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Infectious Diseases Society of Washington

INTERIM GUIDELINES FOR EVALUATION & MANAGEMENT OF COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* SKIN AND SOFT TISSUE INFECTIONS IN OUTPATIENT SETTINGS

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I. Introduction

This document is intended to provide interim clinical guidance for management of *Staphylococcus aureus* skin and soft tissue infections (SSTI) in outpatients in the setting of increasing levels of community-associated methicillin-resistant *S. aureus* (CA-MRSA) until more definitive guidelines are available from the Centers for Disease Control and Prevention and/or medical professional organizations. The guidelines were developed collaboratively by the Infectious Diseases Society of Washington and Public Health – Seattle and King County, Tacoma-Pierce County Department of Health, and Washington State Department of Health. Key points in the document are highlighted in bold.

Clinicians should consider other relevant potential etiologies in addition to MRSA when evaluating patients with SSTI. These guidelines do not address the general approach to management of skin and soft tissue infections or management of hospitalized patients, for which other references are available.

Figure1, a flow diagram (*Management of Suspected S. aureus Skin and Soft Tissue Infection*) and Tables 1 and 2 (*Empiric Oral Antimicrobial Agents for Treatment of Outpatients with Suspected MRSA* and *Eradication of MRSA Colonization*) can be removed from the document and posted for reference in clinical settings.

II. Background

Methicillin-resistant *S. aureus* (MRSA) are resistant to ß-lactam antibiotics, including penicillinase-resistant penicillins (methicillin, oxacillin, nafcillin) and cephalosporins. MRSA are recognized pathogens among hospitalized patients and persons with certain healthcare-associated risk factors. Recent reports suggest that the frequency of MRSA infections among otherwise healthy persons without typical healthcare-associated MRSA (HA-MRSA) risk factors is increasing. The full clinical spectrum, epidemiology, and risk factors for CA-MRSA have yet to be defined. Current evidence suggests that these strains are genetically distinct from HA-MRSA, cause a different spectrum of illness (including SSTI that may be severe), and have different antibiotic susceptibility patterns than HA-MRSA. Severe invasive disease (e.g., bacteremia/sepsis syndrome, pneumonia, pyomyositis, bone and joint infections) due to CA-MRSA has been reported less frequently than SSTI.[1,2,3]

III. Clinical approach to potential *S. aureus* skin and soft tissue infections (SSTI)

The clinical approach is based on available information about risk factors for MRSA, the clinical presentation and severity of the infection, and the presence of co-morbidities (see Figure 1).

- **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.**[7]
  - Antibiotic therapy alone without I & D is not recommended for treatment of fluctuant abscesses.
- **For outpatients with potential MRSA infections, 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.**
- MRSA infections are reportable in some local health jurisdictions.

IV. Assessment of risk factors for MRSA

MRSA should be considered in the differential diagnosis of all patients presenting with skin and soft tissue infections as well as those with more severe illness compatible with *S. aureus* infection. Risk factors associated with CA-MRSA are not well defined and infections have occurred among previously healthy persons with no identifiable risk factors.[3,4] Identifying patients at increased risk for MRSA can guide empiric antibiotic selection and avoid use of agents ineffective against MRSA (particularly cephalosporins).

Risk factors that should increase the level of suspicion for MRSA:[5,6]

- 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
- High prevalence of MRSA in local community or patient population (as indicated by results of local antimicrobial susceptibility testing, clinical experience and surveillance data)
- Recent and/or frequent antibiotic use
- Close contact with someone known to be infected or colonized with MRSA
- Recurrent skin disease
- Crowded living conditions (e.g., homeless shelters)
- Incarceration
- Infection among sports participants who have:
  - Skin-to-skin contact
  - Pre-existing skin damage
  - Shared clothing and/or equipment
- Certain populations (e.g., Pacific Islanders, Alaskans Natives, Native Americans)
- Outbreaks of MRSA have been reported among men who have sex with men

- Also consider MRSA in patients with SSTI and poor response to β-lactam antibiotics

V. Management of *S. aureus* SSTI based on severity (adapted from Eron criteria)[8]

- **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.[9]
  - Consider oral antimicrobials, based on clinical judgment, particularly if I & D is not possible and/or if MRSA is suspected.
    - If oral antimicrobial therapy is administered, therapy with a β-lactam (e.g., cephalexin or dicloxacillin) may be adequate in cases where MRSA is not suspected.
    - If suspicion for MRSA is high based on the presence of one or more risk factors for MRSA, (including high prevalence of MRSA locally), consider empiric therapy with agents active against MRSA (see Table 1).
    - Monitor patients for response to therapy and adjust antimicrobials based on culture and susceptibility results

- **Moderate: Eron Class 2** (Patient is either systemically ill [e.g. febrile] 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 for response to initial oral therapy.
  - Treat empirically for MRSA in patients with risk factors for, or factors potentially associated with, MRSA (including high prevalence of MRSA locally).
  - Adjust antimicrobials based on culture and susceptibility results.

- **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) 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.

VI. 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, particularly those treated with I & D alone.**
- **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."[23] 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.**[17]
- **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, and
    - 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 Group A streptococcal infection is suspected, therapy should include an agent active against this organism (ß-lactam, macrolide, clindamycin). Tetracyclines and trimethoprim-sulfamethoxazole, although active against many MRSA, are not recommended treatments for suspected GAS infections.

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

MRSA is a common healthcare-associated pathogen in the United States. The main mode of transmission of MRSA is via hands (especially healthcare workers' hands) which may become contaminated by contact with a) colonized or infected patients, b) colonized or infected body sites of the personnel themselves, or c) devices, items, or environmental surfaces contaminated with body fluids containing MRSA. [24,25]

- **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 adequate) when providing care for patients, change gloves after having contact with infective material that may contain high concentrations of microorganisms (e.g., wound drainage or dressings). Remove gloves before leaving the patient's room and wash hands immediately with an antimicrobial agent. 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's wound. 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.
    - 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
    - Select EPA-registered disinfectants, if available, and use them in accordance with the manufacturer's instructions.
      - Keep housekeeping surfaces (e.g., floors, walls, tabletops) visibly clean on a regular basis and clean up spills promptly.
      - Use an EPA-registered hospital detergent/disinfectant designed for general housekeeping purposes in patient-care areas when uncertainty exists regarding the presence of multidrug-resistant organisms.
  - **For additional information on infection control, see:**
    - http://www.cdc.gov/ncidod/hip/ARESIST/mrsahcw.htm
    - http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5210a1.htm

VIII. Information for patients with *S. aureus* infection (including MRSA) and their caregivers[5]

- **Patients with *S. aureus* infections including MRSA, their family members and close contacts should be thoroughly 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.
    - Wash hands with soap and warm water or alcohol-based hand rub after touching infected skin and bandages. 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.
    - 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.
    - Consider using clean, disposable, nonsterile gloves to change bandages.
    - 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".
    - Additional information for patients can be found at the following websites:
      - http://www.cdc.gov/ncidod/hip/ARESIST/mrsa_comm_faq.htm
      - http://www.metrokc.gov/health/prevcont/mrsa.htm#others
      - http://www.tpchd.org/antibiotic/index.htm
      - http://www.doh.wa.gov/Topics/antibiotics.htm

IX. 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
    - MRSA infections with ongoing 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

- **Rifampin should never be used as a single agent to treat infection or colonization with MRSA**

Figure 1. Management of Suspected *S. aureus* Skin and Soft Tissue Infection (see text)

Clinical presentation
- Looks like insect or spider bite
- Folliculitis, pustular lesions
- Furuncle, carbuncle (boils)
- Abscess (esp. with tissue necrosis)
- Cellulitis
- Impetigo
- Infected wound

Risk factors associated with MRSA (see text)
- History of MRSA infection, colonization
- History of (within past 12 months): hospitalization; dialysis or renal failure, diabetes; surgery; long term care residence; indwelling catheter or medical device
- Injection drug use, incarceration
- Close contact with someone known to be infected or colonized with MRSA
- High prevalence of MRSA in community or population
- Local risk factors: consult local public health department

- **INCISION & DRAINAGE (I & D) OF ABSCESSES.**[9] If I & D not performed, consider culture of draining wounds, or aspirate or biopsy of central area of inflammation
- **CULTURE & ANTIMICROBIAL SUSCEPTIBILITY TESTING** (include "D-test" for clindamycin resistance if MRSA – see text) [23]

Mild (Eron Class 1)
Afebrile, healthy other than SSTI

Moderate (Eron Class 2)
Febrile, appears ill, but no unstable co-morbidities

Severe or Critically Ill (Eron Class 3 and 4)
Appears toxic, unstable co-morbidity, or limb-threatening infection; sepsis syndrome or life-threatening infection, e.g. necrotizing fasciitis

Outpatient management
- Low suspicion for MRSA: Local care, I & D, +/- topical antibiotics may be sufficient.
- ***If oral antibiotics used:*** β-lactam antibiotics (e.g., cephalexin, dicloxacillin) may be adequate
- If increased suspicion for MRSA based on presence of ≥1 risk factors: consider empiric therapy active against MRSA
- Monitor response to therapy, if not improving, consider changing to regimen active against MRSA

Outpatient management
- Low suspicion for MRSA: β-lactam antibiotics (e.g., cephalexin, dicloxacillin) may be adequate
- If increased suspicion for MRSA based on presence of ≥1 risk factors: empiric therapy active against MRSA
- Adjust antibiotics based on results of culture & susceptibility testing

Hospital management
- Empiric broad-spectrum IV antibiotics including vancomycin for activity against *S. aureus*, including MRSA
- Adjust therapy based on results of culture & susceptibility testing
- Consult ID specialist if no improvement or considering alternative agents (e.g., linezolid, daptomycin)
- Switch to oral therapy based on susceptibility testing if:
  - Afebrile for 24 hours
  - Clinically improved
  - Able to take oral therapy
  - Close follow-up possible

Note: If Group A streptococcal (GAS) infection is suspected, therapy should include an agent active against this organism (ß-lactam, macrolide, clindamycin). Tetracyclines and trimethoprim-sulfamethoxazole, although active against many MRSA, are not recommended for treatment of suspected GAS infections.

Important: To prevent transmission of infection, provide education and information on infection control measures and wound care to all patients and/or caregivers of patients with *S. aureus* infection, particularly those with MRSA per WAC 246-101-105 (7). (See: http://www.doh.wa.gov/notify/other/legal.htm for legal requirements for notifiable condition reporting in Washington State)

Table 1. Empiric Oral Antimicrobial Agents for Treatment of Outpatients with Suspected MRSA

Selection of empiric therapy should be guided by local *S. aureus* susceptibility and modified based on results of culture and susceptibility testing. The duration of therapy for most SSTI is 7-10 days, but may vary depending on severity of infection and clinical response. ***NOTE: Before treating, clinicians should consult complete drug prescribing information in the manufacturer's package insert or the PDR***.

Antimicrobial	Adult Dose	Pediatric Dose
Trimethoprim-sulfamethoxazole (TMP-SMX) DS[10,11,12]	1 tablet (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
Minocycline[12,13,14] or doxycycline[12]	100 mg PO bid	***Not recommended for pediatric use – suggest consultation with infectious disease specialist before use***
Clindamycin[a,12,15,16,20]	300-450 mg PO qid	10-20 mg/kg/day in 3-4 doses; not to exceed adult dose

NOTE: If Group A streptococcal infection is suspected, oral therapy should include an agent active against this organism (ß-lactam, macrolide, clindamycin). Tetracyclines and trimethoprim-sulfamethoxazole, although active against many MRSA, are not recommended treatments for suspected GAS infections.

NOTE: **Outpatient use of quinolones or macrolides.** Fluoroquinolones [12,18,19,20] (e.g.,ciprofloxicin, levofloxacin, moxifloxacin, gatifloxacin) and macrolides (e.g., erythromycin, clarithromycin, azithromycin) are NOT recommended for treatment of MRSA because of high resistance rates. If fluoroquinolones are being considered, consult with infectious disease specialist before use.

NOTE: Outpatient use of Linezolid in SSTI[21,22]. Linezolid is costly and has great potential for inappropriate use, 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.

[a]Isolates resistant to erythromycin and sensitive to clindamycin should be evaluated for inducible clindamycin resistance (MLS_B phenotype) 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.[17]

Table 2: Eradication of MRSA Colonization

Efficacy of decolonization in preventing re-infection or transmission in the outpatient setting is not documented, and is NOT routinely recommended. Consultation with an infectious disease specialist is recommended before eradication of colonization is initiated. Possible regimens include:

- Rifampin (Adult dose: 300mg PO bid x 5 days; pediatric dose: 10-20 mg/kg/day in 2 doses not to exceed 600 mg/d x 5 days) may be used in combination with TMP-SMX, OR rifampin with doxycycline, OR rifampin with minocycline, for recurrent MRSA infection despite appropriate therapy. Never use rifampin monotherapy, due to the rapid emergence of resistance.
- Topical intranasal mupirocin may be used bid for 5 days with or without systemic antimicrobial therapy.
- Skin antisepsis with chlorhexidine or other agents may be used in addition to one or both of the above regimens.

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