

Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America

Dennis L. Stevens,¹ Alan L. Bisno,² Henry F. Chambers,³ E. Patchen Dellinger,⁴ Ellie J. C. Goldstein,⁵ Sherwood L. Gorbach,⁶ Jan V. Hirschmann,⁷ Sheldon L. Kaplan,⁸ Jose G. Montoya,⁹ and James C. Wade¹⁰

¹Division of Infectious Diseases, Department of Veterans Affairs, Boise, Idaho; ²Medical Service, Miami Veterans Affairs Health Care System, Florida; ³San Francisco General Hospital, University of California; ⁴Division of General Surgery, University of Washington, Seattle; ⁵University of California, Los Angeles, School of Medicine, and R. M. Alden Research Laboratory, Santa Monica, California; ⁶Department of Community Health, Tufts University, Boston, Massachusetts; ⁷Medical Service, Puget Sound Veterans Affairs Medical Center, Seattle, Washington; ⁸Department of Pediatrics, Baylor College of Medicine, Houston, Texas; ⁹Department of Medicine, Stanford University, California; and ¹⁰Geisinger Health System, Geisinger Cancer Institute, Danville, Pennsylvania

A panel of national experts was convened by the Infectious Diseases Society of America (IDSA) to update the 2005 guidelines for the treatment of skin and soft tissue infections (SSTIs). The panel's recommendations were developed to be concordant with the recently published IDSA guidelines for the treatment of methicillin-resistant *Staphylococcus aureus* infections. The focus of this guideline is the diagnosis and appropriate treatment of diverse SSTIs ranging from minor superficial infections to life-threatening infections such as necrotizing fasciitis. In addition, because of an increasing number of immunocompromised hosts worldwide, the guideline addresses the wide array of SSTIs that occur in this population. These guidelines emphasize the importance of clinical skills in promptly diagnosing SSTIs, identifying the pathogen, and administering effective treatments in a timely fashion.

EXECUTIVE SUMMARY

Summarized below are the recommendations made in the new guidelines for skin and soft tissue infections (SSTIs). Figure 1 was developed to simplify the management of localized purulent staphylococcal infections such as skin abscesses, furuncles, and carbuncles in

the age of methicillin-resistant *Staphylococcus aureus* (MRSA). In addition, Figure 2 is provided to simplify the approach to patients with surgical site infections. The panel followed a process used in the development of other Infectious Diseases Society of America (IDSA) guidelines, which included a systematic weighting of the strength of recommendation and quality of evidence using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system (Table 1) [1–4]. A detailed description of the methods, background, and evidence summaries that support each of the recommendations can be found in the full text of the guidelines.

I. What Is Appropriate for the Evaluation and Treatment of Impetigo and Ecthyma?

Recommendations

1. Gram stain and culture of the pus or exudates from skin lesions of impetigo and ecthyma are

Received 17 April 2014; accepted 21 April 2014.

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. 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: Dennis L. Stevens, PhD, MD, Infectious Diseases Section, VA Medical Center, 500 W Fort St, Bldg 45, Boise, ID 83702 (dlstevens@mindspring.com).

Clinical Infectious Diseases 2014;59(2):147–59

© The Author 2014. Published by Oxford University Press on behalf of the Infectious Diseases Society of America. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.

DOI: 10.1093/cid/ciu444

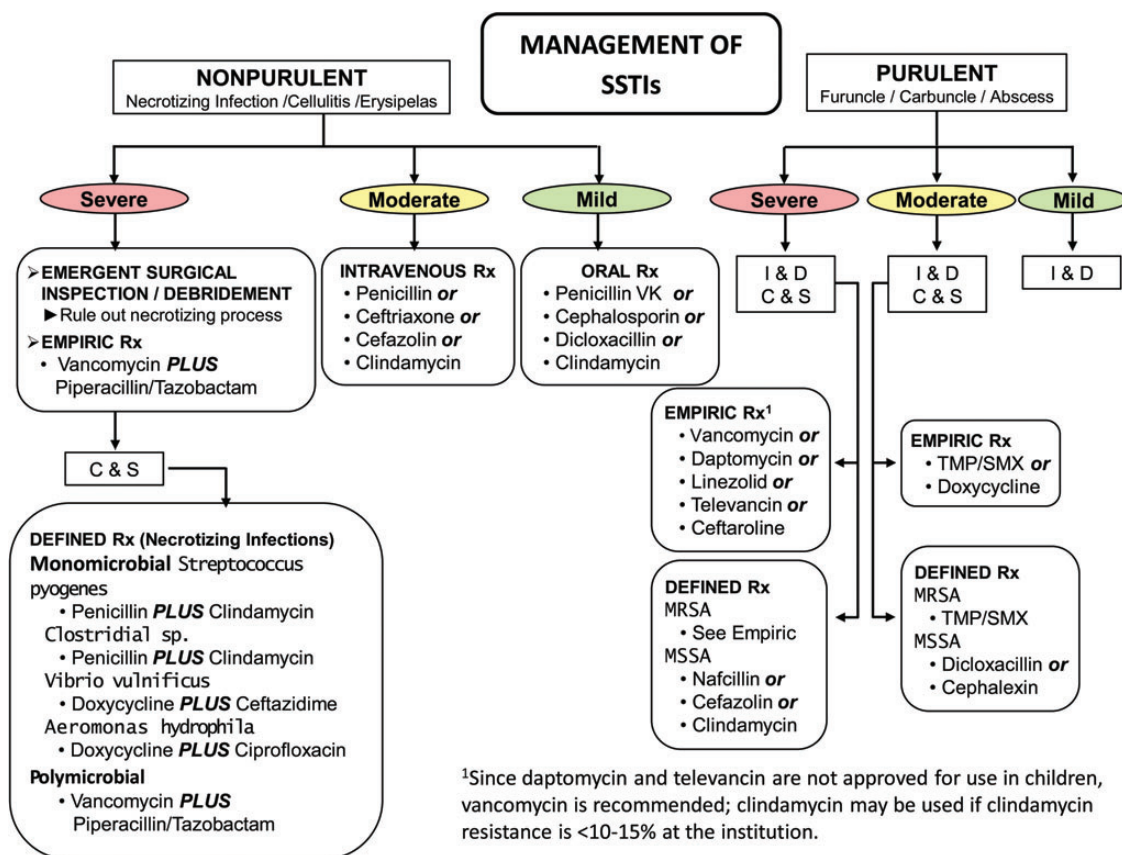


Figure 1. Purulent skin and soft tissue infections (SSTIs). Mild infection: for purulent SSTI, incision and drainage is indicated. Moderate infection: patients with purulent infection with systemic signs of infection. Severe infection: patients who have failed incision and drainage plus oral antibiotics or those with systemic signs of infection such as temperature $>38^{\circ}\text{C}$, tachycardia (heart rate >90 beats per minute), tachypnea (respiratory rate >24 breaths per minute) or abnormal white blood cell count ($<12\,000$ or <400 cells/ μL), or immunocompromised patients. Nonpurulent SSTIs. Mild infection: typical cellulitis/erysipelas with no focus of purulence. Moderate infection: typical cellulitis/erysipelas with systemic signs of infection. Severe infection: patients who have failed oral antibiotic treatment or those with systemic signs of infection (as defined above under purulent infection), or those who are immunocompromised, or those with clinical signs of deeper infection such as bullae, skin sloughing, hypotension, or evidence of organ dysfunction. Two newer agents, tedizolid and dalbavancin, are also effective agents in SSTIs, including those caused by methicillin-resistant *Staphylococcus aureus*, and may be approved for this indication by June 2014. Abbreviations: C & S, culture and sensitivity; I & D, incision and drainage; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; Rx, treatment; TMP/SMX, trimethoprim-sulfamethoxazole.

recommended to help identify whether *Staphylococcus aureus* and/or a β -hemolytic *Streptococcus* is the cause (strong, moderate), but treatment without these studies is reasonable in typical cases (strong, moderate).

2. Bullous and nonbullous impetigo can be treated with oral or topical antimicrobials, but oral therapy is recommended for patients with numerous lesions or in outbreaks affecting several people to help decrease transmission of infection. Treatment for ecthyma should be an oral antimicrobial.

(a) Treatment of bullous and nonbullous impetigo should be with either mupirocin or retapamulin twice daily (bid) for 5 days (strong, high).

(b) Oral therapy for ecthyma or impetigo should be a 7-day regimen with an agent active against *S. aureus* unless cultures yield streptococci alone (when oral penicillin is the recommended agent) (strong, high). Because *S. aureus* isolates from impetigo and ecthyma are usually methicillin susceptible, dicloxacillin or cephalexin is recommended. When MRSA is suspected or confirmed, doxycycline, clindamycin, or sulfamethoxazole-trimethoprim (SMX-TMP) is recommended (strong, moderate).

(c) Systemic antimicrobials should be used for infections during outbreaks of poststreptococcal glomerulonephritis to help eliminate nephritogenic strains of *S. pyogenes* from the community (strong, moderate).

Wound Infection Algorithm

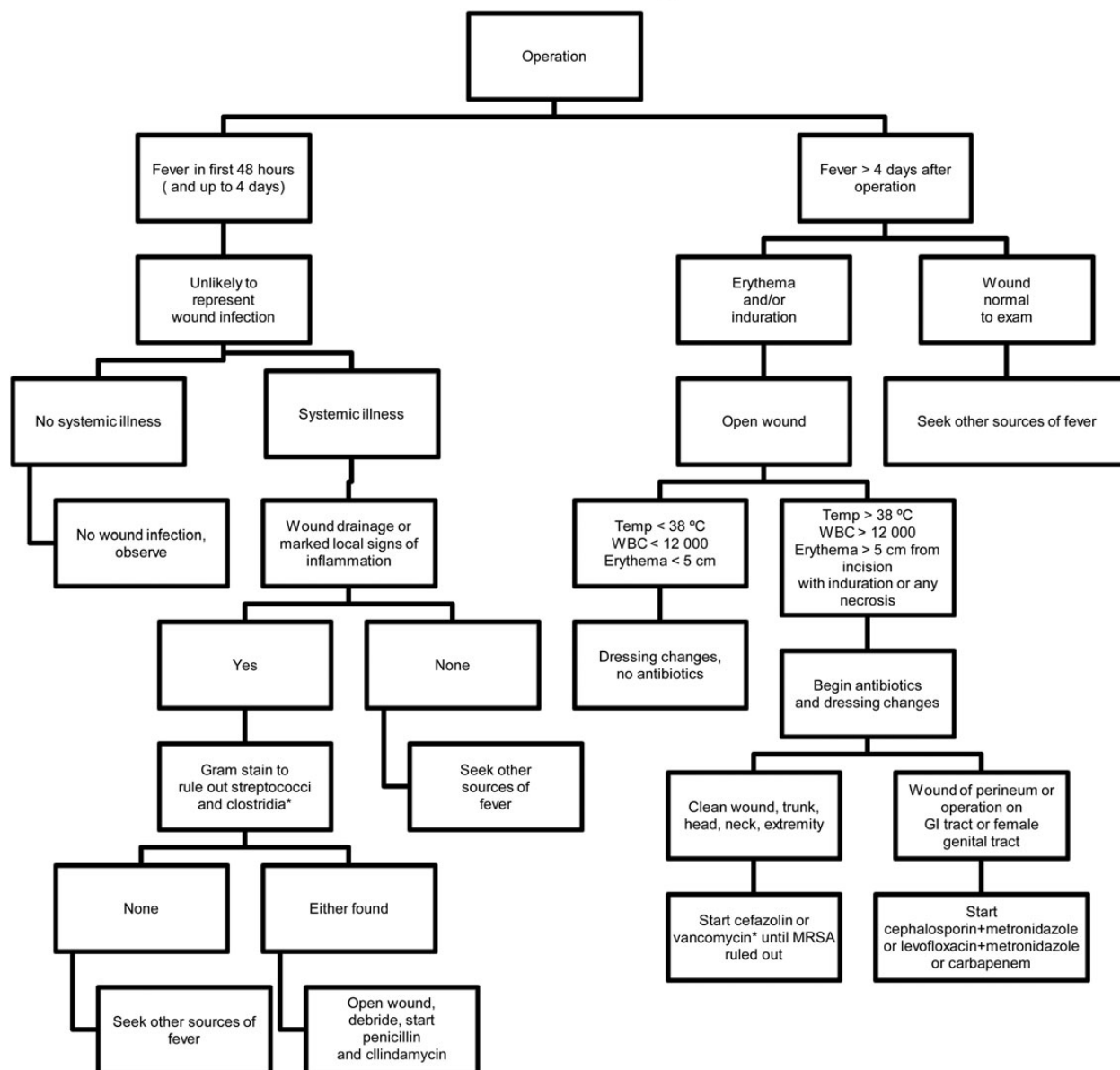


Figure 2. Algorithm for the management and treatment of surgical site infections (SSIs). *For patients with type 1 (anaphylaxis or hives) allergy to β -lactam antibiotics. If Gram stain not available, open and debride if purulent drainage present. Where the rate of infection with methicillin-resistant *Staphylococcus aureus* infection is high, consider vancomycin, daptomycin, or linezolid, pending results of culture and susceptibility tests. Adapted and modified with permission from Dellinger et al [5]. Abbreviations: GI, gastrointestinal; MRSA, methicillin-resistant *Staphylococcus aureus*; WBC, white blood cell count.

II. What Is the Appropriate Evaluation and Treatment for Purulent SSTIs (Cutaneous Abscesses, Furuncles, Carbuncles, and Inflamed Epidermoid Cysts)?

Recommendations

3. Gram stain and culture of pus from carbuncles and abscesses are recommended, but treatment without these studies is reasonable in typical cases (strong, moderate).

4. Gram stain and culture of pus from inflamed epidermoid cysts are not recommended (strong, moderate).

5. Incision and drainage is the recommended treatment for inflamed epidermoid cysts, carbuncles, abscesses, and large furuncles, mild (Figure 1) (strong, high).

6. The decision to administer antibiotics directed against *S. aureus* as an adjunct to incision and drainage should be

Table 1. Strength of Recommendations and Quality of the Evidence

Strength of Recommendation and Quality of Evidence	Clarity of Balance Between Desirable and Undesirable Effects	Methodological Quality of Supporting Evidence (Examples)	Implications
Strong recommendation, high-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research is unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation, low-quality quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence	Recommendation may change when higher-quality evidence becomes available. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Strong recommendation, very low-quality evidence (very rarely applicable)	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence	Recommendation may change when higher-quality evidence becomes available; any estimate of effect for at least 1 critical outcome is very uncertain.
Weak recommendation, high-quality evidence	Desirable effects closely balanced with undesirable effects	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	The best action may differ depending on circumstances or patient's or societal values. Further research is unlikely to change our confidence in the estimate of effect
Weak recommendation, moderate-quality evidence	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies	Alternative approaches likely to be better for some patients under some circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Weak recommendation, low-quality evidence	Uncertainty in the estimates of desirable effects, harms, and burden; desirable effects, harms, and burden may be closely balanced	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Weak recommendation, very low-quality evidence	Major uncertainty in the estimates of desirable effects, harms, and burden; desirable effects may or may not be balanced with undesirable effects	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence	Other alternatives may be equally reasonable. Any estimate of effect, for at least 1 critical outcome, is very uncertain

Abbreviation: RCT, randomized controlled trial.

made based upon presence or absence of systemic inflammatory response syndrome (SIRS), such as temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, tachypnea >24 breaths per minute, tachycardia >90 beats per minute, or white blood cell count $>12\,000$ or <400 cells/ μL (moderate; Figure 1) (strong, low). An

antibiotic active against MRSA is recommended for patients with carbuncles or abscesses who have failed initial antibiotic treatment or have markedly impaired host defenses or in patients with SIRS and hypotension (severe; Figure 1 and Table 2) (strong, low).

Table 2. Antimicrobial Therapy for Staphylococcal and Streptococcal Skin and Soft Tissue Infections

Disease Entity	Antibiotic	Dosage, Adults	Dosage, Children ^a	Comment
Impetigo ^b (<i>Staphylococcus</i> and <i>Streptococcus</i>)	Dicloxacillin	250 mg qid po	N/A	N/A
	Cephalexin	250 mg qid po	25–50 mg/kg/d in 3–4 divided doses po	N/A
	Erythromycin	250 mg qid po ^c	40 mg/kg/d in 3–4 divided doses po	Some strains of <i>Staphylococcus aureus</i> and <i>Streptococcus pyogenes</i> may be resistant.
	Clindamycin	300–400 mg qid po	20 mg/kg/d in 3 divided doses po	N/A
	Amoxicillin-clavulanate	875/125 mg bid po	25 mg/kg/d of the amoxicillin component in 2 divided doses po	N/A
	Retapamulin ointment	Apply to lesions bid	Apply to lesions bid	For patients with limited number of lesions
	Mupirocin ointment	Apply to lesions bid	Apply to lesions bid	For patients with limited number of lesions
MSSA SSTI	Nafcillin or oxacillin	1–2 g every 4 h IV	100–150 mg/kg/d in 4 divided doses	Parental drug of choice; inactive against MRSA
	Cefazolin	1 g every 8 h IV	50 mg/kg/d in 3 divided doses	For penicillin-allergic patients except those with immediate hypersensitivity reactions. More convenient than nafcillin with less bone marrow suppression
	Clindamycin	600 mg every 8 h IV or 300–450 mg qid po	25–40 mg/kg/d in 3 divided doses IV or 25–30 mg/kg/d in 3 divided doses po	Bacteriostatic; potential of cross-resistance and emergence of resistance in erythromycin-resistant strains; inducible resistance in MRSA
	Dicloxacillin	500 mg qid po	25–50 mg/kg/d in 4 divided doses po	Oral agent of choice for methicillin-susceptible strains in adults. Not used much in pediatrics
	Cephalexin	500 mg qid po	25–50 mg/kg/d 4 divided doses po	For penicillin-allergic patients except those with immediate hypersensitivity reactions. The availability of a suspension and requirement for less frequent dosing
	Doxycycline, minocycline	100 mg bid po	Not recommended for age <8 y ^d	Bacteriostatic; limited recent clinical experience
	Trimethoprim-sulfamethoxazole	1–2 double-strength tablets bid po	8–12 mg/kg (based on trimethoprim component) in either 4 divided doses IV or 2 divided doses po	Bactericidal; efficacy poorly documented
MRSA SSTI	Vancomycin	30 mg/kg/d in 2 divided doses IV	40 mg/kg/d in 4 divided doses IV	For penicillin allergic patients; parenteral drug of choice for treatment of infections caused by MRSA
	Linezolid	600 mg every 12 h IV or 600 mg bid po	10 mg/kg every 12 h IV or po for children <12 y	Bacteriostatic; limited clinical experience; no cross-resistance with other antibiotic classes; expensive
	Clindamycin	600 mg every 8 h IV or 300–450 mg qid po	25–40 mg/kg/d in 3 divided doses IV or 30–40 mg/kg/d in 3 divided doses po	Bacteriostatic; potential of cross-resistance and emergence of resistance in erythromycin-resistant strains; inducible resistance in MRSA. Important option for children
	Daptomycin	4 mg/kg every 24 h IV	N/A	Bactericidal; possible myopathy
	Ceftaroline	600 mg bid IV	N/A	Bactericidal
	Doxycycline, minocycline	100 mg bid po	Not recommended for age <8 y ^d	Bacteriostatic; limited recent clinical experience
	Trimethoprim-sulfamethoxazole	1–2 double-strength tablets bid po	8–12 mg/kg/d (based on trimethoprim component) in either 4 divided doses IV or 2 divided doses po	Bactericidal; limited published efficacy data

Table 2 continued.

Disease Entity	Antibiotic	Dosage, Adults	Dosage, Children ^a	Comment
Non-purulent SSTI (cellulitis)	Adult dosage	Pediatric dosage	antimicrobial agents for patients with severe penicillin hypersensitivity	N/A
Streptococcal skin infections	Penicillin 2–4 million units every 4–6 h IV Clindamycin 600–900 mg every 8 h IV Nafcillin 1–2 g every 4–6 h IV Cefazolin 1 g every 8 h IV Penicillin VK 250–500 mg every 6 h po Cephalexin 500 mg every 6 h po	Penicillin 60–100 000 units/kg/dose every 6 h 10–13 mg/kg/dose every 8 h IV 50 mg/kg/dose every 6 h 33 mg/kg/dose every 8 h IV	Clindamycin, vancomycin, linezolid, daptomycin, or telavancin. Clindamycin resistance is <1% but may be increasing in Asia	N/A

Abbreviations: bid, twice daily; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; N/A, not applicable; po, by mouth; qid, 4 times daily; SSTI, skin and soft tissue infection; tid, 3 times daily.

^a Doses listed are not appropriate for neonates. Refer to the report by the Committee on Infectious Diseases, American Academy of Pediatrics [6], for neonatal doses.

^b Infection due to *Staphylococcus* and *Streptococcus* species. Duration of therapy is 7 days, depending on the clinical response.

^c Adult dosage of erythromycin ethylsuccinate is 400 mg 4 times/d po.

^d See [6] for alternatives in children.

III. What Is the Appropriate Treatment for Recurrent Skin Abscesses?

Recommendations

7. A recurrent abscess at a site of previous infection should prompt a search for local causes such as a pilonidal cyst, hidradenitis suppurativa, or foreign material (strong, moderate).
8. Recurrent abscesses should be drained and cultured early in the course of infection (strong, moderate).
9. After obtaining cultures of recurrent abscess, treat with a 5- to 10-day course of an antibiotic active against the pathogen isolated (weak, low).
10. Consider a 5-day decolonization regimen twice daily of intranasal mupirocin, daily chlorhexidine washes, and daily decontamination of personal items such as towels, sheets, and clothes for recurrent *S. aureus* infection (weak, low).
11. Adult patients should be evaluated for neutrophil disorders if recurrent abscesses began in early childhood (strong, moderate).

IV. What Is Appropriate for the Evaluation and Treatment of Erysipelas and Cellulitis?

Recommendations

12. Cultures of blood or cutaneous aspirates, biopsies, or swabs are not routinely recommended (strong, moderate).
13. Cultures of blood are recommended (strong, moderate), and cultures and microscopic examination of cutaneous aspirates, biopsies, or swabs should be considered in patients with malignancy on chemotherapy, neutropenia, severe cell-mediated immunodeficiency, immersion injuries, and animal bites (weak, moderate).
14. Typical cases of cellulitis without systemic signs of infection should receive an antimicrobial agent that is active against streptococci (mild; Figure 1) (strong, moderate). For cellulitis with systemic signs of infection (moderate nonpurulent; Figure 1), systemic antibiotics are indicated. Many clinicians could include coverage against methicillin-susceptible *S. aureus* (MSSA) (weak, low). For patients whose cellulitis is associated with penetrating trauma, evidence of MRSA infection elsewhere, nasal colonization with MRSA, injection drug use, or SIRS (severe nonpurulent; Figure 1), vancomycin or another antimicrobial effective against both MRSA and streptococci is recommended (strong, moderate). In severely compromised patients as defined in question 13 (severe nonpurulent; Figure 1), broad-spectrum antimicrobial coverage may be considered (weak, moderate). Vancomycin plus either piperacillin-tazobactam or imipenem/meropenem is recommended as a reasonable empiric regimen for severe infections (strong, moderate).
15. The recommended duration of antimicrobial therapy is 5 days, but treatment should be extended if the infection has not improved within this time period (strong, high).

16. Elevation of the affected area and treatment of predisposing factors, such as edema or underlying cutaneous disorders, are recommended (strong, moderate).

17. In lower-extremity cellulitis, clinicians should carefully examine the interdigital toe spaces because treating fissuring, scaling, or maceration may eradicate colonization with pathogens and reduce the incidence of recurrent infection (strong, moderate).

18. Outpatient therapy is recommended for patients who do not have SIRS, altered mental status, or hemodynamic instability (mild nonpurulent; Figure 1) (strong, moderate). Hospitalization is recommended if there is concern for a deeper or necrotizing infection, for patients with poor adherence to therapy, for infection in a severely immunocompromised patient, or if outpatient treatment is failing (moderate or severe nonpurulent; Figure 1) (strong, moderate).

V. Should Anti-inflammatory Agents Be Used to Complement Antibiotic Treatment of Cellulitis?

Recommendation

19. Systemic corticosteroids (eg, prednisone 40 mg daily for 7 days) could be considered in nondiabetic adult patients with cellulitis (weak, moderate).

VI. What Is the Preferred Evaluation and Management of Patients With Recurrent Cellulitis?

Recommendations

20. Identify and treat predisposing conditions such as edema, obesity, eczema, venous insufficiency, and toe web abnormalities (strong, moderate). These practices should be performed as part of routine patient care and certainly during the acute stage of cellulitis (strong, moderate).

21. Administration of prophylactic antibiotics, such as oral penicillin or erythromycin bid for 4–52 weeks, or intramuscular benzathine penicillin every 2–4 weeks, should be considered in patients who have 3–4 episodes of cellulitis per year despite attempts to treat or control predisposing factors (weak, moderate). This program should be continued so long as the predisposing factors persist (strong, moderate).

VII. What Is the Preferred Management of Surgical Site Infections?

Recommendations

22. Suture removal plus incision and drainage should be performed for surgical site infections (strong, low).

23. Adjunctive systemic antimicrobial therapy is not routinely indicated, but in conjunction with incision and drainage may be beneficial for surgical site infections associated with a significant systemic response (Figure 2), such as erythema and induration extending >5 cm from the wound edge, temperature

>38.5°C, heart rate >110 beats/minute, or white blood cell (WBC) count >12 000/μL (weak, low).

24. A brief course of systemic antimicrobial therapy is indicated in patients with surgical site infections following clean operations on the trunk, head and neck, or extremities that also have systemic signs of infection (strong, low).

25. A first-generation cephalosporin or an antistaphylococcal penicillin for MSSA, or vancomycin, linezolid, daptomycin, telavancin, or ceftaroline where risk factors for MRSA are high (nasal colonization, prior MRSA infection, recent hospitalization, recent antibiotics), is recommended (strong, low). See also Tables 2 and 3.

26. Agents active against gram-negative bacteria and anaerobes, such as a cephalosporin or fluoroquinolone in combination with metronidazole, are recommended for infections following operations on the axilla, gastrointestinal tract, perineum, or female genital tract (strong, low). See also Table 3.

Table 3. Antibiotics for Treatment of Incisional Surgical Site Infections

Surgery of Intestinal or Genitourinary Tract

Single-drug regimens

Ticarcillin-clavulanate 3.1 g every 6 h IV

Piperacillin-tazobactam 3.375 g every 6 h or 4.5 g every 8 h IV

Imipenem-cilastatin 500 mg every 6 h IV

Meropenem 1 g every 8 h IV

Ertapenem 1 g every 24 h IV

Combination regimens

Ceftriaxone 1 g every 24 h + metronidazole 500 mg every 8 h IV

Ciprofloxacin 400 mg IV every 12 h or 750 mg po every 12 h + metronidazole 500 mg every 8 h IV

Levofloxacin 750 mg IV every 24 h + metronidazole 500 mg every 8 h IV

Ampicillin-sulbactam 3 g every 6 h + gentamicin or tobramycin 5 mg/kg every 24 h IV

Surgery of trunk or extremity away from axilla or perineum

Oxacillin or nafcillin 2 g every 6 h IV

Cefazolin 0.5–1 g every 8 h IV

Cephalexin 500 mg every 6 h po

SMX-TMP 160–800 mg po every 6 h

Vancomycin 15 mg/kg every 12 h IV

Surgery of axilla or perineum^a

Metronidazole 500 mg every 8 h IV

plus

Ciprofloxacin 400 mg IV every 12 h or 750 mg po every 12 h IV po

Levofloxacin 750 mg every 24 h IV po

Ceftriaxone 1 g every 24 h

Abbreviations: IV, intravenous; po, by mouth; SMX-TMP, sulfamethoxazole-trimethoprim.

^a May also need to cover for methicillin-resistant *Staphylococcus aureus* with vancomycin 15 mg/kg every 12 h.

VIII. What Is the Preferred Evaluation and Treatment of Necrotizing Fasciitis, Including Fournier Gangrene?

Recommendations

27. Prompt surgical consultation is recommended for patients with aggressive infections associated with signs of systemic toxicity or suspicion of necrotizing fasciitis or gas gangrene (severe nonpurulent; Figure 1) (strong, low).

28. Empiric antibiotic treatment should be broad (eg, vancomycin or linezolid plus piperacillin-tazobactam or a carbapenem; or plus ceftriaxone and metronidazole), as the etiology can be polymicrobial (mixed aerobic-anaerobic microbes) or monomicrobial (group A streptococci, community-acquired MRSA) (strong, low). See also Table 4.

29. Penicillin plus clindamycin is recommended for treatment of documented group A streptococcal necrotizing fasciitis (strong, low). See Figures 1, 2, and Table 4.

IX. What Is the Appropriate Approach to the Management of Pyomyositis?

Recommendations

30. Magnetic resonance imaging (MRI) is the recommended imaging modality for establishing the diagnosis of pyomyositis. Computed tomography (CT) scan and ultrasound studies are also useful (strong, moderate).

31. Cultures of blood and abscess material should be obtained (strong, moderate).

32. Vancomycin is recommended for initial empirical therapy. An agent active against enteric gram-negative bacilli should be added for infection in immunocompromised patients or following open trauma to the muscles (strong, moderate).

33. Cefazolin or antistaphylococcal penicillin (eg, nafcillin or oxacillin) is recommended for treatment of pyomyositis caused by MSSA (strong, moderate). See Table 2.

34. Early drainage of purulent material should be performed (strong, high).

35. Repeat imaging studies should be performed in the patient with persistent bacteremia to identify undrained foci of infection (strong, low).

36. Antibiotics should be administered intravenously initially, but once the patient is clinically improved, oral antibiotics are appropriate for patients in whom bacteremia cleared promptly and there is no evidence of endocarditis or metastatic abscess. Two to 3 weeks of therapy is recommended (strong, low).

X. What Is the Appropriate Approach to the Evaluation and Treatment of Clostridial Gas Gangrene or Myonecrosis?

Recommendations

37. Urgent surgical exploration of the suspected gas gangrene site and surgical debridement of involved tissue should be performed (severe nonpurulent; Figure 1) (strong, moderate).

38. In the absence of a definitive etiologic diagnosis, broad-spectrum treatment with vancomycin plus either piperacillin/

tazobactam, ampicillin/sulbactam, or a carbapenem antimicrobial is recommended (strong, low). Definitive antimicrobial therapy with penicillin and clindamycin (Figure 1) is recommended for treatment of clostridial myonecrosis (strong, low).

39. Hyperbaric oxygen (HBO) therapy is not recommended because it has not been proven as a benefit to the patient and may delay resuscitation and surgical debridement (strong, low).

XI. What Is the Role of Preemptive Antimicrobial Therapy to Prevent Infection for Dog or Cat Bites?

Recommendations

40. Preemptive early antimicrobial therapy for 3–5 days is recommended for patients who (a) are immunocompromised; (b) are asplenic; (c) have advanced liver disease; (d) have preexisting or resultant edema of the affected area; (e) have moderate to severe injuries, especially to the hand or face; or (f) have injuries that may have penetrated the periosteum or joint capsule (strong, low).

41. Postexposure prophylaxis for rabies may be indicated; consultation with local health officials is recommended to determine if vaccination should be initiated (strong, low).

XII. What Is the Treatment for Infected Animal Bite–Related Wounds?

Recommendation

42. An antimicrobial agent or agents active against both aerobic and anaerobic bacteria such as amoxicillin-clavulanate (Table 5) should be used (strong, moderate).

XIII. Should Tetanus Toxoid Be Administered for Animal Bite Wounds?

Recommendation

43. Tetanus toxoid should be administered to patients without toxoid vaccination within 10 years. Tetanus, diphtheria, and tetanus (Tdap) is preferred over Tetanus and diphtheria (Td) if the former has not been previously given (strong, low).

XIV. In Which Patients Is Primary Wound Closure Appropriate for Animal Bite Wounds?

Recommendation

44. Primary wound closure is not recommended for wounds, with the exception of those to the face, which should be managed with copious irrigation, cautious debridement, and preemptive antibiotics (strong, low). Other wounds may be approximated (weak, low).

XV. What Is the Appropriate Treatment of Cutaneous Anthrax?

Recommendations

45. Oral penicillin V 500 mg 4 times daily (qid) for 7–10 days is the recommended treatment for naturally acquired cutaneous anthrax (strong, high).

46. Ciprofloxacin 500 mg by mouth (po) bid or levofloxacin 500 mg intravenously (IV)/po every 24 hours × 60 days is

Table 4. Treatment of Necrotizing Infections of the Skin, Fascia, and Muscle

Type of Infection	First-line Antimicrobial Agent	Adult Dosage	Pediatric Dosage Beyond the Neonatal Period	Antimicrobial Agent for Patients With Severe Penicillin Hypersensitivity
Mixed infections	Piperacillin-tazobactam plus vancomycin	3.37 g every 6–8 h IV 30 mg/kg/d in 2 divided doses	60–75 mg/kg/dose of the piperacillin component every 6 h IV 10–13 mg/kg/dose every 8 h IV	Clincomycin or metronidazole ^a with an aminoglycoside or fluoroquinolone
	Imipenem-cilastatin	1 g every 6–8 h IV	N/A	N/A
	Meropenem	1 g every 8 h IV	20 mg/kg/dose every 8 h IV	
	Ertapenem	1 g daily IV	15 mg/kg/dose every 12 h IV for children 3 mo–12 y	
	Cefotaxime plus metronidazole or clindamycin	2 g every 6 h IV 500 mg every 6 h IV 600–900 mg every 8 h IV	50 mg/kg/dose every 6 h IV 7.5 mg/kg/dose every 6 h IV 10–13 mg/kg/dose every 8 h IV	N/A
<i>Streptococcus</i>	Penicillin plus clindamycin	2–4 million units every 4–6 h IV (adult) 600–900 mg every 8 h IV	60 000–100 000 units/kg/dose every 6 h IV 10–13 mg/kg/dose every 8 h IV	Vancomycin, linezolid, quinupristin/dalfopristin, daptomycin
<i>Staphylococcus aureus</i>	Nafcillin	1–2 g every 4 h IV	50 mg/kg/dose every 6 h IV	Vancomycin, linezolid, quinupristin/dalfopristin, daptomycin
	Oxacillin	1–2 g every 4 h IV	50 mg/kg/dose every 6 h IV	
	Cefazolin	1 g every 8 h IV	33 mg/kg/dose every 8 h IV	
	Vancomycin (for resistant strains)	30 mg/kg/d in 2 divided doses IV	15 mg/kg/dose every 6 h IV	
	Clindamycin	600–900 mg every 8 h IV	10–13 mg/kg/dose every 8 h IV	Bacteriostatic; potential cross-resistance and emergence of resistance in erythromycin-resistant strains; inducible resistance in MRSA ^b
<i>Clostridium</i> species	Clindamycin plus penicillin	600–900 mg every 8 h IV 2–4 million units every 4–6 h IV (adult)	10–13 mg/kg/dose every 8 h IV 60 000–100 000 units/kg/dose every 6 h IV	N/A
<i>Aeromonas hydrophila</i>	Doxycycline plus ciprofloxacin or ceftriaxone	100 mg every 12 h IV 500 mg every 12 h IV 1 to 2 g every 24 h IV	Not recommended for children but may need to use in life-threatening situations	N/A
<i>Vibrio vulnificus</i>	Doxycycline plus ceftriaxone or cefotaxime	100 mg every 12 h IV 1 g qid IV 2 g tid IV	Not recommended for children but may need to use in life-threatening situations	N/A

Abbreviations: IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; N/A, not applicable; qid, 4 times daily; tid, 3 times daily.

^a If staphylococcus present or suspected, add an appropriate agent.

^b If MRSA is present or suspected, add vancomycin not to exceed the maximum adult daily dose.

Table 5. Recommended Therapy for Infections Following Animal or Human Bites

Antimicrobial Agent by Type of Bite	Therapy Type		
	Oral	Intravenous	Comments
Animal bite			
Amoxicillin-clavulanate	875/125 mg bid	. . .	Some gram-negative rods are resistant; misses MRSA
Ampicillin-sulbactam	. . .	1.5–3.0 g every 6–8 h	Some gram-negative rods are resistant; misses MRSA
Piperacillin-tazobactam	. . .	3.37 g every 6–8 h	Misses MRSA
Carbapenems		See individual info.	Misses MRSA
Doxycycline	100 mg bid	100 mg every 12 h	Excellent activity against <i>Pasteurella multocida</i> ; some streptococci are resistant
Penicillin plus dicloxacillin	500 mg qid/500 mg qid	. . .	
SMX-TMP	160–800 mg bid	5–10 mg/kg/day of TMP component	Good activity against aerobes; poor activity against anaerobes
Metronidazole	250–500 mg tid	500 mg every 8 h	Good activity against anaerobes; no activity against aerobes
Clindamycin	300 mg tid	600 mg every 6–8 h	Good activity against staphylococci, streptococci, and anaerobes; misses <i>P. multocida</i>
Second-generation cephalosporin			Good activity against <i>P. multocida</i> ; misses anaerobes
Cefuroxime	500 mg bid	1 g every 12 h	
Cefoxitin	. . .	1 g every 6–8 h	
Third-generation cephalosporin			
Ceftriaxone	. . .	1 g every 12 h	
Cefotaxime	. . .	1–2 g every 6–8 h	
Fluoroquinolones			Good activity against <i>P. multocida</i> ; misses MRSA and some anaerobes
Ciprofloxacin	500–750 mg bid	400 mg every 12 h	
Levofloxacin	750 mg daily	750 mg daily	
Moxifloxacin	400 mg daily	400 mg daily	Monotherapy; good for anaerobes also
Human bite			
Amoxicillin-clavulanate	875/125 mg bid	. . .	Some gram-negative rods are resistant; misses MRSA
Ampicillin-sulbactam	. . .	1.5–3.0 g every 6 h	Some gram-negative rods are resistant; misses MRSA
Carbapenems			Misses MRSA
Doxycycline	100 mg bid	. . .	Good activity against <i>Eikenella</i> species, staphylococci, and anaerobes; some streptococci are resistant

Abbreviations: bid, twice daily; MRSA, methicillin-resistant *Staphylococcus aureus*; qid, 4 times daily; SMX-TMP, sulfamethoxazole-trimethoprim; tid, 3 times daily.

recommended for bioterrorism cases because of presumed aerosol exposure (strong, low).

XVI. What Is the Appropriate Approach for the Evaluation and Treatment of Bacillary Angiomatosis and Cat Scratch Disease?

Recommendations

47. Azithromycin is recommended for cat scratch disease (strong, moderate) according to the following dosing protocol:

- Patients >45 kg: 500 mg on day 1 followed by 250 mg for 4 additional days (strong, moderate).
- Patients <45 kg: 10 mg/kg on day 1 and 5 mg/kg for 4 more days (strong, moderate).

48. Erythromycin 500 mg qid or doxycycline 100 mg bid for 2 weeks to 2 months is recommended for treatment of bacillary angiomatosis (strong, moderate).

XVII. What Is the Preferred Treatment for Erysipeloid?

Recommendation

49. Penicillin (500 mg qid) or amoxicillin (500 mg 3 times daily [tid]) for 7–10 days is recommended for treatment of erysipeloid (strong, high).

XVIII. What Is the Appropriate Treatment of Glanders?

Recommendation

50. Ceftazidime, gentamicin, imipenem, doxycycline, or ciprofloxacin is recommended based on in vitro susceptibility (strong, low).

XIX. What Is the Appropriate Diagnosis and Treatment of Bubonic Plague?

Recommendation

51. Bubonic plague should be diagnosed by Gram stain and culture of aspirated material from a suppurative lymph node (strong, moderate). Streptomycin (15 mg/kg intramuscularly [IM] every 12 hours) or doxycycline (100 mg bid po) is recommended for treatment of bubonic plague (strong, low). Gentamicin could be substituted for streptomycin (weak, low).

XX. What Is Appropriate for Diagnosis and Treatment for Tularemia?

Recommendations

52. Serologic tests are the preferred method of diagnosing tularemia (weak, low).

53. Streptomycin (15 mg/kg every 12 hours IM) or gentamicin (1.5 mg/kg every 8 hours IV) is recommended for treatment of severe cases of tularemia (strong, low).

54. Tetracycline (500 mg qid) or doxycycline (100 mg bid po) is recommended for treatment of mild cases of tularemia (strong, low).

55. Notify the microbiology laboratory if tularemia is suspected (strong, high).

XXI. What Is the Appropriate Approach to Assess SSTIs in Immunocompromised Patients?

Recommendations

56. In addition to infection, differential diagnosis of skin lesions should include drug eruption, cutaneous infiltration with the underlying malignancy, chemotherapy- or radiation-induced reactions, Sweet syndrome, erythema multiforme, leukocytoclastic vasculitis, and graft-vs-host disease among allogeneic transplant recipients (strong, high).

57. Differential diagnosis for infection of skin lesions should include bacterial, fungal, viral, and parasitic agents (strong, high).

58. Biopsy or aspiration of the lesion to obtain material for histological and microbiological evaluation should always be implemented as an early diagnostic step (strong, high).

XXII. What Is the Appropriate Approach to Assess SSTIs in Patients With Fever and Neutropenia?

Recommendations

59. Determine whether the current presentation of fever and neutropenia is the patient's initial episode of fever and neutropenia, or persistent unexplained fever of their initial episode (after 4–7 days) or a subsequent episode of fever and neutropenia (recurrent) (strong, low).

60. Aggressively determine the etiology of the SSTI by aspiration and/or biopsy of skin and soft tissue lesions and submit these for thorough cytological/histological assessments, microbial staining, and cultures (strong, low).

61. Risk-stratify patients with fever and neutropenia according to susceptibility to infection: high-risk patients are those with anticipated prolonged (>7 days) and profound neutropenia (absolute neutrophil count <100 cells/ μ L) or with a Multinational Association for Supportive Care (MASCC) score of <21; low-risk patients are those with anticipated brief (<7 days) periods of neutropenia and few comorbidities (strong, low) or with a MASCC score of $\geq$ 21 (strong, moderate).

62. Determine the extent of infection through a thorough physical examination, blood cultures, chest radiograph, and additional imaging (including chest CT) as indicated by clinical signs and symptoms (strong, low).

XXIII. What Is the Appropriate Antibiotic Therapy for Patients With SSTIs During the Initial Episode of Fever and Neutropenia?

Recommendations

63. Hospitalization and empiric antibacterial therapy with vancomycin plus antipseudomonal antibiotics such as cefepime, a carbapenem (imipenem-cilastatin or meropenem or doripenem) or piperacillin-tazobactam is recommended (strong, high).

64. Documented clinical and microbiologic SSTIs should be treated based on antimicrobial susceptibilities of isolated organisms (strong, high).

65. It is recommended that the treatment duration for most bacterial SSTIs should be 7–14 days (strong, moderate).

66. Surgical intervention is recommended for drainage of soft tissue abscess after marrow recovery or for a progressive polymicrobial necrotizing fasciitis or myonecrosis (strong, low).

67. Adjunct colony-stimulating factor therapy (granulocyte colony-stimulating factor [G-CSF], granulocyte macrophage colony-stimulating factor [GM-CSF]) or granulocyte transfusions are not routinely recommended (weak, moderate).

68. Acyclovir should be administered to patients suspected or confirmed to have cutaneous or disseminated varicella zoster virus (herpes simplex virus [HSV] or varicella zoster virus [VZV]) infection (strong, moderate).

XXIV. What Is the Appropriate Antimicrobial Therapy for Patients With SSTIs During Persistent or Recurrent Episodes of Fever and Neutropenia?

Recommendations

69. Yeasts and molds remain the primary cause of infection-associated with persistent and recurrent fever and neutropenia; therefore, empiric antifungal therapy (Table 6) should be added to the antibacterial regimen (strong, high).

(a) Empiric administration of vancomycin or other agents with gram-positive activity (linezolid, daptomycin, or ceftaroline, Table 7) should be added if not already being administered (strong, high).

(b) *Candida* species SSTIs should be treated with an echinocandin or, if *Candida parapsilosis* has been isolated, lipid

Table 6. Standard Doses of Antifungal Agents

Antifungal Agent	Oral Dose	IV Dose	Comments
Fluconazole	100–400 mg every 24 h	800 mg loading dose, then 400 mg daily	<i>Candida krusei</i> and <i>Candida glabrata</i> are resistant
Voriconazole ^a	400 mg bid × 2 doses, then 200 mg every 12 h	6 mg/kg IV every 12 h for 2 doses, followed by 4 mg/kg IV every 12 h	Accumulation of cyclodextrin vehicle with IV formulation with renal insufficiency
Posaconazole	400 mg bid with meals	N/A	Covers <i>Mucorales</i>
Lipid complex amphotericin B	N/A	5 mg/kg/d	Not active against fusaria
Liposomal amphotericin B	N/A	3–5 mg/kg/d	Not active against fusaria

Abbreviations: bid, twice daily; IV, intravenous; N/A, not applicable.

^a The use of patient-specific pharmacokinetics is recommended to improve clinical outcome [7].

formulation amphotericin B (strong, high) with fluconazole as an acceptable alternative (strong, moderate). Treatment should be administered for 2 weeks after clearance of bloodstream infection or resolution of skin lesions (strong, moderate).

(c) *Aspergillus* SSTIs should be treated with voriconazole (strong, high), or alternatively, lipid formulations of amphotericin B, posaconazole, or echinocandin for 6–12 weeks (strong, low). *Mucor/Rhizopus* infections should be treated with lipid formulation amphotericin B (strong, moderate) or posaconazole (strong, low) (Table 6). The addition of an echinocandin could be considered based on synergy in murine models of mucormycosis, and observational clinical data (weak, low).

(d) *Fusarium* species infections should be treated with high-dose IV voriconazole or posaconazole (strong, low).

(e) Begin treatment for antibiotic-resistant bacterial organisms (Table 7), in patients currently on antibiotics (strong, moderate).

(f) Intravenous acyclovir should be added to the patient's antimicrobial regimen for suspected or confirmed cutaneous or disseminated HSV or VZV infections (strong, moderate).

70. Blood cultures should be obtained and skin lesions in this population of patients should be aggressively evaluated by culture aspiration, biopsy, or surgical excision, as they may be caused by resistant microbes, yeast, or molds (strong, moderate).

71. The sensitivity of a single-serum fungal antigen test (1,3-β-D-glucan or galactomannan tests) is low particularly in patients receiving antifungal agents, and benefits from laboratory tests for fungal antigen or DNA detection remain inconsistent (strong, moderate).

72. Polymerase chain reaction (PCR) in peripheral blood for HSV and VZV might be helpful in establishing a diagnosis of disseminated infection in patients with unexplained skin lesions (weak, moderate).

XXV. What Is the Appropriate Approach to Assess SSTIs in Patients With Cellular Immunodeficiency?

Recommendations

73. Consider immediate consultation with a dermatologist familiar with cutaneous manifestations of infection in patients with cellular immune defects (eg, those with lymphoma, lymphocytic leukemia, recipients of organ transplants, or those receiving immunosuppressive drugs such as anti-tumor necrosis factors or certain monoclonal antibodies) (weak, low).

74. Consider biopsy and surgical debridement early in the management of these patients (weak, low).

75. Empiric antibiotics, antifungals, and/or antivirals should be considered in life-threatening situations (weak, moderate).

Table 7. Standard Doses of Antimicrobial Agents Active Against Multidrug-Resistant Organisms

Antimicrobial	IV Dose	Comments
Vancomycin	30–60 mg/kg/d in 2–4 divided doses	Target serum trough concentrations of 15–20 µg/mL in severe infections
Daptomycin	4–6 mg/kg/d	Covers VRE, strains nonsusceptible to vancomycin may be cross-resistant to daptomycin
Linezolid	600 mg every 12 h	100% oral bioavailability; so oral dose same as IV dose. Covers VRE and MRSA
Colistin	5 mg/kg load, then 2.5 mg/kg every 12 h	Nephrotoxic; does not cover gram-positives or anaerobes, <i>Proteus</i> , <i>Serratia</i> , <i>Burkholderia</i>

Abbreviations: IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci.

The use of specific agents should be decided with the input of the primary team, dermatology, infectious disease, and other consulting teams (strong, moderate).

Notes

Acknowledgments. The expert panel expresses its gratitude to the external reviewers, Drs. Thomas File, Thomas M. Hooton, and George A. Pankey. The panel thanks the IDSA for supporting the development of this guideline and specifically, Vita Washington for her continued support throughout the guideline development process. We thank Irene Collie and Dr Amy E. Bryant for technical assistance in developing the algorithm in Figure 1.

Financial support. Support for these guidelines was provided by the Infectious Diseases Society of America.

Potential conflicts of interest. The following list is a reflection of what has been reported to IDSA. To provide thorough transparency, IDSA requires full disclosure of all relationships, regardless of relevancy to the guideline topic. Evaluation of such relationships as potential conflicts of interest is determined by a review process that includes assessment by the SPGC chair, the SPGC liaison to the development panel and the board of directors liaison to the SPGC, and, if necessary, the Conflict of Interest (COI) Task Force of the Board. This assessment of disclosed relationships for possible COI will be based on the relative weight of the financial relationship (ie, monetary amount) and the relevance of the relationship (ie, the degree to which an association might reasonably be interpreted by an independent observer as related to the topic or recommendation of consideration). The reader of these guidelines should be mindful of this when the list of disclosures is reviewed. D. L. S. has no current conflicts of interest and currently receives research support from the Department of Veterans Affairs and the National Institutes of Health. A. L. B. has received honoraria from UpToDate. H. F. C. has served as a consultant to Pfizer, AstraZeneca, Theravance, and Trius, and has received stocks/bonds from Merck and Trius. E. P. D. has served as a consultant; has received grants for clinical research and/or lectured for honoraria from Bayer, Merck, Wyeth-Ayerst, AstraZeneca, Pfizer, Ortho-McNeil, Cubist, Vicuron, InterMune, Peninsula, Johnson & Johnson, Cepheid, Replidyne, Kimberley-Clark, Targanta, Schering-Plough, Enturia, Optimer Pharmaceuticals, Cadence, Implicit, Cardinal, Durata, 3M, Applied Medical, and BD-GeneOhm; and has received a clinical trial grant from Tetrphase. E. J. C. G. has served as a consultant to Schering-Plough,

ViraPharm, Replidyne, Oculus Innovative Sciences, Theravance, Cerexa, Merck, and Optimer Pharmaceuticals; has received honoraria from Merck, Johnson & Johnson; and has received research grants from Replidyne, Oculus Innovative Sciences, Cubist, Theravance, Pfizer, Cerexa, Johnson & Johnson, Merck, and Optimer Pharmaceuticals. S. L. G. has received stocks/bonds from Optimer Pharmaceuticals, Cubist Pharmaceuticals, and Cempira Pharmaceuticals has received honoraria from IDSA (Editor, *Clinical Infectious Diseases*); has served as a consultant to Cempira Pharmaceuticals; and has received grants from the National Institutes of Health. S. L. K. has served as a consultant to Novartis, Pfizer, and Wyeth; has been a site PI for Cubist, Cerexa, and Optimer; and has received honoraria from UpToDate and Merck. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. *BMJ* **2008**; 336:1049–51.
2. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* **2008**; 336:924–6.
3. Guyatt GH, Oxman AD, Kunz R, Vist GE, Falck-Ytter Y, Schunemann HJ. What is “quality of evidence” and why is it important to clinicians? *BMJ* **2008**; 336:995–8.
4. Jaeschke R, Guyatt GH, Dellinger P, et al. Use of GRADE grid to reach decisions on clinical practice guidelines when consensus is elusive. *BMJ* **2008**; 337:a744.
5. Dellinger EP, Evans HL, Van Eaton EG. Hospital Infections Chapter 817. In: Ashley SW, Cance WG, Chen H, Jurkovich GJ, Napolitano LM, Pemberton JH, Riall TS, Swanson JS, Valentine JS, eds. Decker, Ontario, CA: ACS Surgery Online, **2012**; 8–26.
6. Pickering LK. Committee on Infectious Diseases, American Academy of Pediatrics. Antimicrobial agents and related therapy. 26th ed. Elk Grove Village, IL: American Academy of Pediatrics, **2003**.
7. Pascual A, Csajka C, Buclin T, et al. Challenging recommended oral and intravenous voriconazole doses for improved efficacy and safety: population pharmacokinetics-based analysis of adult patients with invasive fungal infections. *Clin Infect Dis* **2012**; 55:381–90.