Health PEI

ANTIMICROBIAL STEWARDSHIP SUBCOMMITTEE

Empiric Antimicrobial Therapy for Diabetic Foot Infection in Adults

Clinical Presentation

- Not all diabetic foot wounds are infected.
- Presentation of infected wounds may include:
  - Manifestations of local inflammation including erythema, warmth, swelling, tenderness and/or the presence of purulent drainage in an ulcer or sinus tract.
  - Secondary signs of infection including friable or discoloured granulation tissue, undermining of wound edges, foul odour, non-purulent drainage (i.e. dishwater pus) or tissue necrosis.
  - Signs of severe infection including cutaneous bullae, soft tissue gas, tissue necrosis, and/or gangrene.
  - Systemic signs such as fever, chills, hypotension, tachypnea, and tachycardia.

Definitions

Infection Severity	Clinical Presentation
Mild Infections	• Cellulitis <2 cm around ulcer and without involvement of deeper tissues • Non-foot threatening • No signs of sepsis
Moderate Infections	• Cellulitis >2 cm around ulcer or involvement of deeper tissues (e.g., abscess, deep tissue (i.e. tendon spaces)) • Non-foot threatening
Severe Infections	• Signs of sepsis • Foot threatening • Extensive soft tissue involvement or deeper tissues (i.e. bone, joint or tendon spaces) • Pulseless foot

Most Common Organisms

- **Acute onset (i.e. less than 4 weeks):** Gram-positive organisms such as beta-hemolytic *Streptococci* and *Staphylococcus aureus* (consider methicillin resistant *Staphylococcus aureus* if risk factors).
  - MRSA risk factors include – history of MRSA infection or colonization; household contact with a MRSA colonized individual; IV drug use; crowded living conditions (e.g., homelessness, incarcerated persons); and recent travel to or residing in an MRSA endemic region or community.
- **Chronic or more complex/deep tissue infections (i.e. greater than 4 weeks):** Gram-positive and Gram-negative organisms (Enterobacterales such as *E. coli, Proteus spp,* etc.) as well as anaerobes.
- **Common colonizers:** *Pseudomonas aeruginosa* and *Enterococcus* species, especially when isolated from sub-optimally collected specimens. When found on culture coverage is ONLY required if patient is failing initial empiric therapy regimen.

Investigations & Work-up

- **Cultures:** Tissue specimens post-debridement and post-wound cleansing; surface or wound drainage swabs NOT recommended.
- **Imaging:** Recommend starting with plain radiography for bony abnormalities, gas in soft tissue, and radio-opaque foreign bodies. Radionuclide imaging generally not necessary, is not specific and rarely useful.

- **Assess for Osteomyelitis:**
  - In a **clinically infected wound** a positive probe-to-bone (PTB) test is highly suggestive of osteomyelitis.
  - Plain x-ray also recommended. Repeat in 2 weeks, if initial x-ray is normal and there is high probability of osteomyelitis.

Treatment Considerations

- Essential elements for the management of diabetic foot infections include good glycemic control; proper wound care; vascular assessment (evaluate peripheral pulses and check for necrotic tissue); pressure off-loading from affected areas (e.g., aircasting); debridement of devitalized tissue; and smoking cessation.
- **Review prior microbiology results:** consider prior wound microbiology results when selecting an empiric therapy.
- **Assess severity:** treat according to the severity of the infection.
- **Assess for MRSA:** See risk factors listed above.
- **Tailor regimen** based on culture and susceptibility results and patient response.
- **Chronic ulcer with new onset redness without** purulent drainage, wound breakdown, necrosis, or foul odor may be managed with narrow spectrum agents (e.g., cefadroxil, cephalexin, cefazolin) to cover Gram-positive organisms. Clinical follow-up for response to therapy recommended.

Empiric Treatment

Severity	Preferred	Alternatives
Mild • Outpatient therapy recommended	**Wound less than 4 weeks duration:** • cephalexin 500 – 1000 mg PO q6h* **OR** • cefadroxil 500 – 1000 mg PO q12h* True immediate allergy[1] to a beta-lactam at risk of cross reactivity with cephalexin or cefadroxil: • cefuroxime 500 mg PO q12h*	**Wound less than 4 weeks duration:** • clindamycin 300 – 450 mg PO q6h (only if severe delayed reaction[2] to a beta-lactam) MRSA Suspected: • doxycycline 200 mg PO for 1 dose then 100 mg PO q12h **OR** • sulfamethoxazole+trimethoprim 1600+320 mg PO q12h*[,3]
	Wound greater than 4 weeks duration: • cephalexin 500 – 1000 mg PO q6h* AND metroNIDAZOLE 500 mg PO q12h **OR** • cefadroxil 500 – 1000 mg PO q12h* AND metroNIDAZOLE 500 mg PO q12h **OR** • amoxicillin-clavulanate 875/125 mg PO q12h* True immediate allergy[1] to a beta-lactam at risk of cross reactivity with amoxicillin, cephalexin or cefadroxil: • cefuroxime 500 mg PO q12h* AND metroNIDAZOLE 500 mg PO q12h	**Wound greater than 4 weeks duration and MRSA suspected:** • doxycycline 200 mg PO for 1 dose then 100 mg PO q12h AND metroNIDAZOLE 500 mg PO q12h **OR** • sulfamethoxazole+trimethoprim 1600/320 mg PO q12h*[,3] AND metroNIDAZOLE 500 mg PO q12h

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Severity	Preferred	Alternatives
Moderate • Initial management with outpatient parenteral therapy with rapid step- down to oral therapy after 48-72 hours based on patient response recommended	**Wound less than 4 weeks duration:** • ceFAZolin 2000 mg IV q8h* **Alternative for outpatient IV management:** **[**probenecid 1 g PO, followed 10 - 60 min later by ceFAZolin 2000 mg IV**]** repeated q24h*	**Wound less than 4 weeks duration:** • cefTRIAXone 2 g IV q24h (preferred) **OR** • levoFLOXacin 750 mg IV/PO q24h* MRSA suspected: • vancomycin 25 mg/kg IV x 1 dose, then 15 mg/kg IV q12h* (adjust dose to a target trough of 10 to 15 mg/L)
	Wound greater than 4 weeks duration: • ceFAZolin 2000 mg IV q8h* AND metroNIDAZOLE 500 mg PO q12h **Alternatives for outpatient IV management:** **[**probenecid 1 g PO, followed 10 - 60 min later by ceFAZolin 2000 mg IV**]** repeated q24h* AND metronidazole 500mg PO q12h MRSA suspected, then add to above: • vancomycin 25 mg/kg IV x 1 dose, then 15 mg/kg IV q12h* (adjust dose to a target trough of 10 to 15 mg/L)	**Wound greater than 4 weeks duration:** • cefTRIAXone 2 g IV q24h AND metroNIDAZOLE 500 mg PO q12h **OR** • amoxicillin-clavulanate 2000mg IV q8h* **OR** • levoFLOXacin 750 mg IV/PO q24h* AND metroNIDAZOLE 500 mg PO q12h MRSA suspected, then add to above: • vancomycin 25 mg/kg IV x 1 dose, then 15 mg/kg IV q12h* (adjust dose to a target trough of 10 to 15 mg/L)
Severe • Inpatient management recommended • Urgent vascular assessment if pulseless foot	• piperacillin-tazobactam 4.5 g IV q6h* MRSA suspected, then add to above: • vancomycin 25 mg/kg IV x 1 dose, then 15 mg/kg IV q12h* (adjust dose to a target trough of 10 to 15 mg/L)	• meropenem 1000 mg IV q8h* **OR** • levoFLOXacin 750 mg IV q24h* AND metroNIDAZOLE 500 mg IV/PO q12h MRSA suspected, then add to above: • vancomycin 25 mg/kg IV x 1 dose, then 15 mg/kg IV q12h* (adjust dose to a target trough of 10 to 15 mg/L)

***** Dose adjustment required for renal function

[1] True, immediate IgE-mediated allergies include, but are not limited to: anaphylaxis, angioedema, hypotension, bronchospasm, stridor, urticarial, and pruritis.

[2] Severe delayed reactions include, but are not limited to: Stevens-Johnson syndrome, toxic epidermal necrolysis, immune hepatitis, DRESS, serum sickness, hemolytic anemia, or interstitial nephritis

[3] Use caution and consider avoiding in patients with pre-existing renal disease, elderly patients or those receiving an angiotensin-converting-enzyme inhibitor, angiotensin receptor blocker, amiloride or spironolactone due to the risk of hyperkalemia

Duration & Route of Therapy

- Dependent on site, severity, and extent of infection as well as other patient specific factors such as degree of surgical management and vascular status.
- There is no evidence to support continuing antibiotic therapy until the wound is healed in order to either accelerate closure or prevent subsequent infection.

Site of Infection, by Severity or Extent	Route of Administration	Duration of Therapy	Comments
Soft Tissue Only			
Mild	Oral	5 – 7 days	May extend if slow to resolve
Moderate	Initial parenteral with rapid oral step down within 48 to 72 hours	1 – 2 weeks	May extend if slow to resolve
Severe	Initial parenteral, switch to oral when or if possible	2 weeks	May extend if slow to resolve
Deep Tissue	Initial parenteral, switch to oral when or if possible	2 – 4 weeks	Longer duration and IV route recommended for extensive infections involving deeper tissues (e.g., tendon spaces)
Bone or Joint Involvement			
No residual infected tissue (post-amputation)	Parenteral or Oral	2 – 5 days post-amputation	
Residual infected soft tissue (but no infected bone remaining)	Parenteral or Oral	1 – 4 weeks	Longer duration and IV route recommended if severe and infections involving deeper tissues (e.g., tendon spaces)
Residual infected but viable bone (incomplete surgical resection)	Parenteral (oral switch only if high bioavailability and good bone penetration)	4 – 6 weeks	
No surgical debridement or residual dead bone postoperatively	Initial parenteral therapy, then consider oral switch	Greater than or equal to 6 weeks (up to 3 months) depending on evolution and expert opinion.	Consider ID consult

These guidelines are an adaptation of New Brunswick Anti-infective Stewardship Committee **Empiric Antimicrobial Therapy for Diabetic Foot Infection May 2023**

References:

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2. Lipsky BA, Berendt AR, Cornia PB et al. 2012 Infectious Disease Society of America Clinical Practice Guidelines for the Diagnosis and Treatment of Diabetic Foot Infections. CID 2012:54(12):132-173
3. Lipsky BA, Armstrong DG, Citron DM et al. Ertapenem versus piperacillin/tazobactam for diabetic foot infections (SIDESTEP): prospective, randomized, controlled, double-blinded, multicentre trial. Lancet 2005; 366:1695 – 1703
4. Blond-Hill E, Fryters S. Bugs & Drugs An Antimicrobial/Infectious Diseases Reference - App. Accessed February 23, 2023. Alberta Health Services