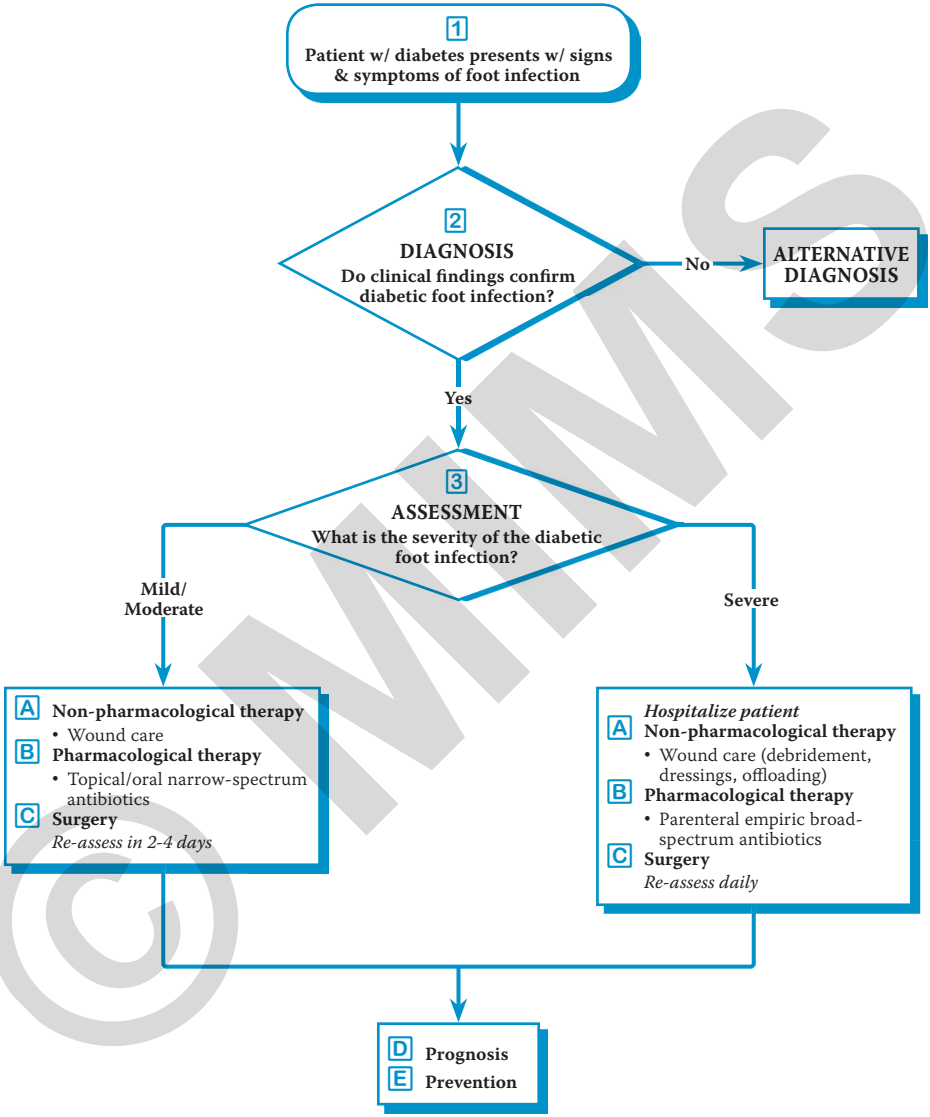
Diabetic Foot Infection (1 of 11)



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1 DIABETIC FOOT INFECTION

- Patients w/ diabetes are prone to have invasion & multiplication of microorganisms in the soft tissue or bone (anywhere below the malleoli) called diabetic foot infection that leads to host inflammatory response that usually results to tissue destruction

Epidemiology

- Based on 2015 prevalence data from the International Diabetes Federation, foot ulcers develop annually in 9.1 to 26.1 million people w/ diabetes worldwide
- An estimated 10% of patients w/ diabetes will have diabetic foot ulcer that precedes more than 80% of non-traumatic amputations
- Lifetime risk of developing a foot ulcer in patients w/ diabetes is 15-25% before but additional data showed between 19% & 34% of persons w/ diabetes will likely to be affected
- Foot infection is very common in patients w/ diabetes, associated w/ the duration of the disease & likelihood of diabetic complications
- Infection of the foot is the most common diabetic complication that would require hospitalization

Etiology

- Staphylococci & streptococci are the most common causative organisms although most diabetic foot infections are polymicrobial
- Copathogens in chronic infections are aerobic Gram-negative bacilli while obligate anaerobes are copathogens in ischemic or necrotic wounds

Pathophysiology

- Most infections typically start w/ a break in the protective cutaneous envelope of the skin that resulted from trauma or neuropathic ulceration
- These open wounds will eventually be colonized by skin flora that in many cases result to infection
  - Due to hyperglycemia-induced advanced glycation end-products, persistent inflammation & apoptosis the wounds in the feet of patients w/ diabetes become chronic
- The following factors predispose the patient w/ diabetes to have foot infection:
  - Deep wound that is long-standing or recurrent or caused by trauma
  - Ill-defined diabetes-related immunological perturbations related to neutrophil function
  - Chronic renal failure
- Spread of infection
  - Microorganisms spread proximally to the subcutaneous tissues including fascia, tendons, muscles, joints & bone
    - This is due to the anatomy of the foot which is divided into several rigid but intercommunicating compartments
  - The infection induces inflammatory response that causes compartmental pressure to exceed capillary pressure, resulting to ischemic tissue necrosis
  - The tendons within the compartments cause proximal spread of infection that usually moves from higher to lower-pressure areas
  - Bacterial virulence may play a role in these complex infections
    - Isolate strains of *Staphylococcus aureus* from clinically non-infected ulcers have been shown to have a lower virulence potential than those that are infected

Signs & Symptoms

- It is not common in patients w/ diabetic foot infection to have systemic symptoms (eg fever & chills), marked leukocytosis or major metabolic disturbance but its presence will indicate a more severe, potentially limb or even life-threatening infection
- Patient may also present w/ symptoms of vascular disease (eg claudication, leg fatigue) & neuropathy (numbness, burning, pain)

Risk Factors

- Patients w/ diabetes who have the following characteristics are predisposed to foot ulcer that leads to infection & ultimately lower extremity amputation:
  - Repetitive stress over an area that is subject to high vertical or shear stress in patients w/ peripheral neuropathy
  - Impaired immunity
  - Peripheral artery disease (PAD)
  - Positive probe-to-bone test
  - Presence of foot ulcer for >30 days
  - Foot wound that is traumatic
  - Previous ulceration or amputation
  - Structural deformity
  - Limited joint mobility
  - Renal insufficiency
  - History of walking barefoot
  - Microvascular complications, peripheral neuropathy w/ loss of protective sensation (LOPS)
  - High levels of hemoglobin A1c
  - Onychomycosis
  - Visual impairment
  - Preulcerative corn or callus
  - Cigarette smoking

1 DIABETIC FOOT INFECTION (CONT'D)

International Working Group on the Diabetic Foot (IWGDF) Risk Classification System

- The IWGDF categorized the risk of patients w/ diabetes for foot ulceration

Category	Ulcer Risk	Characteristics
0	Very low	LOPS & PAD absent
1	Low	LOPS or PAD present
2	Moderate	LOPS & PAD *or* LOPS & foot deformity *or* PAD & foot deformity
3	High	LOPS or PAD *plus* ≥1 of the following: • History of foot ulcer • Lower extremity amputation • End-stage renal disease

2 DIAGNOSIS

Diabetic Foot Soft Tissue Infection

History

- Inquire about the following: Previous history of angioplasty or vascular surgery, renal disease, retinopathy, history of ulceration or amputation, Charcot foot & smoking history

Physical Examination

- Inspect the skin & palpate leg & feet pulses, check for foot deformities & assess patient neurologically w/ a 10-g monofilament test along w/ either pinprick, vibration or temperature assessment
  - Ankle-brachial pressure index should be obtained in patients w/ signs & symptoms of vascular disease
- Skin temperature of the foot, assessed as warmth, is the first indication of inflammation in an insensate foot & may be the first sign of acute Charcot neuroarthropathy resulting from the LOPS in the foot

Clinical Findings

- Clinical findings of local & systemic signs & symptoms of inflammation or purulence is essential in the diagnosis of diabetic foot infection
  - Inflammation is the presence of redness (erythema or rubor), warmth (calor), pain or tenderness (dolor), induration (swelling or tumor)
- Patients w/ diabetes presenting w/ wound in the foot should be evaluated at 3 levels:
  - The patient as a whole (eg cognitive, metabolic, fluid status)
  - The affected foot or limb (eg presence of neuropathy, vascular insufficiency)
  - The infected wound
- If signs of local & systemic infection are diminished, the following secondary features can be taken into consideration:
  - Presence of necrosis
  - Friable or discolored granulation tissue
  - Non-purulent secretions
  - Fetid odor
  - Failure of a properly treated wound to heal
- Signs & symptoms of arterial ischemia, venous insufficiency, presence of protective sensation, & biomechanical problems should also be assessed

Lab Findings

- Leukocytosis & elevated erythrocyte sedimentation rate are highly suggestive of a diabetic foot infection, but their absence does not rule it out

Histological & Microbiological Examinations

- Positive results on both histological & microbiological examinations are essential in the diagnosis of bone infection
- An aseptically obtained bone sample from the base of the debrided wound is used for microbiological examination
  - A deep swab can be done if bone sample cannot be obtained
- Results of microbiological & histological examination may provide useful information on the choice of antibiotic treatment
- To determine the causative organisms & antibiotic sensitivities, wound cultures are done
- During evaluation, wounds should be inspected carefully, debrided of devitalized & necrotic tissue, & probed
  - Cultures of superficial swabs are discouraged because these often yield contaminants
  - Curettage from the base of an appropriately debrided ulcer or deep tissue specimens obtained by biopsy yield true pathogens & more accurate results

2 DIAGNOSIS (CONT'D)

Diabetic Foot Osteomyelitis

- Serious complication of diabetic foot infection that is found in approximately 50-60% of patients hospitalized w/ diabetic foot infection & approximately 10-20% of apparently less severe infections in the ambulatory setting
- It is the infection of the bone of the forefoot & develops by contiguous spread from overlying soft tissue, penetration through the cortical bone & into the medullary cavity
- Foot ulcers that have the following characteristics are suspected to have diabetic foot osteomyelitis:
  - Large (>2 cm) or deep (>3 mm), or that overlay a bony prominence
  - Chronic that do not heal even w/ appropriate wound care
  - Visible or palpable on probing
- Diabetic foot osteomyelitis is suspected when the clinician found an ulcer that lies over a bony prominence especially when it does not heal despite adequate off-loading or when the toe looks erythematous & indurated ("sausage toe")
- Clinical presentation varies w/ site involved, the extent of infected & dead bone, the presence of any associated abscesses or soft tissue involvement, the causative organism(s) & the adequacy of limb perfusion

Probe-to-Bone Test

- Performed in an infected wound as it is a useful clinical diagnostic tool in diagnosing diabetes foot osteomyelitis when done correctly & interpreted appropriately
- When the blunt sterile metal probe gently inserted through a wound strikes bone (detected by its hard, gritty feel), it denotes positive result that has a high likelihood for diagnosis of diabetic foot osteomyelitis
- A negative test in a patient who has low risk for osteomyelitis likely rules out the diagnosis

Bone Biopsy

- A definite diagnosis of osteomyelitis requires both the presence of histological findings consistent w/ bone infection & the isolation of bacteria from aseptically obtained bone sample
- During a surgical intervention or by percutaneous biopsy, a bone sample is obtained
  - Specimen is obtained by going through intact uninfected skin
- In cases of negative culture or one growing only commensal skin flora, it is helpful to have histological examination of bone specimens in interpreting the results of culture
- Bone specimens are processed for both culture & histopathology
- Infected bone usually has inflammatory cells (granulocytes early & mononuclear cells later), while the histomorphology of uninfected bone is normal in diabetic patients, including those w/ neuropathy or peripheral arterial disease
- It is not advised to use results of soft tissue or sinus tract specimens for selecting antibiotic therapy for osteomyelitis as they do not accurately reflect bone culture results
- Bone culture is not always needed when diabetic foot osteomyelitis is suspected, but clinicians should consider this procedure when diagnosis of osteomyelitis remains uncertain despite clinical & imaging evaluations, in cases where data from soft tissue cultures are non-informative, when the infection has failed to respond to initial empiric antibiotic therapy or when considering an antibiotic regimen w/ a higher potential for selecting resistant organisms

Blood Tests

- A highly elevated erythrocyte sedimentation rate increases the likelihood of having diabetic foot osteomyelitis
- C-reactive protein, procalcitonin or blood leukocyte count may be suggestive of diabetic foot osteomyelitis
- A combination of laboratory & clinical findings improves the diagnostic accuracy for diabetic foot osteomyelitis
- Infectious Diseases Society of America (IDSA) had suggested to do PTB test for any diabetic foot infection w/ an open wound to help diagnose or exclude diabetic foot osteomyelitis

Imaging Studies

- Plain radiographs show bony changes w/ presence of gas in the soft tissues or radiopaque foreign bodies in patients w/ diabetic foot osteomyelitis
  - It has low sensitivity & specificity in differentiating osteomyelitis from Charcot changes
- MRI is used when a diagnosis of diabetic foot osteomyelitis is still uncertain & there is a suspicion of soft tissue abscess
  - MRI findings of low focal signal intensity on T1-weighted images, high focal signal on T2-weighted images & high bone marrow signal in short tau inversion recovery sequences are suggestive of diabetic foot osteomyelitis
  - Consider a white blood cell-labelled radionuclide scan or possibly SPECT/CT or 18 F-FDG PET scan when MRI is not available or contraindicated
- The main problems in diagnosing osteomyelitis are that there is a delay in the ability to detect bony changes in early infection on plain radiographs, while later when bony changes occur, it may be difficult to distinguish on imaging studies from those related to Charcot neuroosteoarthropathy
  - Long-standing diabetic foot infections or ulcers are more likely to show underlying bony abnormalities because it takes weeks for bone infection to become radiographically apparent

3 ASSESSMENT OF SEVERITY

- Identifying the severity of infection guides the clinician w/ the choice & route of administration of empiric antibiotic regimen, helps to determine the indication for hospitalization, the potential necessity & time of foot surgery & the likelihood of having an amputation
- In classifying foot infection, the following should be considered:
  - Depth & extent of the tissues involved at initial evaluation
  - Adequacy of arterial perfusion & the possible need for revascularization
  - Systemic toxicity
- The Infectious Diseases Society of America (IDSA) & IWGDF classification of diabetic infection (2012):
  - Uninfected - No signs of infection or no systemic or local symptoms
  - Infected (Mild) - superficial & limited in size & depth:
    - Presence of at least 2 of the following:
      - Local swelling or induration
      - Erythema >0.5-≤2 cm around the wound
      - Local tenderness or pain
      - Local warmth
      - Purulent discharge
  - Other causes of skin inflammatory response have been excluded
    - Infection involves only the skin & subcutaneous tissues
    - No signs or symptoms of systemic infection
  - Infected (Moderate) - deeper or more extensive
    - Infection involves structures deeper than the skin & subcutaneous tissues (eg bone, joint, tendon, muscle)
    - Erythema >2 cm around the wound
    - No signs or symptoms of systemic infection
  - Infected (Severe) - accompanied by systemic signs or metabolic perturbations
    - Presence of systemic inflammatory response syndrome as manifested by at least 2 of the following:
      - Temperature >38°C or <36°C
      - Heart rate >90 beats/minute
      - Respiratory rate >20 breaths/minute or $PaCO_2$ < 4.3 kPa
      - White blood cell count >12,000 or <4,000/mm^3 or >10% immature forms
- Diabetic foot ulcers can also be classified using the Wagner Diabetic Foot Ulcer Classification system that is based on the depth of penetration, the presence of osteomyelitis or gangrene & the extent of tissue necrosis:
  - Grade 0 - Absence of open lesions or ulcer but may have deformity or cellulitis
  - Grade 1 - Diabetic ulcer that is superficial (partial or full thickness)
  - Grade 2 - Ulcer is extended to the ligament, tendon, joint capsule, or deep fascia w/ no abscess or osteomyelitis
  - Grade 3 - Ulcer is deep w/ abscess, osteomyelitis or joint sepsis
  - Grade 4 - Presence of gangrene localized to portion of forefoot or heel
  - Grade 5 - There is extensive gangrene that involves the entire foot
- One of the widely used classification in clinical trials & diabetic foot centers is the University of Texas Wound Classification which assesses wound depth, presence of infection & clinical signs of extremity ischemia:

	GRADE 0	GRADE 1	GRADE 2	GRADE 3
STAGE A	Completely epithelialized preulcerative or postulcerative lesion	Wound is superficial that does not involve bone, capsule or tendon	Wound that penetrates the tendon or capsule	Wound that penetrates the bone or joint
STAGE B	Presence of infection			
STAGE C	Presence of ischemia			
STAGE D	Presence of both infection & ischemia			

  - Increase in wound grade & stage is less likely to heal without revascularization or amputation
- To accurately assess a diabetic foot wound, it usually needs to be debrided of any callus & necrotic tissue to fully visualize the wound

3 ASSESSMENT OF SEVERITY (CONT'D)

- Findings that suggest serious diabetic foot infection & potential indications for hospitalization:
  - Wound that penetrates to subcutaneous tissue w/ cellulitis that is extensive (>2 cm) , distant from ulceration or rapidly progressive
  - Wound has severe inflammation or induration, crepitus, bullae, discoloration, necrosis or gangrene, ecchymoses or petechiae, new anesthesia
  - Infection presents as acute onset/worsening or rapidly progressive
  - Presence of fever, chills, hypotension, confusion, volume depletion
  - Laboratory findings of leukocytosis, elevated C-reactive protein or erythrocyte sedimentation rate, severe/worsening hyperglycemia, acidosis, new/worsening azotemia, electrolyte abnormalities
  - Presence of a foreign body (accidental or surgically implanted), puncture wound, deep abscess, arterial or venous insufficiency, lymphedema, immunosuppressive illness or treatment
  - There is still infection progression while on apparently appropriate antibiotic & supportive therapy
- Findings that suggest hospitalization is indicated:
  - Severe infection
  - Metabolic or hemodynamic instability
  - Intravenous therapy needed
  - Diagnostic testings needed that are not available as outpatient
  - Presence of critical foot ischemia (it may indicate diminishing clinical findings & worsening prognosis)
  - Failure of outpatient management
  - Surgical procedures (more than minor) required
  - Patient is noncompliant w/ outpatient-based treatment
  - Need for more complex dressing changes than patient/caregivers can provide
  - Need for careful continuous observation

PRINCIPLES OF THERAPY

- Management of diabetic foot ulcer in patients w/ diabetes needs an interdisciplinary approach to address glycemic control, infection, offloading of high-pressure areas, lower extremity vascular status & local wound care
- Mild diabetic foot infections are treated in outpatient setting w/ oral antibiotics, wound care & pressure offloading
- Selected patients w/ moderate diabetic foot infections & all patients w/ severe infections will be given intravenous antibiotics & to be evaluated for possible surgical intervention while staying in the hospital
- For diabetic foot wounds that have no evidence of soft tissue or bone infection, antibiotic therapy is not required
- For infected wounds, obtain a post-debridement specimen (preferably of tissue) for aerobic & anaerobic cultures

A NON-PHARMACOLOGICAL THERAPY

Wound Care

- Essentials of wound care in a diabetic patient w/ foot wound include:
  - Debridement
  - Offloading
  - Selection of dressings
- Debridement is the removal of debris, eschar, surrounding callus or devitalized tissue that may impede wound healing & foster infection
  - It is essential in nonischemic wound to have regular debridement of nonviable tissue
  - Generally, sharp/surgical method of debridement is used but mechanical, autolytic or larval debridement techniques may be appropriate for some wounds
- Offloading is the redistribution of pressure off the wound to the entire weightbearing surface of the foot
  - This may be achieved by using temporary footwear until the ulcer heals & foot character stabilizes
  - Pressure-reducing devices (eg removable & irremovable cast walkers & total contact casting) have demonstrated efficacy in plantar surface ulcers
  - Pressure-relief devices that cannot be removed are associated w/ faster healing ulcers than are removable devices as per clinical trials
  - Consultation w/ surgeon skilled in foot surgery is suggested to address bony deformities that prevent the fitting of appropriate footwear &/or offloading of pressure-related ulcers

A NON-PHARMACOLOGICAL THERAPY (CONT'D)

Wound Care (Cont'd)

- Appropriate selection of dressings that allow for moist wound environment & control of excess exudation is necessary in wound care
  - In general, dry wound needs topical treatment that adds moisture while diabetic foot ulcers w/ heavy exudate need a dressing that absorbs moisture
  - Dressings should be changed at least daily, both to apply a clean wound covering & to allow careful examination of the wound for infection
  - Povidone iodine impregnated wound dressings may be considered for infected diabetic foot ulcers
- There is mixed evidence supporting the use of hyperbaric oxygen therapy as an adjunctive treatment to standard diabetic foot wound care

B PHARMACOLOGICAL THERAPY

- Selection of specific antibiotic therapy should be based on:
  - Causative pathogens that are likely or proven
  - Susceptibility to the antibiotic
  - Clinical severity of the infection
  - Evidence of efficacy for diabetic foot infection
  - Costs
- Infected diabetic foot wound that has failed antimicrobial therapy is usually associated w/ progressive tissue destruction & poor wound healing
- The most common pathogens when infection first begins are *Staphylococcus aureus, Streptococcus agalactiae,* & *Streptococcus pyogenes*
  - Anaerobic & Gram-negative pathogens can play a role in the process w/ time & the presence of devitalized tissue that leads to polymicrobial infections
- Parenteral therapy is initially administered in some moderate infections & most severe infections then switch to oral therapy when the infection is responding
- Empiric antibiotic regimen should cover the most common infecting organisms, usually active against standard strains of staphylococci & streptococci, & then be modified according to infection severity & available clinical or microbiological information
- For mild infections, oral narrow-spectrum antibiotics w/ activity against aerobic Gram-positive organisms are preferred to be given for 1-2 weeks
  - It is not advisable to give prolonged antibiotic treatment (eg >14 days) in mild soft tissue diabetic foot infection
- Anti-anaerobic empiric therapy is given for necrotic, gangrenous or foul-smelling wounds that also require debridement
- Combination therapy is given when:
  - The presumed or proven cause of the infection is >1 microorganism
  - The pathogen has a high potential for developing resistance
  - Selecting an agent to which resistance may quickly develop when used alone
- Once the results of the culture & sensitivity tests are available, consider changing to a more specific regimen that targets just the isolated pathogens
- Generally, antibiotic therapy can be discontinued when signs & symptoms of infection have resolved, even if the wound has not healed

Suggested Empiric Antibiotic Therapy

Infection Severity	Recommended Antibiotics
Mild (Gram-positive cocci w/ or without methicillin-resistant *Staphylococcus aureus*)	Co-amoxiclav, Cefdinir, Cephalexin, Clindamycin, Dicloxacillin, Doxycycline, Levofloxacin, Linezolid, Minocycline, Co-trimoxazole
Moderate to Severe (Gram-positive cocci; Gram-negative rods; anaerobes w/ or without multidrug-resistant organisms	Sultamicillin, Cefoxitin, Ceftriaxone, Clindamycin/ fluoroquinolones, Daptomycin, Ertapenem, Imipenem/cilastatin, Linezolid, Levofloxacin, Moxifloxacin, Piperacillin/tazobactam, Ticarcillin/ clavulanate, Tigecycline, Vancomycin
Modify treatment regimen for optimal therapy once culture & susceptibility results are available	

B PHARMACOLOGICAL THERAPY (CONT'D)

Diabetic Foot Osteomyelitis

- When treating diabetic foot osteomyelitis, the following should be considered:
  - Anatomic site of infection
  - Local vascular supply
  - Soft tissue & bone destruction extent
  - Presence of any systemic signs of infection
  - Patient's preference for treatment
- Antimicrobial agent should be based on the results of a bone culture, especially because of the need for long-duration therapy
- When empiric therapy is needed, therapy usually covers *S. aureus* as it is the most common pathogen, but the patient's history or culture results may suggest a need for broader coverage
- Antibiotic therapy of 6 weeks duration is recommended in patients w/ diabetic foot osteomyelitis that did not undergo resection of the infected foot while 1-week duration for those who have all infected bone resected
- Remission rate does not appear to increase when post-debridement antibiotic therapy is extended beyond 6 weeks or if IV treatment is given longer than a week
- Long-term suppressive therapy or intermittent short courses of treatment of recrudescent symptoms can be the appropriate approach for patients who have apparently incurable infection
- Patients w/ diabetic foot ulcers may also be given recombinant human epidermal growth factor as data have shown that it enhances wound healing & shortens healing time

C SURGERY

- Cornerstone of treatment of many deep soft tissue infections & early intervention; may be associated w/ better outcomes
- If the patient has gas gangrene, abscess or necrotizing fasciitis, compartment syndrome or systemic sepsis, immediate surgery is recommended
- Goal of surgical treatment is to drain any deep pus & to minimize tissue necrosis by decompressing foot compartments & to remove devitalized & infected tissue
- Diabetic foot infection surgical intervention should be done by a surgeon w/ thorough knowledge of the anatomy of the foot & the path in which infection spreads through its fascial planes
- Surgical interventions that should be performed in a timely manner may include:
  - Abscess incision & drainage
  - Extensive debridement of necrotic & devitalized tissue
  - Resection
  - Amputation
  - Revascularization
- Incision & drainage is the initial surgical intervention in non-urgent infections
  - If the patient is not responding, further resection is needed
- Debriding necrotic tissue of wound that has a dry eschar, especially in an ischemic foot, should be avoided because often this will resolve w/ autoamputation
- Revascularization, either endovascular or open bypass, is considered for a severely ischemic infected limb in patients w/ diabetes
- Bone resection & amputation is often essential when there is extensive soft tissue necrosis or to provide a more functional foot
- A specimen of bone should be obtained at the time of surgery for analysis by culture & histopathology
- Major amputation is necessary in the following limb situations:
  - Non-viable
  - Affected by a potentially life-threatening infection (eg gas gangrene or necrotizing fasciitis)
  - Functionally useless
  - Prevention of secondary complications

D PROGNOSIS

- Mild diabetic foot infections' signs & symptoms that have been given appropriate treatment almost always resolve without the need for amputation
  - In >80% of cases, long-term control of infection is achieved
- Infections involving deep soft tissue structures or bone often have less favorable outcome & many require surgical debridement, bone resection or partial amputation
- Lower extremity amputation rates may reach 50-60% in patients w/ extensive infection or in medical centers w/ limited expertise or resources
- For hospitalized patients, even in expert centers, almost half of the patients have poor outcomes or will have amputations
- Most amputations can be foot sparing (ie below the malleoli) in the hands of any experienced surgeon
- Presence of limb or foot ischemia can synergize w/ infection that worsen prognosis
- For a patient w/ diabetic foot ulcer, the risk of death at 5 years is 2.5 times as high as the risk for a patient who does not have a foot ulcer
- There is a high likelihood that having had one foot infection can also infect the other
  - There is a 20-30% recurrence of diabetic foot infection especially in those w/ underlying osteomyelitis
- Evidence of remissions includes a decrease in the erythrocyte sedimentation rate, destroyed bone reconstitution on plain radiograph & healing of any overlying soft tissue wound
- Early signs of skin damage, ie abundant callus, blistering or hemorrhage, are among the strongest predictors of ulcer recurrence
- Within a year after ulcer healing, there is roughly 40% chance of having recurrence, almost 60% in 3 years & 65% within 5 years

E PREVENTION

Foot Care

- Educate patient on proper foot care
  - Foot ulcers should be detected & treated early; encourage daily foot inspection
- Have a regular foot examination & evaluation of amputation risk at intervals of 1-3 months
- The IWGDF recommends the following frequency of clinic visits for the prevention of foot ulcers based on ulcer risk:
  - Very low: Annually
  - Low: Every 6-12 months
  - Moderate: Every 3-6 months
  - High: Every 1-3 months
- Have a regular callus debridement
- The use of professionally fitted therapeutic footwear is recommended for the following:
  - High-risk patients w/ diabetes
  - Diabetic patients w/ severe neuropathy, foot deformities or amputation history
  - Patients w/ healed diabetic foot ulcer
- Pressure-relief devices that cannot be removed are associated w/ faster healing ulcers than are removable devices as per clinical trials
- If indicated, consider referring patients to foot care specialists for preventive care & further vascular evaluation

Lifestyle Modification

- Glycemic & blood pressure control
- Smoking cessation

Further Assessment

- Evaluate surgical interventions as indicated
- In selected patients w/ an active foot ulcer that has not responded to nonsurgical treatment, foot surgery can effectively reduce the risk of recurrent plantar & nonplantar ulcers
- Specialist referral should be considered in patients needing further management of deformities, peripheral artery disease & neuropathy

Dosage Guidelines

OTHER ANTIBIOTICS

Drug	Dosage	Remarks
Clindamycin	**Mild/moderate infections:** 300 mg PO 6-8 hrly for 7-14 days	**Adverse Reactions** • GI effects (abdominal pain, nausea, vomiting, diarrhea, esophagitis, esophageal ulcer, jaundice); Dermatological effects (maculopapular rash, urticaria) Other effects (transient neutropenia & eosinophilia, anaphylactoid reactions, dysgeusia, thrombophlebitis) **Special Instructions** • Discontinue if mild cases of pseudomembranous colitis occur • Use w/ caution in patients w/ diarrhea subsequent to the administration of antibacterial agents • Liver & kidney function tests must be performed in prolonged therapy
Linezolid	600 mg PO/IV 12 hrly for 10-14 days	**Adverse Reactions** • GI effects (diarrhea, nausea, vomiting, constipation, dyspepsia, abdominal pain, tongue discoloration); Other effects (headache, insomnia, rash, dizziness, fever, oral & vaginal moniliasis, hypertension, pruritus) **Special Instructions** • Monitor platelet counts for patients w/ preexisting myelosuppression, increased risk of bleeding, receiving concomitant medications that may decrease platelet count • Contraindicated in patients taking MAOIs, w/ uncontrolled hypertension, pheochromocytoma, thyrotoxicosis • Not to be taken by patients taking MAOIs, sympathomimetic agents, dopaminergic agents, SSRIs, TCAs, serotonin 5-HT1 receptor agonists, Meperidine or Buspirone

OTHER BETA-LACTAMS

Drug	Dosage	Remarks
Ertapenem	1 g IV 24 hrly IV infusion over 30 min ***or*** 1 g IM 24 hrly	**Adverse Reactions** • GI effects (diarrhea, nausea, vomiting); Other effects (infused vein complication, phlebitis/thrombophlebitis, infusion site erythema/pain/swelling, rash) **Special Instructions** • Use w/ caution in patients w/ CNS disorders, compromised renal function, whose seizures are well controlled on Valproic acid or Divalproex Na • Before initiating therapy, careful inquiry should be made concerning previous hypersensitivity to penicillins, cephalosporins, other beta-lactams & other allergens • Prolonged use may cause overgrowth of nonsusceptible organisms, pseudomembranous colitis

OTHER DERMATOLOGICALS

Drug	Dosage	Remarks
Recombinant human epidermal growth factor	Apply topically on the ulcer area 12 hrly x 15-20 wks	**Special Instructions** • Avoid use in immunocompromised patients & in patients w/ known hypersensitivity to its components • Clean ulcer area prior to application of the medication

All dosage recommendations are for non-pregnant & non-breastfeeding women, & non-elderly adults w/ normal renal & hepatic function unless otherwise stated.
Not all products are available or approved for above use in all countries.
Products listed above may not be mentioned in the disease management chart but have been placed here based on indications listed in regional manufacturers' product information.

Specific prescribing information may be found in the latest MIMS.

Dosage Guidelines

PENICILLINS

Drug	Dosage	Remarks
Amoxicillin/ clavulanic acid (Co-amoxiclav, Amoxicillin/ clavulanate)	1.2 g IV 8 hrly IV inj for 3-4 min or IV infusion over 30 min **Severe infection:** 1.2 g IV 6 hrly	**Adverse Reactions** • Dermatological effects (maculopapular or urticarial rashes, urticarial reactions, erythematous maculopapular eruptions); GI effects (diarrhea, nausea, vomiting); Hepatic effects (transient elevations of ALT & AST transaminases, bilirubinemia, abnormal hepatic function, jaundice); Other effects (pseudomembranous colitis, hemolytic anemia, thrombocytopenia, eosinophilia, leukopenia) **Special Instructions** • Discontinue if skin rashes or superinfection occur • Use w/ caution in patients w/ lymphatic leukemia or possible HIV infection, taking aminoglycosides • Monitor *Clostridium difficile*-associated diarrhea
Ampicillin/ sulbactam (Sultamicillin: Pro-drug of Ampicillin & sulbactam)	Slow IV inj over at least 10-15 min/IV infusion over 15-30 min/deep IM inj **Mild infection:** 1.5 g 24 hrly **Moderate infection:** 1.5-6 g 24 hrly **Severe infection:** 12 g 24 hrly	
Piperacillin/ tazobactam	3.375 g 6 hrly IV infusion over 30 min	

QUINOLONES

Drug	Dosage	Remarks
Moxifloxacin	400 mg IV infusion 24 hrly then 400 mg PO 24 hrly for 7-21 days	**Adverse Reactions** • GI effects (diarrhea, nausea, vomiting, abdominal pain, dyspepsia); Musculoskeletal effects (back pain, arthralgia); CVS effects (tachycardia, hypertension); CNS effects (headache, dizziness, insomnia, convulsion); Other effects (hematological changes, taste perversion, visual disturbances, rash, pruritus) **Special Instructions** • Use w/ caution in patients w/ seizures, know or suspected CNS disorders, severe hepatic impairment, known QT interval prolongation or patients on concomitant medication known to prolong the QTc interval • Avoid extensive UV exposure

SURGICAL DRESSINGS & WOUND CARE

Drug	Dosage	Remarks
Povidone-iodine	**Antiseptic soln** Apply sufficient amount to skin at least once or as directed **Powd spray** Spray about 6-10 inches away from the area to be treated 3-4 hrly	**Adverse Reactions** • Rarely, allergic skin reactions (itchiness, redness, small blisters) • Very rarely, acute generalized allergic reactions (drop in BP, difficulty in breathing, swelling of the skin & mucosa) **Special Instructions** • Shake powd spray well before applying • If local irritation occurs, discontinue use • Contraindicated in patients w/ hyperthyroidism, thyroid carcinoma, goiter, childn <2 yr

All dosage recommendations are for non-pregnant & non-breastfeeding women, & non-elderly adults w/ normal renal & hepatic function unless otherwise stated.

Not all products are available or approved for above use in all countries.

Products listed above may not be mentioned in the disease management chart but have been placed here based on indications listed in regional manufacturers' product information.

Specific prescribing information may be found in the latest MIMS.

Please see the end of this section for the reference list.