise to consider all patients with a suspected staphylococcal infection to be potentially infected with MRSA until demonstrated otherwise. MRSA should be considered in the differential diagnosis of all patients presenting with SSTIs as well as those with more severe illness compatible with *S. aureus* infection.

The clinical presentation of an MRSA SSTI may be variable and includes:

- An insect or spider bite
- An “infected pimple”
- Impetigo
- Folliculitis or a pustular lesion
- Furuncle, carbuncle (boils)
- Cellulitis
- Infected wound
- Abscess (esp. with deep tissue necrosis)
- Necrotizing fasciitis

* Traditionally cited risk factors for MRSA (community and hospital associated) include: history of MRSA infection or colonization; history in the past year of hospitalization, admission to a long term care facility (nursing home, skilled nursing, or hospice), dialysis and end-stage renal disease, diabetes mellitus, surgery, permanent indwelling catheters or medical devices that pass through the skin into the body; injection drug use; recent and/or frequent antibiotic use; close contact with someone known to be infected or colonized with MRSA; recurrent skin disease (recurrent abscesses, folliculitis, furunculosis or other skin infections); crowded living conditions (e.g., homeless shelters, military facilities); incarceration; certain populations (e.g., Pacific Islanders, Alaskan Natives, Native Americans). In addition, outbreaks of MRSA have been reported among men who have sex with men.

Management

General principles in the management of SSTI include:

- Incision and drainage (I & D) is of paramount importance in treatment of abscesses and should be done whenever possible. For mild uncomplicated abscesses, local wound care including I & D of fluctuant lesions without antibiotic use is a reasonable treatment option.¹⁹
- Antibiotic therapy alone without I & D is not recommended for treatment of fluctuant abscesses.
- For patients with potential MRSA infections, if you plan to initiate antibiotic therapy, it is important to obtain specimens for culture and susceptibility testing before initiating antibiotic treatment.
 - If I & D is not performed, other options include culture of spontaneously draining wounds and/or culture and biopsy of the central area of cellulitis (note: superficial culture of open wounds may yield skin-colonizing bacteria and not the true pathogen).

Clinicians should determine if household or other close contacts of the patient have SSTI or other infections compatible with MRSA, and facilitate their evaluation and treatment if indicated.

Management of suspected *S. aureus* SSTI based on severity (adapted from Eron criteria)²⁰

- **Mild: Eron Class 1** (Patient has no signs or symptoms of systemic toxicity and no uncontrolled co-morbidities [e.g., peripheral vascular disease, diabetes mellitus, chronic venous insufficiency, morbid obesity] that may complicate treatment.)
 - Outpatient management without oral antimicrobials including I & D of abscesses and wound care (with or without topical antimicrobials) may be sufficient in the majority of cases.²¹
 - Consider oral antimicrobials, based on clinical judgment, particularly if I & D is not possible.
 - If oral antimicrobial therapy is administered, therapy with a β -lactam (e.g., cephalexin or dicloxacillin) may be adequate in cases where clinical presentation is cellulitis without abscess and MRSA is not strongly suspected.
 - If suspicion for MRSA is high, consider empiric therapy with agents active against MRSA (see Table 1).
 - Monitor patients closely (i.e. follow-up phone call or visit within 48 – 72 hrs) for response to therapy and adjust antimicrobials based on culture, susceptibility results and clinical response.

- **Moderate: Eron Class 2** (Patient is either systemically ill [e.g. febrile, complains of unusual pain, or rapid progression of lesion] with stable co-morbidities or systemically well with co-morbidities that may complicate or delay resolution of their SSTI.)
 - Manage as in- or outpatient, depending on degree of illness and co-morbidity; may require initial hospitalization and parenteral antimicrobials with subsequent conversion to oral therapy once signs and symptoms of infection are improving.
 - Monitor outpatients carefully (i.e. follow-up phone call or visit within 48 – 72 hrs) for response to initial oral therapy.
 - Treat empirically for MRSA given high prevalence of MRSA locally.
 - Adjust antimicrobials based on culture and susceptibility results and clinical response.
- **Severe: Eron Class 3** (Patient appears toxic [e.g., tachycardia, tachypnea, hypotension, altered mental status], or non-toxic, but has unstable co-morbidities that may complicate therapy.)

AND

- **Critically Ill: Eron Class 4** (Patient has sepsis syndrome or life-threatening infection such as necrotizing fasciitis.)
 - Manage as inpatient with empiric broad-spectrum parenteral antimicrobial coverage active against MRSA, including vancomycin.
 - Surgical intervention may be necessary.
 - Adjust antimicrobials based on culture and susceptibility results.
 - Consult infectious disease specialist if patient does not improve or alternative antimicrobials (e.g., linezolid or daptomycin) are being considered.

Consider discharge to complete a course of outpatient parenteral or oral therapy, based on clinical improvement, toleration of therapy and availability for follow-up.

Empiric oral antimicrobial therapy for suspected MRSA infections (see Table 1)

- There are no data from randomized clinical trials on which to base treatment recommendations.
- In many patients with mild (Eron Class 1) infections, I & D of abscesses without oral antimicrobial therapy is an adequate treatment option.
- Antimicrobial therapy should be reserved for mild infections that cannot be treated with I & D and for more serious infections (Eron Classes 2-4).
- Patients should be monitored for response to therapy.
- Cultures and sensitivities should be obtained if antibiotics will be initiated.
- Empiric antibiotic regimens should be modified based on results of culture and susceptibility testing of isolates from affected skin and soft tissue or wound drainage.

- *S. aureus* isolates resistant to erythromycin and susceptible to clindamycin should be evaluated for inducible clindamycin resistance (MLSB phenotype) using a “D test.”²²
- Consult your clinical laboratory to determine if the “D test” is done routinely or must be specifically requested.
 - If inducible clindamycin resistance is present, an alternative agent should be considered, particularly if the clinical response to clindamycin is poor.²³
- Although vancomycin has been the “gold standard” for invasive MRSA infections, most CA-MRSA infections are localized SSTI that do not require hospitalization or vancomycin therapy.
 - Initial empiric coverage of infections should be based on the prevalence of MRSA in the clinical setting or patient population (ideally guided by local antimicrobial susceptibility patterns for MRSA, if available), as well as the presence of risk factors for, or factors potentially associated with, MRSA.
 - Therapy should be modified as necessary based on results of culture and susceptibility testing.
 - In patients initially hospitalized for IV therapy, criteria allowing the switch to oral therapy and discharge include:
 - Patient is afebrile for 24 hours, and
 - Clinically improved, and
 - Able to take oral medication, has adequate social support and is available for close outpatient follow-up.

NOTE: Group A streptococci (GAS) are another common cause of SSTI, particularly cellulitis and impetigo. If GAS infection is suspected, therapy should include an agent active against this organism (β -lactam, macrolide, clindamycin). Tetracyclines and trimethoprim-sulfamethoxazole, although active against many MRSA, are not recommended treatments for suspected GAS infections.

Prevention

Infection control for outpatient management of *S. aureus* SSTI, including MRSA

MRSA is a common healthcare-associated pathogen in the United States. Similar to the healthcare setting, the main mode of transmission of CA-MRSA is via hands which may become contaminated by contact with others who are colonized or infected or with devices, items, or environmental surfaces contaminated with body fluids containing MRSA.²⁴

- **Contact precautions should be used for ALL patients with open or draining SSTI and all patients known to be infected with MRSA. The standard components of contact precautions adapted for the outpatient setting are:**
 - Examine patient with MRSA in a private room.

- Wear gloves (clean nonsterile gloves are recommended) when providing care for patients and change gloves after having contact with each patient. Remove gloves and discard before leaving the patient's room and wash hands immediately with soap and water or an alcohol-based hand rub. After glove removal and handwashing, do not touch potentially contaminated environmental surfaces or items in the patient's room to avoid transfer of microorganisms to other patients and environments.
- Wear a gown when providing care if there will be substantial contact with the patient. Remove the gown before leaving the examination room.
- Limit the movement and transport of the patient from the examination room to essential purposes only.
- Ensure that patient-care items and potentially contaminated surfaces are cleaned and disinfected after use.
 - Clean noncritical medical equipment surfaces with a detergent/disinfectant.
 - Do not use alcohol to disinfect large environmental surfaces because of fire hazard.
 - Keep housekeeping surfaces (e.g., floors, walls, tabletops) visibly clean on a regular basis and clean up spills promptly.
 - Use an EPA-registered hospital disinfectant designed for general housekeeping purposes in patient-care areas, and use in accordance with the manufacturer's instructions.
 - Use barrier protective coverings as appropriate for noncritical surfaces that are:
 - 1) touched frequently with gloved hands during the delivery of patient care
 - 2) likely to become contaminated with blood or body substances; or,
 - 3) difficult to clean.
- **For additional information on infection control, see:**
 - www.cdc.gov/ncidod/hip/ARE SIST/mrsahcw.htm
 - www.cdc.gov/mmwr/preview/mmwrhtml/rr5210a1.htm

Infection control for patients with *S. aureus* infection (including MRSA) and their caregivers

- **Patients with *S. aureus* infections, including MRSA, their family members and close contacts should be counseled about measures to prevent spread of infection. Drainage from *S. aureus* infections, wound dressings and other materials contaminated with wound drainage are highly infectious.**
 - Infection control messages for patients to prevent transmission of *S. aureus* SSTI, including MRSA include:
 - Keep wounds and lesions covered with clean, dry bandages. This is especially important when drainage is present.
 - Use clean, disposable, nonsterile gloves to change bandages.
 - Wash hands with soap and warm water or alcohol-based hand rub after touching infected skin, bandages or other waste. Advise family members, other close contacts to wash their hands frequently with soap and warm water, especially if they change your bandages or touch the infected area or anything that might have come in contact with the infected area.
 - Put disposable waste (e.g., dressings, bandages) in a separate trash bag and close the bag tightly before throwing it out with the regular garbage.
 - Do not share personal items (e.g., towels, washcloths, razors, clothing, or uniforms) or other items that may have been contaminated by wound drainage.
 - Disinfect all non-clothing (and non-disposable) items that come in contact with the wound or wound drainage with a solution of one tablespoon of household bleach mixed in one quart of water (must be prepared fresh each day) or a store-bought, household disinfectant.
 - Wash soiled linens and clothes with hot water and laundry detergent. Drying clothes in a hot dryer, rather than air-drying, may also help kill bacteria in clothes.
 - Wash utensils and dishes in the usual manner with soap and hot water or using a standard home dishwasher.
 - Avoid participating in contact sports or other skin-to-skin contact until the infection has healed.
 - Be sure to tell any healthcare providers who treat you that you have a MRSA, a “resistant staph infection.”

Eradication of MRSA colonization (decolonization)

Treatment to eradicate MRSA colonization is not routinely recommended.

- The efficacy of methods to reduce MRSA recurrence and transmission by decolonizing persons in the outpatient setting has not been established. It may be reasonable to consider decolonization for:
 - Patients with recurrent MRSA infections despite appropriate therapy, and
 - Ongoing MRSA transmission in a well-defined cohort with close contact.
- Optimal regimens for eradication of colonization have not been established; regimens that have been used include:
 - Oral antimicrobials (usually rifampin and trimethoprim-sulfamethoxazole, or rifampin and doxycycline, or rifampin and minocycline) and/or,
 - Nasal decolonization with intranasal topical mupirocin (bid for 5 days).

Skin antisepsis (e.g. chlorhexidine baths) has been used in addition to the above regimens.

Colonization can persist for months or years, regardless of intervention. Repeat cultures to determine colonization are therefore not recommended. Colonization should not preclude return to work or school.

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Table 1 - Empiric Oral Antimicrobial Treatment of Outpatients with Suspected MRSA Skin and Soft Tissue Infections (SSTI)

Drug	Adult Dose	Pediatric Dose	Drug interactions/Adverse Effects
Trimethoprim-sulfamethoxazole (TMP-SMX)	1 DS (160 mg TMP/800 mg SMX) po BID	Base dose on TMP: 8-12 mg TMP (& 40-60 mg SMX) per kg/day in 2 doses; not to exceed adult dose	Drug interactions: dapsone, anticoagulants, phenytoin, cyclosporin, diuretics, MTX
Doxycycline	100 mg po BID	Not recommended for use in children \leq 8 yrs of age. If > 8 yrs of age, 2-4 mg/kg/day in 2 divided doses; not to exceed adult dose.	Adverse effects: rash, erythema multiforme, photosensitivity, Stevens-Johnson syndrome, interstitial nephritis, nausea, CNS symptoms
Clindamycin*	300-450 po qid	10-20 mg/kg/day in 3-4 doses; not to exceed adult dose	Adverse effects: GI upset and relatively high incidence of C. difficile psuedomembranous colitis compared to other antibiotics

NOTE: if Group A streptococcal infection is suspected, oral therapy should include an agent active against this organism (β -lactam, macrolide, clindamycin). Tetracyclines and TMP-SMX, although active against many MRSA, are not recommended treatment for suspected GAS infections.

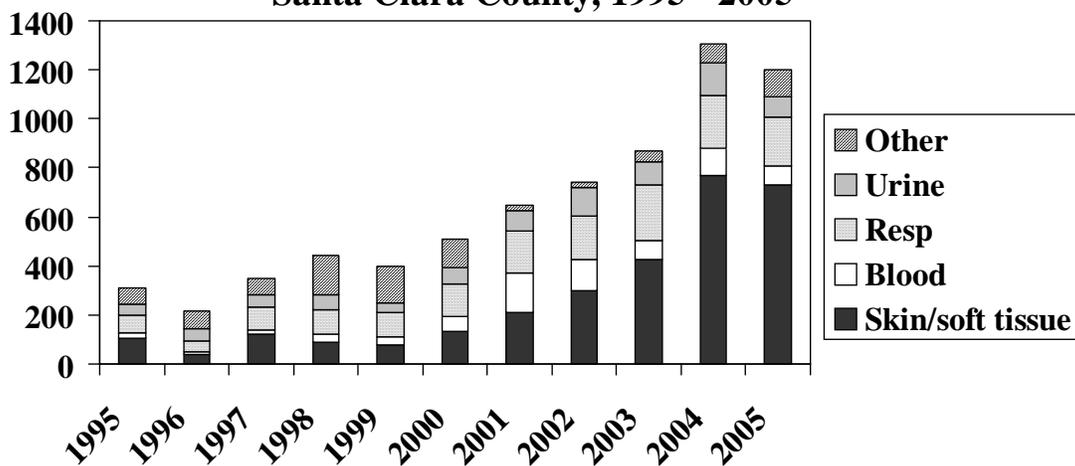
NOTE: Outpatient use of quinolones or macrolides: Fluoroquinolones and macrolides are NOT recommended for treatment of MRSA because of high resistance rates. If fluoroquinolones are being considered, consult with an infectious disease specialist before use.

NOTE: Use of Rifampin alone is NOT recommended. Rifampin may be used in combination with one of the drugs listed above after consultation with an infectious disease specialist.

NOTE: Outpatient use of Linezolid in SSTI: Linezolid is costly and has great potential for inappropriate use, including inducing antimicrobial resistance, and toxicity. Although it is 100% bioavailable and effective in SSTI, it is not recommended for empiric treatment or routine use because of these concerns. It is strongly recommended that linezolid only be used after consultation with an infectious disease specialist to determine if alternative antimicrobials would be more appropriate.

*If considering Clindamycin, isolates resistant to erythromycin and sensitive to clindamycin should be evaluated for inducible clindamycin resistance using the "D test." Consult with your reference laboratory to determine if "D testing" is routine or must be specifically requested. If inducible resistance is present, an alternative agent to Clindamycin should be considered.

**Figure 1: Reported MRSA Cases by Site of Infection
Santa Clara County, 1995 - 2005***



*2005 reports through June 30

**Figure 2: MRSA Rates by Age Group
Santa Clara County, 1995-2004**

