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 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 initially developed collaboratively in 2004 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, and were updated in December, 2007. The main recommendations remain largely unchanged. Some revisions were made in the 2007 version to simplify the text, some points have been expanded for additional detail, and references were updated and key resources added. 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.

Figure 1, 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 have been long recognized as pathogens among hospitalized patients and persons with certain healthcare-associated risk factors. Available data suggest that in recent years, the frequency of MRSA infections among otherwise healthy persons without typical healthcare-associated MRSA (HA-MRSA) risk factors has also been increasing in Washington State and nationally. In a multicenter study of patients presenting to the emergency department with purulent skin and soft tissue infections in 11 US cities (none in Washington State), MRSA was the most common identifiable cause accounting for 59% of the cases[1]. 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.[2,3,4]

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

The clinical approach is based on 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.[5]**
  - Antibiotic therapy alone without I & D is NOT recommended for treatment of fluctuant abscesses.
- **For outpatients with skin and soft tissue infection, 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**.
- **Patient education is a critical component of SSTI management. Clinicians should educate patients, caretakers and household members on specific measures to limit spread of infection to close contacts, including in the household and other living environments (See section VIII. Information for patients with *S. aureus* infection (including MRSA) and their caregivers.**

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 (sepsis syndrome, osteomyelitis, septic arthritis, severe pneumonia and post-influenza pneumonia). A presenting complaint of spider bite should raise suspicion for MRSA infection.

Risk factors associated with CA-MRSA are not well defined and infections have occurred among previously healthy persons with no identifiable risk factors. [4,6] Clinical suspicion for MRSA infection 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 healthcare and/or community associated MRSA: [7,8]

- High prevalence of MRSA in the community or patient population (as indicated by results of antimicrobial susceptibility testing, clinical experience and surveillance data)
- History of MRSA infection or colonization
- Close contact with someone known to be infected or colonized with MRSA
- Recent or frequent antibiotic use
- Recurrent skin disease
- Crowded living conditions (e.g., incarceration, homeless shelters, barracks)
- Cluster of infections among sports participants or other groups who have skin-to-skin contact or shared clothing, equipment, or personal hygiene items
- Complaint of "spider or insect bite"
- SSTI with failure to respond to β-lactam antibiotics
- MRSA transmission through sexual contact has been reported [9]
- 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
  - Indwelling catheters or medical devices that pass through the skin into the body
  - Injection drug use

V. Management of *S. aureus* SSTI based on severity (adapted from Eron criteria)[9]

- **Mild:** 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.[10]
    - Consider oral antimicrobials, based on clinical judgment, particularly if I & D is not possible and when the skin lesion is $\geq$5 cm[10,11]
  - If MRSA is suspected based on the presence of one or more risk factors (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.
    - Therapy with a β-lactam (e.g., cephalexin or dicloxacillin) is preferred for susceptible *S aureus and Group A streptococci*.

- **Moderate:** Patient is either systemically ill (e.g. febrile) with stable co-morbidities or systemically well with co-morbidities that may increase risk for severe or complicated SSTI
  - Treat empirically for MRSA.
  - 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.
  - Adjust antimicrobials based on culture and susceptibility results.

- **Severe:** 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:** Patient has sepsis syndrome or life-threatening infection such as necrotizing fasciitis
  - Manage as inpatient with empiric broad-spectrum parenteral antimicrobial coverage including vancomycin for activity against MRSA.
  - 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.

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 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.**
- **All 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 (MLS_B phenotype) using a "D test."** [25] **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.**[19]
- **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 or 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 transmitted primarily through skin-to-skin contact, including via hands (especially healthcare workers' hands) which may become contaminated by contact with a) colonized or infected patients, b) one's own colonized or infected body sites, or c) devices, items, or environmental surfaces contaminated with body fluids containing MRSA. [26,27]

A combination of standard and transmission based precautions (i.e., contact precautions), is recommended for patients with MRSA colonization and infection in the outpatient setting [27-30]. **Contact precautions (gown and gloves) should be used for ALL patients with open or draining SSTI and when contact with uncontrolled infectious secretions is possible.**

Patient Placement and Room Usage:

- Place patient in private exam room, if feasible.
- Patients may be placed in a room with another patient as long as there is spatial separation and adherence to standard and transmission based precautions.
- A "dirty" procedure room for MRSA patients is not necessary.
- Patients do not have to wait until the end of the day for procedures, ambulatory surgery or care.

Standard Precautions include:

- Perform **hand hygiene** before and after each patient contact. This may consist of an alcohol-based hand sanitizer if hands are not visibly soiled or soap and water.
- **Mask coughing patients**; if coughing patient is unable to mask or when performing a respiratory exam the healthcare worker, including provider, will wear a mask with eye protection.
- After glove removal and hand hygiene, do not touch potentially contaminated environmental surfaces or items in the patient's room to avoid transfer of microorganisms to other patients and environments.
- Use **barrier protective coverings** as appropriate for noncritical surfaces that are 1) touched frequently with during the delivery of patient care; 2) likely to become contaminated with blood or body substances; or 3) difficult to clean

Contact Precautions include:

- Wear **gloves** when touching non-intact skin or mucous membranes, visibly soiled linen, or visibly soiled equipment and surfaces.
- **Gown** if body contact with patient or contaminated secretions is anticipated
- Wear gloves, gown, and **face protection** (surgical mask with eye shield) when performing wound care procedures: irrigating, debriding, performing I & D, or working with complex wounds.
- Discard gloves/gown and perform hand hygiene immediately before leaving exam room.
- Minimize environmental contamination through use of environmental barriers (blue pads, trash bags).
- Do not close room down when patient is discharged.

Environmental Cleaning

- Use an EPA registered cleaner/disinfectant for environmental cleaning and follow manufacturer's instructions for use. Do not use alcohol alone to disinfect the environment or equipment.
- Wear gloves when cleaning/disinfecting the environment. Always perform hand hygiene after removing gloves.
- Wear gown if clothing is likely to be soiled during the cleaning process.
- Wipe thoroughly all environmental surfaces touched by patient or staff during encounter with a disinfectant and allow to air dry.
- If surface has visible body substance contamination: clean surface, discard towel, re-wipe or spray with disinfectant, and let dry.
- Change cleaning cloths (paper towel or wipes) frequently between surfaces.
- Room may be used immediately after cleaning/disinfecting environmental surfaces.

Equipment and Supplies

- Perform hand hygiene prior to accessing clean and sterile supplies to prevent cross contamination of supplies.
- Clean all equipment touched by patient and staff with an approved disinfectant.
- Disinfect or sterilize, as appropriate, all reusable items immediately after use and prior to storage (includes bandage scissors).
- Discard unused contaminated disposable supplies, i.e., unopened supplies on a used procedure tray.

Trash and Laundry

- Contain trash and laundry at the point of use.
- Discard soiled cloth laundry in a fluid resistant laundry hamper or plastic bag.
- Discard disposable paper sheets and gowns in regular trash

For additional information on infection control, see:

- CDC. Information About MRSA for Healthcare Personnel http://www.cdc.gov/ncidod/dhqp/ar_mrsa_healthcareFS.html
- CDC. Management of Multidrug-Resistant Organisms In Healthcare Settings, 2006. Siegel JD, et al; the Healthcare Infection Control Practices Advisory Committee. http://www.cdc.gov/ncidod/dhqp/pdf/ar/mdroGuideline2006.pdf
- What to do about MRSA Toolkit for Outpatient Clinics/Medical Offices (Handbook and wall charts on infection control included), http://www.tpchd.org/mrsa

VIII. Information for patients with *S. aureus* infection (including MRSA) and their caregivers[6]

- **Patient education is a critical component of SSTI management. Clinicians should educate patients, caretakers and household members on specific measures to limit spread of infection to close contacts, including in the household and other living environments.** *Washington Administrative Code (WAC 246-101-105) specifies that healthcare providers shall provide adequate and understandable instruction in disease control measures to each patient who has been diagnosed with a case of a communicable disease, and to contacts who may have been exposed to the disease (http://apps.leg.wa.gov/WAC/default.aspx?cite=246-101-105).*
- **Key infection control messages for patients to prevent transmission of *S. aureus* SSTI, including MRSA:**
  - Take antibiotics as prescribed until the all the medicine is taken.
  - Notify your healthcare provider immediately if you are having trouble taking the medication, or the infection is getting worse.
  - Frequent hand hygiene is very important for everyone in the patient's environment to prevent spread.
    - Alcohol based hand sanitizers will kill MRSA and other pathogens within 15 seconds.
    - Use soap and water when hands are visibly soiled and after touching dressings or anything else soiled.
  - Keep wounds and lesions covered with clean, dry bandages, especially when drainage is present.
  - Patients that can not maintain adequate hygiene and keep wounds covered with clean, dry bandages should be excluded from activities where close contact with other individuals occurs, such as daycare or athletic practice, until their wounds are healed.
  - Use clean, disposable, nonsterile gloves to change bandages.
  - Put disposable waste (e.g., dressings, bandages) in a separate trash bag and close the bag tightly before putting it in 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.
  - Use an environmental disinfectant or dilute bleach solution to regularly clean and disinfect contaminated surfaces, i.e., doorknobs, light switches, counters, phones, toilets, sinks, computer keyboards and mouse. MRSA can live for weeks to months on surfaces.
  - 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 use a standard home dishwasher.
  - Avoid skin-to-skin contact including contact sports until the infection has healed.
  - Be sure to tell any healthcare providers who treat you that you have a MRSA, a "resistant staph infection".

VIII. Information for patients with *S. aureus* infection (including MRSA) and their caregivers, continued

Additional information for patients can be found at the following websites:

- Centers for Disease Control and Prevention
  - http://www.cdc.gov/ncidod/dhqp/ar_mrsa_ca.html
- Tacoma-Pierce County Department of Health
  - http://www.tpchd.org/MRSA (Includes *Living with MRSA*, a booklet that was developed with and for patients and their families, provides guidance on wound care, personal hygiene, environmental cleaning, and prevention of transmission.)
- Public Health – Seattle & King County
  - http://www.metrokc.gov/health/prevcont/mrsa.htm
- Washington State Department of Health
  - http://www.doh.wa.gov/Topics/Antibiotics/default.htm

IX. Eradication of MRSA colonization (decolonization).

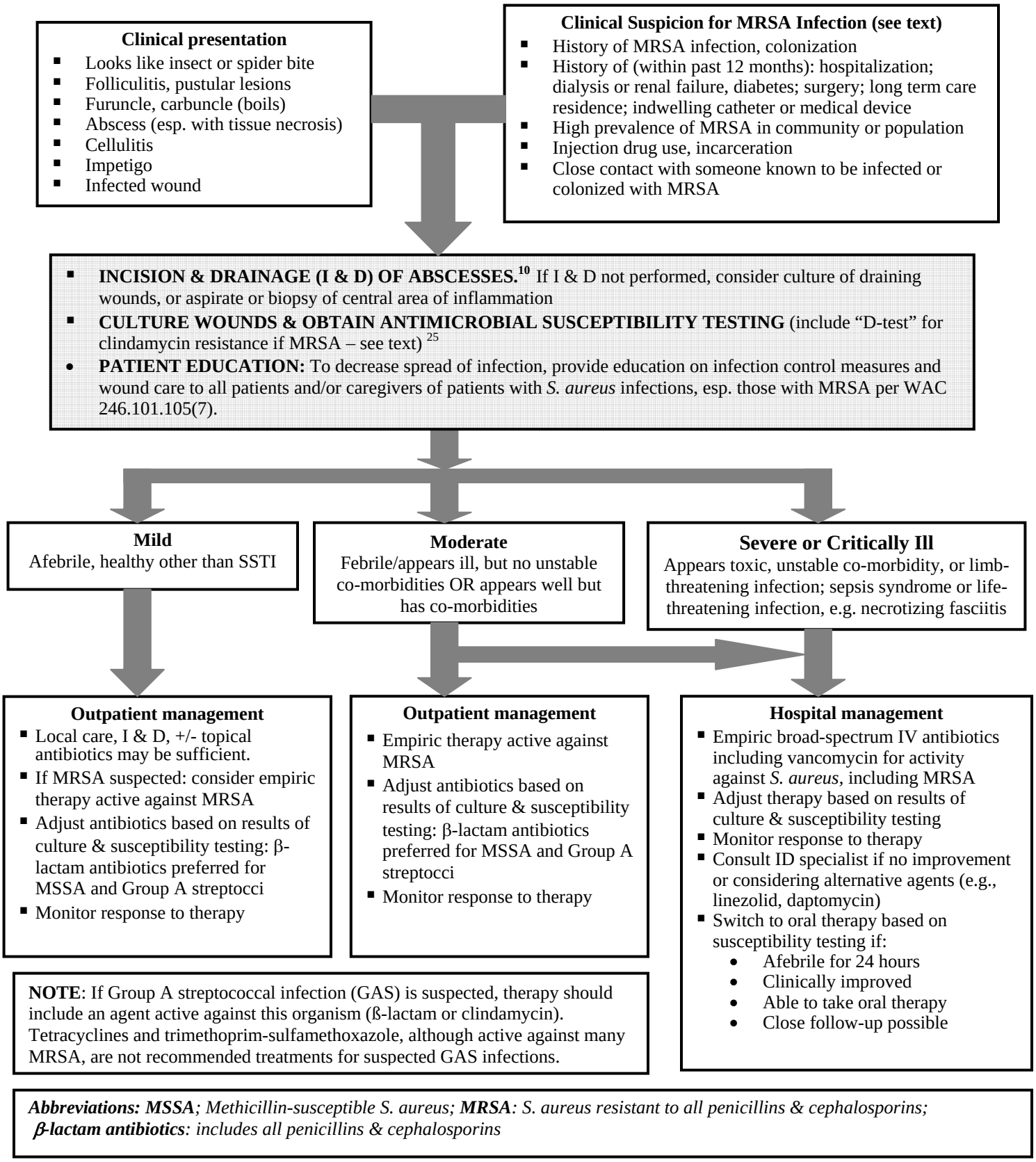
- **Treatment to eradicate MRSA colonization is not routinely recommended.** Consultation with an infectious disease specialist is recommended before eradication of colonization is initiated.
- The efficacy of methods to reduce MRSA recurrence and transmission by decolonizing persons in the outpatient 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 and may include one or more of the following:
  - Nasal decolonization with intranasal topical 2% mupirocin (bid for 5 days)
  - Skin antiseptics (i.e. chlorhexidine or dilute bleach baths) [31, 32]
  - Oral antimicrobials (usually rifampin plus trimethoprim-sulfamethoxazole, or rifampin plus doxycycline, or rifampin plus minocycline)

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

See Table 2. Eradication of MRSA colonization

X. Figure 1. Management of Suspected *S. aureus* Skin and Soft Tissue Infection - December, 2007

Infectious Diseases Society of Washington, Public Health – Seattle and King County, Tacoma-Pierce County Department of Health, and Washington State Department of Health (See text for details)



X1. Table 1. Guidelines for Empiric Oral Antimicrobial Treatment of Outpatients with Suspected MRSA Skin and Soft Tissue Infections (SSTI)

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[12,13,14]	1-2 tablets (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[14,15,16] or doxycycline[14]	100 mg PO bid	***Not recommended for pediatric use – suggest consultation with infectious disease specialist before use***
Clindamycin[a,14,17,18,22]	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 or 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 [14,20,21,22] (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[23,24]. 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]If considering clindamycin, 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.[19]

XII. 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 may include one or more of the following:

Topical intranasal 2% mupirocin may be used bid for 5 days.
Skin antiseptics (i.e. chlorhexidine or dilute baths)
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 with doxycycline, OR with minocycline, for recurrent MRSA infection despite appropriate therapy. ***Never use rifampin monotherapy, due to the rapid emergence of resistance. Rifampin interacts with methadone, oral hypoglycemics, hormonal contraceptives, anticoagulants, protease inhibitors, phenytoin, theophylline, cardiac glycosides and other drugs.***

Recommended Resources

Information for health care providers

- Strategies for Clinical Management of MRSA in the Community: Summary of an Experts' Meeting Convened by the Centers for Disease Control and Prevention. March 2006. (http://www.cdc.gov/ncidod/dhqp/pdf/ar/CAMRSA_ExpMtgStrategies.pdf)

General Information on MRSA

Tacoma Pierce County Health Department (http://www.tpchd.org/mrsa): "Living with MRSA" pamphlet and fact sheets

- Public Health - Seattle & King County (www.metrokc.gov/health/prevcont/mrsa.htm): MRSA fact sheet and links to other MRSA resources
- Centers for Disease Control and Prevention (http://www.cdc.gov/ncidod/dhqp/ar_mrsa_ca.html): Information on community-associated MRSA for public and clinicians
- Public Health Grand Rounds (www.publichealthgrandrounds.unc.edu/antimicrob_resist/): Webcast featuring interviews with Public Health Seattle & King County and local health care providers

MRSA in schools

- Centers for Disease Control and Prevention: MRSA in Schools (http://www.cdc.gov/ncidod/dhqp/ar_mrsa_in_schools.html)
- *Journal of School Nursing* , "Community-acquired methicillin-resistant Staphylococcus aureus: Considerations for school nurses," 23(4), 210-213 (nasn.allenpress.com): Review article for school nurses; abstract available for free, subscription required for full text
- Tacoma Pierce County Health Department (http://www.tpchd.org/mrsa): MRSA Toolkit for middle and high schools
- County of Los Angeles Public Health (lapublichealth.org/acd/MRSA.htm): See "Community Associated MRSA/Staph: A Guideline for Athletic Departments" as well as "Information for Athletes about MRSA' at the bottom of the "Frequently used resources" list – includes handouts for athletes

MRSA in athletes

- From CDC, http://www.cdc.gov/ncidod/dhqp/ar_MRSA_AthletesFAQ.html

MRSA in the workplace

- National Institute for Occupational Safety and Health (www.cdc.gov/niosh/topics/mrsa/): "MRSA and the workplace," including frequently asked questions
- EPA registered disinfectants effective against MRSA (epa.gov/oppad001/chemregindex.htm): See "List H"

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