

2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections^a

Benjamin A. Lipsky,¹ Anthony R. Berendt,² Paul B. Cornia,³ James C. Pile,⁴ Edgar J. G. Peters,⁵ David G. Armstrong,⁶ H. Gunner Deery,⁷ John M. Embil,⁸ Warren S. Joseph,⁹ Adolf W. Karchmer,¹⁰ Michael S. Pinzur,¹¹ and Eric Senneville¹²

¹Department of Medicine, University of Washington, Veterans Affairs Puget Sound Health Care System, Seattle; ²Bone Infection Unit, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, Oxford; ³Department of Medicine, University of Washington, Veterans Affairs Puget Sound Health Care System, Seattle; ⁴Divisions of Hospital Medicine and Infectious Diseases, MetroHealth Medical Center, Cleveland, Ohio; ⁵Department of Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands; ⁶Southern Arizona Limb Salvage Alliance, Department of Surgery, University of Arizona, Tucson; ⁷Northern Michigan Infectious Diseases, Petoskey; ⁸Department of Medicine, University of Manitoba, Winnipeg, Canada; ⁹Division of Podiatric Surgery, Department of Surgery, Roxborough Memorial Hospital, Philadelphia, Pennsylvania; ¹⁰Department of Medicine, Division of Infectious Diseases, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts; ¹¹Department of Orthopaedic Surgery and Rehabilitation, Loyola University Medical Center, Maywood, Illinois; and ¹²Department of Infectious Diseases, Dron Hospital, Tourcoing, France

Foot infections are a common and serious problem in persons with diabetes. Diabetic foot infections (DFIs) typically begin in a wound, most often a neuropathic ulceration. While all wounds are colonized with microorganisms, the presence of infection is defined by ≥ 2 classic findings of inflammation or purulence. Infections are then classified into mild (superficial and limited in size and depth), moderate (deeper or more extensive), or severe (accompanied by systemic signs or metabolic perturbations). This classification system, along with a vascular assessment, helps determine which patients should be hospitalized, which may require special imaging procedures or surgical interventions, and which will require amputation. Most DFIs are polymicrobial, with aerobic gram-positive cocci (GPC), and especially staphylococci, the most common causative organisms. Aerobic gram-negative bacilli are frequently copathogens in infections that are chronic or follow antibiotic treatment, and obligate anaerobes may be copathogens in ischemic or necrotic wounds.

Wounds without evidence of soft tissue or bone infection do not require antibiotic therapy. For infected wounds, obtain a post-debridement specimen (preferably of tissue) for aerobic and anaerobic culture. Empiric antibiotic therapy can be narrowly targeted at GPC in many acutely infected patients, but those at risk for infection with antibiotic-resistant organisms or with chronic, previously treated, or severe infections usually require broader spectrum regimens. Imaging is helpful in most DFIs; plain radiographs may be sufficient, but magnetic resonance imaging is far more sensitive and specific. Osteomyelitis occurs in many diabetic patients with a foot wound and can be difficult to diagnose (optimally defined by bone culture and histology) and treat (often requiring surgical debridement or resection, and/or prolonged antibiotic therapy). Most DFIs require some surgical intervention, ranging from minor (debridement) to major (resection, amputation). Wounds must also be properly dressed and off-loaded of pressure, and patients need regular follow-up. An ischemic foot may require revascularization, and some nonresponding patients may benefit from selected adjunctive measures. Employing multidisciplinary foot teams improves outcomes. Clinicians and healthcare organizations should attempt to monitor, and thereby improve, their outcomes and processes in caring for DFIs.

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^aIt 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: Benjamin A. Lipsky, MD, University of Washington, VA Puget Sound Health Care System, 1660 S Columbian Way, Seattle, WA 98108 (balipsky@uw.edu).

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EXECUTIVE SUMMARY

Diabetic foot infections (DFIs) are a frequent clinical problem. Properly managed, most can be cured, but many patients needlessly undergo amputations because of improper diagnostic and therapeutic approaches. Infection in foot wounds should be defined clinically by the presence of inflammation or purulence, and then classified by severity. This approach helps clinicians make decisions about which patients to hospitalize or to send for imaging procedures or for whom to recommend surgical interventions. Many organisms, alone or in combinations, can cause DFI, but gram-positive cocci (GPC), especially staphylococci, are the most common.

Although clinically uninfected wounds do not require antibiotic therapy, infected wounds do. Empiric antibiotic regimens must be based on available clinical and epidemiologic data, but definitive therapy should be based on cultures of infected tissue. Imaging is especially helpful when seeking evidence of underlying osteomyelitis, which is often difficult to diagnose and treat. Surgical interventions of various types are often needed and proper wound care is important for successful cure of the infection and healing of the wound. Patients with a DFI should be evaluated for an ischemic foot, and employing multidisciplinary foot teams improves outcomes.

Summarized below are the recommendations made in the new guidelines for diabetic foot infections. The expert 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 [1–6] (Table 1). A detailed description of the methods, background, and evidence summaries that support each of the recommendations can be found online in the full text of the guidelines.

RECOMMENDATIONS FOR MANAGING DIABETIC FOOT INFECTIONS

I. In which diabetic patients with a foot wound should I suspect infection, and how should I classify it?

Recommendations

1. Clinicians should consider the possibility of infection occurring in any foot wound in a patient with diabetes (strong, low). Evidence of infection generally includes classic signs of inflammation (redness, warmth, swelling, tenderness, or pain) or purulent secretions, but may also include additional or secondary signs (eg, nonpurulent secretions, friable or discolored granulation tissue, undermining of wound edges, foul odor) (strong, low).

2. Clinicians should be aware of factors that increase the risk for DFI and especially consider infection when these factors are present; these include a wound for which the probe-to-bone (PTB) test is positive; an ulceration present for >30 days; a history of recurrent foot ulcers; a traumatic foot wound; the presence of peripheral vascular disease in the affected limb; a previous lower extremity amputation; loss of protective sensation; the presence of renal insufficiency; or a history of walking barefoot (strong, low).

3. Clinicians should select and routinely use a validated classification system, such as that developed by the International Working Group on the Diabetic Foot (IWGDF) (abbreviated with the acronym PEDIS) or IDSA (see below), to classify infections and to help define the mix of types and severity of their cases and their outcomes (strong, high). The DFI Wound Score may provide additional quantitative discrimination for research purposes (weak, low). Other validated diabetic foot classification schemes have limited value for infection, as they describe only its presence or absence (moderate, low).

II. How should I assess a diabetic patient presenting with a foot infection?

Recommendations

4. Clinicians should evaluate a diabetic patient presenting with a foot wound at 3 levels: the patient as a whole, the affected foot or limb, and the infected wound (strong, low).

5. Clinicians should diagnose infection based on the presence of at least 2 classic symptoms or signs of inflammation (erythema, warmth, tenderness, pain, or induration) or purulent secretions. They should then document and classify the severity of the infection based on its extent and depth and the presence of any systemic findings of infection (strong, low).

6. We recommend assessing the affected limb and foot for arterial ischemia (strong, moderate), venous insufficiency, presence of protective sensation, and biomechanical problems (strong, low).

7. Clinicians should debride any wound that has necrotic tissue or surrounding callus; the required procedure may range from minor to extensive (strong, low).

III. When and from whom should I request a consultation for a patient with a diabetic foot infection?

Recommendations

8. For both outpatients and inpatients with a DFI, clinicians should attempt to provide a well-coordinated approach by those with expertise in a variety of specialties, preferably by a multidisciplinary diabetic foot care team (strong, moderate). Where such a team is not yet available, the primary treating clinician should try to coordinate care among consulting specialists.

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 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 patients 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, 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 or may be closely balanced	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.

9. Diabetic foot care teams can include (or should have ready access to) specialists in various fields; patients with a DFI may especially benefit from consultation with an infectious disease or clinical microbiology specialist and a surgeon with experience and interest in managing DFIs (strong, low).

10. Clinicians without adequate training in wound debridement should seek consultation from those more qualified for this task, especially when extensive procedures are required (strong, low).

11. If there is clinical or imaging evidence of significant ischemia in an infected limb, we recommend the clinician

consult a vascular surgeon for consideration of revascularization (strong, moderate).

12. We recommend that clinicians unfamiliar with pressure off-loading or special dressing techniques consult foot or wound care specialists when these are required (strong, low).

13. Providers working in communities with inadequate access to consultation from specialists might consider devising systems (eg, telemedicine) to ensure expert input on managing their patients (strong, low).

IV. Which patients with a diabetic foot infection should I hospitalize, and what criteria should they meet before I discharge them?

Recommendations

14. We recommend that all patients with a severe infection, selected patients with a moderate infection with complicating features (eg, severe peripheral arterial disease [PAD] or lack of home support), and any patient unable to comply with the required outpatient treatment regimen for psychological or social reasons be hospitalized initially. Patients who do not meet any of these criteria, but are failing to improve with outpatient therapy, may also need to be hospitalized (strong, low).

15. We recommend that prior to being discharged, a patient with a DFI should be clinically stable; have had any urgently needed surgery performed; have achieved acceptable glycemic control; be able to manage (on his/her own or with help) at the designated discharge location; and have a well-defined plan that includes an appropriate antibiotic regimen to which he/she will adhere, an off-loading scheme (if needed), specific wound care instructions, and appropriate outpatient follow-up (strong, low).

V. When and how should I obtain specimen(s) for culture from a patient with a diabetic foot wound?

Recommendations

16. For clinically uninfected wounds, we recommend not collecting a specimen for culture (strong, low).

17. For infected wounds, we recommend that clinicians send appropriately obtained specimens for culture prior to starting empiric antibiotic therapy, if possible. Cultures may be unnecessary for a mild infection in a patient who has not recently received antibiotic therapy (strong, low).

18. We recommend sending a specimen for culture that is from deep tissue, obtained by biopsy or curettage after the wound has been cleansed and debrided. We suggest avoiding swab specimens, especially of inadequately debrided wounds, as they provide less accurate results (strong, moderate).

VI. How should I initially select, and when should I modify, an antibiotic regimen for a diabetic foot infection? (See question VIII for recommendations for antibiotic treatment of osteomyelitis)

Recommendations

19. We recommend that clinically uninfected wounds not be treated with antibiotic therapy (strong, low).

20. We recommend prescribing antibiotic therapy for all infected wounds, but caution that this is often insufficient unless combined with appropriate wound care (strong, low).

21. We recommend that clinicians select an empiric antibiotic regimen on the basis of the severity of the infection and the likely etiologic agent(s) (strong, low).

a. For mild to moderate infections in patients who have not recently received antibiotic treatment, we suggest that therapy just targeting aerobic GPC is sufficient (weak, low).

b. For most severe infections, we recommend starting broad-spectrum empiric antibiotic therapy, pending culture results and antibiotic susceptibility data (strong, low).

c. Empiric therapy directed at *Pseudomonas aeruginosa* is usually unnecessary except for patients with risk factors for true infection with this organism (strong, low).

d. Consider providing empiric therapy directed against methicillin-resistant *Staphylococcus aureus* (MRSA) in a patient with a prior history of MRSA infection; when the local prevalence of MRSA colonization or infection is high; or if the infection is clinically severe (weak, low).

22. We recommend that definitive therapy be based on the results of an appropriately obtained culture and sensitivity testing of a wound specimen as well as the patient's clinical response to the empiric regimen (strong, low).

23. We suggest basing the route of therapy largely on infection severity. We prefer parenteral therapy for all severe, and some moderate, DFIs, at least initially (weak, low), with a switch to oral agents when the patient is systemically well and culture results are available. Clinicians can probably use highly bioavailable oral antibiotics alone in most mild, and in many moderate, infections and topical therapy for selected mild superficial infections (strong, moderate).

24. We suggest continuing antibiotic therapy until, but not beyond, resolution of findings of infection, but not through complete healing of the wound (weak, low). We suggest an initial antibiotic course for a soft tissue infection of about 1–2 weeks for mild infections and 2–3 weeks for moderate to severe infections (weak, low).

VII. When should I consider imaging studies to evaluate a diabetic foot infection, and which should I select?

Recommendations

25. We recommend that all patients presenting with a new DFI have plain radiographs of the affected foot to look for bony abnormalities (deformity, destruction) as well as for soft tissue gas and radio-opaque foreign bodies (strong, moderate).

26. We recommend using magnetic resonance imaging (MRI) as the study of choice for patients who require further (ie, more sensitive or specific) imaging, particularly when soft tissue abscess is suspected or the diagnosis of osteomyelitis remains uncertain (strong, moderate).

27. When MRI is unavailable or contraindicated, clinicians might consider the combination of a radionuclide bone scan and a labeled white blood cell scan as the best alternative (weak, low).

VIII. How should I diagnose and treat osteomyelitis of the foot in a patient with diabetes?

Recommendations

28. Clinicians should consider osteomyelitis as a potential complication of any infected, deep, or large foot ulcer, especially one that is chronic or overlies a bony prominence (strong, moderate).

29. We suggest doing a PTB test for any DFI with an open wound. When properly conducted and interpreted, it can help to diagnose (when the likelihood is high) or exclude (when the likelihood is low) diabetic foot osteomyelitis (DFO) (strong, moderate).

30. We suggest obtaining plain radiographs of the foot, but they have relatively low sensitivity and specificity for confirming or excluding osteomyelitis (weak, moderate). Clinicians might consider using serial plain radiographs to diagnose or monitor suspected DFO (weak, low).

31. For a diagnostic imaging test for DFO, we recommend using MRI (strong, moderate). However, MRI is not always necessary for diagnosing or managing DFO (strong, low).

32. If MRI is unavailable or contraindicated, clinicians might consider a leukocyte or antigranulocyte scan, preferably combined with a bone scan (weak, moderate). We do not recommend any other type of nuclear medicine investigations (weak, moderate).

33. We suggest that the most definitive way to diagnose DFO is by the combined findings on bone culture and histology (strong, moderate). When bone is debrided to treat osteomyelitis, we suggest sending a sample for culture and histology (strong, low).

34. For patients not undergoing bone debridement, we suggest that clinicians consider obtaining a diagnostic bone biopsy when faced with specific circumstances, eg, diagnostic

uncertainty, inadequate culture information, failure of response to empiric treatment (weak, low).

35. Clinicians can consider using either primarily surgical or primarily medical strategies for treating DFO in properly selected patients (weak, moderate). In noncomparative studies each approach has successfully arrested infection in most patients.

36. When a radical resection leaves no remaining infected tissue, we suggest prescribing antibiotic therapy for only a short duration (2–5 days) (weak, low). When there is persistent infected or necrotic bone, we suggest prolonged (≥ 4 weeks) antibiotic treatment (weak, low).

37. For specifically treating DFO, we do not currently support using adjunctive treatments such as hyperbaric oxygen therapy, growth factors (including granulocyte colony-stimulating factor), maggots (larvae), or topical negative pressure therapy (eg, vacuum-assisted closure) (weak, low).

IX. In which patients with a diabetic foot infection should I consider surgical intervention, and what type of procedure may be appropriate?

Recommendations

38. We suggest that nonsurgical clinicians consider requesting an assessment by a surgeon for patients with a moderate or severe DFI (weak, low).

39. We recommend urgent surgical intervention for most foot infections accompanied by gas in the deeper tissues, an abscess, or necrotizing fasciitis, and less urgent surgery for wounds with substantial nonviable tissue or extensive bone or joint involvement (strong, low).

40. We recommend involving a vascular surgeon early on to consider revascularization whenever ischemia complicates a DFI, but especially in any patient with a critically ischemic limb (strong, moderate).

41. Although most qualified surgeons can perform an urgently needed debridement or drainage, we recommend that in DFI cases requiring more complex or reconstructive procedures, the surgeon should have experience with these problems and adequate knowledge of the anatomy of the foot (strong, low).

X. What types of wound care techniques and dressings are appropriate for diabetic foot wounds?

Recommendations

42. Diabetic patients with a foot wound should receive appropriate wound care, which usually consists of the following:

- a. Debridement, aimed at removing debris, eschar, and surrounding callus (strong, moderate). Sharp (or surgical) methods are generally best (strong, low), but mechanical, autolytic, or larval debridement techniques may be appropriate for some wounds (weak, low).
- b. Redistribution of pressure off the wound to the entire weight-bearing surface of the foot (“off-loading”).

While particularly important for plantar wounds, this is also necessary to relieve pressure caused by dressings, footwear, or ambulation to any surface of the wound (strong, high).

- c. Selection of dressings that allow for moist wound healing and control excess exudation. The choice of dressing should be based on the size, depth, and nature of the ulcer (eg, dry, exudative, purulent) (strong, low).

43. We do not advocate using topical antimicrobials for treating most clinically uninfected wounds.

44. No adjunctive therapy has been proven to improve resolution of infection, but for selected diabetic foot wounds that are slow to heal, clinicians might consider using bioengineered skin equivalents (weak, moderate), growth factors (weak, moderate), granulocyte colony-stimulating factors (weak, moderate), hyperbaric oxygen therapy (strong, moderate), or negative pressure wound therapy (weak, low).

Notes

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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, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* **2008**; 336:924–6.
2. Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. *BMJ* **2008**; 336:1049–51.
3. 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.
4. Kish MA. Guide to development of practice guidelines. *Clin Infect Dis* **2001**; 32:851–4.
5. Schunemann HJ, Oxman AD, Brozek J, et al. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. *BMJ* **2008**; 336:1106–10.
6. Guyatt GH, Oxman AD, Kunz R, et al. Incorporating considerations of resources use into grading recommendations. *BMJ* **2008**; 336:1170–3.