Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus Aureus* Infections in Adults and Children: Executive Summary

Catherine Liu,[1] Arnold Bayer,[3,5] Sara E. Cosgrove,[6] Robert S. Daum,[7] Scott K. Fridkin,[8] Rachel J. Gorwitz,[9] Sheldon L. Kaplan,[10] Adolf W. Karchmer,[11] Donald P. Levine,[12] Barbara E. Murray,[14] Michael J. Rybak,[12,13] David A. Talan,[4,5] and Henry F. Chambers[1,2]

[1]Department of Medicine, Division of Infectious Diseases, University of California-San Francisco, San Francisco, California; [2]Division of Infectious Diseases, San Francisco General Hospital, San Francisco, CA, [3]Division of Infectious Diseases, Harbor-UCLA Medical Center, Torrance, CA, [4]Divisions of Emergency Medicine and Infectious Diseases, Olive View-UCLA Medical Center, Sylmar, CA; [5]Department of Medicine, David Geffen School of Medicine at University of California Los Angeles; [6]Division of Infectious Diseases, Johns Hopkins Medical Institutions, Baltimore, Maryland; [7]Department of Pediatrics, Section of Infectious Diseases, University of Chicago, Chicago, Illinois; [8,9]Division of Healthcare Quality Promotion, Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; [10]Department of Pediatrics, Section of Infectious Diseases, Baylor College of Medicine, Houston, Texas; [11]Division of Infectious Diseases, Beth Israel Deaconess Medicine Center, Harvard Medical School, Boston, Massachusetts; [12] Department of Medicine, Division of Infectious Diseases, Wayne State University, Detroit Receiving Hospital and University Health Center, Detroit, Michigan; [13]Deparment of Pharmacy Practice, Wayne State University, Detroit Michigan; and [14]Division of Infectious Diseases and Center for the Study of Emerging and Re-emerging Pathogens, University of Texas Medical School, Houston, Texas

Evidence-based guidelines for the management of patients with methicillin-resistant *Staphylococcus aureus* (MRSA) infections were prepared by an Expert Panel of the Infectious Diseases Society of America (IDSA). The guidelines are intended for use by health care providers who care for adult and pediatric patients with MRSA infections. The guidelines discuss the management of a variety of clinical syndromes associated with MRSA disease, including skin and soft tissue infections (SSTI), bacteremia and endocarditis, pneumonia, bone and joint infections, and central nervous system (CNS) infections. Recommendations are provided regarding vancomycin dosing and monitoring, management of infections due to MRSA strains with reduced susceptibility to vancomycin, and vancomycin treatment failures.

EXECUTIVE SUMMARY

MRSA is a significant cause of both health care–associated and community-associated infections. This document constitutes the first guidelines of the IDSA on the treatment of MRSA infections. The primary objective of these guidelines is to provide recommendations on the management of some of the most common clinical syndromes encountered by adult and pediatric clinicians who care for patients with MRSA infections. The guidelines address issues related to the use of vancomycin therapy in the treatment of MRSA infections, including dosing and monitoring, current limitations of susceptibility testing, and the use of alternate therapies for those patients with vancomycin treatment failure and infection due to strains with reduced susceptibility to vancomycin. The guidelines do not discuss active surveillance testing or other MRSA infection–prevention strategies in health care settings, which are addressed in previously published

Received 28 October 2010; accepted 17 November 2010.

It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. The IDSA considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

Correspondence: Catherine Liu, MD, Dept of Medicine, Div of Infectious Diseases, University of California–San Francisco, San Francisco, California, 94102 (catherine.liu@ucsf.edu).

Clinical Infectious Diseases 2011;52(3):285–292

1058-4838/2011/523-0001$37.00
DOI: 10.1093/cid/cir034

guidelines [1, 2]. Each section of the guidelines begins with a specific clinical question and is followed by numbered recommendations and a summary of the most-relevant evidence in support of the recommendations. Areas of controversy in which data are limited or conflicting and where additional research is needed are indicated throughout the document and are highlighted in the Research Gaps section. The key recommendations are summarized below in the Executive Summary; each topic is discussed in greater detail within the main body of the guidelines.

Please note that specific recommendations on vancomycin dosing and monitoring are not discussed in the sections for each clinical syndrome but are collectively addressed in detail in Section VIII.

I. What is the management of skin and soft-tissue infections (SSTIs) in the era of community-associated MRSA (CA-MRSA)?

SSTIs

1. For a cutaneous abscess, incision and drainage is the primary treatment **(A-II).** For simple abscesses or boils, incision and drainage alone is likely to be adequate, but additional data are needed to further define the role of antibiotics, if any, in this setting.
2. Antibiotic therapy is recommended for abscesses associated with the following conditions: severe or extensive disease (eg, involving multiple sites of infection) or rapid progression in presence of associated cellulitis, signs and symptoms of systemic illness, associated comorbidities or immunosuppression, extremes of age, abscess in an area difficult to drain (eg, face, hand, and genitalia), associated septic phlebitis, and lack of response to incision and drainage alone **(A-III)**.
3. For outpatients with purulent cellulitis (eg, cellulitis associated with purulent drainage or exudate in the absence of a drainable abscess), empirical therapy for CA-MRSA is recommended pending culture results. Empirical therapy for infection due to β-hemolytic streptococci is likely to be unnecessary **(A-II)**. Five to 10 days of therapy is recommended but should be individualized on the basis of the patient's clinical response.
4. For outpatients with nonpurulent cellulitis (eg, cellulitis with no purulent drainage or exudate and no associated abscess), empirical therapy for infection due to β-hemolytic streptococci is recommended **(A-II).** The role of CA-MRSA is unknown. Empirical coverage for CA-MRSA is recommended in patients who do not respond to β-lactam therapy and may be considered in those with systemic toxicity. Five to 10 days of therapy is recommended but should be individualized on the basis of the patient's clinical response.
5. For empirical coverage of CA-MRSA in outpatients with SSTI, oral antibiotic options include the following: clindamycin **(A-II)**, trimethoprim-sulfamethoxazole (TMP-SMX) **(A-II),** a tetracycline (doxycycline or minocycline) **(A-II)**, and linezolid **(A-II)**. If coverage for both β-hemolytic streptococci and CA-MRSA is desired, options include the following: clindamycin alone **(A-II)** or TMP-SMX or a tetracycline in combination with a β-lactam (eg, amoxicillin) **(A-II)** or linezolid alone **(A-II)**.
6. The use of rifampin as a single agent or as adjunctive therapy for the treatment of SSTI is not recommended **(A-III).**
7. For hospitalized patients with complicated SSTI (cSSTI; defined as patients with deeper soft-tissue infections, surgical/traumatic wound infection, major abscesses, cellulitis, and infected ulcers and burns), in addition to surgical debridement and broad-spectrum antibiotics, empirical therapy for MRSA should be considered pending culture data. Options include the following: intravenous (IV) vancomycin **(A-I)**, oral (PO) or IV linezolid 600 mg twice daily **(A-I)**, daptomycin 4 mg/kg/dose IV once daily **(A-I)**, telavancin 10 mg/kg/dose IV once daily **(A-I),** and clindamycin 600 mg IV or PO 3 times a day **(A-III)**. A β-lactam antibiotic (eg, cefazolin) may be considered in hospitalized patients with nonpurulent cellulitis with modification to MRSA-active therapy if there is no clinical response **(A-II).** Seven to 14 days of therapy is recommended but should be individualized on the basis of the patient's clinical response.
8. Cultures from abscesses and other purulent SSTIs are recommended in patients treated with antibiotic therapy, patients with severe local infection or signs of systemic illness, patients who have not responded adequately to initial treatment, and if there is concern for a cluster or outbreak **(A-III).**

Pediatric considerations

9. For children with minor skin infections (such as impetigo) and secondarily infected skin lesions (such as eczema, ulcers, or lacerations), mupirocin 2% topical ointment can be used **(A-III).**
10. Tetracyclines should not be used in children <8 years of age **(A-II).**
11. In hospitalized children with cSSTI, vancomycin is recommended **(A-II).** If the patient is stable without ongoing bacteremia or intravascular infection, empirical therapy with clindamycin 10–13 mg/kg/dose IV every 6–8 h (to administer 40 mg/kg/day) is an option if the clindamycin resistance rate is low (eg, <10%) with transition to oral therapy if the strain is susceptible **(A-II)**. Linezolid 600 mg PO/IV twice daily for children ≥12 years of age and 10 mg/kg/dose PO/IV every 8 h for children <12 years of age is an alternative **(A-II)**.

II. What is the management of recurrent MRSA SSTIs?

Recurrent SSTIs

12. Preventive educational messages on personal hygiene and appropriate wound care are recommended for all patients with SSTI. Instructions should be provided to:

i. Keep draining wounds covered with clean, dry bandages (**A-III**).

ii. Maintain good personal hygiene with regular bathing and cleaning of hands with soap and water or an alcohol-based hand gel, particularly after touching infected skin or an item that has directly contacted a draining wound (**A-III**).

iii. Avoid reusing or sharing personal items (eg, disposable razors, linens, and towels) that have contacted infected skin (**A-III**).

13. Environmental hygiene measures should be considered in patients with recurrent SSTI in the household or community setting:

i. Focus cleaning efforts on high-touch surfaces (ie, surfaces that come into frequent contact with people's bare skin each day, such as counters, door knobs, bath tubs, and toilet seats) that may contact bare skin or uncovered infections (**C-III**).

ii. Commercially available cleaners or detergents appropriate for the surface being cleaned should be used according to label instructions for routine cleaning of surfaces (**C-III**).

14. Decolonization may be considered in selected cases if:

i. A patient develops a recurrent SSTI despite optimizing wound care and hygiene measures (**C-III**).

ii. Ongoing transmission is occurring among household members or other close contacts despite optimizing wound care and hygiene measures (**C-III**).

15. Decolonization strategies should be offered in conjunction with ongoing reinforcement of hygiene measures and may include the following:

i. Nasal decolonization with mupirocin twice daily for 5–10 days (**C-III**).

ii. Nasal decolonization with mupirocin twice daily for 5–10 days and topical body decolonization regimens with a skin antiseptic solution (eg, chlorhexidine) for 5–14 days or dilute bleach baths. (For dilute bleach baths, 1 teaspoon per gallon of water [or ¼ cup per ¼ tub or 13 gallons of water] given for 15 min twice weekly for ~3 months can be considered.) (**C-III**).

16. Oral antimicrobial therapy is recommended for the treatment of active infection only and is not routinely recommended for decolonization (**A-III**). An oral agent in combination with rifampin, if the strain is susceptible, may be considered for decolonization if infections recur despite above measures (**CIII**).

17. In cases where household or interpersonal transmission is suspected:

i. Personal and environmental hygiene measures in the patient and contacts are recommended (**A-III**).

ii. Contacts should be evaluated for evidence of *S. aureus* infection:

a. Symptomatic contacts should be evaluated and treated (**A-III**); nasal and topical body decolonization strategies may be considered following treatment of active infection (**C-III**).

b. Nasal and topical body decolonization of asymptomatic household contacts may be considered (**C-III**).

18. The role of cultures in the management of patients with recurrent SSTI is limited:

i. Screening cultures prior to decolonization are not routinely recommended if at least 1 of the prior infections was documented as due to MRSA (**B-III**).

ii. Surveillance cultures following a decolonization regimen are not routinely recommended in the absence of an active infection (**B-III**).

III. What is the management of MRSA bacteremia and infective endocarditis?

Bacteremia and Infective Endocarditis, Native Valve

19. For adults with uncomplicated bacteremia (defined as patients with positive blood culture results and the following: exclusion of endocarditis; no implanted prostheses; follow-up blood cultures performed on specimens obtained 2–4 days after the initial set that do not grow MRSA; defervescence within 72 h of initiating effective therapy; and no evidence of metastatic sites of infection), vancomycin (**A-II**) or daptomycin 6 mg/kg/dose IV once daily (**AI**) for at least 2 weeks. For complicated bacteremia (defined as patients with positive blood culture results who do not meet criteria for uncomplicated bacteremia), 4–6 weeks of therapy is recommended, depending on the extent of infection. Some experts recommend higher dosages of daptomycin at 8–10 mg/kg/dose IV once daily (**B-III**).

20. For adults with infective endocarditis, IV vancomycin (**A-II**) or daptomycin 6 mg/kg/dose IV once daily (**A-I**) for 6 weeks is recommended. Some experts recommend higher dosages of daptomycin at 8–10 mg/kg/dose IV once daily (**B-III**).

21. Addition of gentamicin to vancomycin is not recommended for bacteremia or native valve infective endocarditis (**A-II**).

22. Addition of rifampin to vancomycin is not recommended for bacteremia or native valve infective endocarditis (**A-I**).

23. A clinical assessment to identify the source and extent of the infection with elimination and/or debridement of other sites of infection should be conducted (**A-II**).

24. Additional blood cultures 2–4 days after initial positive cultures and as needed thereafter are recommended to document clearance of bacteremia (**A-II**).

25. Echocardiography is recommended for all adult patients with bacteremia. Transesophageal echocardiography

(TEE) is preferred over transthoracic echocardiography (TTE) (**A-II**).

26. Evaluation for valve replacement surgery is recommended if large vegetation (>10 mm in diameter), occurrence of ≥1 embolic event during the first 2 weeks of therapy, severe valvular insufficiency, valvular perforation or dehiscence, decompensated heart failure, perivalvular or myocardial abscess, new heart block, or persistent fevers or bacteremia are present (**A-II**).

Infective Endocarditis, Prosthetic Valve

27. IV vancomycin plus rifampin 300 mg PO/IV every 8 h for at least 6 weeks plus gentamicin 1 mg/kg/dose IV every 8 h for 2 weeks (**B-III**).

28. Early evaluation for valve replacement surgery is recommended (**A-II**).

Pediatric considerations

29. In children, vancomycin 15 mg/kg/dose IV every 6 h is recommended for the treatment of bacteremia and infective endocarditis (**A-II**). Duration of therapy may range from 2 to 6 weeks depending on source, presence of endovascular infection, and metastatic foci of infection. Data regarding the safety and efficacy of alternative agents in children are limited, although daptomycin 6–10 mg/kg/dose IV once daily may be an option (**C-III**). Clindamycin or linezolid should not be used if there is concern for infective endocarditis or endovascular source of infection but may be considered in children whose bacteremia rapidly clears and is not related to an endovascular focus (**B-III**).

30. Data are insufficient to support the routine use of combination therapy with rifampin or gentamicin in children with bacteremia or infective endocarditis (**C-III**); the decision to use combination therapy should be individualized.

31. Echocardiogram is recommended in children with congenital heart disease, bacteremia more than 2–3 days in duration, or other clinical findings suggestive of endocarditis (**A-III**).

IV. What is the management of MRSA pneumonia?

Pneumonia

32. For hospitalized patients with severe community-acquired pneumonia defined by any one of the following: (1) a requirement for intensive care unit (ICU) admission, (2) necrotizing or cavitary infiltrates, or (3) empyema, empirical therapy for MRSA is recommended pending sputum and/or blood culture results (**A-III**).

33. For health care–associated MRSA (HA-MRSA) or CA-MRSA pneumonia, IV vancomycin (**A-II**) or linezolid 600 mg PO/IV twice daily (**A-II**) or clindamycin 600 mg PO/IV 3 times daily (**B-III**), if the strain is susceptible, is recommended for 7–21 days, depending on the extent of infection.

34. In patients with MRSA pneumonia complicated by empyema, antimicrobial therapy against MRSA should be used in conjunction with drainage procedures (**A-III**).

Pediatric considerations

35. In children, IV vancomycin is recommended (**A-II**). If the patient is stable without ongoing bacteremia or intravascular infection, clindamycin 10–13 mg/kg/dose IV every 6–8 h (to administer 40 mg/kg/day) can be used as empirical therapy if the clindamycin resistance rate is low (eg, <10%) with transition to oral therapy if the strain is susceptible (**A-II**). Linezolid 600 mg PO/IV twice daily for children ≥12 years of age and 10 mg/kg/dose every 8 h for children <12 years of age is an alternative (**A-II**).

V. What is the management of MRSA bone and joint infections?

Osteomyelitis

36. Surgical debridement and drainage of associated soft-tissue abscesses is the mainstay of therapy and should be performed whenever feasible (**A-II**).

37. The optimal route of administration of antibiotic therapy has not been established. Parenteral, oral, or initial parenteral therapy followed by oral therapy may be used depending on individual patient circumstances (**A-III**).

38. Antibiotics available for parenteral administration include IV vancomycin (**B-II**) and daptomycin 6 mg/kg/dose IV once daily (**B-II**). Some antibiotic options with parenteral and oral routes of administration include the following: TMP-SMX 4 mg/kg/dose (TMP component) twice daily in combination with rifampin 600 mg once daily (**B-II**), linezolid 600 mg twice daily (**B-II**), and clindamycin 600 mg every 8 h (**B-III**).

39. Some experts recommend the addition of rifampin 600 mg daily or 300–450 mg PO twice daily to the antibiotic chosen above (**B-III**). For patients with concurrent bacteremia, rifampin should be added after clearance of bacteremia.

40. The optimal duration of therapy for MRSA osteomyelitis is unknown. A minimum 8-week course is recommended (**A-II**). Some experts suggest an additional 1–3 months (and possibly longer for chronic infection or if debridement is not performed) of oral rifampin-based combination therapy with TMP-SMX, doxycycline-minocycline, clindamycin, or a fluoroquinolone, chosen on the basis of susceptibilities (**C-III**).

41. Magnetic resonance imaging (MRI) with gadolinium is the imaging modality of choice, particularly for detection of early osteomyelitis and associated soft-tissue disease (**A-II**). Erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) level may be helpful to guide response to therapy (**B-III**).

Septic Arthritis

42. Drainage or debridement of the joint space should always be performed (**A-II**).

43. For septic arthritis, refer to antibiotic choices for osteomyelitis (recommendation 37 above). A 3–4-week course of therapy is suggested (**A-III**).

Device-related osteoarticular infections

44. For early-onset (<2 months after surgery) or acute hematogenous prosthetic joint infections involving a stable implant with short duration (≤3 weeks) of symptoms and debridement (but device retention), initiate parenteral therapy (refer to antibiotic recommendations for osteomyelitis) plus rifampin 600 mg daily or 300–450 mg PO twice daily for 2 weeks followed by rifampin plus a fluoroquinolone, TMP-SMX, a tetracycline or clindamycin for 3 or 6 months for hips and knees, respectively (**A-II**). Prompt debridement with device removal whenever feasible is recommended for unstable implants, late-onset infections, or in those with long duration (>3 weeks) of symptoms (**A-II**).

45. For early-onset spinal implant infections (≤30 days after surgery) or implants in an actively infected site, initial parenteral therapy plus rifampin followed by prolonged oral therapy is recommended (**B-II**). The optimal duration of parenteral and oral therapy is unclear; the latter should be continued until spine fusion has occurred (**B-II**). For late-onset infections (>30 days after implant placement), device removal whenever feasible is recommended (**B-II**).

46. Long-term oral suppressive antibiotics (eg, TMP-SMX, a tetracycline, a fluoroquinolone [which should be given in conjunction with rifampin due to the potential emergence of fluoroquinolone resistance, particularly if adequate surgical debridement is not possible should be given in conjunction with rifampin], or clindamycin) with or without rifampin may be considered in selected cases, particularly if device removal not possible (**B-III**).

Pediatric considerations

47. For children with acute hematogenous MRSA osteomyelitis and septic arthritis, IV vancomycin is recommended (**A-II**). If the patient is stable without ongoing bacteremia or intravascular infection, clindamycin 10–13 mg/kg/dose IV every 6–8 h (to administer 40 mg/kg/day) can be used as empirical therapy if the clindamycin resistance rate is low (eg, <10%) with transition to oral therapy if the strain is susceptible (**A-II**). The exact duration of therapy should be individualized, but typically a minimum 3–4-week course is recommended for septic arthritis and a 4–6-week course is recommended for osteomyelitis.

48. Alternatives to vancomycin and clindamycin include the following: daptomycin 6 mg/kg/day IV once daily (**C-III**) or linezolid 600 mg PO/IV twice daily for children ≥12 years of age and 10 mg/kg/dose every 8 h for children <12 years of age (**C-III**).

VI. What is the management of MRSA infections of the CNS?

Meningitis

49. IV vancomycin for 2 weeks is recommended (**B-II**). Some experts recommend the addition of rifampin 600 mg daily or 300–450 mg twice daily (**B-III**).

50. Alternatives include the following: linezolid 600 mg PO/IV twice daily (**B-II**) or TMP-SMX 5 mg/kg/dose IV every 8–12 h (**C-III**).

51. For CNS shunt infection, shunt removal is recommended, and it should not be replaced until cerebrospinal fluid (CSF) cultures are repeatedly negative (**A-II**).

Brain abscess, subdural empyema, spinal epidural abscess

52. Neurosurgical evaluation for incision and drainage is recommended (**A-II**).

53. IV vancomycin for 4–6 weeks is recommended (**B-II**). Some experts recommend the addition of rifampin 600 mg daily or 300–450 mg twice daily (**B-III**).

54. Alternatives include the following: linezolid 600 mg PO/IV twice daily (**B-II**) and TMP-SMX 5 mg/kg/dose IV every 8–12 h (**C-III**).

Septic Thrombosis of Cavernous or Dural Venous Sinus

55. Surgical evaluation for incision and drainage of contiguous sites of infection or abscess is recommended whenever possible (**A-II**). The role of anticoagulation is controversial.

56. IV vancomycin for 4–6 weeks is recommended (**B-II**). Some experts recommend the addition of rifampin 600 mg daily or 300–450 mg twice daily (**B-III**).

57. Alternatives include the following: linezolid 600 mg PO/IV twice daily (**B-II**) and TMP-SMX 5 mg/kg/dose IV every 8–12 h (**C-III**).

Pediatric considerations

58. IV vancomycin is recommended (**A-II**).

VII. What is the role of adjunctive therapies for the treatment of MRSA infections?

59. Protein synthesis inhibitors (eg, clindamycin and linezolid) and intravenous immunoglobulin (IVIG) are not routinely recommended as adjunctive therapy for the management of invasive MRSA disease (**A-III**). Some experts may consider these agents in selected scenarios (eg, necrotizing pneumonia or severe sepsis) (**C-III**).

VIII. What are the recommendations for vancomycin dosing and monitoring?

These recommendations are based on a consensus statement of the American Society of Health-System Pharmacists, the IDSA, and The Society of Infectious Diseases Pharmacists on guidelines for vancomycin dosing [3, 4].

Adults

60. IV vancomycin 15–20 mg/kg/dose (actual body weight) every 8–12 h, not to exceed 2 g per dose, is recommended in patients with normal renal function (**B-III**).

61. In seriously ill patients (eg, those with sepsis, meningitis, pneumonia, or infective endocarditis) with suspected MRSA infection, a loading dose of 25–30 mg/kg (actual body weight) may be considered. (Given the risk of red man syndrome and possible anaphylaxis associated with large doses of vancomycin, one should consider prolonging the infusion time to 2 h and use of an antihistamine prior to administration of the loading dose.) (**C-III**).

62. Trough vancomycin concentrations are the most accurate and practical method to guide vancomycin dosing (**B-II**). Serum trough concentrations should be obtained at steady state conditions, prior to the fourth or fifth dose. Monitoring of peak vancomycin concentrations is not recommended (**B-II**).

63. For serious infections, such as bacteremia, infective endocarditis, osteomyelitis, meningitis, pneumonia, and severe SSTI (eg, necrotizing fasciitis) due to MRSA, vancomycin trough concentrations of 15–20 μg/mL are recommended (**B-II**).

64. For most patients with SSTI who have normal renal function and are not obese, traditional doses of 1 g every 12 h are adequate, and trough monitoring is not required (**B-II**).

65. Trough vancomycin monitoring is recommended for serious infections and patients who are morbidly obese, have renal dysfunction (including those receiving dialysis), or have fluctuating volumes of distribution (**A-II**).

66. Continuous infusion vancomycin regimens are not recommended (**A-II**).

Pediatrics

67. Data are limited to guide vancomycin dosing in children. IV vancomycin 15 mg/kg/dose every 6 h is recommended in children with serious or invasive disease (**B-III**).

68. The efficacy and safety of targeting trough concentrations of 15–20 μg/mL in children requires additional study but should be considered in those with serious infections, such as bacteremia, infective endocarditis, osteomyelitis, meningitis, pneumonia, and severe SSTI (ie, necrotizing fasciitis) (**B-III**).

IX. How should results of vancomycin susceptibility testing be used to guide therapy?

69. For isolates with a vancomycin minimum inhibitory concentration (MIC) ≤2 μg/mL (eg, susceptible according to Clinical and Laboratory Standards Institute [CLSI] breakpoints), the patient's clinical response should determine the continued use of vancomycin, independent of the MIC (**A-III**).

i. If the patient has had a clinical and microbiologic response to vancomycin, then it may be continued with close follow-up

ii. If the patient has not had a clinical or microbiologic response to vancomycin despite adequate debridement and removal of other foci of infection, an alternative to vancomycin is recommended regardless of MIC.

70. For isolates with a vancomycin MIC >2 μg/mL (eg, vancomycin-intermediate *S. aureus* [VISA] or vancomycin-resistant *S. aureus* [VRSA]), an alternative to vancomycin should be used (**A-III**).

X. What is the management of persistent MRSA bacteremia and vancomycin treatment failures in adult patients?

71. A search for and removal of other foci of infection, drainage or surgical debridement is recommended (**A-III**).

72. High-dose daptomycin (10 mg/kg/day), if the isolate is susceptible, in combination with another agent (e.g. gentamicin 1 mg/kg IV every 8 h, rifampin 600 mg PO/IV daily or 300-450 mg PO/IV twice daily, linezolid 600 mg PO/IV BID, TMP-SMX 5 mg/kg IV twice daily, or a beta-lactam antibiotic) should be considered (**B-III**).

73. If reduced susceptibility to vancomycin and daptomycin are present, options may include the following: quinupristin-dalfopristin 7.5 mg/kg/dose IV every 8 h, TMP-SMX 5 mg/kg/dose IV twice daily, linezolid 600 mg PO/IV twice daily, or telavancin 10 mg/kg/dose IV once daily (**C-III**). These options may be given as a single agent or in combination with other antibiotics.

XI. What is the management of MRSA infections in neonates?

Neonatal pustulosis

74. For mild cases with localized disease, topical treatment with mupirocin may be adequate in full-term neonates and young infants (**A-III**).

75. For localized disease in a premature or very low-birthweight infant or more-extensive disease involving multiple sites in full-term infants, IV vancomycin or clindamycin is recommended, at least initially, until bacteremia is excluded (**A-II**).

Neonatal MRSA sepsis

76. IV vancomycin is recommended, dosing as outlined in the Red Book (**A-II**) [160].

77. Clindamycin and linezolid are alternatives for non-endovascular infections (**B-II**).

The prevalence of MRSA has steadily increased since the first clinical isolate was described in 1961, with an estimated 94,360 cases of invasive MRSA disease in the United States in 2005 [5]. Initially almost exclusively health care–associated, by the mid-1990s, MRSA strains were reported as causing infections among previously healthy individuals in the community who lacked

health care–associated risk factors [6]. Unlike HA-MRSA, these so-called CA-MRSA isolates are susceptible to many non–ß-lactam antibiotics. Furthermore, they are genetically distinct from HA-MRSA isolates and contain a novel cassette element, SCCmec IV and exotoxin, Panton-Valentine leukocidin (PVL). The epidemiology of MRSA has become increasingly complex as CA-MRSA and HA-MRSA strains have co-mingled both in the community and in health care facilities [7, 8]. Not unexpectedly, MRSA disease has had an enormous clinical and economic impact [9, 10].

The wide spectrum of illness caused by MRSA includes SSTIs, bacteremia and endocarditis, pneumonia, bone and joint infections, CNS disease, and toxic shock and sepsis syndromes. CA-MRSA was the most common cause of SSTI in a geographically diverse network of emergency departments in the United States [11]; however, there may be differences in local epidemiology to consider when implementing these guidelines. SSTIs may range in clinical presentation from a simple abscess or cellulitis to deeper soft-tissue infections, such as pyomyositis, necrotizing fasciitis, and mediastinitis as a complication of retropharyngeal abscess [12–15]. Bacteremia accompanies the majority (75%) of cases of invasive MRSA disease [5]. A multitude of disease manifestations have been described, including, but not limited to, infective endocarditis; myocardial, perinephric, hepatic, and splenic abscesses; septic thrombophlebitis with and without pulmonary emboli [16]; necrotizing pneumonia [17–21]; osteomyelitis complicated by subperiosteal abscesses; venous thrombosis and sustained bacteremia [16, 22, 23]; severe ocular infections, including endophthalmitis [24]; sepsis with purpura fulminans [25]; and Waterhouse-Friderichsen syndrome [26].

The Expert Panel addressed the following clinical questions in the 2010 Guidelines:

I. What is the management of SSTIs in the CA-MRSA era?

II. What is the management of recurrent MRSA SSTIs?

III. What is the management of MRSA bacteremia and infective endocarditis?

IV. What is the management of MRSA pneumonia?

V. What is the management of MRSA bone and joint infections?

VI. What is the management of MRSA infections of the CNS?

VII. What is the role of adjunctive therapies for the treatment of MRSA infections?

VIII. What are the recommendations for vancomycin dosing and monitoring?

IX. How should results of vancomycin susceptibility testing be used to guide therapy?

X. What is the management of persistent MRSA bacteremia and vancomycin treatment failures?

XI. What is the management of MRSA in neonates?

Acknowledgments

The Expert Panel wishes to express its gratitude to Drs. Gordon Archer, Frank Lowy, and Brad Spellberg for their thoughtful reviews of earlier drafts of the guideline. The Expert Panel also recognizes the following for their important contributions in identifying critical gaps where funding of research is needed to advance clinical treatment and care: William Burman, David M. Margolis, and Louis B. Rice (IDSA Research Committee), Stanley C. Deresinski (IDSA SPGC), and Padma Natarajan (IDSA staff). The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Financial support. IDSA.

Potential conflicts of interest. H.F.C. has received honoraria and research grants and has served as a consultant to Cubist, Ortho-McNeil, Pfizer, Theravance, and Targanta. S. E. C. has received honoraria from Forest and RibX, has served as a consultant for Merck and has received research support from Astellas, Cubist and AdvanDx. R.D. has received research funding from Pfizer, Clorox, Sanofi Pasteur, Sage, and GeneOhm. S.L.K. has received grant funding from Pfizer, has served as MRSA Leadership Advisor to Pfizer, and is participating in a pediatric daptomycin study. A.W.K. has received honoraria and grants from Cubist Pharmaceuticals, Merck, Wyeth, and Pfizer and has served as a consultant for Cubist Pharmaceuticals, Theravance, Astellas, Pfizer, Merck, and Ortho-McNeil and has owned stock from Cubist Pharmaceutical, Pfizer, and Johnson and Johnson. D.P.L. has received research support from Cubist, Johnson & Johnson, and Theravance and has served as a speaker for Cubist. B.E.M. has served as a consultant and received research support from Johnson & Johnson, Astellas, Pfizer, Cubist, Theravance, Targanta, Sanofi-Aventis, Vicuron Pharmaceuticals, and Wyeth-Ayerst. M.R. has received grants and or has served as a consultant speaker for the Pfizer, Cubist, Theravance/Astellas, Targanta, and Johnson & Johnson. D.A.T. has served on the advisory board to Pfizer, Ortho-McNeil, Astellas, Schering-Plough, and Replidyne. All other authors: no conflicts.

References

1. Calfee DP, Salgado CD, Classen D, et al. Strategies to prevent transmission of methicillin-resistant *Staphylococcus aureus* in acute care hospitals. Infect Control Hosp Epidemiol **2008**; 29(Suppl 1):S62–S80.
2. Anderson DJ, Kaye KS, Classen D, et al. Strategies to prevent surgical site infections in acute care hospitals. Infect Control Hosp Epidemiol **2008**; 29(Suppl 1):S51–S61.
3. Rybak M, Lomaestro B, Rotschafer JC, et al. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm **2009**; 66:82–98.
4. Rybak MJ, Lomaestro BM, Rotschafer JC, et al. Vancomycin therapeutic guidelines: a summary of consensus recommendations from the Infectious Diseases Society of America, the American Society of Health-System Pharmacists, and the Society of Infectious Diseases Pharmacists. Clin Infect Dis **2009**; 49:325–7.
5. Klevens RM, Morrison MA, Nadle J, et al. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. JAMA **2007**; 298:1763–71.
6. Herold BC, Immergluck LC, Maranan MC, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. JAMA **1998**; 279:593–8.
7. Liu C, Graber CJ, Karr M, et al. A population-based study of the incidence and molecular epidemiology of methicillin-resistant *Staphylococcus aureus* disease in San Francisco, 2004–2005. Clin Infect Dis **2008**; 46:1637–46.
8. D'Agata EM, Webb GF, Horn MA, et al. Modeling the invasion of community-acquired methicillin-resistant *Staphylococcus aureus* into hospitals. Clin Infect Dis **2009**; 48:274–84.

9. Purcell K, Fergie J, Peterson MD. Economic impact of the community-acquired methicillin-resistant *Staphylococcus aureus* epidemic on the Driscoll Children's Health Plan. Pediatr Infect Dis J **2006**; 25:178–80.
10. Noskin GA, Rubin RJ, Schentag JJ, et al. The burden of *Staphylococcus aureus* infections on hospitals in the United States: an analysis of the 2000 and 2001 Nationwide Inpatient Sample Database. Arch Intern Med **2005**; 165:1756–61.
11. Moran GJ, Krishnadasan A, Gorwitz RJ, et al. Methicillin-resistant *S. aureus* infections among patients in the emergency department. N Engl J Med **2006**; 355:666–74.
12. Lee TC, Carrick MM, Scott BG, et al. Incidence and clinical characteristics of methicillin-resistant *Staphylococcus aureus* necrotizing fasciitis in a large urban hospital. Am J Surg **2007**; 194:809–12; discussion, 12–13.
13. Pannaraj PS, Hulten KG, Gonzalez BE, et al. Infective pyomyositis and myositis in children in the era of community-acquired, methicillin-resistant *Staphylococcus aureus* infection. Clin Infect Dis **2006**; 43:953–60.
14. Miller LG, Perdreau-Remington F, Rieg G, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles. N Engl J Med **2005**; 352:1445–53.
15. Wright CT, Stocks RM, Armstrong DL, et al. Pediatric mediastinitis as a complication of methicillin-resistant *Staphylococcus aureus* retropharyngeal abscess. Arch Otolaryngol Head Neck Surg **2008**; 134:408–13.
16. Gonzalez BE, Teruya J, Mahoney DH Jr., et al. Venous thrombosis associated with staphylococcal osteomyelitis in children. Pediatrics **2006**; 117:1673–9.
17. Francis JS, Doherty MC, Lopatin U, et al. Severe community-onset pneumonia in healthy adults caused by methicillin-resistant *Staphylococcus aureus* carrying the Panton-Valentine leukocidin genes. Clin Infect Dis **2005**; 40:100–7.
18. Hageman JC, Uyeki TM, Francis JS, et al. Severe community-acquired pneumonia due to *Staphylococcus aureus*, 2003-04 influenza season. Emerg Infect Dis **2006**; 12:894–9.
19. Centers for Disease Control and Prevention. Severe methicillin-resistant *Staphylococcus aureus* community-acquired pneumonia associated with influenza–Louisiana Georgia, December 2006-January 2007. MMWR Morb Mortal Wkly Rep **2007**; 56:325–9.
20. Gonzalez BE, Hulten KG, Dishop MK, et al. Pulmonary manifestations in children with invasive community-acquired *Staphylococcus aureus* infection. Clin Infect Dis **2005**; 41:583–90.
21. Finelli L, Fiore A, Dhara R, et al. Influenza-associated pediatric mortality in the United States: increase of *Staphylococcus aureus* coinfection. Pediatrics **2008**; 122:805–11.
22. Arnold SR, Elias D, Buckingham SC, et al. Changing patterns of acute hematogenous osteomyelitis and septic arthritis: emergence of community-associated methicillin-resistant *Staphylococcus aureus*. J Pediatr Orthop **2006**; 26:703–8.
23. Crary SE, Buchanan GR, Drake CE, et al. Venous thrombosis and thromboembolism in children with osteomyelitis. J Pediatr **2006**; 149:537–41.
24. Rutar T, Chambers HF, Crawford JB, et al. Ophthalmic manifestations of infections caused by the USA300 clone of community-associated methicillin-resistant *Staphylococcus aureus*. Ophthalmology **2006**; 113:1455–62.
25. Kravitz GR, Dries DJ, Peterson ML, et al. Purpura fulminans due to *Staphylococcus aureus*. Clin Infect Dis **2005**; 40:941–7.
26. Adem PV, Montgomery CP, Husain AN, et al. *Staphylococcus aureus* sepsis and the Waterhouse-Friderichsen syndrome in children. N Engl J Med **2005**; 353:1245–51.