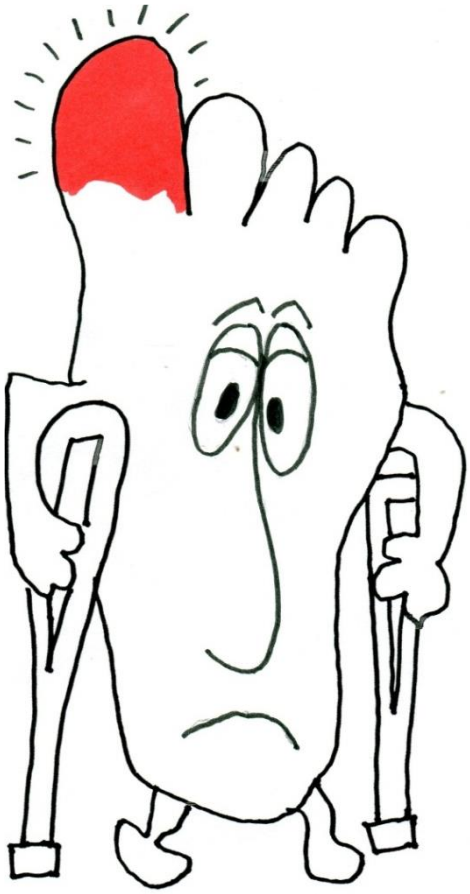
Diabetic Foot Infection for the Houseofficer

Managing Diabetic Foot infection—a Manual for Housestaff and Clinicians



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Infectious disease specialists are used to seeing patients with this condition and are rightly cautious about its' potential for harm. While it might appear fairly straightforward ("this is just a simple cellulitis!), the diabetic foot infection (DFI) remains a challenging problem—despite our best efforts, patients sometimes end up losing life or limb.

The importance of this diabetic foot infection can hardly be overestimated. As you see diabetic patients, keep in mind the following facts [1]:

- ✓ In the United States, twelve million men (11.2% of all men 20 years and older) and 11.5 million women (10.2% of all women 20 years and older) suffer from diabetes.
- ✓ Diabetes in this country alone costs $200 billion annually. This figure includes direct medical costs for medication, surgery and hospitalization—as well as the indirect costs associated with lost productivity, early retirement, and disability.
- ✓ About 60-70% of people with diabetes have mild to severe forms of nervous system damage, putting them at risk for subsequent diabetic foot infection and limb loss.
- ✓ In the United States, there are approximately *86,000* lower-limb amputations on diabetics a year—worldwide, there are over *one million* amputations each year!
- ✓ Experts believe nearly half of all amputations could have been prevented with appropriate examinations and education.

As you will see, nothing is straightforward about diabetic foot infection and the proper management of certain complications is not always completely clear. Nevertheless, a consistent approach—utilizing a few simple principles—will lead to a favorable outcome in the majority of cases. While we can't provide all the answers, I hope this booklet allows you to feel comfortable in managing these sometimes-difficult cases.

Source: [1]www.randomhistory.com (accessed 2/12/11)

How to read this booklet—a quick guide for the uninitiated

Unfortunately, despite the availability of "guidelines", many questions about proper management of these infections remain unanswered and the best course of management is not always clear. This brief booklet is designed to give you an approach to identify and managing these sometimes extremely challenging infections. It is divided into the following sections:

1. Ten things you need to know about diabetic foot infection

This indeed should be "read first"—it will give you a quick overview of "what to do" when confronted with a DFI patient. As you get more deeply involved with the case, subsequent sections will help answer some of the more complicated questions.

2. Pedal pointers…Clues on physical examination

Know how to perform a proper physical examination in order to recognize—and document—important physical findings.

3. X-ray visions…The radiology of diabetic foot infection

From plain films to MRI—here are the skills you need to properly judge the possibility of osteomyelitis and related complications.

4. Infection in the diabetic foot—microbiology and management

What bacteria do you really need to cover and what is the optimal antibiotic therapy? This section will give you an overview of DFI microbiology and initial empiric antimicrobial treatment.

5. Flow to toe…when to call in the vascular surgeon

When healing or response is slow, consider the possibility of poor vascular supply—here is a simple approach to patient evaluation outlining vascular interventions that can help your patient heal.

6. Saved by the scalpel…surgical management of the diabetic foot

Antibiotics aren't always enough—this chapter reviews the "surgical" approach to DFI including the need for specific, selected amputation.

7. Podiatric imposters—diabetic foot infection mimics

Things are always as they appear—there are a number of conditions that "mimic" DFI and can fool the unwary. This section examines the most common "mimics" and provides advice about early diagnosis and therapy.

8. A "foot on fire"—Charcot foot

This is such an important "mimic" that it gets its' own chapter—learn how to recognize and treat Charcot osteolysis to minimize the chance of long term disability.

9. "Special situations"—diabetic foot dilemmas

Not everything fits into a neat category—this section highlights a number of "specialized" problems that occur with the diabetic foot including puncture wounds, heel ulcers and the "the black and blue toe".

10. Managing the diabetic foot wound

The open foot wound is almost a sine qua non for DFI—here is an overview of current wound care concepts and effective therapies that you can use to accelerate healing.

11. The diabetic foot infection "checklist"

As in section 1, here is a "master" checklist that gives you a summary of DFI management in the individual patient.

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Chapter 1

Ten things you need to know about diabetic foot infection

Whether or not you read the rest of this booklet, here are some things that every internist should know about diabetic foot infection (DFI)…

1. **The "at risk" patient:** Patients with a serious DFI usually have a history of long-standing (5-10 years) diabetes with evidence of underlying peripheral neuropathy or related diabetic "complications" (e.g. vascular disease, retinopathy etc.). In some cases, the diagnosis of diabetes mellitus is made when the patient presents with infection—presumably the condition has been present for years but unrecognized because if lack of overt symptoms. This observation suggests a simple maxim—in a patient with an unexplained foot infection, always consider the possibility of diabetes mellitus and check a fasting blood glucose or serum HgbA1c.

2. **What to look for on physical exam:** When you first see the patient with a DFI, check the vital signs (? fever or tachycardia), document the presence of ulceration (? Size, location and depth of the ulcer) and measure the extent of the surrounding erythema. Findings such as necrotic (black) tissue—and soft tissue air (crepitance)—suggest the possibility of gangrene and the need for aggressive surgical intervention.

3. **Microbiology—the gram positive connection:** While any organism may be responsible for DFI, most acute infections are due to gram-positive organisms such as *Staph aureus* and streptococcal species (group B streptococcus is particularly common). Culture any purulent material —in those with a deep or long-standing ulcer, a "deep debridement" generally obtains more reliable samples compared to more "superficial" swabs.

4. **"Bare to the bone"—osteomyelitis assessment:** Obtain a plain film on all patients with a significant DFI—in addition to demonstrating underlying osteomyelitis, it may show a foreign body, signs of trauma (fracture), or evidence of gangrene (soft tissue gas). If the patient has an ulcer, try to "probe-to-bone" with a blunt object—if the test is "positive", the patient probably has underlying osteomyelitis and *doesn't* need an MRI unless you suspect a complication such as a deep, soft tissue abscess.

5. **"Bugs and drugs"—Antibiotic therapy for DFI:** No one is really sure what the "best" initial antibiotic regimen for DFI; however, empiric therapy should definitely include coverage against the most common pathogens seen in this condition—gram positive organisms such as *Staph aureus* and streptococcal species.

   In choosing empiric therapy, keep in mind the following common regimens:

   - **Non-toxic; outpatient**: Cephalexin, amoxicillin/clavulanic acid ***or*** clindamycin (PO)
   - **Non-toxic; ward admission:** Ceftriaxone + metronidazole ***or*** cefoxitin ***or*** ampicillin/sulbactam
   - **Seriously ill patient; ICU:** Piperacillin/tazobactam + vancomycin

   These are brief recommendations—check the remainder of the text for additional considerations. In general, unless they are seriously ill—or have grown the organisms previously—most patients don't require empiric coverage for *Pseudomonas aeruginosa* or MRSA.

6. **Time on treatment:** There are many uncertainties regarding antibiotic treatment of DFI, including the optimal antibiotic regimen, need for parenteral treatment and the length of treatment (? 2 vs. 12 weeks). Keep in mind the following simple "rules":

   - **IV vs. oral:** Patients who require hospital admission should generally start with parenteral (IV) therapy—the decision to 'stepdown" to oral antibiotics can be made if the patient rapidly improves and seems to have minimal inflammation or drainage.
   - **Cellulitis:** Patients with "simple" cellulitis often do well with 10-14 days of therapy
   - **Osteomyelitis:** Those with suspected osteomyelitis should receive approximately 8-12 weeks of therapy—if you choose initial parenteral treatment, evaluate the patient after 1-4 weeks and switch to oral therapy if the patient has had a clinical response.

7. **Go with the flow—vascular evaluation:** When you first see the patient, palpate for presence of the *dorsalis pedis* and *posterior tibial* pulse—if these are absent (or weak) order an ankle brachial index (ABI) and consider additional tests (e.g. arterial duplex; MRA; angiogram) to document presence of underlying vascular disease. If there is minimal flow to the lower extremity, vascular procedures such as open surgical bypass or endovascular techniques (e.g. angioplasty; stent placement) may be necessary for complete healing.

8. **When to call the surgeon:** Any patient with a significant diabetic foot infection should have a podiatry evaluation as part of the initial assessment—proper cultures obtained by "deep debridement" will better allow for appropriate antibiotic treatment. When osteomyelitis is a certainty (e.g. bony destruction on plain radiograph) attempts to cure these with "antibiotics-alone" are usually unsuccessful—in such cases, partial amputation (bone resection) or limited amputation will often be necessary.

9. **Charcot's foot and the DFI "mimics":** Remember that there are a number of conditions that "mimic" DFI including Charcot's foot (Charcot's neuroarthropathy), gout and vascular gangrene. These conditions can completely mimic DFI and typically *do not* improve with antibiotics. Early recognition of Charcot's foot is critical since the foot needs to be "off-loaded" as soon as possible—placing the patient in a wheelchair or on crutches will hopefully minimize the bone destruction that inevitably occurs if the patient continues walking on the foot.

10. **Don't be fooled:** Although the initial infection may seem relatively "minor" (patient is afebrile and "looks good"), don't underestimate the extent of the infection—findings on physical exam can be misleading (the "tip of the "iceberg" phenomenon) and patients can rapidly develop more extensive infection leading to gangrene and limb loss. If you choose to treat a patient as an outpatient, make an effort to see the patient within 48-72 hours—failure of the infection to improve implies inadequate treatment, and possibly the need for more aggressive parenteral therapy.

Never underestimate the potential seriousness of a diabetic foot infection—follow outpatients closely, make sure they understand the gravity of the condition and don't hesitate to hospitalize the patient (for parenteral antibiotics) if they fail to improve.

Chapter 2

Pedal "pointers"—Physical examination of the Diabetic Foot

You are called about a patient with diabetic foot infection (DFI) and expected to make recommendations about therapy. In addition to the patient's history, the first "step" in evaluating the infection is a careful examination of the patient's foot, with attention to features including predisposing factors (e.g. neuropathy), anatomic abnormalities and the depth—and extent—of the infection. This chapter addresses the following questions:

- **Podiatric primer:** What special podiatric conditions put the patient "at risk" for diabetic foot infection?
- **The neuropathic foot:** What is the "intrinsic minus" foot and how does this predispose the patient to DFI?
- **Evaluation of the infected foot:** "Staging" the severity of the infection

Bunions, calluses and corns—a diabetic podiatric "primer"

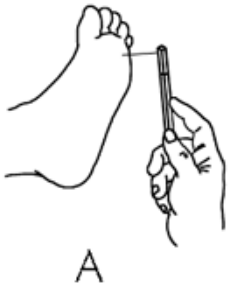
This isn't the place for extensive primer on podiatry; however, diabetics often have the following foot problems that place them at greater risk for subsequent infection or discomfort. During your exam, keep an eye out for the following common problems:

- **Dry skin:** Because of an underlying autonomic neuropathy—and excess glycosylation of tissues—diabetics are more likely to have dry skin and callus formation.
- **Callus:** A "callus" is a hyperkeratotic area of skin thickening on the skin caused by excessive pressure.. These lesions can be dangerous since they may hide deeper infection that can lead to foot ulceration and its' complications.
- **Corns:** A "corn" is a focal area of hyperkeratosis (similar to a callus) that occurs over a boney prominence. A "hard" corn is a firm, "button-like" skin callus that is often painful and can break down with repeated trauma.. A "soft" corn occurs in moist areas between the toes—though less painful than the hard corn, breakdown of the macerated tissue can lead to ulceration and infection.
- **Bunions:** As part of the neuropathic diathesis, diabetics have a greater risk of *hallux valgus*—lateral deviation of the great toe with prominent boney hypertrophy of the 1st metatarsophalangeal joint, sometimes accompanied by a subcutaneous bursa over the joint. Bunions are frequently painful and increase the risk of local tissue breakdown, ulceration and subsequent infection.
- ***Tinea pedis*:** More common in diabetics, *tinea pedis* may appear "harmless" but it can lead to special dangers for the diabetic—the skin 'breaks" associated with the infection place the patient at greater risk for bacterial cellulitis with attendant complications.

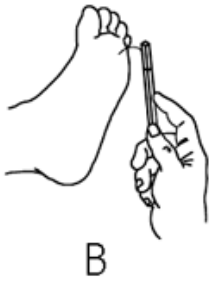
Although these problems can be seen in "normal" patients, they tend to be more common in diabetics and place the patient at greater risk for subsequent infection. Although none of them represent an emergency, they are a special risk to the diabetic patient because of the possibility of skin breakdown and subsequent infection. In the diabetic, even relatively "minor" conditions can turn deadly in certain circumstances!

A "gnawing numbness"—evaluation of neuropathy: Almost all patients with diabetic foot infections have some degree of neuropathy. In clinic—as part of your routine "screening"—abnormal sensation is a marker for potential of "high risk" infections. On examination, look for the following:

- ✓ **Sensory exam:** A simple question (Do you have numbness in your feet?) and a bedside exam for absence of fine touch (touch the plantar surface of the foot with your finger or a cotton applicator) or pain sensation (pin prick with sterile needle) are standard bedside tests to screen for significant neuropathy.
- ✓ **Vibratory sense (128-Hz tuning forks):** The tuning fork is widely used in clinical practice and provides an easy and inexpensive test of vibratory sensation. Vibratory sensation should be tested over the tip of the great toe bilaterally—an abnormal response can be defined as when the patient loses vibratory sensation and the examiner still perceives it while holding the fork on the tip of the toe.
- ✓ **Reflexes:** Absence of ankle or knee jerks suggests advanced neuropathy in the diabetic patient.
- ✓ **Semmes-Weinstein Monofilament test:** This test simple but requires a standardized monofilament nylon fiber that—when applied to the skin—buckles under 10 grams of pressure. The inability to sense the stimulus suggests "loss of protective sensation" that places the patient at risk for diabetic foot ulceration (See below).



Apply the monofilament perpendicular to the skin's surface



Apply sufficient force to cause the filament to bend or buckle

Source: http://ndep.nih.gov/publications (accessed 4/14/13)

The bottom line…If you carry around a Semmes-Weinstein monofilament in your back pocket (for emergencies!), you probably don't need to read this booklet. For most of us, obtaining a good history from the patient (How long have you had diabetes? Do you have numb feet?) , along with a few simple "bedside" findings (check for fine touch, position sense and vibratory sensation) are probably all that is necessary.

Diabetes heroes: Paul W. Brand and the "legacy of leprosy"

Born to a missionary family in India—but trained as a surgeon in Great Britain—Paul W. Brand (1914-2003) returned to India in 1946 in order to serve as director of a "leprosy" hospital. A keen observer and clinician, Brand saw that skin infections (cellulitis) associated with neuropathy caused an enormous amount of disability in the Hansen's population. As part of his therapeutic regimen for skin ulcers, Brand emphasized the importance of off-loading" the foot during recovery—this minimized pressure on the ulcerated skin and hastened the healing process. In 1966, Brand became director of the National Hansen's Disease Center in Carville, Louisiana. With his continued work, he was struck by the similarities between the neuropathies of diabetes and Hansen's disease. In addition to the similar anatomic abnormalities (e.g. hammer/claw toe; pes cavus), both groups ran the risk of Charcot neuroarthropathy and suffered from skin ulceration with subsequent infection. Early identification of the neuropathy—combined with simple measures to protect the "at risk" foot—went a long way towards preventing many of the devastating complications associated with these conditions. Brand's pioneering work at Carville greatly benefited Hansen's patients and laid the foundation for the modern management of the diabetic foot.

Source: Diabetes Metab Res Rev 2012; 28(Suppl 1): 3–7

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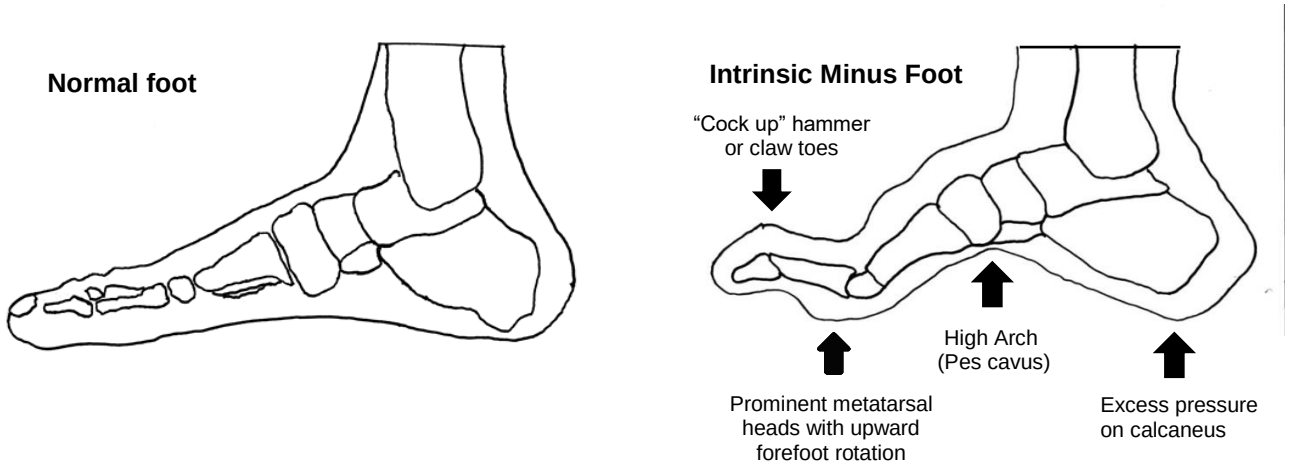
The "Intrinsic Minus Foot"—a casualty of neuropathy

The term "intrinsic minus foot" refers to the structural changes that occur in the diabetic foot as a result of long-standing neuropathy. Diabetic neuropathies progress from distal to proximal—the intrinsic muscles of the foot (lumbricals) are innervated by the longest nerves and are the first to be affected by the neuropathy. Weakness of these muscles leads to visible findings including "hammer toes", upward rotation of the forefoot and prominence of the plantar arch (see drawing). On exam, look for the following findings:



Features associated with the "intrinsic minus" foot include the following….

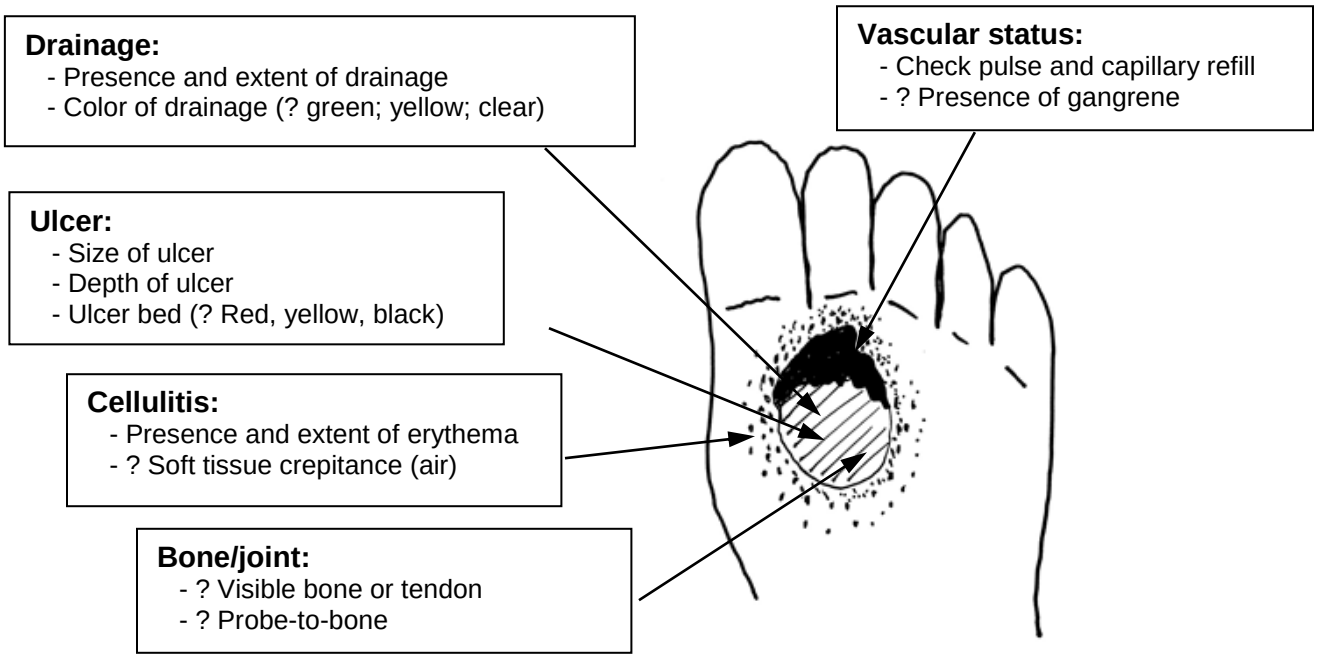
Wasting of lumbricals	Following progression of denervation, muscle wasting leads to visible channels (lumbrical wasting) between the metatarsals on the dorsum of the foot.
Hammer toes	The lumbricals flex the metatarsal-phalangeal (MP) joints and extend the interphalangeal (IP) joints—denervation disrupts muscle balance at these joints leading to flexion of the IP joints and extension of the MP joints with the resultant hammer toes.
Prominent plantar metatarsal heads	Extension of the MP joints leads to **upward rotation of the forefoot** and the appearance of bony prominences (the metatarsal heads) at the base of each toe. At first, these prominences are found only at the bases of the first and fifth toes; however, with progression, all of the toes are affected and calluses can be palpated under each metatarsal head..
Distal migration of the plantar metatarsal fat pads	In the normal physical examination, fat pads underneath the metatarsal heads are thick enough to be pinched by the examiner. With time and alterations of the foot, distal migration of the fat pads leaves the metatarsal heads more exposed to pressure and subsequent ulceration.
Cock-up deformity of the hallux longus with prominent extensor tendon	Weakening of the lumbricals and impaired flexion at the MTP joint leads to special prominence of the 1st (great) toe. When this occurs, the extensor tendon of this toe is usually visibly prominent.
Other findings	Upward rotation of the forefoot and soft tissue glycation leads to tightening of the plantar fascia with a resulting "high" longitudinal arch or "**pes cavus**". The underlying autonomic neuropathy leads a **dry (xerotic) skin**, a condition that further promotes callus formation and increases the risk of skin breakdown and ulceration.

Every time you see a patient with diabetes, always remove the patient's shoe and socks and inspect the feet. If all of us followed this simple rule, this would have a big impact on reducing amputations in diabetes.

Paul W Brand M.D.

The infection "connection"—evaluation of cellulitis and ulcers

When you first see the patient, document the presence and extent of the infection. Look for erythema, the presence of drainage and evidence of underlying osteomyelitis (e.g. visible bone and tendon; + probe-to-bone test). The literature contains a number of "scoring" systems (e.g. Wagner classification; University of Texas wound classification system) used to assess the extent and severity of infection. Although valuable, most of these systems are not known by the average physician and can be confusing for the uninitiated. The Infectious Disease Society of America (IDSA) Guidelines (see chapter on "Infection") provides a simple "severity scoring system" (mild-moderate-severe) that helps with documentation and decisions about therapy.



In your evaluation, look for the presence of the following physical examination findings…

- ✓ **Ulcer:** Note the location, size and depth of the ulcer
- ✓ **Cellulitis:** Is there surrounding cellulitis greater than 2 cm in span? More than 2 cm of surrounding cellulitis suggests more severe disease and the need for initial parenteral therapy.
- ✓ **Drainage:** Is there purulent drainage? Does it have a smell? A "Foul" smelling drainage suggests the presence of anaerobes and the need for antibiotics such as metronidazole, clindamycin or ampicillin/sulbactam.
- ✓ **? Gangrene:** Are there any black or necrotic areas? Presence of this finding suggests gangrene and the need for aggressive debridement.
- ✓ **? Visible bone or tendons:** Visualization of deeper structures almost guarantees the likelihood of underlying bone infection and the need for more prolonged antibiotic therapy.
- ✓ **? Probe to bone:** If you are able to "probe to bone" with a blunt object, there is over an 80% chance of underlying osteomyelitis, even if the initial bone radiograph appears normal.
- ✓ **"Squeeze" test:** When faced with an open ulcer, give a firm "squeeze" to the tissues surrounding the ulcer—if pus squirts out, the patient likely has deeper infection requiring debridement.

A circulatory "checkup"—the vascular examination: Does the patient have significant underlying "large-vessel" (Macrovascular) disease? A quick bedside assessment will ensure that the patient has adequate blood flow to permit antibiotic delivery and wound healing. On examination, look for the following:

- ✓ **Pulse evaluation:** Make a special effort to feel both the *dorsalis pedis* and *posterior tibial* pulse. Although the dorsalis pedis is occasionally absent (5-10% of patients), absence in a DFI patient suggests more proximal obstructions and the need for additional vascular studies. In those with decreased distal pulses, check more proximal vessels (e.g. popliteal and femoral arteries) for evidence of "macrovascular" disease (? Bruits)..
- ✓ **Capillary flow:** Firmly press the foot skin with your thumb and then let go—if it remains "blanched" for longer than 20 seconds, the patient has poor vascular supply to the extremity.
- ✓ **Dependent rubor:** If there is minimal swelling and pain, drop the leg over the side of the bed—if the leg turns red—this suggests "dependent rubor", a sign of underlying vascular disease.

How sick is the patient?—the sepsis "continuum"

How sick is the patient? Do they have gangrene? Do they appear toxic or septic? On your initial examination, look for the following signs and "grade" the severity of the infection on the sepsis "continuum" scale (see table below):

- ✓ **Vital signs:** Note the patient's temperature, heart rate and blood pressure—fever and hypotension suggest possible sepsis and require aggressive therapy with hospital admission and intravenous antibiotics.
- ✓ **? Gangrene:** Is there evidence of gangrene or tissue gas—if so, obtain a surgical consult as soon as possible since debridement or amputation might be necessary?
- ✓ **Toxicity:** In addition to the standard signs of sepsis, if the patient appears seriously ill, especially if they are hypotensive and severe soft tissue pain, consider the possibility of a necrotizing soft tissue infection (e.g. gas gangrene) requiring ICU admission and aggressive therapy.

Increasing Severity →

SIRS (Systemic Inflammatory Response Syndrome)	Sepsis	Severe Sepsis	Septic Shock
2 or more of the following criteria: • Temp > 38°C or < 36°C • HR > 90 bpm • RR > 20 per min or $PaCO_2$ < 32 mm Hg • WBC > 12K or < 4K or > 10% bands	Documented infection together with 2 or more SIRS criteria	Sepsis + organ dysfunction • Lactic acidosis • Oliguria • Hypoxemia • Coagulation do • Altered mental status	Sepsis + hypotension (<90 mm Hg) despite adequate fluid resuscitation

The severity of the infection will guide initial antibiotic therapy—treat "septic" patients with parenteral antibiotic therapy till the patient is stabilized and cultures are available.

When you evaluate a patient with a diabetic foot infection, look for the following on examination…

- **Anatomic abnormalities:** Examine the foot, looking for the "common" podiatric problems of diabetics (e.g. tinea, corns, calluses) as well as the findings associated with the neuropathic foot (e.g. toe abnormalities; pes cavus; "rocker-bottom" foot). In a patient with foot infection and long-standing diabetes, it is unusual not to see any of these abnormalities.
- **Define an entry point:** In many cases, you'll be able to find an "entry point"—a break in the skn barrier where the infection started. Look for evidence of *tinea pedis* (check between the toes) and ask the patient about foot trauma and blister development.
- **Measure the ulcer and cellulitis:** Examine the "infection" component of the foot with special attention to the following:
  - ✓ **Location, size and depth of the ulcer:** Document the size, location and depth of the ulcer—the larger and deeper the ulcer, the longer it will take to heal.
  - ✓ **Presence of purulent drainage:** Make note of the nature of the discharge (? Amount; ? color) as well as the presence of any odor that might suggest a specific pathogen (e.g. foul odor with anaerobes; musty "grape-like" odor with *Pseudomonas aeruginosa*).
  - ✓ **Extent of erythema:** If possible, outline the extent of the cellulitis with a marking pen—this will allow other examiners follow the progression of the infection over the next several days.
  - ✓ **? Visible bone/tendon:** Use a blunt object (e.g. forceps) in an attempt to "probe to bone" through the ulcer—presence of a positive "PTB" test is highly predictive of underlying osteomyelitis.
- **Check for neuropathy:** It's great if you have a Semmes Weinstein monofilament or a tuning fork—if these are not available, ask the patient about neuropathy symptoms (Do you have numbness in your feet?) and perform a simple exam looking for intact fine touch and position sense.
- **Examine the pulses:** Look for and document the presence of the *dorsalis pedis* and *posterior tibialis* pulse. If these are weak—or not present—extend your exam to the popliteal and femoral arteries—obstruction at higher levels suggests "macrovascular" disease that could benefit from surgical bypass.
- **Look for "red flags":** Make note of any gangrene or soft tissue air (crepitance)—these signs speak to the presence of dead tissue and the possibility of a life-threatening necrotizing soft tissue infection (e.g. gas gangrene).
- **Is the patient "septic"?** How sick or "toxic" is the patient—signs of "sepsis" including high fever, hypotension and evidence of organ dysfunction imply the possibility of bacteremia and the need for immediate antibiotic therapy and surgical consultation.

Physical examination of the diabetic foot—what you need to know…

- The diabetic patient with long-standing neuropathy develops a condition known as an "intrinsic-minus" foot—atrophy of the "intrinsic" muscles of the foot (lumbricals) that leads to a host of anatomic abnormalities due to excess pressure on the metatarsal heads ((hammer/claw toe; pes cavus) that can lead to skin breakdown.
- Common foot problems in diabetics (Calluses; corns; bunions; dry skin; tinea pedis) can also result in skin breakdown and increase the diabetic's risk of foot infection.
- In the patient with cellulitis, look for an entry point (? *tinea pedis*;? skin ulceration) and document the extent of the inflammation.
- If the patient has distinct ulceration, note the size and depth of the ulcer, the nature of the drainage (e.g.clear, pus or bloody) and the presence of visible bone or tendon (findings that suggest underlying bone infection).
- Check the *dorsalis pedis* pulse and overall vascular flow to the foot (capillary refill)—if the pulse is absent, request an Ankle-Brachial Index (ABI) and full vascular evaluation (arterial duplex scan) in order to screen for underlying vascular obstruction.
- With a blunt object (forceps or swab), perform a "probe to bone" test; the presence of visible bone—or a positive "PTB" test— is highly suggestive of underlying osteomyelitis. Patients with proven osteomyelitis, in addition to more prolonged antibiotic therapy, may require surgical excision of the infected bone.
- Document the patient's vital signs—if the patient appears "toxic" or has signs of "sepsis" (high fever, hypotension,tachycardia)—they will likely need immediate hospitalization, along with parenteral antibiotic therapy.
- In a diabetic patient, always remove the shoes and examine the feet—early identification and treatment of relatively "minor" foot problems can often prevent the devastating complications of infection and limb loss.

Chapter 3

X-ray "visions"—the radiology of diabetic foot infection

Radiology plays a critical role in evaluating diabetic foot infection (DFI)—it documents underlying osteomyelitis and helps detect other complications such as fracture, Charcot's foot and gas gangrene. In managing the patient with suspected DFI, keep in mind the following "principles" of radiological diagnosis in this population:

- **The importance of the "plain" radiograph:** Although not as sensitive as some of the other radiological studies, always start with a" plain" radiograph—in addition to picking up some of the complications of diabetic foot, it will serve as a baseline for future management.
- **Evaluating osteomyelitis:** Despite their importance in ruling out osteomyelitis, plain films are frequently negative "early" in the process (e.g. the first 2-3 weeks of infection). In this situation, clinical findings such as the presence of a large, deep ulcer—or a "positive" probe-to-bone test—may be just as helpful in guiding therapy. In these cases, a repeat radiograph—2 to 4 weeks later—may show distinct bony abnormalities, confirming the diagnosis of osteomyelitis and the need for more prolonged antibiotic treatment.
- **The "gold standard" of MRI—possibilities and pitfalls:** More and more, specialists are turning to the MRI as the "gold standard" for diagnosing osteomyelitis. Despite its' potential benefits, it's important to know the possible pitfalls of this technique included added expense and the possibility of "false positive" scans.

Know the "numbers"…The following table (Table 1) gives the "numbers" (sensitivity and specificity) of the standard radiological modalities in the diagnosis of diabetic osteomyelitis. Keep these figures in mind as you make choices about the various studies available

Table 1: Comparison of radiographic modalities in diabetic foot infection

Modality	Sensitivity	Specificity
Plain radiograph	50-90%	30-90%
Bone scan*	80%	30%
Indium-111-labeled WBC scan*	75%	70%
MRI	30-100%	70-95%

Source: Veves A et al. The Diabetic Foot. 2nd edition. Human Press
***see Dinh MT et al. Clin Infect Dis 2008;47:519-27.**

The power of "plain"—the plain radiograph in diabetic foot infection

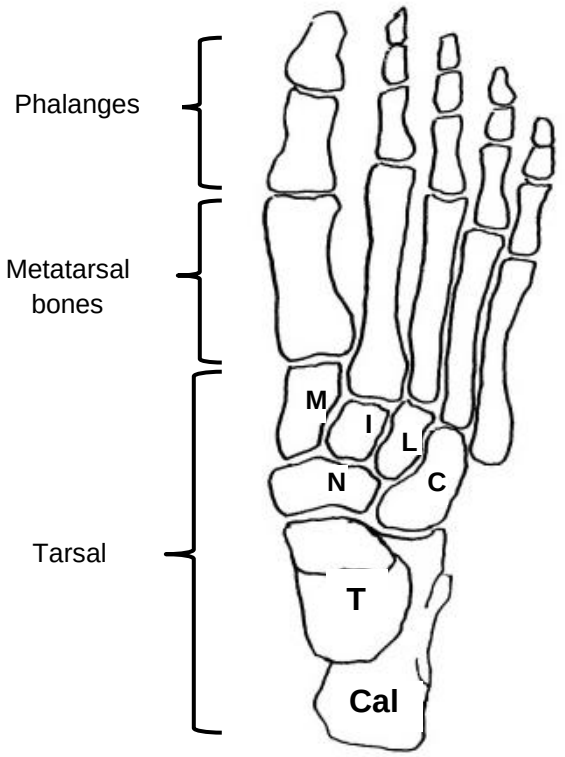
For decades, physicians have relied upon the "plain" radiographic as an aid in the initial evaluation of the infected diabetic foot. Modern digital radiographic techniques—with the option of changing image contrast and magnification—has advanced the utility of this modality even further.

In most cases of DFI, if the patient has not had a recent plain radiograph, it's important to obtain one— both to search for immediate complications as well as provide a "baseline" for future studies. When you review the initial film, here are some things to look for…

- **Presence of ulcer:** Although best seen on physical exam, ulceration may be visible on X-ray—the presence of bone destruction immediately adjacent to an infected ulcer is powerful evidence for osteomyelitis.
- **Soft tissue swelling and such gas:** In the infected patient, the presence of soft tissue gas immediately raises the possibility of gas gangrene and associated necrotizing soft tissue infection. While such a finding is critical, don't be fooled by a "negative" study—necrotizing fasciitis secondary to group A streptococcal infection (the "flesh-eating" bacteria), typically does not produce soft tissue gas!
- **Signs of osteomyelitis:** On plain films, look for evidence of cortical bone destruction, focal (or diffuse) bone osteopenia, or periosteal new bone formation, all signs of potential osteomyelitis. Remember that these may not be present on the initial film, so a repeat film (2-4 weeks later) may be helpful in confirming the diagnosis.
- **Vascular calcification:** Rarely found in other conditions, calcification of medium sized arteries is the first clue that the patient's diabetes is long-standing and accompanied by significant peripheral arterial disease.
- **Presence of fracture:** Diabetics have a higher incidence of foot fractures. In a patient with long-standing diabetes, fracture with minimal history of trauma suggests the possibility of underlying Charcot's arthropathy.
- **Foreign bodies:** Because of their underlying neuropathy, patients may fail to recognize injury incurred following "stepping on nail" or some other foot trauma. Obtain a plain radiograph to look for the presence of radiopaque metal or glass foreign bodies. Wood fragments or vegetable matter won't show up on plain film and are better imaged by MRI scan.

"Dem bones"—the radiographic anatomy of the foot

As you read radiology reports and speak with consultants, it's important to know your way around the local anatomy. Examine the following drawing and make sure you are familiar with the bony anatomy of the foot.



Keep in mind this med school mnemonic in order to remember the tarsal bones of the foot:

Tall: Talus
California: Calcaneus
Naval: Navicular
Medical: Medial cuneiform
Interns: Intermediate cuneiform
Love: Lateral cuneiform
Cuties: Cuboid

Diabetes Heroes

W.C. Roentgen and the case of the debilitated "dancer"

In late 1895, while experimenting with a cathode ray tube, the German physicist W.C. Roentgen discovered "x-rays"—radiation emanating from the device was capable of penetrating normal tissue and offered a means to image the "hidden" structures within the body. Although physicians were initially skeptical of radiography, the legal profession quickly adopted the new technology and it was not long before radiographs were introduced as evidence in a trial. The first recorded judicial use of x-rays occurred in September 1895 during a lawsuit brought against a London theater by the popular British burlesque/comedy actress, Gladys Ffolliott (Yes, that's the correct spelling!). Following a performance, the actress stumbled on a broken staircase, injured her foot and—hoping to recoup the financial losses she suffered from the accident—sued the theater owners. In the ensuing trial, Ffolliott's lawyers presented a foot radiograph that clearly demonstrated a dislocated cuboid bone, proving the injury was "genuine" and not an act. The novel films carried the day—impressed by the findings, the jury found in favor of Ms. Ffolliott and awarded her hefty damages. Publicity surrounding such cases further increased interest in the new "X-rays" and ensured their rapid adoption by both the medical and legal community. Despite the current availability of sophisticated imaging techniques, the plain radiograph remains a critical tool in the initial evaluation of the diabetic foot—in the patient with a diabetic foot infection, order a plain film to rule out unrecognized pathology and to serve as a baseline for future studies.

Source: Lichtenstein. "Forensic Radiology" Edited by B .G. Brogdon CRC Press 1998

Going "nuclear"—WBC and bone scans

Prior to the widespread adoption of MRI technology, the radionuclide bone scan was the most common way to confirm the presence of osteomyelitis. When choosing to go the "nuclear" route, keep the following in mind:

- ✓ **Bone scan—a false alarm?** Depending upon the study, the technetium 99 phosphate labeled bone scan is fairly sensitive (~80%) but relatively non-specific (~30%) in confirming osteomyelitis. The poor specificity (e.g. high false-positive rate…see Table 1) is due to the fact that other conditions such as fracture, Charcot's neuroarthropathy and gout can lead to abnormal tracer uptake.
- ✓ **A WBC scan rescue:** Compared to bone scan, the Indium-111-labeled leukocyte scan has similar sensitivity but improved specificity (~80%). Despite the improved specificity, other non-infectious conditions such as gout or fracture can still lead to "false positive" scans.
- ✓ **? Combos:** Although the scans are sometimes felt to provide complementary information, most radiologists do not feel there is a strong role for ordering both scans in an individual patient.

In diabetic foot evaluation, routine nuclear scans have largely been supplanted by MRI technology; however, nuclear imaging remains useful, especially in those where an MRI is not available or permitted by insurance. In the future, emerging technologies such as PET scanning may also prove useful, although experience with this modality remains relatively limited at the present time.

Making the most of magnets—Magnetic Resonance Imaging (MRI)

Although plain radiography is clearly the first test to order in the patient with diabetic foot infection, the MRI scan has become an indispensable modality in managing patients with this condition. In addition to its' superior ability to image soft tissue conditions (e.g. cellulitis, tendonitis, soft tissue abscess), it has now become the "tie-breaker" in cases where the presence of osteomyelitis is uncertain.

Talk like a radiologist…As review films with the radiologist, know the MRI findings of osteomyelitis (see Table 2) and familiarize yourself with the following "lingo"—it will help with communication and make you sound like you know what you are talking about!

- **T1 weighted scan:** A "T1" weighted scan, characterized by a short TR (repetition time) and a short TE (echo time), is dependent on the fat content of tissue. This sequence gives a "bright" or more intense signal from tissue with a high fat content and is generally felt to provide the best anatomic detail. Normal bone (marrow) is bright (white) on T1 weighted scans—infected bone (osteomyelitis) is "dark".
- **T2 weighted scan:** The "T2" weighted scan with a long TR (> 1000) and long TE time demonstrates a "bright" (white) focus in areas of increased water content. In the T2 weighted scan, bone is normally dark—areas of osteomyelitis or cellulitis will be "bright" or white.
- **"Fat-sat" scan:** In fat suppressed T2-weighted images, (including STIR scan: short T1-inversion recovery sequence), fat is suppressed (dark) and water is bright—this allows for improved imaging of edema within bone and soft tissues.

Table 2: MRI findings in osteomyelitis

	T1 Scan	T2 Scan
Normal bone	Bright (white)	Dark
Osteomyelitis	Dark (black)	Bright (white)

What to look for…When reviewing MRI scans, keep in mind the following…

- **Osteomyelitis:** Nearly all diabetes-related foot osteomyelitis results from the contiguous spread of infection from an adjacent foot ulcer. Areas of suspected osteomyelitis will appear dark on T1 weighted scans (normal white bone; infected bone: dark) and bright on T2 weighted scans (Normal bone: dark; infected bone: bright)..
- ✓ **Cellulitis:** Both tissue edema (uninfected) and cellulitis will appear "bright" (white) on T2 weighted scan.); intravenous gadolinium contrast with a T1 weighted scan will help differentiate the two (e.g. increased contrast enhancement of cellulitis; minimal enhancement with edema-alone).
- ✓ **Abscess:** MRI scans permits visualization of deep, soft tissue or bone abscesses. Such lesions may require surgical drainage or debridement for ultimate cure. While an abscess may be apparent on T2 weighted scans, a T1 scan (with gadolinium) is likely to give the best visualization of this process.
- ✓ **Tenosynovitis:** On T2 scans, look for a fluid with a "bright" (white) signal around the tendon with enhancement on a T1W contrast scan.
- ✓ **Septic arthritis:** As with tenosynovitis, joint fluid will be "bright" white in infected joints.
- ✓ **Charcot's foot:** The MRI changes of Charcot osteolysis can completely mimic those seen with diabetic osteomyelitis; however, the anatomic location of the process can help differentiate between the two conditions: . Charcot osteolysis is more likely to be seen in mid-foot bones (e.g. tarsal) whereas diabetic osteomyelitis is more common in the forefoot (e.g. phalanges; metatarsals) and hindfoot (e.g. calcaneus) bones.

Source: Donovan A, Schweitzer ME. Use of MR Imaging in Diagnosing Diabetes-related Pedal Osteomyelitis. Radiographics; 2010; 30:723-736.

Remember…After the initial radiograph, MR imaging is the modality of choice for the evaluation of pedal osteomyelitis and soft-tissue infection, with sensitivity of 90% + and specificity of 83%.

MRI of osteomyelitis—a timely trio of instructive scans

The following MRI scans (a 61 year old male with diabetic foot infection of the 2nd phalanx) demonstrate the typical MRI features of osteomyelitis in the diabetic foot. Note the ulcer on the medial aspect of the 2nd phalanx (skin disruption between the two arrows) with involvement of the associated bone (identified by the arrowhead). The final scan in the set (Figure 4) confirms the high likelihood of osteomyelitis with increased contrast enhancement of the bone marrow and surrounding tissue.

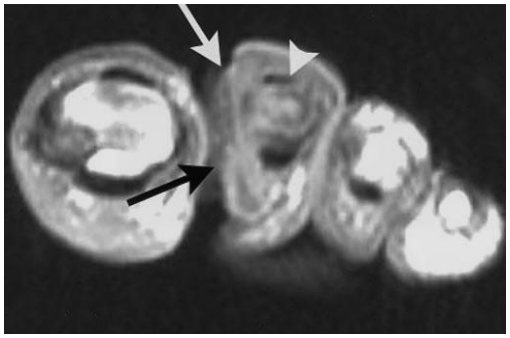


Fig 2. Coronal T1-weighted (T1W) scan

Note the skin interruption (between arrows) due to the skin ulceration that is the likely source of the bone infection. Compare the bone signal in the first (large toe) with the signal in the involved 2nd toe (arrowhead)—the first toe shows "normal" bone signal (bright/white on T1W scan) and the involved 2nd toe has a dark or decreased signal that suggests osteomyelitis.

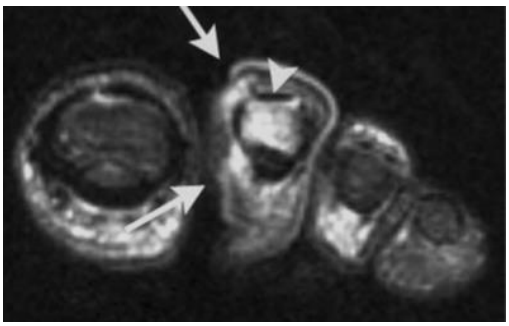


Fig 3. Coronal T2-weighted (T2W) scan

This scan demonstrates the reverse with a "normal" decreased signal in the first toe, and an increased (bright/white) signal in the bone of the second phalanx, suggesting the presence of osteomyelitis.

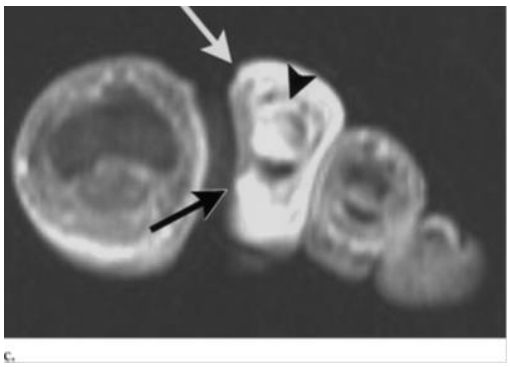


Fig. 4. Coronal T1-weighted fat-suppressed scan with IV contrast

This scan further suggests the presence of osteomyelitis. Following intravenous administration of gadolinium, the proximal 2nd phalanx (and surrounding tissue) enhances, confirming the presence of osteomyelitis with associated cellulitis.

(Source: Lederman HP et al. Radiology 2002; 223-747-755.)

A word of caution— MRI "pitfalls":

MRI can be costly and time consuming and is not always readily available—some insurance plans won't permit it without special authorization. When making a decision about the MRI, keep in mind the following:

- **"Plain" radiographs:** If the patient has clear bone destruction on plain radiographs, the MRI is not likely to provide additional information, unless you are looking for the presence of an underlying abscess or soft tissue infection (e.g. tenosynovitis; septic arthritis). .
- **"False positive" MRI:** Be cautious about over-interpretation of the MRI. While it is a very sensitive test (95%+), a "positive" bone signal does not always mean osteomyelitis—the specificity is around 80% and other conditions such as bone marrow edema (osteitis) may be falsely read as osteomyelitis.

- **Preoperative podiatry roadmap:** If they are planning surgery, podiatrists sometimes request a scan in order to "map out" the anatomy and extent of infection in advance.

Remember… The MRI is an excellent modality for evaluating diabetic foot infection; however, it's not needed in most cases—a plain radiograph is much cheaper and can often demonstrate signs of underlying osteomyelitis that will help guide subsequent therapy. If a patient is unable to undergo an MRI, a bone scan may be just as valuable in providing the necessary information to help manage the patient.

Use this checklist when evaluating radiological studies in DFI…

- ❑ **Obtain a plain radiograph** on all patients with suspected osteomyelitis, especially individuals with deep or long standing ulceration. Look for the following…
  - ✓ **Soft tissue gas:** Suggests gangrene
  - ✓ **Vascular calcification:** Raises question of vascular compromise
  - ✓ **Periostitis:** This is a later finding and suggests underlying osteomyelitis, especially if it occurs near a soft tissue ulcer.
  - ✓ **Osteomyelitis**, as evidenced by a bone rarefaction (compare with previous films if available), osteolysis or bone fragmentation

- ❑ **Consider a bone scan** or white cell scan if you have a strong suspicion of osteomyelitis and an MRI is not available.

- ❑ **Order an MRI** if osteomyelitis needs to be confirmed, especially if there is planned surgery (e.g. amputation or soft tissue debridement). On this exam , look for the following:
  - ✓ **Cellulitis:** Look for increased signal in soft tissues on T2W scan.
  - ✓ **Soft tissue abscess:** This is best delineated with a post-contrast T1 weighted or STIR scan.
  - ✓ **Tenosyovitis:** There will be enhancement of the tendon "sleeve" following IV contrast administration
  - ✓ **Osteomyelitis:** Look for decreased signal (dark) on T1W scan and increased signal ("bright" or white) on T2W scans.

Imaging the diabetic foot, what you need to know…

- Patients with diabetic foot infection should have a plain foot radiograph in order to help exclude serious complications (gas gangrene; osteomyelitis) as well as other conditions that might be pertinent to the case (e.g. fracture; foreign body; Charcot's foot).
- In patients with suspect osteomyelitis, look at the film for evidence of cortical bone destruction, diffuse osteopenia (of a specific bone) and periostitis. If the initial film is negative, consider repeating the plain film in 2-4 weeks—the "classic" radiographic findings of osteomyelitis may take several weeks to appear.
- A technetium 99 phosphate labeled bone scan s is fairly sensitive (~80%) but less specific (~30%) for osteomyelitis. Other conditions such as stress fracture, vascular infarct and Charcot's neuroathropathy may produce "false positive" scan.
- An Indium-111-labeled leukocyte scan (WBC scan) has a similar sensitivity to the bone scan, but is more specific (~80%) and less prone to false-positive results.
- The MRI is the most sensitive and specific radiographic procedure for early detection of osteomyelitis. In addition to its' sensitivity for bone infection, it allows for detection of soft tissue abscess, tenosynovitis and is a helpful adjunct in planning a surgical approach to amputation or abscess drainage.
- On a T-1 weighted MRI scan, normal bone is "bright" (white) and osteomyelitis is "dark" or black. A T2-weighted image is just the opposite—normal bone is dark and osteomyelitis is "bright".
- While the MRI can be helpful in selected cases, most patients with diabetic foot infection do not need the procedure—simple measures such as a plain radiograph or the "probe to bone" test are often sufficient to detect osteomyelitis and guide subsequent therapy.

Chapter 4

Infection in the Diabetic Foot—Microbiology and management

Diabetic foot infection (DFI) remains one of the most serious complications of diabetes; even "trivial" infections—if not properly managed—can lead to life-threatening complications such as gas gangrene or necrotizing fasciitis. This chapter focuses on the microbiology and antibiotic management of this all-to-common affliction.

Important considerations concerning diabetic foot infection include the following:

- **How serious is the infection?** Cellulitis, osteomyelitis or gangrene—where does your patient fall on the "spectrum" of diabetic foot infection? This chapter will introduce a simple "staging" system that will give you a handle on the severity of the infection and the appropriate level of management.
- **Microbiology of DFI:** What are the most common organisms associated with diabetic foot infection? Although studies suggest that many patients have "mixed" infection with both aerobic and anaerobic species, *Staphylococcus aureus* and streptococcal species are most often cultured, especially in patients with acute infection.
- **Empiric antibiotic therapy:** What is the most appropriate, initial antibiotic therapy? At clinical presentation, "broad-spectrum" therapy (with coverage against both gram positives and gram negatives), with more "narrow spectrum" agents once culture results are available.
- **Indications for surgery:** Does the patient have a complication (e.g. soft tissue abscess, gas gangrene, necrotizing fasciitis) requiring immediate surgery?

Hovering over all of this is the "big" question—can diabetic foot infection (especially osteomyelitis) really be cured? Although we are often successful in treating "simple" soft tissue cellulitis, the ability to cure documented osteomyelitis remains uncertain. What follows here is an overview of the staging, microbiology and empiric antibiotic therapy for this condition:

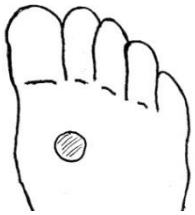
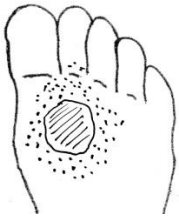
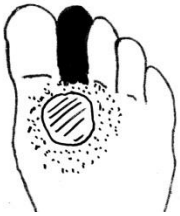
Figure 1: The Diabetic Foot Infection "Spectrum"

All the worlds a "stage"—the spectrum of diabetic foot infection

There is nothing simple about diabetic foot infection. The first step in managing these infections is to get an idea of the extent and depth of infection. Think of DFI as a "spectrum" (see above) that includes "simple" cellulitis, "deeper" infection (ulceration), underlying osteomyelitis and full blown gangrene:

- **Cellulitis:** This is the most common infection in the diabetic. In most cases, an acute cellulitis is usually caused by "gram positive" organisms such as *Staphylococcus aureus* or streptococcal species. Non-toxic patients with "simple" cellulitis may respond to outpatient oral antibiotics; however, such cases need to be followed closely since even a "simple" cellulitis can evolve into a deep, life-threatening necrotizing fasciitis.
- **Ulcer:** The presence of an ulcer usually reflects more long-standing diabetes with underlying neuropathy and altered foot biomechanics. The microbiology here tends to be more complicated and often includes "mixed" infection with gram negative bacteria and anaerobes.
- **Osteomyelitis:** In those with a "deep" ulcer, underlying osteomyelitis is a definite possibility. Look for a + "probe to bone" test (this is highly suggestive of osteomyelitis) or an abnormal radiograph. If in doubt, a bone scan or should help to confirm (or exclude) underlying bone infection. The presence of osteomyelitis is an important finding—patients with clear evidence of bone infection need more prolonged antibiotic therapy (e.g. 8-12 weeks) and may require surgical intervention (e.g. deep debridement or partial amputation).
- **Gangrene:** Overt gangrene—or signs of severe systemic toxicity—suggests the possibility of an underlying necrotizing soft tissue infection such as necrotizing fasciitis or gas gangrene. In addition to immediate antibiotic therapy, these patients prompt evaluation by a surgeon since emergency surgery may be necessary for survival.

As mentioned earlier, "staging" the infection is important to estimate the severity of infection and determine the best therapy. When you examine the patient, look for the following findings and "grade" the extent of the infection using the diabetic foot infection severity score developed by the Infectious Disease Society of America (IDSA):

IDSA Diabetic Foot Infection Severity Score			
Stage:	**Mild Infection**	**Moderate infection**	**Severe infection**
			
Inflammation	Cellulitis/erythema ≤ 2 cm. around ulcer ↘↙ 2 cm. span	Cellulitis extending > 2 cm	Cellulitis > 2 cm beyond ulcer with (or without) presence of gangrene
Wound	Purulent Shallow (≤ 3 mm)	Purulent May be deep (> 3mm)	Purulent May be deep (> 3mm)
Visible bone/tendon	Bone/tendon not visible	Bone/tendon may be visible + "probe to bone" test" suggests osteomyelitis	Bone/tendon may be visible + "probe to bone" test"
? Gangrene	None	None	May be present
Systemic symptoms	No systemic toxicity	No systemic toxicity or "mild" SIRS* signs including fever, tachycardia	Moderate to severe toxicity including high fever, rigors, nausea/vomiting and/or hypotension,
*SIRS criteria: Temperature" <36 °C (96.8 °F) or >38 °C (100.4 °F; Heart rate: >90/min; Respiratory rate: >20/min or PaCO2<32 mmHg: White Blood count: <4000/mm³), >12,000/mm³), or 10% bands			

As you examine the foot, look for the following in order to help "stage" the infection…

- ❑ **Extent of inflammation:** Examine the wound (or foot) for the 4 cardinal signs of inflammation—pain, tenderness, erythema and warmth/induration. Measure the extent of the infection of infection beyond the entry point (if visible).
- ❑ **Wound status:** If present, measure the size (and depth) of the ulcer. Look for purulent drainage and—if present—obtain a culture (aerobic/anaerobic) and Gram stain. While "superficial" cultures can be helpful, if possible, ask the podiatrist to obtain a "deep" culture following deep debridement—this is more likely to give you an accurate representation of the microbiology.
- ❑ **? Bone/tendon involvement:** If there is visible muscle or tendon—or you can "probe to bone"—there is a high likelihood of underlying osteomyelitis.
- ❑ **Presence of gangrene:** Black, devitalized tissue may be due to pure vascular compromise (dry gangrene) or may be accompanied by fluid/drainage (wet gangrene). In any event, it is a serious finding suggesting the need for evaluation and followup by a vascular surgeon.
- ❑ **Systemic symptoms:** Specifically look for "**SIRS**" signs such as fever (Temperature: >38 °C), tachycardia (rate >90/beats per min.) or increased respiratory rate (>20/min). Patients with severe toxicity, hypotension (BP < 90 mm Hg) or signs of end organ damage have **severe SIRS** and are likely to need immediate broad spectrum antibiotic therapy and possibly, surgical evaluation.

Cellulitis vs Osteomyelitis—clinical clues

In most cases, no single finding permits immediate diagnosis of osteomyelitis; however, selected findings (long-standing ulcer, visible bone, high sedimentation rate, plain film abnormalities) suggest a high probability of underlying osteomyelitis and the need for further evaluation. Making this decision is important since osteomyelitis generally requires more prolonged therapy, and—in some cases—a major or minor amputation.

Use the following table as an aid in deciding whether the patient has underlying osteomyelitis. If there is significant doubt about the presence of bone infection, an MRI (or bone scan) is likely to be helpful as a tie-breaker:

Finding	Cellulitis	Osteomyelitis
Onset	Recent (< 1 week)	Long standing
Physical examination	Minimal or no ulcer	Deep ulcer/probe to bone
Sedimentation rate	Less than 30 mm/hr	> Greater than 70 mm/hr
Radiograph (plain film)	Negative	Osteomyelitis
MRI or bone scan	Negative	Positive

Some things to remember…

- ✓ **Chronic ulcer:** A long-standing ulcer (> 4 weeks) with "inability to heal" is more likely to be associated with underlying osteomyelitis. Visible bone—or the ability to probe to the bone with a blunt object—is highly predictive of osteomyelitis.
- ✓ **Elevated sedimentation rate:** Presence of a very high ESR (> 70 mm/hr.) is also predictive of osteomyelitis.
- ✓ **X-ray clues:** Obtain a plain radiograph on all patients with significant DFI. If this is negative—and the possibility of bone infection remains high—consider repeating the film in two weeks to look for signs of osteomyelitis (e.g. periostitis, osteopenia or bone destruction).

Remember… Infection with osteomyelitis generally requires more prolonged therapy (8-12 weeks) than patients with "simple" cellulitis. If the presence of osteomyelitis remains uncertain after the above considerations, it may be appropriate to obtain a bone scan or MRI.

Pedal pathogens—the microbiology of diabetic foot infection

The many studies of DFI suggest a common theme—"gram positive" bacteria such as *Staphylococcus aureus* and streptococcal species (Grp A, Grp B and viridans streptococci) remain key pathogens in patients with acute infection. This is especially important in patients with acute infection and "simple" cellulitis. For patients with more complicated infection (e.g. deep ulcer or gangrene), the microbiology may be more complicated. A recent study of 433 patients with moderate to severe diabetic foot infection (see Table 1) took special efforts to ensure proper specimen collection—specimens were obtained *after* deep debridement and were sent for *both* aerobic and anaerobic cultures. The results of this study reflect the microbiology of more "complicated" diabetic foot infection:

Table 1: Microbiology of diabetic foot infection

Microorganism(s)	% patients	Microorganism(s)	% patients
Aerobic gram-positive cocci		**Gram-negative facultative bacilli**	
Staphylococcus aureus	20	*Enterobacteriaceae*	12
Staphylococcus epidermidis	15	*Pseudomonas* species	3
Streptococcus species	15	**Obligate anaerobes**	
Enterococcus species	12	Anaerobic cocci	45
Corynebacterium species	10	Anaerobic GNR	
		Prevotella sp.	14
		Porphyromonas	11
		Bacteroides fragilis	10
		Polymicrobial	84
433 patients as reported in: Citron et al. J Clin Micro 2007: 2819-28.			

In addition to confirming the importance of "gram positives" (staphylococci; streptococci), this study also highlighted the importance of polymicrobial infection—especially anaerobic bacteria—in patients with moderate to severe diabetic foot infection. An important caveat in any such studies is the way the culture is taken— whenever possible, try to obtain a "deep" culture (via debridement) that bypasses the superficial wound flora.

A review of such studies suggests the following important observations…

- ✓ **Staph/strep:** Gram positive organisms such as *Staphylococcus aureus* and streptococci (grp A; grp B and viridans streptococci) remain the most common pathogens in patients with acute diabetic foot infection.
- ✓ **Group B streptococci** (*Streptococcus agalactiae*) are especially common in diabetics and account for almost 50% of all streptococcal isolates.
- ✓ **MRSA:** The incidence of MRSA in DFI was not especially high in the above study (MRSA 4.4 % vs. MSSA 14%), suggesting that empiric MRSA coverage may not be necessary in all patients. Consider empiric MRSA coverage (e.g. vancomycin, TMP/SMX) in seriously ill patients or those who are "known" MRSA carriers.
- ✓ **Gram negative bacteria** (*Enterobacteriaceae*; *Pseudomonas*) actually represent a relatively small percentage of DFIs (less than 10% of patients)—think of these bugs in patients with a history of more chronic, long-standing foot ulceration.
- ✓ **Anaerobes:** With proper culture techniques, anaerobic cocci (45% of cases) and anaerobic GNRs (*Prevotella*, *Porphyromonas* and *Bacteroides* species) turn out to be surprisingly common—add antibiotic coverage for these organisms (e.g. metronidazole; clindamycin; ampicillin/sulbactam, cefoxitan) in patients with overt gangrene or those with "foul smelling" drainage.
- ✓ **Mixed infection** with both aerobes and anaerobes appears to be common (84% of infections were "polymicrobial") suggesting that broad-spectrum antibiotic therapy—with coverage against both aerobes and anaerobes—is a wise idea in most situations until culture results are available.

Diabetes Heroes

Giuseppe Brotzu and the birth of the cephalosporins

Because of the breakdown in public health measures, typhoid fever was an especially common problem throughout Italy at the end of WWII. Giuseppe Brotzu, a microbiologist and public health officer on the island of Sardinia, was intrigued by a curious anomaly in the local epidemiology of the disease—although typhoid was common on the island, it rarely occurred among individuals who swam —or ate shellfish—from waters close to discharge from a local sewage pipe. Inspired by the recent discovery and development of penicillin, Brotzu cultured waters close to the pipe and isolated a mold (*Cephalosporium acremonnium)* that secreted antibiotic-like substances capable of inhibiting bacterial growth. He sent the isolate to Oxford University where researchers isolated an active compound (Cephalosporin C) with a ß-lactam ring structure and activity quite similar to penicillin. Chemical modification of the parent molecule led to a whole series of compounds (the cephalosporins) with activity against both gram positive (e.g. staphylococci; streptococci) *and* gram negative bacilli (*E. coli, Salmonella, Vibrio* and *Brucella* species). Later modifications of the parent molecule further broadened the spectrum to include *Pseudomonas aeruginosa* (e.g. ceftazidime; cefepime), anaerobes (e.g. cefoxitan; cefotetan) and MRSA (e.g. ceftaroline). Cephalosporins—first isolated from sewage effluent by a curious microbiologist—have gone on to become some of the most important anti-bacterial drugs of the modern era.

From:Oru B et al. Giuseppe Brotzu and the discovery of cephalosporins. European Conference of Medical and Health Libraries. Cologne,Germany.September. 2002. veprints.unica.it/148/1/orru-poster.pdf accessed 9/18/12

Empiric antibiotic selection—first choices

Presence of cellulitis or infection generally demands immediate empiric antibiotic therapy. The decision about hospital admission—and antibiotic selection—depends on several factors:

- **Timing and likely pathogens:** A patient with an "abrupt" onset (less than 2-3 days) is more likely to have *Staph aureus* or streptococcal species as pathogens. Think of "facultative" gram negative bacilli (e.g. *Enterobacteriaceae)* in patients with more "chronic" infection (> 7 days); consider "strict" anaerobes (e.g. *Bacteroides* and *Fusobacterium* species; anaerobic streptococci) in those with gangrene or a foul smelling ulcer.
- **Severity of disease:** Patients with moderate to severe infection, generally require hospital admission or initial parenteral antibiotic therapy. If the patient has signs of "severe sepsis" or septic shock (e.g. toxicity; hypotension; acidosis), administer broad spectrum therapy that includes coverage of both *Pseudomonas* (Piperacillin/tazobactam, carbapenem or ciprofloxacin) and MRSA (vancomycin, ceftaroline or linezolid).
- **? Able to take oral medications:** If the patient has significant nausea and vomiting, start parenteral treatment and don't rely on oral therapy.
- **? Allergies:** Avoid ß-lactams in a patient with a history of an anaphylactic reaction (e.g. hives, wheezing, hypotension) to penicillin—cephalosporins are often safe if the previous reaction was just a "rash" but the patient should be watched closely to ensure safe administration.

Some additional things to consider…

- ✓ **? Hospital admission:** When considering hospital admission, err on the side of caution—patients with diabetic foot infection can deteriorate rapidly and end up in septic shock.
- ✓ **Pseudomonas** coverage is generally reserved for those with severe disease (e.g. sepsis; ICU admission) or patients with documented *Pseudomonas aeruginosa* on recent culture.
- ✓ **? Possible MRSA:** Consider empiric coverage for methicillin resistant *Staph aureus* (MRSA) for those with more severe disease (sepsis or ICU admission) or patients known to be MRSA carriers.
- ✓ **Anaerobic coverage:** Anaerobic infection is more likely to be present in patients with long-standing ulceration, or in those with "foul-smelling" purulent drainage.

Use the following table to "stage" the patient and administer initial antibiotic Rx:

Stage of infection	Suggested empiric antibiotics
Mild infection Purulent wound with… • Cellulitis/erythema extending ≤ 2 cm • Pt afebrile c no systemic toxicity	Cephalexin 500 mg PO Q 6 hr *or* Clindamycin 450 mg PO Q 6hr *or* Amoxicillin/clavulanic acid (875 mg PO BID) *or* Levofloxacin 750 mg PO Qday
Moderate infection Purulent wound with… • Cellulitis extending > 2 cm. • Lymphangitic streaking • Fever ≤ 38.7 C (102 F) • Spread to deeper soft tissues including muscle, tendon, joint or bone	Ceftriaxone (2 gm IV Qday) + metronidazole (500 mg PO q8hr) *or* Cefotetan (2gm IV Q 12 hr) *or* Ampicillin/sulbactam (3 gm IV q6hr) *or* Ciprofloxacin 750 mg PO q12 hr + Clindamycin 450 mg PO/IV q6 hr
Severe infection Patient with signs of systemic toxicity including.. • High fever and shaking chills • Hypotension • Confusion • Leukocytosis • Severe hyperglycemia or metabolic acidosis • Severe "toxicity" .	Piperacillin/tazobactam (4.5 gm IV q8hr) + Vancomycin (1 gm IV Q 12 hr) or Doripenem (500 mg IV q8hr) + Vancomycin (1 gm IV Q 12 hr) or Ciprofloxacin (400 mg IV Q 12 hr) + Clindamycin (900 mg IV q 8hr)
Note: All dosing is based on normal renal function	

Does your patient have necrotizing fasciitis (or gas gangrene)?

On first examination, this patient might appear to have just a simple streptococcal cellulitis—patients with uncomplicated streptococcal cellulitis often have impressive soft tissue swelling accompanied by signs of moderate "toxicity" including high fever and tachycardia. Nevertheless, *always* keep in mind the possibility of a serious necrotizing soft tissue infection such as gas gangrene or necrotizing fasciitis (NF)—survival in these cases requires early surgical intervention. In evaluating your patient with DFI, look for the following clues to the possibility of necrotizing soft tissue infection:

- ✓ **Quality of the pain:** The severity of the pain—often out of proportion to findings on physical examination—is an important clue to the possibility of NF; the pain is unrelenting and often poorly responsive to opiates or NSAIDS.
- ✓ **Physical exam findings:** While there may be minimal findings on the initial examination, any signs suggesting soft tissue gas (crepitation) or cutaneous necrosis (hemorrhagic or dusky bullae) increases the possibility of necrotizing fasciitis. Despite the severe pain, localized cutaneous anesthesia is common with further spread of the infection.
- ✓ **Patient "toxicity":** Patients with NF and related conditions often develop severe toxicity (e.g. hypotension, confusion, respiratory distress, severe tachycardia) suggesting underlying sepsis. Patients with type II NF (group A streptococci) may develop signs and symptoms compatible with toxic shock syndrome (TSS). A

sense of extreme anxiety or fear ("I feel like I am going to die") is not uncommon in patients with life-threatening gas gangrene or NF.

- ✓ **Clinical progression:** The progression of NF can be variable—although most patients become severely ill quite rapidly, some cases develop over several days and have a more subacute presentation.
- ✓ **Laboratory findings:** Patients with progressive NF frequently develop elevated CPK, increasing leukocyte counts (often over 10K) and laboratory findings consistent with metabolic acidiosis (↑ lactic acid levels; ↓ serum bicarbonate).
- ✓ **Radiographic abnormalities:** Presence of gas in the soft tissue on routine plain films or CT scan suggests the possibility of a Type 1 necrotizing fasciitis (mixed aerobic/anaerobic infection) or gas gangrene (due to *Clostridia perfringens*). Be careful—absence of gas does not rule out a NSTI; patients with group A streptococcal necrotizing fasciitis typically *do not* have soft tissue gas.

While no single factor "proves" that the patient has a necrotizing soft tissue infection,severe, unremitting pain, soft tissue gas on radiographs and the appearance of "patient toxicity" all point to the diagnosis. In suspect cases, involve a surgeon as early as possible—definitive diagnosis and treatment requires surgical intervention.

A "Gallery of Gangrene"—Classification of necrotizing soft tissue infection

The classification of necrotizing soft tissue infections remains confusing and the specific diagnosis may not always be clear in any one case. While some of these syndromes have a subacute onset and delayed progression, most are marked by a relatively rapid onset of severe disease with associated sepsis and high mortality. With this in mind, here is a list of some of the more common syndromes likely to be seen by the clinician:

- **Necrotizing fasciitis:** These soft tissue infections are marked by prominent, necrotizing involvement of the fascial plane, often with sparing or late involvement of the overlying muscle. This syndrome is further subdivided by the underlying microbiology…
  - ➢ **Type 1 NF:** These patients have infection with mixed organisms, including at least one anaerobic species (e.g. *Bacteroides* sp.; *Peptostreptococcus*) in combination with a "facultative" anaerobe such as streptococcus or *Enterobacteriaceae* (e.g. *E coli, Enterobacter, Klebsiella, Proteus* species). Because of the presence of facultative anaerobes, soft tissue gas is a prominent feature of type 1 NF.
  - ➢ **Type 2 NF:** This form of the infection is associated with group A streptococcal infection; although clinically similar to type 1 NF, the presence of signs associated with streptococcal toxic shock syndrome (generalized erythematous "sunburn-like" rash) is a clue to this particular pathogen. In contradistinction to type 1 NF, soft tissue gas *is not* seen in type 2 NF.
  - ➢ **MRSA-associated NF:** Recent reports suggest that community-acquired MRSA infection (CA-MRSA) may present with a clinical syndrome similar to type 2 NF. For this reason, most specialists add empirical antibiotic coverage for this organism (e.g. vancomycin, clindamycin) until culture results are available.
- **Clostridial myositis (Gas gangrene):** This is the classic "gas gangrene" seen in diabetics with soft tissue gas, intense muscle pain, and "dishwater" pus coming from affected wounds. This may occur following relatively minor trauma and is usually due to *Clostridium perfringen* or related clostridial species. Gram stain of the purulent drainage demonstrates gram-positive rods (clostridia) but few leukocytes—the organism secretes a toxin responsible for cell lysis.

ID Checklist: Managing antibiotic therapy in diabetic foot infection…

- ❑ **Stage the wound:** Using the above system (mild, moderate, severe) stage the virulence of the infection based on size of surrounding cellulitis, depth of infection (? Muscle, tendon, bone involvement) and severity of associated symptoms (High fever, sepsis, acidosis, renal failure)
- ❑ **Obtain a culture:** Try to obtain a "deep" swab of any purulent material. Whenever possible, have podiatry debride the wound in order to obtain a more reliable specimen. Obtain blood cultures in patients with fever who are hospitalized.
- ❑ **Consider hospital admission** and parenteral therapy in patients with moderate to severe infection, especially those with rapidly spreading cellulitis or any evidence of systemic toxicity (e.g. fever, hypotension). If you choose to treat the patient as an "outpatient", arrange for followup within the next 24-48 hours to make sure the infection remains under control or is clinically improving.
- ❑ **Choose empiric antibiotic** therapy based on the severity of infection described in the above table (IDSA criteria). In patients with "severe" infection (DFI + signs of severe SIRS), use broad spectrum therapy that includes agents with activity against *Pseudomonas* and MRSA until culture results are available.
- ❑ **Obtain a surgical consult** in patients with evidence of gangrene, soft tissue air, myositis or severe infection (? Underlying occult fasciitis). Always keep in mind the possibility of a necrotizing soft tissue infection requiring surgical intervention for diagnosis and treatment.
- ❑ **Reevaluate the patient** in 24-48 hours—make sure the patient is improving and consider modifying the antibiotics depending upon the culture results.

Managing the diabetic foot infection—what you need to know…

- Never underestimate the severity and potential for harm of a diabetic foot infection--even seemingly "trivial" infections can lead to life-threatening complications such as gangrene, loss of limb, and rarely death.
- Using the IDSA guidelines, "stage" the infection as mild, moderate or severe using simple criteria such as ulcer dimension (size, depth), presence of purulence, degree of erythema and systemic symptoms (fever; tachycardia, hypotension, "toxicity).
- When indicated, debride the ulcer and obtain a deep culture for aerobes and anaerobes. Compared to a superficial swab, a "deep" culture is more likely to reflect the true microbiology of the infection.
- In patients with "acute" infection, gram positive organisms such as *Staph aureus* and streptococci (group B streptococci) are the most common pathogens. In those with a long-standing ulcer (e.g. > one month), there is a higher incidence of infection with "facultative" gram negative bacteria (e.g. *E. coli; Klebsiella*) and strict anaerobes (*Bacteroides* sp.; anerobic streptococci).
- For "mild" infection (shallow ulcer; no toxicity), treat with oral antibiotics (cephalexin; amoxicillin/clavulanic acid; clindamycin or levofloxacin).
- In those with "moderately" severe infection (deep ulcer; signs of "SIRS but not toxic), administer intravenous antibiotics such as cefoxitin, ampicillin/sulbactam or ceftriaxone + metronidazole).
- In patients with "severe" disease (gangrene; toxicity; hypotension; high fever), obtain cultures and administer broad spectrum antibiotics that includes antibiotics with activity against *Pseudomonas aeruginosa,* MRSA and anaerobes.
- In patients with "severe" cellulitis (e.g. severe pain, patient toxicity, leukocytosis, soft tissue gas), always keep in mind the possibility of necrotizing soft tissue syndromes such as necrotizing fasciitis or gas gangrene. In these cases, involve a surgeon as early as possible—both diagnosis and management of these conditions requires surgical evaluation.

Chapter 5

"Saved by the Scalpel"- Surgery in the diabetic foot

Antibiotics don't always work—severe diabetic foot infections (DFIs), frequently require surgical intervention such as debridement or amputation for ultimate cure. This chapter pays special attention to the following issues:

- **Surgical anatomy of the diabetic foot:** What anatomic features of the foot are important to the surgeon? We will give a brief overview of the anatomy of foot "compartments" and their importance in any surgical intervention.
- **Surgical indications:** What circumstances lead to surgical intervention in patients with DFI? Operative management of DFI includes abscess drainage, debridement, and resection of infected bone or major amputation.
- **An amputation "primer":** Surgical amputation is a common outcome in patients with severe diabetic foot infection—this section outlines the major types of amputation as well as the impact of these procedures on a patient's mental well-being and ability to ambulate.

The "decision for incision"—when surgery is necessary

In the patient with diabetic foot infection, aggressive surgical intervention is most frequently required in the following situations…

- **Deep soft tissue abscess:** If you suspect a deep, soft-tissue abscess—or there is presence of soft tissue gas—obtain surgical advice as soon as possible. Early, aggressive drainage/debridement—along with antibiotic therapy—may allow you to "save" the rest of the foot.
- **Osteomyelitis:** In patients with clear evidence of osteomyelitis (bony destruction on plain film; + "probe-to-bone" test), early surgery—including debridement or partial amputation—may be necessary. Even if a "full" amputation is not necessary, early debridement of infected bone allows the surgeon to obtain adequate deep cultures, information that can be quite helpful in guiding subsequent antibiotic therapy.
- **Gangrene/Necrotizing fasciitis:** If there is evidence of gangrene (e.g. black, necrotic tissue) or necrotizing soft tissue infection (e.g. cellulitis/myositis with severe pain and patient toxicity) obtain a consult as soon as possible—early, immediate surgical evaluation with debridement/amputation may be essential and prove life-saving.

Surgical anatomy of the foot—what you need to know

Significant diabetic foot infections frequently end up in the hands of a surgeon. In a few simple bullet points, here is what you need to know about the basic surgical approach to soft tissue abscesses:

- ✓ **Four main compartments:** The forefoot has a four main compartments defined by fascial planes (see Fig. 1 next page) including the following: 1) Medial compartment, 2). Central compartment, 3). Lateral compartment

and 4). Intraosseus compartment. Initial soft tissue abscesses tend to remain confined within these compartments.

- ✓ **Pathway to the calf:** Infection of the central compartment with its' associated tendons is the most likely route for spread of infection beyond the ankle and into the calf.
- ✓ **"Compartment" syndromes:** Foot infections may lead to "compartment syndromes" with elevated intracompartmental pressures, vascular compromise and subsequent gangrene.

Fig 1: The four compartments of the foot

Transverse section of the foot with 4 compartments including:

1**). Medial compartment**: 1st toe and associated muscles

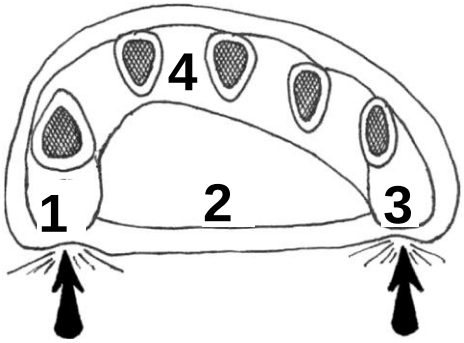
2). **Central compartment**: 2nd, 3rd, and 4th toes with intrinsic muscles of the foot.

3). **Lateral compartment**: 5th toe and associated muscles

4.) **Interosseous compartment**. 2nd,3rd, 4th MT with interosseous muscles

The arrows demonstrate points of maximal pressure and common locations for ulceration (arrows).

Source: van Baal J G Clin Infect Dis. 2004;39:S123-S128



Surgical considerations

In their approach to the infected diabetic foot, surgeons have a number of considerations that help to determine the type of surgery and—if necessary—the level of amputation. They keep the following in mind as they plan the procedure:

- **Presence of pus and necrosis:** Does the patient have a "deep infection" with pus (e.g. abscess) and necrotic bone? Although this is often anticipated prior to surgery, sometimes the extent of the infection will only be apparent at the time of the operation.
- **Functional outcome:** If some type of amputation or bone resection is necessary, what will be the functional outcome of the foot? Although more limited "foot-sparing" surgery (e.g. ray resection or transmetarsal amputation) may allow the patient to ambulate, altered biomechanics may increase the rate of ulceration on the remaining foot.

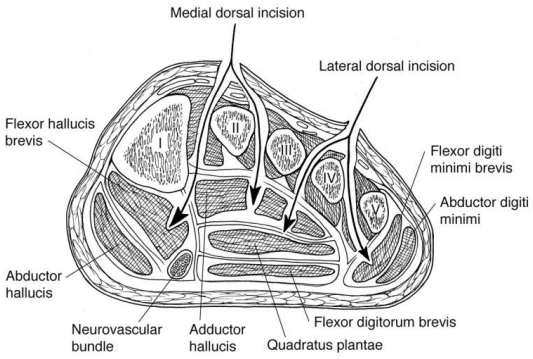


Fig. 2. Surgical approach to deep soft tissue infection

Source: Injury to the Tarsometatarsal Joint Complex JAAOS **July/August 2003** vol. 11 no. 4 **260-267**

- **Vascular status:** Poor capillary fill time and the absence of a "healthy" *dorsalis pedis* pulse raise questions about the patient's vascular status and the ability of the wound to heal. While there are ways to assess vascular status prior to surgery (see Chapter 6), the adequacy of the vascular supply can be assessed at the time of surgery by the amount of bleeding and a visualization of the perfused tissues.
- **? Soft tissue flap:** With any amputation procedure, the surgeon will need to decide if there is adequate, perfused soft tissue (skin) available that will allow creation of a flap and healing of the wound.

The Double-Dorsal Incision: For drainage of deep soft tissue abscesses or management of "compartment" syndromes of the foot, dorsal incision ("the double dorsal" incision—see figure 2) is usually preferred by the surgeon---this allows for quicker healing and reduces the degree of pain when patients subsequently begin ambulation

R. D. Lawrence—a "layer cake" and foot sparing surgery

Robert Daniel Lawrence (1892-1978) was a British medical student who himself suffered from intractable diabetes. In 1925, believing his condition to be incurable (insulin had yet to be discovered) he traveled to Venice to live out his remaining days surrounded by warm weather and culture. Following the discovery of insulin (1926), Lawrence hastily returned to Great Britain and became one of the first English diabetic patients to receive the new drug. As a physician with a unique perspective on the condition, Lawrence dedicated his subsequent career to treating diabetic patients and complications associated with the condition. For long-term diabetics, Lawrence recognized that simple provision of insulin was not enough—improved patient survival led to additional complications such as peripheral neuropathy and associated foot infection. In an era of limited antibiotic therapy, such a complication could well be fatal—simple infection could quickly become life-threatening, necessitating the need for a major amputation to ensure patient survival. Hoping to avoid this outcome in one of his patients with a localized foot infection, Lawrence convinced a surgical colleague (K.C. McKeown) to consider a more limited "ray" or "wedge" resection of the affected foot, a procedure he compared to "taking a slice out of a layer cake". The first such operation took place in 1941 during the London blitz—despite the trying circumstances of the surgery, the procedure was a success and the patient fully recovered with a functional foot that appeared almost normal. Lawrence's insights paved the way for modern surgical approaches to the diabetic foot—such "foot-sparing" surgery avoids "major" amputations and maintains patient mobility by minimizing tissue and bone loss.

Source: Mc Keown KC,The History of the Diabetic Foot. *Diabetic Medicine* 1995;12:19-23.

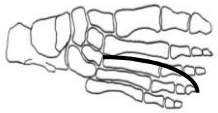
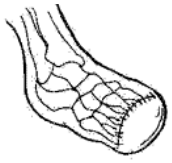
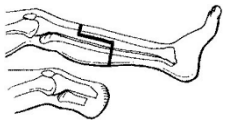
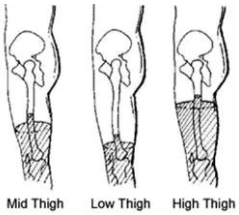
Choosing the Level of Amputation

If an amputation is necessary, surgeons are usually the ones to make the decision about the feasibility and level of amputation in a specific situation. As the surgeon evaluates the case, here are some of the important considerations that come to mind:

- **Extent of infection:** Any amputation must remove all infected and necrotic tissue, allowing for a healthy "margin" that will permit wound healing.
- **Vascular considerations:** There must be adequate blood supply for wound healing to occur. Simple procedures (e.g. Doppler studies of blood pressure; pulse volume analysis) can help predict whether the amputation will be successful at a specific level.
- **A "functional" stump:** The amputation must preserve a "functional" stump that has a minimal chance of repeat skin "breakdown" and—in those with "higher" amputations (e.g. amputations above the foot)—provides an adequate base for a functioning prosthesis.
- **Patient fitness:** The patient's underlying health is a critical in the ultimate decision—complicated "foot-sparing" surgery (with its' more prolonged healing times) may be unwise in a patient with severe congestive heart failure who is unlikely to be ambulatory. In this situation, a below the knee amputation (with a "clean" margin) may be a better choice, leading to faster healing of the stump and more rapid recovery.

A Compendium of lower extremity amputations

Once a decision is made to perform an amputation or debridement, the surgeon must decide at what level the amputation will occur. Whenever possible, the surgeon will make all efforts to try to perform amputation as far distally as possible. In general, most "foot-sparing" amputations (e.g. ray resection; transmetatarsal) will leave the patient with a "functional" foot and able to ambulate. The following table outlines the types of amputations likely to be necessary in the patient with severe infection:

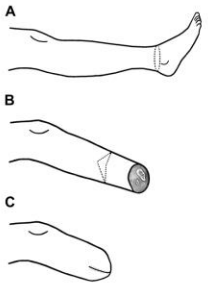
Type of Amputations	Comments
Toe amputation 	Toe ulceration/infection is common in diabetics and, a "limited" toe resection is the most common type of amputations in these patients. Fortunately, most of these procedures are well tolerated and result in relatively minimal cosmetic deformity and gait impairment. Amputation of the **5th toe** is the most common amputation in diabetics—it has little effect on stance, appearance and gait. Amputation of the **1st toe** is also common; stance and walking are normal except for a mild limp with rapid ambulation. Amputation of the **2nd toe** is likewise well-tolerated; however, there is a higher incidence of subsequent severe *hallus valgus*, a deformity associated with ulceration.
Ray amputation 	Digital ulceration with more proximal involvement may require a **"ray" resection** with excision of part of the metartarsal bone along with the distal phalanx. The head of the first metatarsal is a primary weig ht bearing surface—resection of the first ray often leads to gait imbalance and a limp. Surprisingly enough, despite the more extensive bone loss, amputation of the medial two (and even three) rays often provides a functional, weight-bearing foot with relatively normal gait. Border ray amputations (3rd, 4th, 5th toes) are well-tolerated and do not significantly interfere with normal ambulation.
Transmetatarsal amputation 	More proximal infection with involvement of several toes or the distal metatarsal bones may require a **transmetatarsal amputation** (TMA)—an amputation across the midfoot level that leaves the proximal two thirds of the foot intact. Although the TMA is more disabling than a simple toe (or ray) amputation, patients remain ambulatory and have no need for a prosthesis except for a molded shoe filler. Nevertheless, the absence of the positive fulcrum in the ball of the foot (and loss of the "push off" function of the foot) leads to an impaired gait with a higher incidence of post-surgical complications including hematoma, infection and non-healing ulcer. The presence of deep forefoot infection with cellulitis and lymphangitis extending up the foot are *contraindications* to this procedure.
Below the knee amputation 	The below-the-knee (BTK) amputation is indicated when there is major vascular compromise to the distal foot, especially when proximal extension of the infection (to the ankle) precludes a partial foot amputation (e.g. transmetatarsal amputation). The amputation is well tolerated (with good healing) and has good rehab potential in a medically stable patient—approximately 70% of patients are able to walk with prosthesis. Relative *contraindications* to this procedure include severe infection/gangrene of the mid-calve, severe proximal vascular disease (occlusion of the profundo-femoris artery) and permanent flexion contracture of the knee (this makes use of a prosthesis unrealistic).
Above Knee Amputation 	When the infection has progressed and a below the knee amputation isn't adequate, an above –the-knee amputation (AKA) may be necessary. Although it is a drastic procedure, the AKA has a high healing rate (> 90%) in most studies. The higher amputation leads to a high energy demand (80-120% above normal) if patients are able to ambulate with a prosthesis. This can be a special challenge in individuals with underlying medical problems such as cardiac disease—older diabetics are usually unable to walk following this procedure and often confined to a wheelchair. Depending upon extent of infection, there are three potential levels for amputation (see drawing)—not surprisingly, the lower the level of amputation, the greater the likelihood of ambulation with a prosthesis.

A “guillotine” for gangrene—surgical “staging” of amputation

In patients with “wet” gangrene requiring amputation of the foot, the extent of proximal infection is not always clear—primary closure of an “infected” wound may lead to subsequent wound infection with a need for further surgery. One solution to this problem is a “two-stage” approach—the patient has an initial “guillotine” amputation at the ankle (without wound closure) followed by a more proximal “formal” amputation with secondary wound closure (see Figure 3). The initial stage allows the surgeon to evaluate the extent of infection, and if necessary, provide antibiotic therapy for the next several days prior to the more definitive “standard” amputation. Although it requires an additional operation, this “two-stage” approach has a lower subsequent complication rate (decreased incidence of “stump” infection) and may reduce the need for a subsequent, more disfiguring amputation. In the two-stage approach, antibiotic therapy is typically continued during the gap between the first and second surgeries.

See Fisher et al. J Vasc Surg 1988 8(4): 428-33.

Figure 3: A “guillotine” amputation: An illustration of a “guillotine” amputation showing:



A).The level of the initial cut,

B).The end of stump following the initial surgery

C).**T**he subsequent revision to below-the-knee amputation.

Source: Vinod K Panchbhavi et al. Guillotine Ankle Amputation. Medscape http://emedicine.medscape.com/article/1894411-overview accessed 12/16/14

The “Will to Walk”—Amputation and its’ aftermath

As clinicians, we are sometimes too cavalier about the prospect of amputation—although it may be the “right” medical decision, it is often refused by the patient if we fail to address their fears and the potential toll on the “psyche”.

Trauma vs Infection—the current face of amputation

In Western countries, limb amputation occurs primarily for one of two reasons—trauma (now increasingly associated with military service)—and medical causes, usually amputation due to underlying vascular disease such as diabetes. The psychological “fallout” of amputation may be different for these two groups. While amputation associated with trauma can certainly be challenging, patients tend to be younger, have fewer underlying medical problems and generally have better rehabilitation prospects The situation is likely to be different for the diabetic patient—in these individuals, underlying medical conditions (e.g. stroke; heart failure; severe fatigue) make the post-amputation rehabilitation much more difficult.

In light of these considerations, when the question of amputation/ arises in the patient with diabetic foot infection, the clinician needs to understand—and address—the following patient fears:

- **Fear of disfigurement:** How will I look following an amputation--will this change my image of myself?
- **Fear of immobility**: Will I lose the ability to walk on my own?
- **Fear of others**: Will others treat me differently? Will my family members (or partner) lose interest in me?
- **Fear of death:** Is this a prelude to additional medical problems and my ultimate death?

As you counsel patients, it is important that you (and the patient) understand the following "realities" of lower extremity amputation:

1. **Level of amputation:** The "level" of amputation plays an important role in the ultimate ability to maintain ambulation— provided that their medical status is good (e.g. no stroke or severe heart disease), most patients with partial foot amputations (e.g toe; digit; transmetatarsal) will be able to walk. Patients with "higher" amputations (e.g. below-the-knee; above –the-knee) may be able to walk depending upon their determination and underlying medical status (see Table 2).
2. **Energy of walking:** Higher level amputations (BTK; ATK) increased energy expenditure associated with ambulation, a fact that will have a significant impact on the patient's ultimate recovery. Patients with a below-the-knee (BTK) amputation have a 50% increase in energy expenditure when walking; despite this, somewhere between 60 to 90% will walk successfully following intensive training. The data isn't as good with above-the-knee (ATK) amputations—these patients have double the energy expenditure (90-120% increase) and less than 30% of individuals will achieve ambulatory status.
3. **Underlying medical condition:** Patients with vascular disease and diabetes are older and have additional underlying medical conditions—these may hamper recovery following amputation and interfere with long-term attempts to maintain ambulation.

Table 2: Ambulation following Lower Extremity Amputation (LEA) in the older patient

Type of LEA	% Total of LEA	% Additional energy required for normal bipedal ambulation	% Using prosthesis after intensive physical therapy program
Partial foot	50	0	Not applicable
Below the knee (Trans-tibial)	25	40-60	60-90
Above the knee (Trans-femoral)	25	90-120	0-40

Source: Table modified from Coletta EM. Care of the elderly patient with lower extremity amputation. J Am Board Fam Pract 2000;13-23-34

What you can do to explain amputations to patients…

- **Be honest about the potential complications** including infection, poor healing and the possibility of eventual need for higher amputation.
- **Emphasize the potential benefits** of a surgical or amputation procedure, including early intervention as a way of minimizing a more disfiguring amputation due to uncontrolled infection.
- **Review the possibilities of "rehab"**—most patients with partial foot amputations have a good outcome and—in most cases—a good chance at remaining ambulatory. In some cases, an amputation—with a well healed wound—permits earlier ambulation compared to a patient with a chronic, painful wound where ambulation is likely to be limited.
- **Encourage the patient** to discuss the amputation with friends and family—they need to be reminded that they are still "the same person" and valuable despite the loss.
- **Be patient:** When first approached, a patient may refuse amputation (though necessary), requesting a trial of antibiotics. In non-life-threatening situations (simple osteomyelitis of the digit), this may be appropriate. If it doesn't work, the patient may be more willing to undergo partial amputation at a later date.

Surgical management of the diabetic foot infection—what you need to know…

- Major indications for surgery in diabetic foot infection include 1). Soft tissue abscess 2). Osteomyelitis and 3). Gangrene or necrotizing soft tissue infection.
- Deep foot abscess is initially confined to one of 4 major anatomic compartments within the foot—these are best approached by incisions from the dorsal or lateral approach.
- The decision about the level of amputation depends upon several factors including the proximal extent of the infection, the state of the vascular supply (Will the wound heal?) and the patient's underlying medical condition (Are they capable of ambulation?).
- A toe amputation— the most common amputation seen in diabetic foot infection—is associated with minimal disability and near normal ambulation in patients with "good" medical status.
- A "ray" amputation includes part of the metatarsal in addition to the toe. Once it heals, the patient should achieve full amubulatory status.
- A transmetatarsal amputation in necessary if patients have multiple digit involvement with proximal spread. Compared to other amputations, patients may have a higher rate of post-operative hematoma and wound breakdown; however, once healed, the patient should be able to achieve full ambulatory status.
- Patients with extensive foot infection or severe vascular disease often require a below-the-knee amputation—with proper healing, patients should be able to ambulate, but with a 30-50% increase in energy requirements.
- An above-the-knee amputation is necessary in diabetic patients with necrotizing infection of the calf—many of these individuals are unable to ambulate following surgery because of poor underlying medical status and a close to 100% increase in energy requirements required for ambulation.

Chapter 6

"Flow to toe"—Vascular evaluation in foot infection

Perhaps your patient's wound is "failing to heal" despite appropriate antibiotic therapy. You notice that the foot is relatively cool and you have trouble feeling the *dorsalis pedis* pulse—maybe the patient has significant vascular disease? This chapter will outline techniques for early identification of these patients as well as possible management strategies in the diabetic whose peripheral arterial disease (PAD) is impairing recovery. As you think about vascular disease in diabetics, keep the following in mind:

- **A problem with the "pipes"—vascular disease in diabetics:** Vascular disease is common in long-standing diabetics and contributes to the risk of infection as well as the delayed wound healing. In addition to large-vessel (macrovascular) disease, diabetics are also plagued small-vessel, microvascular involvement.
- **Tests for PAD—identifying and confirming the problem:** Simple bedside screening tests (e.g. arterial palpation; ankle-brachial index [ABI]) help identify underlying vascular disease where additional studies (e.g. arterial ultrasound; angiography) permit confirmation of the condition.
- **Bypassing a blockage—management approaches:** Once you've identified PAD, several techniques including balloon angioplasty and surgical intervention (e.g. vascular bypass) can improve blood flow and hasten wound closure.

A sugary "saga"—PAD in diabetics

Depending upon their age—and length of time they have been diabetic—anywhere between 25 and 33% of diabetic patients may have significant underlying vascular disease. Despite the well-known problem of "microvascular" disease, many diabetics have disease in "larger" vessels that might be amenable to surgical intervention. As you evaluate the patient with a diabetic foot infection, look for the "red flags" that suggest the need for additional vascular evaluation:

- ✓ **History of claudication:** The presence of "cramping" or "fatigue" in legs with exercise suggest the possibility of underlying claudication due to vascular obstruction. Foot or leg pain at rest that improves when the patient hangs the foot over the side of the bed is also suggestive of underlying vascular disease.
- ✓ **Dependent rubor** of the foot—or other signs of vascular insufficiency (e.g. loss of hair, evidence of gangrene/cyanosis, cold dry skin, thick nails)—are additional evidence in support of vascular disease.
- ✓ **Absence of *dorsalis pedis* pulse:** Absence of the *dorsalis pedis* or *posterior tibialis* pulse is a definite warning sign of underlying vascular disease; however, be cautious about jumping to conclusions—approximately 10% of "normal" individuals lack a palpable DP pulse (see Table 2).
- ✓ **Failure to heal:** A diabetic foot wound that fails to heal in the presence of a diminished (or absent) pulses suggests the possibility of underlying PAD.

Peripheral vascular disease (PVD) can be seen in both diabetics and non-diabetics; although the clinical presentation may be similar in the two populations, there are some important clinical differences that need to be kept in mind:

- **Symptom disconnect:** Diabetics with peripheral neuropathy have a different presentation of exercise-induced claudication—diabetics are more likely to complain of leg "fatigue" or weakness with exercise rather than strict claudication-type pain..
- **Location, location, location:** Although "large vessel" disease (aortoiliac and femoral artery) is frequent in diabetics, compared to non-diabetic patients with PAD, involvement of more peripheral, below-the-knee vessels (tibia and peroneal arteries) is more common. This has important implications for attempts at revascularization—vascular surgery in diabetics often requires bypass (or angioplasty) of more distal vessels, a more complicated procedure with a higher failure rate.

The above observations sometimes lead delays in the recognition and treatment of vascular disease in diabetics—if there is any question about vascular status, obtain a simple screening test (e.g ABI or Ankle-Brachial Index) and—based on these findings—obtain more sophisticated testing (e.g. arterial ultrasound) to document the extent of the obstructions.

Put your best "toe" forward…Vascular evaluation 101

In patients with diabetic foot infection, a few simple tests will help determine the likelihood of an underlying vascular obstruction…

- **Physical exam:** Check for a *dorsalis pedis* and *posterior tibial* pulse using a simple grading system (Table 1). Clear absence of *both* of these pulses suggests underlying vascular disease; however, keep in mind that up to 10% of the "normal" population has a non-palpable *dorsalis pedis* pulse (Table 2).

Table 1: Pulse force grading system

Level	Interpretation
3+	Full, bounding
2+	Normal
1+	Weak
0	Absent

Source: J Diag Med Sonography. 2004. 20:5-13

Table 2: Dorsalis pedis artery—prevalence of diminished/Absent Pulsation

Status	% Cases	Status	% Cases
Nondiabetic		**Diabetic**	
Age 35-54	8.6	Age 35-54	16.2
Age 55-74	13.7	Age 55-74	23.5

Source: 1976-80 Second National Health and Nutrition Examination Survey

In patients with absent or diminished peripheral pulses, make sure you examine more proximal vessels. Examine the abdomen for an aneurysm or bruit (? internal iliac obstruction) and palpate for presence of femoral and popliteal pulses. Although we often stress the problems of "microvascular" disease in diabetics, these individuals are also at risk for large vessel obstructions that can be readily bypassed.

- **Ankle Brachial Index (ABI):** Using a blood pressure cuff—and Doppler ultrasound probe—the ABI is a simple "bedside" test that can help screen for underlying vascular disease. Conduct the test with the patient supine and calculate the ABI for each leg by comparing the ratio of the ankle to brachial systolic pressure. In general, values less than 1.0, with anything below 0.8 suggesting the possibility of significant vascular obstruction. Use the following table as a guide to the test results:

Table 3: Ankle-Brachial Index (ABI) Interpretation

ABI ratio	Interpretation
≥ 1.30	Noncompressible vessel
1.00—1.29	Normal
0.91—1.00	Borderline (equivocal)
0.41—0.90	Mild to moderate PAD
0.00 to 0.40	Severe PAD

Source: Begelman SM and Jaff MR. Cleveland Clinic Journal of Medicine 2006;73 (supplement 4): S22-S29.

When interpreting the results, keep in mind the following caveats…

- ✓ **ABI accuracy:** Normal ankle pressure exceeds the brachial pressure by 10-15 mm Hg. Relative to a contrast enhanced arteriogram (the "gold standard" for vascular evaluation), an ABI of 0.90 (or less) has a sensitivity of 95% and a specificity of 100% for detecting a stenotic lesion of at least 50% in the limb.

- ✓ **Warning—an elevated "ABI" (≥ 1.30):** A high ratio (≥ 1.30) suggests a *non-compressible* vessel due to underlying medial artery calcification. In these patients, the ABI is unreliable and additional tests should be ordered. If you have the proper equipment, some experts recommend a toe-brachial index (TBI—see below) in this situation.
- ✓ **Toe-brachial Index:** Since "medial artery calcification" does not generally affect the smaller blood vessels supplying the toes, a TBI (Toe-brachial index) may permit allow a more accurate assessment of vascular status in patients with an artificially "high" ABI. In this situation, a toe-brachial index of less than 0.70 is considered diagnostic of underlying vascular disease.

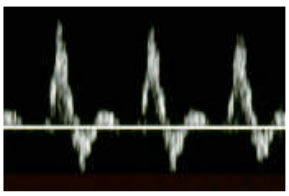
- **Transcutaneous oxygen tension ($TcPO_2$):** Though not always available, measurement of transcutaneous oxygen tension provides an accurate reflection of oxygen availability at the tissue level.

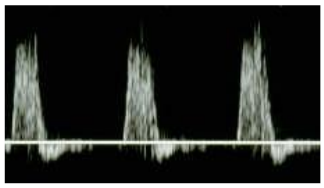
Table 4: Transcutaneous oxygen tension ($TcPO_2$)

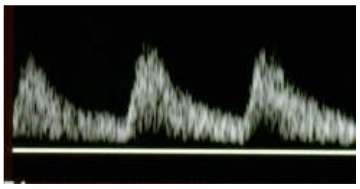
Level	Interpretation
≥ 50 mm Hg	Normal tissue oxygenation levels
< 35 mm Hg	Compromised tissue
< 20 mm Hg	Wound healing unlikely to occur

- **Arterial Duplex Sonography:** If any of the above "screening" tests are positive—or if you still have a high index of suspicion for arterial disease (e.g. claudication; failure of ulcer to heal)—the next test is usually some form of arterial ultrasound with measurement of segmental blood pressures (down the leg, proceeding from mid-thigh) and analysis of the peripheral artery Doppler waveform.

Analysis of Doppler waveform







Triphasic	Biphasic	Monophasic
"**Normal**" vessel with 3-phase flow: - *Initial rapid systolic peak flow* - *Early diastolic flow reversal* - *Late diastolic forward flow*	Early atherosclerosis with diminished diastolic flow reversal	Late atherosclerosis with monophasic pattern and diminished flow.

Source: J Diag Med Sonography. 2004. 20:5-13

The "normal" artery demonstrates a "triphasic" pattern with three distinct components—an initial, rapid upstroke to peak systolic velocity (PSV), followed by a flow reversal in early diastole, and a subsequent lower, late systolic peak (forward flow). As atherosclerosis develops—and the vessel becomes less elastic and compliant—the waveform takes on a biphasic, and later monophasic appearance.

As the ultrasonographer systematically images the descending vascular tree, they may pick up areas of obstruction with a drop in blood pressure across the blockage. Although overall flow is reduced, patients with a significant obstruction will have an *increased* peak systolic velocity immediately distal to a blockage. Such findings permit localization of the obstruction and will help planning for subsequent surgery (or angioplasty) should it prove necessary.

- **Angiography:** The above testing represents non-invasive "screening" tests for peripheral arterial disease. Once it is determined that significant obstructions exist, any subsequent surgical procedure generally requires an angiographic procedure.
  - ✓ **Magnetic Resonance Angiography** (MRA) has excellent accuracy (Sensitivity: MRA 94% vs. duplex ultrasound 89%) and is able to acquire images of almost all major lower extremity vessels including the *dorsalis pedis*. Although quite sensitive, MRA has a tendency to overestimate extent of stenosis (calling a "moderate" stenosis "severe") and cannot reliably detect calcium—a feature that may limit revascularization attempts.
  - ✓ **Computerized tomographic arteriography**: Current CT scanners (64 channel "multidetector") allow for more rapid image acquisition than MRA with an almost equivalent sensitivity/specificity for detecting vascular obstruction. Drawbacks include the possibility of nephrotoxicity following contrast administration, and the potential for radiation exposure if the test needs to be repeated.
  - ✓ **Contrast angiography:** This is the "gold standard" for imaging the lower extremity vascular tree and is now mainly reserved for patients who will be undergoing vascular bypass surgery or—at the time of procedure—balloon angioplasty.

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Andreas Gruentzig and transluminal balloon angioplasty

In the 1964, Dr Charles Dotter, a vascular radiologist at the University of Oregon in Portland, developed the technique of transluminal angioplasty—he introduced increasingly large catheters into a vessel in order to "open up" an arterial obstruction in a peripheral artery. Schooled in Dotter's techniques, a young German physician named Andreas Gruentzig wondered about adding a "balloon" to the end of a catheter in order to open up obstructions in hard-to-reach locations. Working on prototypes in his kitchen, he developed a double lumen catheter fitted with a polyvinylchloride balloon designed to be "inflated" in order to relieve vascular obstruction. In 1975, Gruentzig presented his findings at a meeting of the American Heart Association—unfortunately, they were met with little interest and some degree of skepticism. Going back to the laboratory, Gruentzig continued to refine his apparatus and—in 1976— performed the first human coronary angioplasty during a cardiac bypass procedure at St Mary's Hospital in San Francisco. When he presented this work at the 1977 AHA meeting, the reception was completely different; the audience recognized the pioneering nature of his work and gave him a standing ovation upon conclusion of his presentation. Dotter and Gruentzig's work has had a profound impact on the modern management of diabetic vascular disease—patients unable to tolerate major vascular surgery can still benefit from improved arterial flow utilizing relatively "simple"—and safer—outpatient angioplasty procedures.

Source: http://www.ptca.org/archive/bios/gruentzig.html Accessed: 1/09/11

"Reborn" with a bypass—vascular surgery intervention

Patients with poor wound healing or symptomatic claudication should undergo the above studies in order to document the presence of vascular insufficiency. If vascular studies suggest the presence of large-vessel obstruction, they may well benefit from surgical intervention (e.g. vascular bypass; vascular stent; balloon angioplasty) in order to reestablish flow.

In this situation, it's generally up to the vascular surgeon (in consultation with radiology) to determine the best approach to relieving the obstruction. This may require surgical intervention (vascular bypass) or an endovascular invasive technique such as balloon angioplasty or stent placement. Each of these approaches has their own pros and cons…

- **Surgical bypass:** In those with signs of vascular insufficiency (e.g. poorly controlled infection; delay in wound healing) and radiographically documented macrovascular disease, surgical bypass may be the way to go. Although "open" surgery has a higher rate of potential complications, comparative studies suggest a higher graft "patency" rate one to two years following the procedure.

  While surgical bypass has certain advantages, not every patient is a candidate. Patients with significant underlying medical conditions (e.g. CHF; coronary artery disease) may not be able to tolerate a major surgical procedure. Previous saphenous vein harvest for other procedures such as coronary bypass, may make the vessels unavailable for peripheral vascular surgery. Diabetics typically have more peripheral disease with significant vascular calcification—this frequently reduces the chances of finding a patent distal "target" vessel and—if surgery is carried out—increases the long term risk of re-occlusion.

- **Endovascular procedures:** During the past decade, additional "non-invasive" techniques have been developed to help manage peripheral arterial disease. These include balloon angioplasty, vascular stents and endovascular atherectomy. Compared to open surgical bypass, such procedures can be performed on an outpatient basis and are better tolerated by the medically infirm patient, unable to undergo major surgery. Although comparative studies are few, such endovascular procedures seem to have equivalent outcomes with relation to mortality, limb salvage (~80% at 1 yr.) and wound healing (~60% at one year).

Literature Alert

Vascular bypass to distal vessels—success vs. failure?

For surgical management of vascular disease, most physicians are familiar with the favorable results obtained with "large" vessel procedures such as aorto-femoral (aorto-iliac lesions) or femoral-popliteal bypass (femoral artery lesions). Diabetics; however, are more likely to have peripheral obstructions including disease in the popliteal, tibial and peroneal arteries. The development of "*dorsalis pedis* bypass" techniques (vascular graft from femoral or popliteal vessels to the dorsalis pedis artery) permits targeting of more distal obstructions and has become more common in the diabetic population with peripheral vascular disease.

To assess outcomes of this approach, investigators in Boston reviewed their experience of 1000 cases (70% male; median age 67 years), treated between 1990 and 2000. Their findings include the following:

- ✓ Diabetes remains a common factor in these "distal" lesions—over 90% of patients in this study had underlying diabetes.
- ✓ While all patients had grafts to distal vessels, the starting point of the graft ("inflow" artery) varied and included the common femoral (~30%), popliteal (~55%) and superficial femoral (~10%) arteries.
- ✓ The operations were a success in the majority of cases—at a 5 year assessment, 60% of grafts appeared "patent" and close to 80% of patients were able to avoid limb amputation.
- ✓ Despite these innovations, the long term outcome in this population remains guarded —mortality was 50% at 5 years and 75% at 10 years. The increased mortality is usually due to associated conditions such as stroke and coronary artery disease.

Bypassing these more "distal" lesions requires grafts with a potentially higher failure rate and the need for greater surgical skill.. Such findings suggest that--in the proper hands--distal vascular bypass procedures may be quite beneficial in diabetics with limb ischemia.

"Open" surgery vs. endovascular procedures—making the decision

Despite these favorable reports, there are both "pros" and "cons" of the various approaches (e.g. surgery vs. endovascular). Some of these include the following:

- ✓ **Endovascular procedures** (e.g. angioplasty; stents) have a *higher* rate of long term re-occlusion when compared to open vascular surgery with grafting.

- ✓ For **open surgical procedures**, native venous grafts (e.g. greater saphenous vein) have a greater patency rate when compared to artificial grafts—previous use of the vein for other procedures (e.g. coronary bypass) favors use of an endovascular approach.
- ✓ **Critical ischemia:** Patients with life-threatening, critical limb ischemia with a potential for large-volume tissue loss—or major amputation—are more likely to benefit from an open surgical vascular graft.

As you discuss the vascular issues with your consultants, the following table might be helpful in sorting out the "issues" involved in a "bypass" versus an "endovascular" procedure:

	Surgical bypass favored	**Endovascular procedure favored**
Patient surgical risk	Average (<5%)	High
Life expectancy	≥ 2 years	Limited
Severity of ischemia	Major tissue loss; poor hemodynamics	Minor ulcer; marginal hemodynamics
Anatomy	Multi-level, TASC C/D	Single level; TASC A-C
Vein availability	Great saphenous vein or good alternate	Inadequate

Abbreviations: TASC: Trans-Atlantic Inter-Society Cpncensus on management of peripheral arterial disease (Score)
Source: Conte MD. Diabetic Revascularization:Endovascular Versus Open Bypass—Do We Haven the Answer?. Sem in Vasc Surg 2012 25:108-114.

In the end, the decision (surgery vs. endovascular procedure) depends upon several factors, including the *severity and extent* of the ischemia, the *overall medical condition* of the patients, and the *expertise of your consultants*. A timely intervention in a patient with a poorly healing ulcer may prevent an amputation and increase the chances of ulcer resolution.

What you need to know—vascular disease and diabetics

- Always consider the possibility of underlying peripheral arterial disease (PAD) in a patient with a poorly responding diabetic foot infection or a recalcitrant ulcer.
- Look for underlying vascular disease in your patients with diabetes—check for presence of a *dorsalis pedis* pulse and obtain simple screening tests (ABI—Ankle Brachial Index) in those with a weak pulse or poor capillary refill.
- DFI patients with abnormal "screening" tests should have additional studies such as arterial duplex sonography, magnetic resonance angiography (MRA) and—in selected cases—contrast arterial angiography in anticipation of vascular reconstruction.
- Although many longstanding diabetics have small vessel disease, a significant proportion of advanced cases also have "large" vessel obstruction (femoral and popliteal artery) that is amenable to vascular bypass.
- Compared to non-diabetic PAD patients, diabetics have an increased incidence of disease in more distal "infrapopliteal" vessels such as the peroneal and tibial arteries. Such anatomy makes vascular bypass surgery more challenging but does not necessarily preclude procedures such as a *femoral-to-dorsalis pedis* bypass.
- For patients unable to undergo "open" vascular surgery, less invasive endovascular procedures such as balloon angioplasty or vascular stents may help reestablish blood flow necessary to heal a recalcitrant ulcer.
- In a patient with a diabetic foot infection, recognize the possibility of underlying vascular disease (check pulses), obtain the appropriate screening tests (e.g. ABI; arterial duplex) and refer the patient to a vascular surgeon if significant disease exists.

Chapter 7

Podiatric "imposters"— Foot infection mimics

Although infection is at the top of the list when you see an "inflamed" diabetic foot, you also need to consider the possibility of a diabetic foot infection "mimics"—conditions that can mimic infection and lead you down the wrong treatment path. Keep these conditions in mind if the presentation is atypical or the patient doesn't appear to be improving with antibiotics:

1. Charcot foot—a pedal puzzle

The patient with Charcot foot (Charcot neuroarthropathy) typically presents with a warm, swollen, erythematous foot that can completely mimic cellulitis. The condition is most commonly seen in long-standing diabetics with significant neuropathy but relatively well maintained blood supply. Although a clear history of trauma may be absent, relatively minor trauma (e.g. minor fall, excess walking, minor trauma to the foot, recent surgery) sometimes triggers the condition.

The initial radiographs may be negative; however, patients with more advanced disease, typically have bone/joint abnormalities (e.g. fractures, bone destruction, joint dislocation) that can be confused with diabetic osteomyelitis. Look for the following features as means of separating diabetic cellulitis/osteomyelitis from Charcot foot:

- ✓ **Symptoms:** Although the foot is typically warm and swollen, Charcot patients generally lack fever and don't appear particular toxic. Patients with Charcot's may have pain, but are often surprisingly pain free.
- ✓ **Absence of ulcer:** Ulcers are usually absent in early acute Charcot foot; however, later—when they have developed significant deformity—ulcers may occur at sites with protruding bone and lead to associated osteomyelitis.
- ✓ **Physical exam:** Although both conditions have neuropathy, Charcot patients typically have well preserved vascular supply—pulses are usually "bounding" and the foot appears well perfused. With Charcot foot, erythema often lessens with elevation of the foot, something that is less likely in cellulitis (In cellulitis, the erythema remains, even if the foot is elevated).
- ✓ **Midfoot involvement:** While Charcot's can affect any part of the foot (including ankle and forefoot), involvement is most common in the midfoot, leading to loss of the arch and the classic "rocker bottom" foot due to destruction of the tarsal-metatarsal joints. Although diabetic osteomyelitis can involve the midfoot, it is typically more common in the forefoot (toes; metatarsals) and calcaneus.
- ✓ **Radiographs:** In Charcot foot, the initial plain film is often normal; however, later films show the typical mid-foot deformity with bone destruction, joint subluxation and fractures of the tarsal bones.
- ✓ **Other findings:** Although Charcot patients are usually afebrile, laboratory abnormalities (elevated ESR, CRP and WBC) can mimic infection and lead to inappropriate antibiotic use.

The early, "acute" Charcot foot can mimic cellulitis, leading to prolonged and unnecessary antibiotic therapy. Clues suggesting Charcots include lack of fever, absence of ulcer or skin break and a relatively "non-toxic" patient. Even then, cellulitis may still be a possibility and the diagnosis uncertain. If in doubt, it is better to administer broad-spectrum antibiotic therapy and reevaluate the patient in a few days—a prompt response to antibiotics suggests that cellulitis was the real culprit; failure of the patient to improve should raise the possibility of an alternative diagnosis such as Charcot foot.

Early recognition of Charcot foot is especially important—immediate "off-loading" the foot (using crutches or a wheelchair) is necessary to minimize the progression with associated bone destruction that accompanies the condition. Charcot foot is so important in evaluation of the diabetic foot that we have devoted the following chapter to a more detailed description of the management of this condition.

2. Diabetic bullous dermopathy—baffling blisters

"Diabetic bullous dermopathy" (*Bullous diabeticorum*) is a condition characterized by the sudden, spontaneous onset of blisters on the hands or feet in diabetic patients. The actual cause of the condition is unclear; however, it is thought related to underlying diabetic "microvascular" disease and typically seen in patients with long-standing disease. Features that are characteristic of this condition include the following:

- ✓ **History:** Patients generally present with the sudden onset of blisters on the extremities, usually on the digits and often without a clear history of trauma.
- ✓ **Physical exam:** The blisters are often irregularly shaped and filled with clear fluid—there is usually little pain and minimal surrounding erythema. If erythema if prominent—and the fluid is "cloudy—keep in mind the possibility of infection and obtain a needle aspiration for culture and Gram stain.
- ✓ **Biopsy results:** Biopsy findings can be variable depending upon the level of the "split" in the skin, from "superficial" (e.g. intraepidermal or subcorneal) to the deeper, dermal-epidermal separation more commonly seen in "fresh" blisters.
- ✓ **Treatment:** Treat these lesions as you would a diabetic foot ulcer, with a covering bandage to protect it from trauma. Although a brief course of antibiotics may be appropriate (if you are unsure about secondary infection), avoid overtreatment with prolonged, high-dose intravenous antibiotics. With conservative therapy, the lesions take about 4-6 weeks to heal, usually without scarring.

The most common problem associated with diabetic bullous dermopathy is initial misdiagnosis—most clinicians haven't heard of the condition, tend to misdiagnose infection and are prone to over-treat with antibiotics. Although *bullous diabeticorum* is generally benign, a ruptured bulla and skin break can lead to infection with all its' attendant complications—follow the patient carefully to make sure they do not develop active infection requiring antibiotic therapy.

3. Calciphylaxis—a dialysis danger

Your patient on dialysis with diabetic renal disease wakes up one morning with a purplish, mottled lesion on their lower extremity—you suspect the presence of infectious "gangrene", but are puzzled by the lack of fever and other signs of inflammation/infection. In this situation, consider the possibility of "**calciphylaxis**", a form of vascular gangrene associated with excess deposition of calcium in the walls of medium-sized arterial vessels.

- ✓ **Clinical presentation:** In calciphylaxis, patients develop cutaneous gangrene that is secondary to vasacular necrosis of underlying fatty tissue. The process can be present in almost any location, but most typically involves the extremities, buttocks and abdominal wall.
- ✓ **Epidemiology:** Although it may occur in patients without renal impairment, calciphylaxis is especially common in patients with end stage renal disease. The presence of underlying hyperparathyroidism is a potential exacerbating factor, leading to deposition of excess calcium in peripheral vessels.

- ✓ **Diagnosis:** In addition to the characteristic appearance on physical examination, patients usually have findings on plain radiography. Plain radiographs of the area invariably demonstrate arteriosclerosis due to calcium deposition in medium sized arteries In uncertain cases, an incisional biopsy may confirm the disease (it demonstrates medial calcification); however, biopsy may worsen the condition and should not be performed routinely.
- ✓ **Therapy:** Debridement of the wound with local wound care may be helpful; however, there are risks to overly aggressive therapy since wounds may take a long time to heal. Patients with hyperparathyroidism may benefit from a parathyroidectomy to bring down calcium levels.

The prognosis in calciphylaxis is guarded—even with aggressive treatment measures, patients have a significant mortality rate over the subsequent year, a reflection of the severity of the patient's underlying renal disease with it's attendant complications.

4. Contact dermatitis—a cutaneous conflagration

Patients put all kinds of creams and ointments on their skin, often without telling their physicians. At times, reactions to these compounds may lead to acute contact dermatitis—a condition with signs of inflammation (e.g. erythema, blisters, drainage) that can completely mimic bacterial infection.

Before you put in the PICC line for long-term antibiotics, keep in mind the following:

- ✓ **Clinical presentation:** Patients present with signs of inflammation (e.g. erythema, warmth) over the affected area that looks like cellulitis; sometimes there are associated blisters that mimic impetigo. Despite the appearance of cellulitis, patients are usually afebrile. The appearance of "bilateral" disease (distinctly uncommon in cellulitis) should prompt consideration of cellulitis "mimics" such as contact or stasis dermatitis.
- ✓ **Topical sensitizers:** Patients use a number of topical creams/ointments that can cause this problem including moisturizers, topical antibiotics and rarely, even topical corticosteroids. Topical neomycin—available over-the-counter—is a special culprit; patients use the ointment to "prevent infection" in a wound but often end up increasing the likelihood of inflammation, especially if they continue to apply the product as the condition gets worse! In addition to topical antibiotics, ask the patient about the "holistic" products such as herbal products (e.g. aloe vera) and topical "vitamins" (vitamin E).
- ✓ **Shoes and socks:** Patients may have reaction to shoe components—this will present as a symmetrical (both feet) erythematous, inflammatory reaction that occurs on the dorsum of the feet in areas of contact with the offending agents. Ask the patient about new shoes or socks—various compounds utilized in shoe manufacture (e.g. dyes, rubber) may lead to an acute reaction in at risk patients.
- ✓ **Treatment:** Once you suspect the diagnosis, make sure the patients stops using the offending agent. The erythema will often improve following application of a mid-potency topical steroid.

Remember! Contact dermatitis can completely mimic a cellulitis with itching, erythema and—in some cases—"weeping" blisters. In your diabetic patients with an apparent acute infection (but without fever), always ask about application of topical agents (e.g.antibiotic ointments, herbal products, vitamin E) that could lead to an acute contact dermatitis.

5. Acute gout—the crystal conundrum

Your patient may have a history of gout. They may have recently started a thiazide diuretic. They complain of the sudden onset of severe foot pain that wakes them up in the middle of the night. Examination shows a painful, red swollen foot—while cellulitis is a possibility, keep in mind the possibility of gout and remember the following points:

- ✓ **Clinical mimic:** Gout can completely mimic cellulitis with fever, pain and erythema of the foot. Involvement of the 1st metatarsophalangeal (MTP) joint is classic although other joints may be involved including the midfoot (tarsal) joints, the ankle, other MTP joints.
- ✓ **Other findings:** Ask the patient about a previous diagnosis of gout or bouts of unexplained 1st MTP pain (e.g. podagra). Look for evidence of tophi on extensor surfaces around joints (e.g. elbows), digits or earlobes.
- ✓ **Laboratory Diagnosis:** The serum uric acid may not always be elevated during an acute gouty attack—if gout is a possibility, tap the offending joint and look for the classic crystals.
- ✓ **Treatment:** Antibiotics won't work for gout—in suspect cases start the patient on high-dose NSAIDS or colchicine. Patients unable to take these agents (individuals with gastritis or renal insufficiency) may benefit from a brief course of high-dose corticosteroids.

Gout can completely mimic cellulitis—in a patient that doesn't respond to antibiotics, keep the diagnosis in mind and look for the telltale clinical signs.

Ben Franklin, gout and the autumn crocus

Although Ben Franklin died at age 84 from an acute pneumonia, he long suffered from gouty arthritis with associated kidney/bladder stones. Franklin had numerous risk factors for gout including alcohol, diet (he loved high purine foods such as meat and seafood), genetics (gout ran in his family) and lead exposure—he worked for many years as a printer and his favorite Madeira wines were often stored in lead containers. During his travels in Europe, Franklin heard about the therapeutic benefits of the autumn crocus, a plant which had been used since ancient times for treatment of arthritis and "rheumatism". Upon his return to the United States in 1785, Franklin brought bulbs back to the United States and introduced cultivation of the plant to the New World. We now know that the autumn crocus contains colchicine—a compound that poisons microtubule activity and inhibits neutrophil migration, leading to an anti-inflammatory effect. Franklin's gout ultimately proved quite incapacitating—in order to attend the Constitutional Convention he had to be transported from his lodging on a daily basis by carriers who bore him in a special "sedan". Despite his many infirmities, Franklin's wise advice helped shape the founding document and—for sufferers of gout—provided access to an effective treatment for this painful and sometime debilitating condition.

Source: http://www.everydayhealth.com/gout-pictures/7-gout-lessons-from-the-past.aspx#08 accessed: 6/21/15

6. Pyoderma gangrenosum—a painful pustule

Your patient presents with a blister or painful pustule that ulcerates, leaving a deep, excavated and purulent ulcer. Despite antibiotics, the ulceration persists and is accompanied by severe pain. While infection is always a possibility, consider the possibility of pyoderma gangrenosum, an idiopathic, ulcerative condition marked by purulent drainage and extreme pain. Despite the presence of bacteria on superficial cultures, treatment of this condition with antibiotics generally has little effect—paradoxically, the treatment of choice is corticosteroids or immunosuppressive agents. Consider the possibility of "PG" in the following situations:

- ✓ **Clinical presentation:** The PG ulcer is typically deep, with undermined edges and purplish discoloration of the surrounding tissues. If some healing has occurred, clinicians describe a "net-like" pattern of fibrosis or pigmentation around the ulcer. *Severe pain* is a common complaint and a hallmark of pyoderma gangrenosum.
- ✓ **Response to antibiotic treatment:** By the time you see the patient, they may have received previous antibiotics with little clinical response. PG ulcers typically fail to improve following antibiotic therapy—this is a clue to the condition and should raise the possibility of a soft-tissue infection "mimic".
- ✓ **Associated conditions:** Although the etiology of pyoderma gangrenosum is unclear, it is associated with underlying conditions such as inflammatory bowel disease (Crohn's disease; Ulcerative colitis), rheumatologic disease (e.g. rheumatoid arthritis) and hematological disease (e.g. underlying leukemia). Cutaneous ulceration in the presence of any of these conditions should immediately raise the possibility of pyoderma gangrenosum.

- ✓ **Diagnosis:** In addition to the clinical characteristics (e.g. failure to respond to antibiotics; associated underlying conditions; severe pain) a tissue biopsy may be helpful—histopathology demonstrates leukocytic infiltrate *without* evidence of vasculitis. Although not pathognomonic, these findings are suggestive and help to exclude underlying vasculitis or cutaneous neoplasm.
- ✓ **Treatment of pyoderma gangrenosum:** Failure to respond to antibiotics should suggest the possibility of PG. In suspect cases, treatment with immunosuppressives (e.g. corticosteroids; cyclosporine) typically leads to dramatic improvement with ulcer healing and reduction in pain/drainage.

Remember! If you suspect the possibility of pyoderma gangrenosum, obtain a dermatology consult—the dermatologist can organize a proper biopsy (to rule out other conditions) and are familiar with the immunosuppressive agents required to treat this condition.

7. Stasis dermatitis—a venous "scourge"

Patients with this condition are often mistakenly thought to cellulitis of the lower extremity—clues to the diagnosis include 1) a history of venous disease or thrombophlebitis, 2) involvement of the "gaiter" area near the ankle, and 3) frequent involvement of both lower extremities.

The cause of acute stasis dermatitis is unclear but is likely related to underlying venous valvular disease with backup or "leakage" of fluid into surrounding tissues. This leads to inflammation, pericapillary fibrosis (on skin biopsy) and subsequent scarring and pigmentation. In the acute stage, the inflammation mimics acute cellulitis. Involvement of subcutaneous adipose tissue leads to "**lipodermatosclerosis**", a condition that pathologically mimics an acute panniculitis on biopsy. When you consider stasis dermatitis, keep in mind the following:

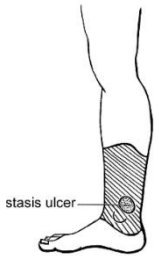
- ✓ **Clinical appearance:** Acute stasis dermatitis often begins in the "gaiter" area—the anatomic region encompassing the lower third of the leg and medial malleoli (see below). Initially, the patient has erythema and warmth that mimics acute cellulitis—with prolonged disease, hyperpigmentation occurs and there may be ulceration close to the medial malleolus.

"Gaiter"—A Dictionary Definition:

gait·er ˈgātər/
Noun: **gaiter**; plural noun: **gaiters**

1. A garment similar to leggings, worn to cover or protect the ankle and lower leg.
2. A shoe or overshoe extending to the ankle or above.
3. A lower leg covering, buttoned up the side and worn as part of the traditional costume of an Anglican bishop.

Source: https://www.google.com accessed: 3/22/15
Image: http://www.wsiat.on.ca/images/mlo/venous_gaiter2.jpg



"**Gaiter" region of lower extremity**

- ✓ **Epidemiology:** This condition is more common in women patients and typically affects individuals in their 5th decade (age 40-50) with a history of previous venous disease (e.g. venous insufficiency; varicose veins).
- ✓ **Inflammation:** During the onset of the condition, there may be erythema and pain that mimic acute cellulitis; however, the absence of fever—and the presence of *bilateral* lower extremity involvement (in some cases)—are clues to the condition. If you are uncertain about presence of infection, empiric antibiotic therapy may be appropriate—in the appropriate clinical situation, failure to respond to treatment should raise the possibility of acute stasis dermatitis.
- ✓ **Diagnosis:** Although biopsy can be helpful, most dermatologists try to avoid biopsy in this region because of poor blood supply and delayed healing. The clinical presentation—and failure to respond to antibiotic therapy—are clues to the diagnosis.
- ✓ **Treatment:** In addition to general measure to reduce lower extremity edema (e.g. leg elevation; diuretics; venous surgery), topical corticosteroids, wet dressings (in the patient with acute inflammation) and/or closed

topical dressings (e.g. Unna boot) are often used. Patients with severe acute stasis dermatitis may benefit from a short course of oral prednisone (e.g. 20-30 mg PO for 5-7 days).

In patients with lipodermatosclerosis, some studies have a shown a benefit from using oral dipyridamole. In general, while gentle cleansing of the lesions may be beneficial, try to avoid using topical antibiotics such as neomycin or bacitracin since these agents may lead to contact sensitization. If you feel that a topical antibiotic is necessary, topical muropiricin or erythromycin are less likely to lead to contact sensitization.

Stasis dermatitis is an important cause of lower extremity edema, inflammation and ulceration. A lack of response to antibiotic therapy—along with a history of venous disease—is a clue to the underlying diagnosis.

Check out the internet!

A brief review like this lacks the ability to provide photos of the above conditions. The internet provides many photos that will allow you to see the broad range—and characteristic clinical features—of these diseases. Take the time to review what's available—you will be richly rewarded with an expanded clinical "toolbox" and greater diagnostic acumen.

Diabetic foot infection 'mimics"—what you need to know…

- Charcot foot is a condition most commonly seen in long-standing diabetics with a history of peripheral neuropathy. Patients with acute Charcot foot typically develop erythema and swelling that mimics cellulitis (although they are usually afebrile!).
- With more advanced disease, Charcot's patients develop characteristic foot deformities ("rocker bottom" foot) with associated radiographic changes. Early recognition of acute Charcot foot is critical since treatment involves prompt off-loading of the foot in order to minimize progression.
- Patients with diabetic bullous dermopathy (*bullous diabeticorum*) present with the sudden onset of spontaneous cutaneous bullae that mimic impetigo or diabetic foot infection. Although these may appear "infected" they typically are culture negative (by needle aspirate) and have minimal surrounding inflammation.
- Calciphylaxis is typically seen in patients with end-stage renal disease and underlying vascular disease. Patients present with purple, mottled skin lesions that progress to skin necrosis, mimicking infectious gangrene. On plain radiograph, patients usually have evidence of calcium deposition (arteriosclerosis) in mid-sized vessels.
- Calciphylaxis lesions sometimes respond to cautious debridement; however, due to the underlying vascular disease, healing is slow and patients are sometimes left with chronic, unhealed wounds. The overall long-term prognosis of patients presenting with this condition is generally poor—the presence of calciphylaxis is a marker for extensive vascular disease with all its' attendant complications.
- Acute contact dermatitis is due to contact sensitization of the skin from various chemical products. Although patients present with skin findings that mimic acute cellulitis (e.g. erythema; blisters; weeping skin), they are usually afebrile and non-toxic, clues to the possibility of a non-infectious "mimic".
- In patients with "inflamed" skin, ask about chemical exposure (including herbal products such as aloe vera and Vitamin E), new shoes (? shoe "dermatitis") and the use of topical antibiotics (e.g. neomycin; bacitracin). If patients with "cellulitis" fail to respond to antibiotic therapy, consider the possibility of acute contact dermatitis and—in those with a clear exposure history—consider a course of topical corticosteroids.
- Acute gout of the first toe (e.g. podagra) or ankle can completely mimic cellulitis and/or septic arthritis. Ask the patient about previous attacks of gout and medications (e.g. thiazide diuretics; B-blockers; aspirin; cyclosporine) that are known to precipitate acute attacks. A definitive diagnosis of gout requires a diagnostic arthrocentesis of the suspected joint to look for uric acid crystals.
- Pyoderma gangrenosum is a condition that can present with deep, painful and purulent ulcers that fail to respond to antibiotic therapy. Although it is often associated with an underlying condition (e.g. inflammatory bowel disease; rheumatologic disorders; hematologic malignancies), it may occur spontaneously following cutaneous trauma. After biopsy (to rule out vasculitis), consider a trial of corticosteroids or immunosuppressive agents –in suspect cases, patients will often have improvement of the ulcer and a dramatic relief of pain.
- Patients with acute stasis dermatitis usually have a history (or clinical signs) of preexisting venous disease (e.g. varicose veins; lower extremity edema) and typically develop signs of acute inflammation and ulceration over and around the medial malleoli of the ankle. Lack of response to antibiotic—and the presence of bilateral "cellulitis" of both lower extremities—are additional clues to the condition. In addition to measures to reduce lower extremity edema (e.g. lower extremity elevation; diuretics; compression stockings), a trial of topical or oral corticosteroids may be helpful in managing any acute inflammation.

Chapter 8

A "Foot on Fire"— Charcot arthropathy

Charcot foot (Charcot neuroarthropathy or "CNO" for short) is one of the most important diabetic foot infection (DFI) mimics—failure to diagnosis this at an early stage (a common mistake!) often leads to considerable bony destruction and disability. This section will review some of the key features of this condition, including the following:

- **Who is at risk?** Charcot foot (Charcot's neuroarthropathy) usually presents during the 5th or 6th decade in patients with long-standing diabetes and peripheral neuropathy.
- **Diabetic foot infection "mimic":** Patients present with a warm, erythematous foot that can mimic cellulitis or osteomyelitis.
- **Radiology confirmation:** Involvement of the midfoot (Tarsal-metatarsal bones) is characteristic of the condition and leads to the characteristic "rocker bottom" foot deformity in later stages.
- **The importance of early recognition:** Early diagnosis and treatment (prompt "off-loading" of the foot) is critical for a successful outcome in patients with CNO.

Clinical presentation of Charcot foot

Whatever the cause of Charcot foot, early recognition is critical in order to minimize the subsequent foot deformities. The diagnosis of the condition in diabetics starts at the bedside with presentation of a warm, swollen, erythematous foot that appears infected. Although the patient may complain of pain, in general, pain is less than expected and most patients do not appear particularly "toxic".

In considering Charcot foot, keep in mind the following clinical points…

- ✓ **Erythema/swelling:** Edema, erythema and warmth are common in findings in acute Charcot foot and often mimic DFI. In general, patients with Charcot's have less pain and are usually not febrile.
- ✓ **Neuropathy:** Peripheral neuropathy appears to be a necessary prerequisite for the development of Charcot foot. Most patients with the condition have had long-standing diabetes (10-15 years) with associated neuropathy.
- ✓ **Blood supply:** In Charcot foot, the vascular supply is generally intact with bounding or palpable pedal pulses. Absence of intact pulses should make you question the diagnosis.
- ✓ **Trauma:** Over 50% of patients with Charcot foot remember some trauma; even relatively "trivial" trauma could act as an inciting event.
- ✓ **Deformity:** With progression of the disease, patients develop a "rocker bottom" foot abnormality (see below) with subsequent plantar skin ulceration.

Clinical Clue: If you suspect Charcot's osteoarthropathy, raise the foot and place it on a bed—erythema may lessen with diabetic foot infection but will persist in patients with Charcot's.

French vs. Germans—a neurologic *contretemps*

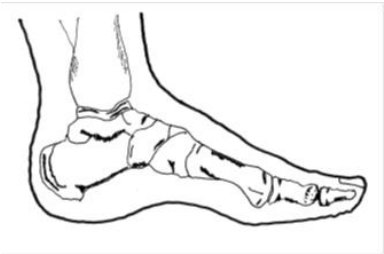
One hundred years ago, early speculation about the pathogenesis of Charcot's arthropathy broke down into two main opposing theories. The "French" school (this is what Charcot himself believed) emphasized the importance of the "neurovascular" cause—loss of the "trophic" influence from peripheral nerves led to alterations in blood flow and resultant bone resorption. The "German" school emphasized the importance of trauma—loss of pain sensation (a consequence of the neuropathy) led to excessive foot trauma with consequent bone resorption and fracture. In patients with Charcot foot, both neurological and vascular components appear important. Most patients with the condition have had diabetes for at least 10-15 years and have demonstrable neuropathy on exam. With regard to blood supply, it is uncommon to see CNO in diabetic patients with poor blood supply to the foot—most individuals have "bounding" or palpable pulses that signify "good" blood supply from major vessels. Indeed, there are well-described cases where patients developed CNO immediately *after* they had undergone vascular bypass to improve blood supply! While the exact pathophysiology of Charcot foot still remains unclear, both vascular and neuropathic factors are likely to play a critical role

Diagnosis of Charcot foot

Since Charcot foot can completely mimic diabetic foot infection, how can you tell the difference and make the diagnosis? While there is no definitive test for CNO, keep in mind the diagnosis in the following clinical situations…

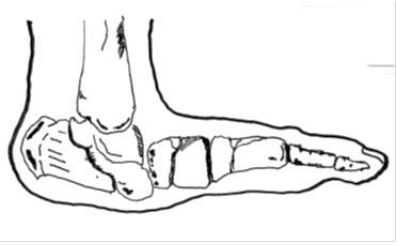
- **Clinical presentation:** Consider the possibility of Charcot neuroarthropathy in a diabetic patient with a warm, swollen foot and the "right" epidemiological circumstances including, 1) History of diabetes x 10-15 years; 2). Presence of peripheral neuropathy, and 3) Good vascular supply as evidenced by palpable pulses.
- **Physical exam:** Charcot patients typically have a peripheral neuropathy and a bounding pulse. In more advanced disease, bone osteolysis/destruction leads to foot deformities such as a "rocker-bottom" foot. Despite the impressive foot findings (erythema; swelling), patients with Charcot foot don't usually have fever and toxicity seen in clinical infection.
- **Laboratory:** There are no definitive laboratory findings that will rule in—or exclude—Charcot neuroarthropathy. Although the sedimentation rate is often abnormal in Charcot foot (sometimes completely mimicking infection), a normal ESR or CRP is a point in favor of Charcot's.
- **Radiographs:** The plain radiograph is often normal early in the clinical course; however, with more prolonged involvement, patients will develop evidence of bone resorption, including bone fragmentation and joint dislocation. Although the Charcot's process may affect any portion of the foot (see below), involvement is especially common in the midfoot (e.g. tarsal-metatarsal joints) leading to the characteristic "rocker bottom" foot and radiographic.

  If the plain film is negative, an abnormal bone scan or MRI may suggest early development of CNO. MRI may also help in differentiation of Charcot osteolysis from diabetic osteomyelitis—presence of skin ulcer and sinus tract (with adjacent bone involvement) suggests underlying bacterial infection.



Normal foot

Note normal longitudinal arch



Charcot foot

Characteristic "Rocker bottom" midfoot deformity with loss of arch

Diabetes Heroes

Jean-Martin Charcot—an unexpected podiatric pioneer

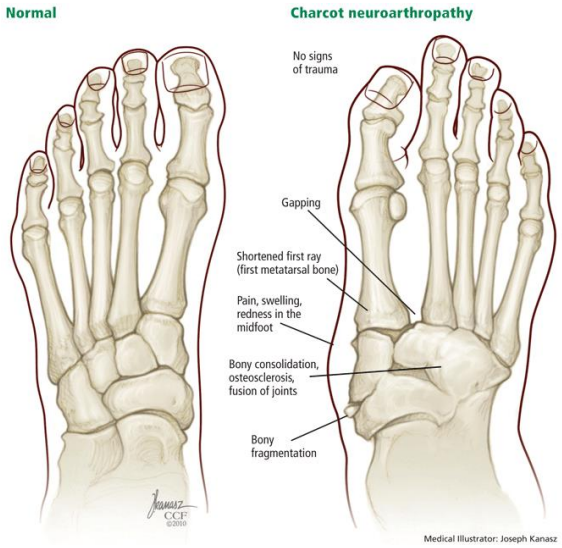
Jean-Martin Charcot (1825-1893)—called the "father" of clinical neurology—provided some of the first descriptions of "classic" neurological diseases such as amyotrophic lateral sclerosis, Parkinson's disease and progressive muscular dystrophy (Charcot-Marie-Tooth disease). While working at the grand asylum Saltpeiere (in Paris) Charcot, described an "arthropathy of ataxia" in his patients with *tabes dorsalis*--a late stage of neurosyphilis with severe proprioceptive defects due to nerve and spinal cord involvement. Longstanding cases sometimes developed an erythematous and swollen joint, mimicking infection; destruction of the underlying joint led to a "bag of bones" associated with articular bone fragments. Although diabetes was known in Charcot's time, survival was short and patients rarely lived long enough to develop long-term complications of the disease. The introduction of insulin in the late 1920s permitted longer survival and led to the recognition of long-term complications such as neuropathy. In 1936, the Chicago physician William Riely Jordan described the first case of Charcot neuroarthropathy of the foot/ankle in a patient with long-standing diabetic neuropathy. In the modern era, *tabes dorsalis* has almost completely disappeared and diabetes—with its' associated complications—has now become the most common cause of Charcot neuroarthropathy. Although Charcot himself never described a diabetic Charcot "foot", his keen clinical observations—and recognition of the underlying pathophysiology—led to the description of the entity that now bears his name.

Source: Harkless LB, Felder-Johnson K. Foot and Ankle Secrets. Hanley and Belfus Inc. Philadelphia 1998.

Radiology of Charcot's foot—pedal patterns and the 5 "Ds"

As you evaluate the diabetic foot, specific radiologic findings may play an important role in helping to suggest the possibility of Charcot neuroarthropathy. Important points to keep in mind include the following:

- **Early "normal":** On initial clinical presentation, (Eichenholz stage 0), a plain radiograph may be completely normal—bone scan or MRI are likely to show findings such as bone edema or stress fracture.
- **Location:** Charcot's NO typically involves tarsal bones in the mid-foot (Frykberg Type 2,3—70% of cases); however, the process may any part of the foot including the anterior foot, heel and ankle.
- **X-ray findings:** While Charcot foot may mimic osteomyelitis (and other foot conditions), advanced Charcot's has typical findings including areas of increased density, bone fragmentation, joint dislocation/destruction (see the 5 "D" s of Charcot foot) and loss of the normal longitudinal arch.



The 5 "D"s of Charcot foot

1. **D**ensity increase (Subchondral sclerosis)
2. **D**estruction of the joint
3. **D**ebris (Intra-articular loose bodies)
4. **D**islocation
5. **D**isorganization

Image: Botek et al. Cleve Clin J Med. 2010 Sep;77(9):593-9.

Know the score—classification of Charcot neuroarthropathy

There are several schemes available to "classify" Charcot foot, either based on the progression of the process (Eichenholz classification) or the pattern involvement (Sanders and Frykberg Classification). The Frykberg classification (see Table in appendix) outlines the multiplicity of patterns that might occur:

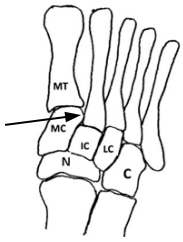
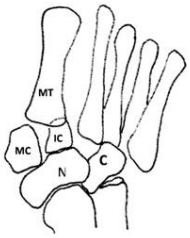
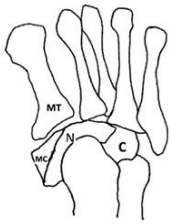
Type 1: Forefoot involvement—15% of cases
Type 2: Tarsometatarsal joints (Lisfranc joint)—40% of cases
Type 3: Naviculocuneiform joints (Chopart joint)—30% of cases
Type 4: Ankle (+/- Subtalar joint)—10% of cases
Type 5: Calcaneus—5% of cases

Most commonly, patients with Charcot foot present with midfoot (Type 2 or Type 3 pattern) complications; however, they may also develop forefoot (Type 1), ankle (Type 4) or calcaneal (Type 5) involvement. The importance of these less common presentations is that they may also mimic osteomyelitis or infection—before you commit the patient to long term antibiotics, always consider the possibility that the clinical or radiologic process might be secondary to a Charcot's process.

The midfoot—"epicenter" for Charcot's destruction

Although Charcot neuroarthropathy may involve any part of the foot (See Sanders-Frykberg classification), it typically involves the midfoot (tarso-metatarsal joints), leading to the characteristic "rocker-bottom" pattern of joint deformity..

The following table demonstrates radiographic findings characteristic of Charcot's involvement of the midfoot.

Normal radiograph	**Charcot foot-SF type 2** (Tarso-metatarsal involvement)	**Charcot foot-SF type 3** (Naviculocuneiform, Talonavicular and Calcaneocuboid involvement)
		
"Normal" alignment of Lisfranc's joint including 2nd metatarsal mortise (arrow)	Tarso-metatarsal joint dislocation Lateral displacement of metatarsals Abnormal "gaps" between bones Erosion and dissolution of bones	Involvement of Chopart's joint Collapse of navicular bone Loss of talonavicular joint Destruction of cuneiform bones
Abbreviations: C: cuboid; IC: Intermediate cuneiform; LC: Lateral cuneiform; MC: Medial cunteiform; MT: Metatarsal; N: Navicular SF: Sanders-Frykberg classification		

Diabetic osteomyelitis due to associated skin ulceration, is far more likely to involve the forefoot (phalanges; metatarsal bones) and calcaneus. While not perfect (see below: Charcot's osteolysis versus osteomyelitis), this distinction (e.g. midfoot versus forefoot or calcaneus) often allows for rapid differentiation between Charcot foot and diabetic pedal osteomyelitis

Diagnostic dilemma: Charcot's 'osteolysis' versus osteomyelitis

It's a common diagnostic dilemma, a diabetic patient presents with a warm foot and an abnormal radiograph—do the bone changes represent Charcot osteolysis—a non-infectious complication—or diabetic "osteomyelitis"—secondary infection of the bone? Here are a couple of clues that will help you sort out this common dilemma:

- ✓ **Midfoot involvement:** If the bony changes occur in the "midfoot" (tarsal bones), this is more likely to signify Charcot's osteolysis—in the diabetic, osteomyelitis is far more common in the forefoot or heel.
- ✓ **? Presence of ulcer:** Most osteomyelitis is associated with a cutaneous ulcer (or entry point) close to the affected bone—if midfoot ulceration is absent, radiographic changes are more likely to represent Charcot's arthropathy/osteolysis rather than osteomyelitis.
- ✓ **Constitutional symptoms** (fever; shaking chills; tachycardia) are more suggestive of concomitant infection. Although the ESR and leukocyte count may be elevated in Charcot neuroarthropathy, significant elevations are more suggestive of infection.
- ✓ **Cuboid bone:** With breakdown of the midfoot in Charcot's, ulceration of the plantar surface with involvement of the cuboid bone is common. In this situation, presence of a sinus tract—along with MRI evidence of osteomyelitis--suggest a higher likelihood of osteomyelitis in addition to advanced Charcot's.

Admittedly, the differentiation between Charcot's and osteomyelitis is not always easy—a special difficulty occurs when the patient with a Charcot foot develops secondary osteomyelitis. Sometimes the clinician has to assume the possibility of infection and treat accordingly. Nevertheless, keep in mind that the radiographic appearance of Charcot foot can almost completely mimic osteomyelitis—in this situation, weeks of high dose antibiotics may prove fruitless and lead to unwanted complications.

"Take a load off your feet"—management of Charcot foot

The first step in management of Charcot foot is ***recognition***—despite the presence of clinical findings, studies show that there is typically a delay of over 24 weeks in diagnosis of this condition. Initial therapy is conservative—**off-loading of the foot** is critical since continued weight-bearing inevitably worsens the condition. Here are recommended (and some experimental) therapies for this condition:

- **Total contact cast (TCC):** This is a special cast that redistributes pressure and permits gradual healing of the foot. Unfortunately, this is a slow process—on average, it takes over 18 weeks for the foot temperature to normalize.
- **Drug therapy:** Two **bisphosphonate** agents, pamidronate (IV) and alendronate (PO) have been tested in Charcot foot—these agents reduce bone turnover markers but remain experimental at the present time. More recently, a therapeutic trial of **calcitonin** seems to have had some benefit; however, these therapies is routinely recommended at the present time.
- **Surgery:** Surgical therapy may be indicated if medical therapy fails or if the patient has a severe deformity or ulcer. Available surgical procedures include the following…
    - ✓ **Isolated tendo-achilles lengthening:** Patients with advanced diabetic neuropathy often have reduced Achilles elasticity, a condition leading to increased plantar pressure. Excessive midfoot pressure can lead to the characteristic dislocations and fractures seen in Charcot foot. Surgical lengthening of the Achilles tendon will weaken the tension and may help prevent progression of the deformity.
    - ✓ **Exostectomy:** With midfoot collapse, patients may have a "rocker bottom" foot with ulceration under a prominent cuboid or navicular bone. Partial or whole excision of these bones may permit wound healing.
    - ✓ **Total surgical reconstruction:** In those with more serious deformities, an extensive reconstruction with osteotomy, bone realignment, and internal fixation may be an option. This procedure isn't easy—it is lengthy (3-6 hours), requires a prolonged convalescence, and, increases the risk (40-60%) of a Charcot foot in the non-operated extremity.

Managing a possible case of Charcot foot…

- **Suspect the diagnosis:** In a diabetic patient with a warm, swollen and erythematous foot, keep Charcot neuroarthropathy in mind—especially if they are afebrile and there is no obvious entry point (e.g. ulcer) or purulence suggestive of infection.
- **Obtain a radiograph:** Although the plain radiograph may be negative early in the condition, involvement of the midfoot is especially common in Charcot foot.
- **? Coinfection:** It may be difficult to completely exclude infection—if some signs suggest infection (purulent ulcer, severe pain, fever, toxicity), obtain cultures and cover the patient with antibiotic.
- **Consider a scan:** If the plain radiograph is negative, a bone scan or MRI might demonstrate early osteolysis or bone involvement.
- **Offload the foot:** Charcot neuroosteoarthropathy can progress quite rapidly (within days) if the patient continues to weight bear—in those with suspected CNO, offload the foot as soon as possible.
- **Obtain a podiatry consult:** Early consultation with podiatry is critical in proper management of suspected Charcot's patients—in addition to off-loading the joint, in select cases they will advise shoe inserts (orthotics)and employ techniques (Total Contact Casting) that will help delay progression and allow the bones to heal..

Charcot foot (neuroarthropathy)—what you need to know…

- Charcot neuroarthropathy (CNO) presents with clinical findings that mimic diabetic foot infection including signs of warmth, erythema and swelling.
- The condition is most commonly seen in diabetics during their 5th or 6th decade of life—most have a significant history of peripheral neuropathy and evidence of *good* blood supply (+2 pulses) on foot exam.
- Although Charcot's can affect any portion of the foot; the most common site is the tarsal bones of the midfoot (70% of cases), leading to the classic "rocker bottom" joint deformity of the foot. .
- The radiographic features of Charcot's (e.g. soft tissue edema, bone destruction) can completely mimic osteomyelitis/infection. Decisions about appropriate therapy depend upon the clinical presentation—presence of an ulcer (with purulent drainage) next to the affected bone suggests the possibility of concomitant osteomyelitis.
- The treatment for Charcot neuroarthropathy is "off-loading" the foot—continued ambulation and pressure on the foot will lead to eventual bone breakdown and foot deformity. If you suspect CNO, off load the foot (e.g. the patient should use crutches or wheelchair) promptly and have the patient see a podiatrist as early as possible.
- Advanced CNO can lead to significant foot deformity and disability. Although patients with advanced Charcot's often end up requiring an amputation, some individuals benefit from limited bone resection (exostectomy) and/or total reconstruction of the foot.
- Early recognition of Charcot foot remains a key in management principle—prompt off-loading of the foot may spare the patient progressive joint destruction with associated deformity.

Chapter 9

Special situations…
Diabetic foot dilemmas

This chapter focuses on the "special situations" in diabetic foot infections—some are common—and some are rather esoteric or unusual. When you see a diabetic foot problem, keep these unique presentations in mind…

"Doc…I stepped on a nail"—Puncture wounds in the diabetic foot

Puncture wounds are common in diabetics—with the underlying neuropathy, patients may continue to ambulate, ignoring the potential severity of the injury until infection sets in. Fortunately, most of these injuries do not result in infection—one study (See: East et al. BMC Surgery 2011, Oct 17;11;37) reported that "puncture" injuries healed in 45% of 77 patients without medical intervention. Nevertheless, such injuries must be taken seriously in light of the genuine potential for infection and limb loss. What appears to be a superficial wound may mask a much deeper infection, or even a foreign body, which is another risk factor for secondary infection. In addition, when a patient "steps on a nail", bacteria from the shoes insole (sometimes *Pseudomonas aeruginosa*) may be inoculated deep into the foot, leading to osteomyelitis or deep space infection (See:Rubin et al. J Foot Ankle Surg.;49(5):421-5.).

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Study Alert

Puncture wounds in the diabetic foot

Lavery et al. (Diabetes Care. 1995 Dec;18(12):1588-91) reported their experience with 146 patients (77 diabetics; 69 non-diabetics) hospitalized with infected foot puncture wounds. In comparing this injury in diabetic—versus non-diabetic patients—they made the following key observations:

- Diabetic patients were more likely to have underlying neuropathy, and to have acquired their injury while "walking barefoot".
- Compared to non-diabetic patients, diabetics were more likely to have osteomyelitis (35% of diabetics vs. 13% of nondiabetics).
- Although *Pseudomonas aeruginosa* was seen (It was the most common cause of infection in *non-diabetics*), *Staphylococcus aureus* and polymicrobial infection turned out to be the most common pathogens isolated in diabetics with puncture wound infections.

When confronted by an infection associated with puncture wound, keep in mind the following:

- ✓ Obtain a plain radiographic early in the diagnostic process—you might spot a radiopaque foreign body (requiring removal) or evidence of tissue gas (masked on your exam by the thick plantar skin and fascia).
- ✓ An ultrasound may be helpful in identifying non-opaque foreign bodes such as wood, plastic or rubber (See: .Rubin G et al. *J Foot Ankle Surg*. 2010;49:421-425.)
- ✓ Request a podiatry or surgical consult at an early stage—although these injuries may appear superficially "benign", such wounds may mask deeper infection that requires surgical exploration and debridement.
- ✓ When choosing empiric antibiotic coverage, include antibiotics active against *Pseudomonas aeruginosa* (e.g. ciprofloxacin, cefepime or a carbapenem), especially in patients with "serious" infections.

Decubitus ulcers…Healing the hapless heel

The necrotic heel ulcer is not uncommon in diabetics, especially in the "bed bound" patient with underlying neuropathy and vascular insufficiency. Do not underestimate the potential seriousness of these lesions—the eschar may hide a deep sinus tract with infection of the underlying calcaneus.

Management of this situation includes the following:

- Patients with wet gangrene and purulent drainage need deep debridement and surgical exploration.
- Cautious observation (with offloading of the ulcer) may be appropriate in those with minimal drainage and a dry eschar. It is unclear how much antibiotics will help this situation; however, consider a course of empiric therapy if there is any drainage or suspicion of underlying infection.
- Obtain a radiograph and look for underlying osteomyelitis of the calcaneus. In those with evidence of significant bone destruction, a calcanectomy may be necessary.

See: Suzuki, K. (editor). Current Insights On Treating Heel Pressure Ulcers. Podiatry Today 2009.Volume 22 - Issue 5 - May 2009; Page 22-26. *Accessed: 9/16/12 http://www.podiatrytoday.com/print/1780*

"Perilous" pets—animal bite infections

Animal bite wounds are especially dangerous in the diabetic patient—such infections may lead to life-threatening gangrene or sepsis. The history of animal exposure may not be readily apparent unless you ask. We've seen one patient (with underlying cirrhosis and a "weeping" edematous foot) whose dog licked his feet on a daily basis—the patient developed *Pasteurella* bacteremia and almost died. *Pasteurella multocida*—a gram-negative coccobacillus often associated with "bite" infections—is typically resistant to first generation cephalosporins (e.g. cephalexin; cefazolin) but sensitive to penicillin, third generation cephalosporins, quinolones and tetracyclines.

Additional situations that have been reported include…

- **Dogs and group G strep:** A series of group G strep (*Streptococcus canis*) infections in dog owners with diabetic foot ulcers. (See: Lam MM et al. Clin Microbiol. 2007 Jul;45(7):2327-9. Epub 2007 May 2.)
- **Rat bites:** In the developing world, there is a literature devoted to foot wounds following "rat bites". (See: Kalra B et al. Diabetologia. 2006 Jun;49(6):1452-3. Epub 2006 Apr 4).
- **Pet-assisted surgery:** In one case, a 35 year old diabetic with severe neuropathy presented with traumatic amputation of great toe—her small dog (*Lhapsa apso*) bit off the toe when she was unconscious during an insulin reaction. A similar experience occurred in another patient, an undiagnosed diabetic whose dog was attracted to the foot because of his poorly controlled blood sugar (See: Ballard WT, Iowa Orthop J. 1994;14:171-3.].

"Battered" bones—Neuropathic foot fractures in diabetics:

Patients with diabetes and underlying neuropathy have a higher incidence of osteopenia and a greater risk of foot fractures. Common sites of fractures include the metatarsal head or bone shaft and the phalanxes. Patients who walk barefoot are at risk for 5thdigit fractures when they catch the toe on furniture, causing forced eversion of the toe.

When managing these injuries, keep in mind the following:

- ✓ **Be careful**—following trauma, the initial radiograph may be normal. In this situation, if you strongly suspect a fracture, obtain a bone scan or MRI.
- ✓ **Charcot foot:** A fracture may precipitate—or be the first sign—of underlying an underlying Charcot foot.
- ✓ **Delay in healing:** Fractures in the patients with more advanced diabetes typically take two to three times longer to heal.

"Black and blue"—managing the necrotic toe

Diabetic patients are at risk for the sudden development of a "blue" or "black" toe, usually secondary to vascular compromise related to underlying arteriosclerosis. The differential diagnosis of this condition includes embolic disease, infection (gangrene) as well as miscellaneous conditions including vasculitis and hematologic conditions.

The distinction between "wet" and "dry" gangrene is a critical one—patients with wet gangrene almost are always infected and require broad spectrum intravenous antibiotic therapy along with aggressive wound debridement.

When managing a patient with the sudden onset of a "black" toe, keep in mind the following:

- ✓ An acute pedal infection may cause a sudden onset of a gangrenous toe, especially if the infection arises in the interdigital space and suddenly compromises blood flow to the digit.
- ✓ Consider the possibility of embolization from a more remote site. Examine the patient for a "cardiac" source (e.g.? arrhythmias; ? infective endocarditis) as well as vascular involvement of the abdominal aorta (e.g ? Aortic aneurysm) or peripheral blood vessels (e.g. ? Decreased/absent pulses;? bruits).
- ✓ Patients who have undergone recent vascular procedures (e.g. angiography) may have cholesterol emboli syndrome characterized *by livedo reticularis*, renal insufficiency and mild eosinophilia.
- ✓ Dry gangrene can often be managed conservatively as the digit may "autoampute" by itself within a few months. In these cases, place a gauze dressing separating the impaired digit from the normal digits to either side—this will prevent bacterial spread in case there is some degree of low grade infection. Some experts treat the patient with empiric oral antibiotics to minimize the likelihood of "wet" gangrene.
- ✓ In an afebrile, non-toxic patient, antibiotic therapy can sometimes convert wet gangrene into dry gangrene. These patients should be observed cautiously, since deterioration of their condition will often require aggressive surgery including amputation.

Elliot Proctor Joslin—American diabetes pioneer

Elliott Proctor Joslin, M.D. (1869-1962)—the founder of Boston's Joslin clinic (the Joslin Diabetes Center) was one of the first physicians in the United States to specialize in the therapy of diabetes. A graduate of Harvard medical school, Joslin was inspired to study diabetes because of an aunt who suffered from the disease. He admitted patients to the New England Deaconess Hospital in Boston and performed careful studies on the effects of diet on metabolism and glucose control. Relying on study of over a 1000 of his own cases, Joslin published a monograph in 1916 (*The Treatment of Diabetes Mellitus*) where he claimed a 20 percent decrease in the mortality of patients who followed a strict program of diet and exercise. Joslin was an early adopter of insulin treatment and created a comprehensive approach to managing the disease that include a team of physicians, nurses and patient educators. With the improved survival of diabetic patients, Joslin recognized the long-term complications such as foot infection and made sure that podiatric care and evaluation were an important part of the center program. The Joslin Diabetes Center has pioneered in many aspects of diabetes treatment including the introduction of preprandial glucose testing in hospitalized patients, development of laser photocoagulation for treatment of diabetic retinopathy, and—harkening back to Joslin's earlier views—an emphasis on the importance of diet and exercise in minimizing the development of Type II diabetes.

Source: Wikipedia. Accessed 4/17/15

"Fire and ice"…Diabetic foot burns

Diabetic patients with long-standing disease and peripheral neuropathy have a special risk for serious wounds due to burns. Patients with neuropathy often have a sensation of "cold" extremities—attempts to warm the foot (with hot packs, heaters; see Table) may lead to inadvertent burns, sometimes with life-threatening complications.

At a special burn center, a 10 year review of 68 diabetic patients (87% male; mean age 58 years) with lower extremity burn wounds noted the following:

- **Delayed healing:** Although the wounds were relatively small by burn center standards (4.2% Body surface area [0.5–15% range; 57% full thickness]) patients required longer stays (an average of 2 weeks) when compared to non-diabetic patients.
- **High rate of infection:** Close to half of patients developed infection (28 cellulitis; 4 osteomyelitis; 2 deep plantar infections) and 11 patients required some type of amputation (7 Below-the-knee, 4 transmetatarsal, and 20 toes).
- **Predisposing factors:** In diabetics with burn wounds, there was a high incidence of underlying cardiovascular disease (57%) and renal disease (20% of patients were on hemodialysis).

When faced with the possibility of a diabetic "burn wound", keep in mind the following:

- ✓ Tell your patients to avoid walking barefoot and warn them about the risk of thermal wounds due to hot water, heating pads and fireplaces.
- ✓ Patients with a full thickness wound should be seen by a burn surgeon or referred to a special burn center—they may require excision of necrotic tissue and surgical grafting.
- ✓ Prophylactic topical antibiotics (e.g. Silver sulfadiazine [Silavadene]) may be appropriate to minimize the risk of infection; however, consider "triple antibiotic" ointment with silver.
- ✓ Don't underestimate the potential seriousness of a burn wound injury in the diabetic—even patients with relatively "small" wounds may end up with secondary infection and limb loss.

Table 1: Causes of diabetic "burn" infections

Walking on hot surface
Soaking feet in hot water
Warming feet with heater or fire
Spilling hot water on feet
Using hot water bottle
Burn due to hot paraffin bath
Frostbite

A sidewalk "scorcher": In a region where summer day temperatures rise above 100°F, pavement temperatures may reach well above 140° F, a level that can lead to deep burns in only seconds! Caution your patients about walking barefoot on hot surfaces.

Source: Greenhalgh DG et al. Temperature threshold for burn injury: an oximeter safety study. J Burn Care Rehabil 2004;25:411–15.

Special situations in the diabetic foot—what you need to know…

- Diabetic patients with peripheral neuropathy are at risk for "puncture" wounds of the foot when they unknowingly step on nails or other sharp objects. Such injuries can be dangerous since the "innocuous" surface appearance may mask deeper infection within the foot..
- In a diabetic patient with a deep puncture wound, involve a surgical specialist as early as possible—the wound may require surgical exploration and debridement in order to exclude a foreign body and obtain cultures.
- Following wound debridement, administer antibiotics active against staphylococci and streptococci, the most common pathogens in this situation. Pending culture results, many practitioners also add a quinolone (e.g. ciprofloxacin or levofloxacin) since *Pseudomonas aeruginosa* is a well-recognized pathogen in this situation.
- In the bedridden patient, examine the patient's heel for evidence of a decubitus ulcer. Patients with evidence of infection (purulent discharge and surrounding erythema) require antibiotic treatment along with debridement. Those with "just" a dry black eschar can be off-loaded and observed—most specialists avoid debridement unless there is clear evidence of infection or underlying osteomyelitis.
- Always ask the patient about any pets or animal exposure—select organisms (e.g. *Pasteurella multocida,* grp G streptococci) may be part of the animal's normal oral flora and cause infection if the animal licks the wound or the patient walks around barefoot.
- Diabetic patients have an increased risk of foot fracture, as well as an increase delay in healing should one occur. A foot fracture that is unexplained—or related to minimal trauma—may be an early sign of Charcot neuroarthropathy (Charcot foot) and a reflection of underlying osteopenia.
- If a patient suddenly develops a black or blue toe, in addition to trauma, consider the following possibilities: 1). interdigital infection with impairment of local blood supply 2).embolization from a distant source (e.g. heart, aorta, peripheral vessels) and 3).cholesterol emboli following a vascular procedure.
- Patients with "dry" gangrene of the toe may autoamputate if managed conservatively. Place a gauze bandage between the toes (to prevent spread of infection following contact with the devitalized toe) and consider administering an oral antibiotic to minimize the chance that the lesion may convert to "wet" gangrene
- Diabetics with peripheral neuropathy are at special risk for injuries following excessive heat (burns) or cold (frostbite) since the impaired sensation may delay appreciation of any thermal insult. Counsel your patients to avoid walking barefoot on hot surfaces and to exercise caution in soaking the foot in hot water or applying external heat (e.g. hot water bottles, heaters).

Chapter 10

Managing the diabetic foot wound

The mark of successful therapy in diabetic foot ulcer is complete healing of the wound. Indeed, prior to seeing a physician (or ending up in the emergency room), patients will often try various "home remedies" or self-treatments in an effort to avoid the trip to the doctor. Most of these treatments are ineffective if not downright harmful. This chapter will review the "scientific" approach to wound healing and provide a practical approach to managing your patient's wounds. In the next few pages, we will cover the following:

- **Principles of wound care:** This section will review the basic principles of wound care, including scientific data about the importance of wound moisture.
- **Assessing the wound:** Wound classification schemes can be confusing—we will present a simple "color-based" tool that helps you assess the wound and make proper decisions about therapy.
- **Debridement and wound dressing:** Wound healing requires proper debridement of necrotic wounds and the appropriate choice of a wound dressing—this section will outline the principles behind debridement and the pros—and cons—of available wound dressings.
- **Healing the chronic wound:** Wounds sometimes "stall" and fail to heal despite your best efforts—this part will look at the factors that lead to delayed healing and some measures that might help speed things along.

"Lessons" for lesions—the principles of wound healing in the diabetic

Although we've had over two thousand years of written experience with wound healing (the Ancient Egyptians placed honey on wounds—a technique that is still sometimes employed today!), it is only in recent times that we have developed principles backed up by scientific studies. When you approach a diabetic foot wound, keep in mind the importance of the following principles:

- **Moisture is best:** Mom's advice to "let the air get at it" and "allow it to breath" is out of date—classic studies from the early sixties (see below) demonstrated that "moist", covered wounds heal faster than "dry" wounds. Exposing a wound to air and allowing it to "dry out" impairs the nascent growth of epidermal tissue and increases the risk of infection. Choose dressings that protect the wound by providing a continuous moist environment.
- **Take a load off it—offloading wounds:** Most diabetic wounds occur in locations with excess mechanical pressure—failure to offload the wound during early treatment stages will ultimately lead to failure of healing. Whenever possible, prohibit direct weight bearing and work with physical therapy (or an orthotics specialist) to offload or redistribute wound pressures. This may mean total offloading (e.g. use of crutches) or orthotics (e.g. boots, special shoes, inserts) designed to redistribute the weight.
- **Blood supply is critical:** Inadequate blood supply (weak or absent *dorsalis pedis* pulse) is a predictor for ultimate failure to heal a wound. When in doubt about perfusion, order additional studies (e.g. ABI index;

arterial Doppler; TcO_2P; toe pressure) to evaluate blood supply and revascularize the limb (e.g. balloon angioplasty; bypass surgery) with help from experts.

- **A bone "alone"—the osteomyelitis connection:** Underlying ongoing bone infection (osteomyelitis) is another reason for "failure to heal" in the DFU—progression of bone destruction on radiographs (despite appropriate antibiotic therapy) is a harbinger of ultimate healing failure. In this situation, a limited, strategic bone resection may permit adequate healing and spare loss of the rest of the foot or limb.
- **A miscellany of factors:** In addition to the above features, a number of other factors play a role in healing diabetic foot wounds. These include…**control of diabetes** (is glucose under good control as evidenced by HgbA1c?), **nutrition** (Is the patient malnourished or have a low albumin?) and, if a smoker, is the patient still **smoking**.

George D. Winter—a modern medical "Myth Buster"

George D. Winter (1927-1981) was a British researcher interested in the scientific basis of wound healing. Conventional medical wisdom suggested that healing was more rapid if the wound was allowed to "dry out" and form a scab. Uncertain about this dictum, Winter devised a study to answer the question in a scientific fashion. Working on an animal model of wound care, he created multiple partial thickness wounds on the backs of pigs—half the wounds were left open to the air and the remainder covered with polymer film. Contrary to medical wisdom, the moist, "covered" wounds healed significantly faster, showing more rapid migration of epithelium to the wound bed. The results clearly showed that "moist" wound dressings accelerated the rate of wound healing. His subsequent paper (*Formation of the scab and the rate of epithelisation of superficial wounds in the skin of the young domestic pig*; Nature 193:293 1962) turned out to be a landmark investigation that revolutionized the practice of wound care. Winter's simple but elegant study demonstrated the importance of a "moist" wound bed and spawned an entire industry devoted to developing dressings that would aid this process.

Source: http://en.wikipedia.org/wiki/George_D._Winter (accessed 1/09/11).

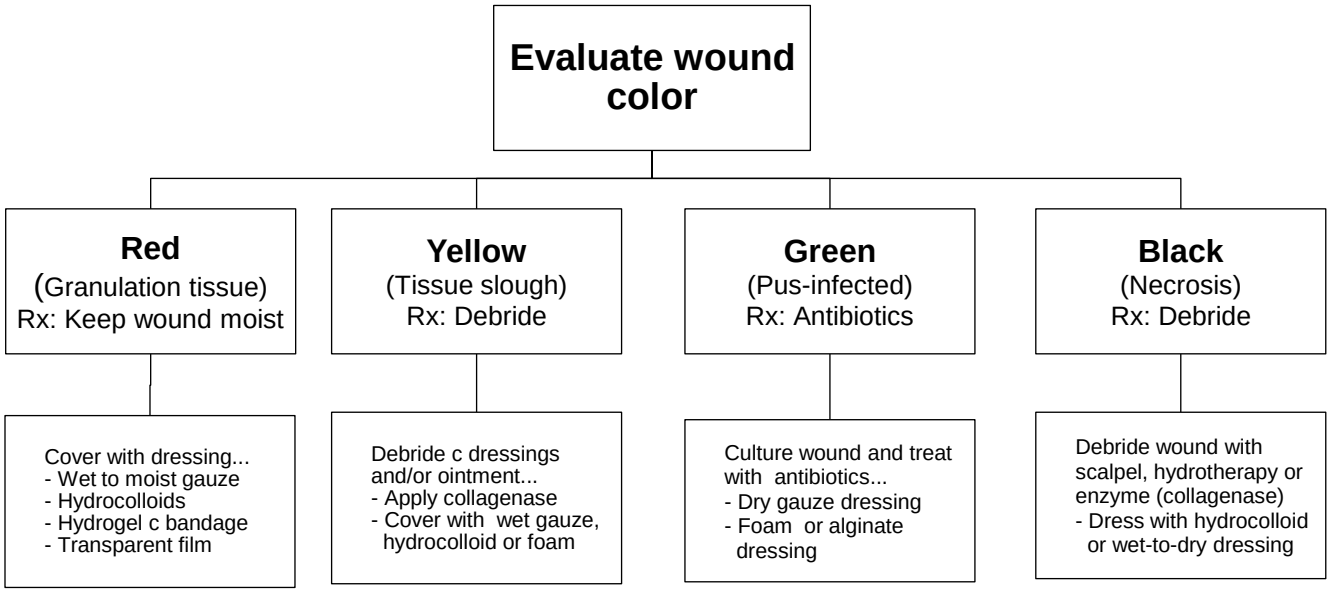
A quick guide to wound assessment—size, color and drainage

As a first "step", evaluate the type of wound with respect to size, depth, "color" (presence of necrosis), drainage and blood supply. While not foolproof, the "color" of an open wound helps provide a handy guide to helping choose management technique. When choosing a wound dressing, consider the following four factors…

1. **Size and depth:** Measure the wound size and record the wound depth—not surprisingly, "large" (> 2 cm^2), deep (> 3mm) wounds take longer to heal and are more likely to be associated with underlying osteomyelitis.
   - ✓ **Partial thickness wound:** This type of wound is relatively superficial and involves only the epidermis—there is no evidence of underlying adipose tissue (fat), muscle, tendon or bone. Retention of the dermis means that these wounds (with proper care) are likely to heal.
   - ✓ **Full thickness wound:** These wounds penetrate directly through the skin into lower layers (adipose tissue, muscle, tendon, bone). These wounds heal more slowly and are more likely to be associated with underlying osteomyelitis.
2. **Color:** The color of the wound can help sort out the stage of healing as well as the need for debridement. Use the following chart (nest page) to assess the wound and the required therapy.
3. **Amount of drainage:** Document the nature (clear, sanguineous, purulent) and amount (scant, moderate or large) of the drainage? If the wound appears infected (yellow or green purulent drainage), obtain a culture and consider antibiotic therapy. Wounds with excessive drainage should be covered with an "absorptive" dressing such as dry gauze (changed frequently), foam or alginate compounds.

4. **Blood supply:** Adequate blood supply is critical to wound healing—assess (and document) pulses, capillary refill and tissue warmth. A wound on a cold, "pulseless" foot is unlikely to heal.

Use the following schematic to assess the type of wound present…



Wound color	Interpretation	Management technique
Red	This suggests a relatively healthy granulation tissue that is on its' way to healing. In this situation, dressings that foster a moist environment are likely to have the best effect.	Maintain a moist environment with wet gauze (don't let it dry out) or a specialized dressing made of hydrocolloid, hydrogel or foam.
Yellow	The presence of "yellow" material containing debris or "slough" generally consists of excess fibrin or proteinaceous material. Removal of this material—via gentle debridement (mechanical or chemical)—is necessary to promote wound healing.	Need to clean the wound to remove the yellow layer—can use chemical debridement or hydrotherapy (pulsatile lavage). Cover the wound with a hydrocolloid, foam or wet gauze dressing
Green	"Green" drainage suggests the possibility of an infected wound—obtain a culture and treat with appropriate antibiotics	Culture the wound, cover it with gauze (soaked with Betadine) and treat with appropriate PO or IV antibiotics
Black	Presence of this color suggests gangrenous or devitalized tissue—aggressive debridement will be necessary if wound healing is to occur.	Needs extensive debridement—either conservative sharp debridement (via scalpel), hydrotherapy (whirlpool, pulsatile lavage) or chemical (Panafil gel).

A "Dictionary" of debridement

Debridement—the "usually surgical removal of lacerated, devitalized or contaminated tissue" (French *débridement,* from *débrider* to remove adhesions—Merriam Webster 2014)—is a critical component of wound healing. Wounds that contain dead, necrotic and infected tissue generally don't heal or have slow rate of healing. Although the term typically implies "surgical" debridement, there are actually several forms of debridement, some of them non-surgical and easily administered by the non-surgeon:

1. **Autolytic debridement:** In this method, the practitioner applies an occlusive dressing over the wound and allows the "natural" accumulation of "tissue fluids" (containing macrophages, neutrophils and enzymes) to autolyze the necrotic tissue.
2. **Mechanical debridement:** This is the basis for the "wet to dry" dressing form of wound debridement—once the wound "dries", removing the gauze pulls off any devitalized tissue that has stuck to the bandage. Although it seems to have fallen out of favor (see below), there are still circumstances where wet-to-dry dressings might prove useful.
3. **Enzymatic debridement:** In this method, the practitioner applies topical enzymes such as collagenase (Accuzyme) in order to lyse dead collagen and related proteins in the wound. This is especially effective in in wounds with extensive tissue "slough" or in wounds where surgical debridement is for contraindicated.
4. **Surgical debridement:** Usually reserved for wounds with significant necrosis, this implies using a scalpel to debride the wound at the bedside for relatively small wounds ("sharp" debridement), or in the operating room for large/extensive wounds (surgical debridement).

When "wet to dry" is best… If you have a necrotic wound with lots of dead, non-vital tissue that needs debridement, the "wet to dry" dressing may be just the thing. As the wound dries out, the gauze (the 2x2 or 4x4 gauze bandage) sticks to underlying tissue and hastens mechanical debridement as the bandage is peeled away. While simple, this is not always the best way to go—in addition to causing pain, pulling off the dressing may also disrupt the delicate epithelial growth next to the non-vital tissue. If this is a problem, consider other mechanisms of debridement (see above) including autolytic dressings, enzyme debridement (e.g. collagenase) and surgical debridement at the bedside or in the operating room.

Debridement—a word of caution…

Although it seems straight-forward, surgical debridement (removing dead tissue with a scalpel) can sometimes lead to complications and should be approached cautiously by the inexperienced practitioner. Some states require training/certification for non-physician practitioners involved in wound debridement. If you choose to go ahead with surgical wound debridement, keep the following in mind:

- ✓ **Avoid critical structures:** Be careful around tendons, nerves and arteries—cutting through these tissues might be downright dangerous and could increase the likelihood of long-term impairment.
- ✓ **Know when debridement is contraindicated:** Keep in mind that there are situations where debridement is relatively *contraindicated* since the wound may *worsen* following debridement. Pyoderma gangrenosum (see chapter on DFI "mimics") is a painful, "pyogenic" condition that will typically worsen follow debridement. Even with the diabetic foot, there are situations (e.g. dry eschar on the heel) where most experts recommend against debridement, unless there is clear evidence of underlying infection.
- ✓ **Make sure the blood supply is adequate:** Be cautious about debridement in patients with a poor blood supply—overaggressive surgery make the situation worse (increasing the size of the wound) and raise the risk of limb loss. Prior to the procedure, make sure that pulses are palpable and consider some basic clinical studies (ankle-brachial index; arterial Doppler) to document adequate blood supply.
- ✓ **Control pain:** Although not always a problems in the diabetic (they may have a severe neuropathy that minimizes pain), surgical debridement can be quite painful—prior to the procedure, assess the patient's level of pain tolerance and consider premedication—or local anesthetic—in those likely to have problems. Patients requiring extensive debridement may well require general anesthesia and an operating room procedure.
- ✓ **Know your skills:** While it may seem straightforward to the uninitiated, a "simple" procedure can suddenly turn "complicated" if the patient has severe pain or suffers from difficult-to-control bleeding. If you are not an expert, it is usually best to leave "serious" wound debridement to the surgeon who is aware of the pitfalls and problems.

The "Dressing Dilemma"—making decisions about local wound care

There are now literally thousands of products available for covering wounds—most of these preparations fall into one of several "broad" categories:

Dressing Type	Comments
Gauze	Gauze dressings are probably the most common ones you are familiar with. They are made of woven cotton and can be dry or impregnated with petrolatum or antibiotic solutions (Xeroform; iodoform; salts). ✓ Needs solution (normal saline) or gel to maintain wet/moist surface. ✓ Good for debridement (wet-to-dry dressing) but may debride normal tissue. ✓ Use with solution (or petrolatum) in dry wounds (maintain moist surface); use as dry dressing in exudative wounds.
Hydrocolloid	Sodium carboxymethylcellulose compound on a film or foam backing. ✓ Inexpensive, maintains moist surface and protects wound ✓ Generally used on "clean", non-infected wounds ✓ Change every 3-5 days or when exudate strikethrough occurs
Alginates	Calcium containing polysaccharides derived from seaweed—have large absorptive capacity and are beneficial in wounds with heavy exudate. ✓ Best for infected wounds or wounds with heavy exudate ✓ Change Qday or BID depending upon the amount of exudate ✓ Do not use in "dry" wounds or wounds with eschar
Foam	This is an open cell, polyurethane on a film backing. It has high absorptive capacity and is good for "wet" wounds with large amount of exudate. ✓ Use on exudating wounds—avoid on "dry" wounds ✓ Generally does not adhere to wound—minimal pain on removal
Hydrogel	Three-dimensional, water swollen (90% water), cross-linked polymer (paste or sheet) that adds moisture to wounds. ✓ Available in amorphous form (tube) that can conform to and fill dead space ✓ Little antibacterial activity—secondary bacterial invasion can occur when used alone ✓ Will keep wound bed moist but may produce surrounding maceration
Transparent films	Clear plastic film that breaths (+ entry of oxygen and water vapor) but blocks entry of water and bacteria. ✓ Used in flat, dry wounds with good granulation. ✓ Clear plastic permits observation of wound ✓ Less commonly used in diabetic foot infection (more commonly used with decubitus ulcers).
Enzymes	Creams, ointment, or spray containing one of the following enzymes: collagenase, fibrinolysin, or trypsin ✓ Especially useful for chemical debridement of wounds with eschar or fibrin. ✓ Relatively slow and expensive; however, cream or ointment preparations maintain wound moisture ✓ Discontinue creams when eschar has disappeared.

Source: http://www.apsna.org

Keep in mind the following recommendations…

- **"Clean" wounds** (e.g. little exudate; minimal infection; well debrided): Consider a simple gauze dressing (with providone-iodine [e.g. Betadine]) or hydrocolloid dressings.
- **"Infected" wounds** (e.g. purulent with high levels of exudate): A simple dry gauze may suffice but also consider use of "absorptive" foam or alginate dressings. Of course, in these cases, antibiotic therapy is also an important component of management.
- **Necrotic wounds** (e.g. evidence of eschar or necrosis)**:** If patient is unable to undergo sharp debridement, consider "wet-to-dry" gauze dressing or utilize ointments or creams with enzymes (e.g. collagenase; trypsin).

Wound care magic— a "simple" approach to the diabetic foot wound

The above approach to wound care may seem complicated and is not always easy to remember. Once you have debrided and cultured the wound—and started the patient on antibiotics (if necessary)—the following protocol is a "time-tested" approach that is used by many podiatrists and wound care specialists:

- **Assess the wound:** Measure (size; depth) the wound and using the above system (Red-yellow-green-black). Assess the likelihood of infection and need for debridement and antibiotic therapy.
- **Obtain a culture:** Obtain aerobic and anaerobic cultures, preferably taken from a "deep" sample at the time of the debridement (Although sometimes necessary, try to avoid a "superficial" swab).
- **? Debride the wound:** If necessary (black "necrotic" tissue or yellow "slough") debride the wound using either a mechanical (e.g. sharp debridement with scalpel; wet-to-dry dressing) or non-mechanical (e.g. autolytic; enzyme debridement) method.
- **Cover the wound** with a two layer dressing…
  The "primary" dressing (close to the skin) is a iodine (Betadine) soaked gauze pad
  The second dressing (on top of the first gauze layer) is a dry gauze pad
- **Wrap the dressing** with a Kerlix bandage
- **Change the dressing** once a day—this allows the patient to inspect the wound and to make sure it is not infected (increased green or clear drainage) or becoming necrotic (black tissue).
- **Offload the wound:** Make sure the patient knows to offload the wound by using crutches, sitting in a wheelchair or using a cane (for forefoot lesions, walk on the heel and avoid putting pressure on the front of the foot).

Clinical Trials

What to expect…How fast can diabetic wounds heal?

Patients (and clinicians) are always frustrated by the time it takes to heal a diabetic foot wound, but how long does it really take? A recent study (looking at a new wound care product) examined wound healing in approximately 200 patients with diabetic foot ulcers. The wounds were relatively small (average wound area 2.8 cm^2 [0.2-42.4 cm^2] and the study excluded those with "infected" wounds or severe vascular disease. The adjacent table outlines the likelihood of "closure" or full wound healing at various times.

Time to healing-Diabetic foot ulcers*

Time (weeks)	% Complete Healing
4	10
8	25
12	35

*Source: Diabetes Care 2003:2003: 26(6):1879-82.

Message of the study...

- Examine the patient at 4 weeks—failure of the patient to demonstrate a 50% reduction in wound size (from baseline) means trouble and suggests a high likelihood (close to 90%) that they will "fail to heal".
- Even with optimal conditions (shallow ulcer; good wound care; no infection; vascular supply intact), only about 35% of non-infected diabetic foot ulcers will completely heal by 12 weeks!
- When wound size appear s to "plateau'—and lacks evidence of progressive healing--look for complicating factors such as poor patient compliance, infection or vascular insufficiency. In addition, think about the use of more advanced wound care techniques or consider a consultation with a wound care expert!

Source: Sheehan P et al. Percent change in wound area of diabetic foot ulcers over a 4-week period is a robust predictor of complete healing in a 12-week prospective trial. Diabetes Care. 2003. Jun;26(6):1879-82.

“Chronic” wounds—definition and pathophysiology

“Normal” , acute wounds go through a set of progressive stages leading to complete reepitheliazation—specialists consider a wound to be “chronic” when it “stalls” at one of these stages and fails to complete the healing process. The precise reason this occurs is not completely clear; however, the following factors seem to play a role in the failure of a wound to heal:

- ✓ **Ischemia** is an important factor in chronic wounds, especially in diabetics or older patients with underlying vascular disease. The presence of ischemia leads to inflammation and the release of chemokines favoring neutrophil invasion—these cells contain the enzyme myeloperoxidase which increses production of oxygen radicals (Reactive Oxygen Species) resulting in tissue damage.
- ✓ **Infection:** Chronic wounds are more likely to be “colonized” or infected with bacteria, a state that attracts neutrophils with consequent enzyme release and tissue damage. With passage of time (and multiple courses of antibiotics), bacteria become more resistant to standard agents—chronic wounds are more likely to be colonized with methicillin resistant *Staph aureus* (MRSA) and resistant gram negatives such as *Pseudomonas aeruginosa.*
- ✓ **Off-loading:** Constant pressure on a foot wound—as occurs in walking—may hamper healing of the lesion. “Offloading” a wound is an important component of wound healing and must be assessed in any patient with a wound that fails to heal.
- ✓ **Growth factors:** In the chronic wound, there is altered chemical balance with decreased growth factors such as platelet derived Growth factor (PDGF) and increased levels of “harmful” inflammatory enzymes (metalloproteinases; elastases) that cause tissue damage and delay healing.

Grafts, Growth factors and “Grubs”—Alternative wound care options

Once you’ve ruled out some of the common causes of “failure to heal” (see above), it’s time to obtain expert help and consider the use of some of the “alternative” wound care options. Though the efficacy is debated (it’s not always clear that they work better than “standard” approaches), these techniques sometimes lead to closure of a previously open, non-healing wound—they may be worth a try in a previously recalcitrant case. Among some of the options, are the following…

- ✓ **Tissue grafts:** Native or specially engineered tissue grafts (e.g. Apligraft) may help close a wound that has failed to heal by other means.
- ✓ **Growth factors:** Genetically engineered platelet derived growth factor (.01% becaplermin gel) is expensive but has been shown to accelerate wound healing in at least one, large randomized controlled trial. Presence of wound infection is a relative contraindication to the use of this agent.
- ✓ **Negative wound pressure therapy:** Application of external negative pressure via a “wound vac” has become a popular option for poorly healing diabetic foot ulcers.
- ✓ **Hyperbaric oxygen:** Although efficacy is debated—and the treatment is expensive, requiring a specially equipped chamber—high oxygen concentrations appears to have a positive effect on some chronic wound problems.
- ✓ **Sugar or honey:** High osmolar honey or sugar paste has long been recognized as a folk remedy that encourages wound healing. This has led to commercial products with medical grade honey (e.g. MediHoney; Therahoney) as well as home remedies employing a paste made of table sugar (see: http://www.peoplespharmacy.com/2013/03/03/sugar-for-wound-care).
- ✓ **Maggots:** Although this has an undoubted “ick” factor, fly larvae (maggots) feed on necrotic material and respect healthy tissue—this has been touted in patients with chronic, foul-smelling wounds that require extensive debridement.

Chronic wound "woes"..what to do when healing is delayed

The patient arrives in your office, takes off their bandage and shows you a chronic, non-healing wound—they expect you to provide the solution. The following checklist offers a list of possibilities (and possible corrections) when the regular treatment doesn't seem to be working…

- ❑ **? "Off-loading" the wound:** Is the patient the patient continuing to ambulate and put pressure on the wound—failure to "off-load" the wound (especially plantar ulcers) is one of the most common reasons for failure of the wound to heal. Make sure the patient is off-loading the wound (on crutches, via wheelchair or cane) and consider a total contact cast or special boot.
- ❑ **Antibiotic failure:** In those with documented infection, review any previous culture results and make sure the "bugs" are susceptible to patient's antibiotic regimen. Also, confirm that the patient is taking the drug and keep in mind the possibility of poor intestinal absorption in those on oral regimens.
- ❑ **Is the wound infected?** Look for purulent material or an increase in amount of drainage—wound infection may well contribute to delay in healing. If there is increased drainage, consider repeating cultures
- ❑ **Rule out osteomyelitis:** The presence of underlying osteomyelitis may hamper wound healing—obtain a repeat plain radiograph and look for evidence of progressive bone destruction. If the plain films are negative, consider an MRI or bone scan. Definite evidence of bone destruction suggests the need for partial amputation of the infected bone.
- ❑ **Check the blood supply:** Check pulses and—if you haven't done so already—obtain a screening ABI (ankle brachial index). Marked impairment of the blood supply (ABI < 0.7) should prompt additional studies (arterial duplex; MRA) and a vascular surgery evaluation.
- ❑ **Consider alternative measures** including native or engineered tissue grafts, topical growth factors and negative pressure wound therapy. With stubborn wounds, some experts have had success with honey or granulated sugar!
- ❑ **? Diabetic foot infection mimics:** Keep in mind that a number of conditions, including vasculitis, neoplasm and gout can lead to ulceration that mimics diabetic foot infection. Patients with Charcot foot develop foot deformities that lead to poorly healing pressure ulcers if not immediately off-loaded.

"Word to the Wise": Offloading a wound isn't always so easy— patients will often continue to walk on the wound despite your instructions. This is a recipe for disaster and remains one of the most common reasons for failure of wound closure. It is imperative that patients understand the importance of "offloading" the wound by using crutches, a wheelchair or a cane. If the patient appears unreliable, a total contact cast (somewhat time-consuming to apply) or an orthotic walking device (be careful, patients sometimes take it off!) are other options.

Wound care for the diabetic foot ulcer—what you need to know…

- The cause of diabetic foot ulceration is often multifactorial with neuropathy, vascular insufficiency and infection playing a prominent role in the initiation—or persistence—of skin breakdown.
- Careful wound care plays an important role in the healing of the diabetic foot wound—clinical research has repeatedly demonstrated that "moist" wounds heal faster than wounds that are allowed to dry out.
- While there are numerous available wound care products (some of them quite expensive!), a simple dressing (Iodine moistened gauze with a covering bandage) appears to provide adequate protection for most diabetic foot wounds.
- For plantar ulcers, "off-loading" the wound is a key factor—wounds will not heal if the patient continues to ambulate and place excessive pressure on the wound.
- A chronic wound is present when the wound fails to heal and reepithelialize—the biology of these wounds suggests that they have increased inflammatory mediators leading to tissue damage and delayed healing.
- There are a number of reasons why a wound may fail to heal including infection, failure to "offload" the wound, underlying vascular insufficiency and diabetic foot wound "mimics" (neoplasm; vasculitis; Charcot foot).
- If a wound fails to heal with simple measures, more exotic treatments include tissue grafts, growth factors, negative wound pressure (e.g. WoundVac) and "high" osmolar preparations (e.g. honey; granulated sugar).

Chapter 11

Putting it all together…a diabetic foot infection "checklist"

You are confronted by a patient with a diabetic foot infection (DFI), follow this checklist and algorithm in order to provide proper management…

- ❑ **Examine the patient** with special attention to the following…
  - **Vital signs:** Does the patient have signs of SIRS including hypotension, fever and tachycardia—such findings suggest more serious infection and the need for more aggressive treatment (e.g. initial parenteral antibiotics; surgery).
  - **? Overall foot anatomy:** Look for signs of a "diabetic" foot including hammer toes, "cocked up" toes with prominent *extensor hallucis longus*, high arch, midfoot collapse (Charcot foot).
  - **If gangrene or soft-tissue air is present**, call a surgeon immediately—the patient may have gas gangrene and require immediate surgery.
  - **Is there a foul smell?** Anaerobes are likely to be present and require antibiotic coverage.
  - **Examine the toes** for evidence of *tinea pedis* or onychomycosis—these seemingly "harmless" infections may be the entry point for life-threatening bacterial infection of the foot.
  - **Measure and probe any ulcer**: Look for presence of bone or tendon—if you can "probe to bone" with a blunt object, osteomyelitis is likely to be present.
  - **Squeeze the affected area—**if you can express pus the patient will likely require surgical drainage of an underlying soft-tissue abscess suppurative tenosynovitis.
  - **Check the patient's peripheral sensation—**most patients with diabetic foot infection have some degree of peripheral neuropathy that may dull the pain of the infection.
  - **Check and record pulses in the lower extremity—**a poor blood supply will hamper healing and impair antibiotic delivery. In those with poor pulses, check an ankle-brachial index (ABI)—an ABI < 0.8 is abnormal and suggests the ulcer is unlikely to heal.

- ❑ **Obtain a culture and laboratory studies**: Culture (and request a Gram stain) any purulent drainage —if possible, call a surgeon and obtain a "deep" culture from a deep debridement. Patients with fever and toxicity requiring hospital admission should have **blood cultures**—the yield may not be high but it can be quite helpful in zeroing in on the likely pathogen. In addition to cultures and routine studies (e.g. CBC, chemistry panel), obtain an erythrocyte sedimentation rate **(ESR)** and C-reactive protein **(CRP)**—these studies will help monitor response to therapy (CRP) and aid in assessment of osteomyelitis (ESR usually > 60 mm/hr).

- ❑ **Review the radiograph of the foot:** Any patient with a foot ulcer should have plain radiographs looking for a fracture, foreign body, soft-tissue air or underlying osteomyelitis. Consider obtaining an MRI of the foot in the following circumstances:
  - High suspicion of underlying osteomyelitis (e.g. patient with deep ulcer) despite a negative plain radiograph.
  - Patients with a poor clinical response to appropriate antibiotics.
  - Possibility of a deep, soft-tissue abscess or tenosynovitis.
  - Uncertainty about the extent of infection (the "tip of the iceberg" phenomenon).

- **Evaluate the vascular supply…** As stated above, check and record pulses in the lower extremity—if pulses are absent (or decreased), consider obtaining an arterial "duplex" of the lower extremity including an "**ABI**"—ankle-brachial index (an ABI < 0.8 is abnormal and suggests the need for revascularization).

- **? Osteomyelitis vs. cellulitis…** Using a few simple parameters, try to determine whether the patient has osteomyelitis or just "plain" cellulitis (see table). Although specificity varies, a higher number of "positive" parameters suggests an increased likelihood of osteomyelitis. The presence of osteomyelitis has implications for the length of therapy—the greater the likelihood of "osteo", the greater the need for more prolonged antibiotics (2 weeks for cellulitis vs. 8-12 weeks for osteomyelitis). If in doubt, treat the patient for 4 weeks and obtain a repeat plain film in 4 weeks—new evidence of bony resorption or poor ulcer healing suggests underlying osteomyelitis.

Parameter	***Cellulitis***	***Osteomyelitis***
Ulcer present > 30 days	No	Yes
Bone lesion on radiograph	No	Yes
"Probe to bone test"	Negative	Positive
ESR > 60 mm/hr.	No	Yes

❑ "Stage" the patient's infection…

Using a simple system* (see below), "stage" the extent of the infection

Mild infection	Moderate infection	Severe infection
Purulent wound or signs of inflammation (Pain, tenderness, erythema, warmth or induration) with the following…	Purulent wound or signs of inflammation (Pain, tenderness, erythema, warmth or induration) with the following…	Purulent wound or signs of inflammation (Pain, tenderness, erythema, warmth or induration) with the following…
• **Cellulitis/erythema ≤ 2 cm**. around ulcer • **No Systemic toxicity**	• **Cellulitis/erythema > 2 cm**. around ulcer • **Evidence of osteomyelitis, tendon or deep infection** • **No or minimal Systemic toxicity**	• **Systemic toxicity including some of the following findings…** ✓Fever, chills, toxicity ✓Hypotension ✓Confusion ✓Vomiting ✓Leukocytosis ✓Metabolic acidosis ✓Severe hyperglycemia ✓Azotemia

* Based on IDSA diabetic foot scoring system

- **Consider the possibility of a cellulitis "mimic":** Don't forget that several syndromes can mimic diabetic foot infection…
  - **Charcot foot** can completely mimic DFI with pain, swelling and erythema—look for midfoot involvement ("rocker bottom" foot deformity with loss of longitudinal and transverse arch), peripheral neuropathy and "good" blood supply with "bounding" pulses (usually).
  - **Gout:** Ask about a history of "podagra" (1st metatarsophalangeal involvement), order a serum uric acid and consider a joint tap to look for crystals.
  - **Ischemia:** Palpate the major LE pulses and look for "dry" gangrene or "wet" (infected) gangrene.

- **Deep venous thrombosis:** Check venous duplex in suspect cases

❑ **Call a surgeon…** In patients with moderate or severe infection—especially if there is any evidence of **gangrene, necrotizing soft tissue infection** or **"deep"** infection requiring incision and drainage. They will help assess the foot, determine the need for drainage, debridement and/or amputation. In patients with impaired vascular supply, obtain vascular studies and involve a vascular surgeon (or interventional radiologist) as soon as possible.

❑ **Start empiric antibiotic therapy…**Once you suspect a possible infection, start empiric antibiotic therapy, depending upon the "stage" of the infection.

Mild infection **(Oral)**	**Moderate infection** **(Oral or IV)**	**Severe infection** **(IV)**
Cephalexin (PO) or Amoxicillin/clavulanic acid or Clindamycin PO or Levofloxacin or TMP/SMX† + cephalexin	Oral therapy (see Mild infection) or Ceftriaxone + metronidazole (PO) or Cefoxitan (or cefotetan) or Ceftaroline or Ampicillin/sulbactam	Piperacillin + vancomycin or Doripenem + vancomycin Or Ciprofloxacin + vancomycin + metronidazole
Amoxicillin/clav 875 mg PO BID Cephalexin 500 mg PO QID Clindamycin 450 mg PO QID Levofloxacin 500 mg PO Qday Trimethoprim/sulfamethoxazole (1-2 DS tablets PO BID)	Ampicillin/sul 3 gm IV Q 6 hr Cefoxitan 1-2 gm IV Q 8 hr Ceftaroline 600 mg IV Q 12 hr Ceftriaxone 1-2 gm IV Q 24 hr Tigecycline 100 mg load; 50 mg IV Q 12 hr	Ciprofloxacin 400 mg IV Q 12 hr Doripenem 500 mg IV Q 8 hr Metronidazole 500 mg IV Q 8 hr Pip/tazo 4.5 mg IV Q 8 hr Vancomycin 1 gm IV Q 12 hr

* Dosing for 70 kg patient with normal renal function
† In patient with possible MRSA

When choosing antibiotic therapy, keep in mind the following…

✓ **Staph/strep:** Most diabetic foot infections (> 50%) are due to staphylococcus (*S. aureus*) or streptococcus (Grp A, Grp B strep and/or viridans streptococci)

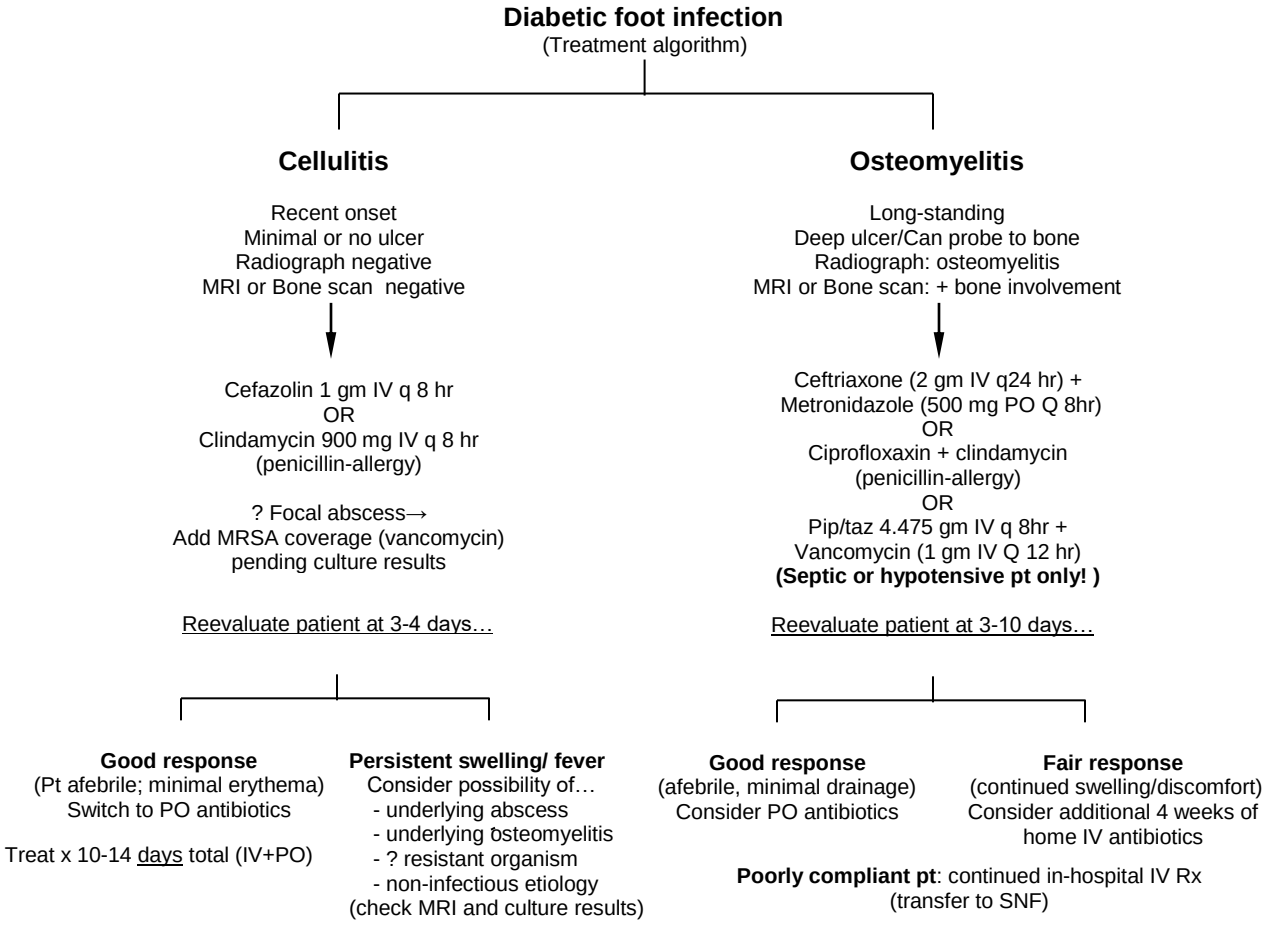
✓ **Oral antibiotics:** With appropriate followup, most patients with mild (or moderate) disease can be treated with oral agents.

✓ **MRSA:** We reserve MRSA coverage (e.g. vancomycin) for those with a previous history of documented MRSA infection or "sicker" patients requiring ICU care.

✓ **Anaerobes:** If the drainage has a "foul" smell, anaerobes are likely—include antibiotics with anaerobic coverage in initial therapy (e.g. metronidazole; clindamycin; BL/BLI [amp/sulbatam or piperacillin/tazobactam], cefotetan, tigecycline or carbapenem).

✓ ***Pseudomonas aeruginosa*** is uncommon in diabetic foot infection—most of the time it represents a superficial contaminant; however, it should be covered in critically ill patients (ICU; severe sepsis) until culture results are available.

✓ **Severity of infection:** Reserve hospital admission for patients with "severe" infection (signs of sepsis or "toxicity") or cases where oral therapy may be unreliable (e.g. poor compliance; GI distress; poorly controlled diabetes).


Diabetic foot infection
(Treatment algorithm)
Cellulitis
Recent onset
Minimal or no ulcer
Radiograph negative
MRI or Bone scan negative
Cefazolin 1 gm IV q 8 hr
OR
Clindamycin 900 mg IV q 8 hr
(penicillin-allergy)
? Focal abscess→
Add MRSA coverage (vancomycin)
pending culture results
Reevaluate patient at 3-4 days…
Good response
(Pt afebrile; minimal erythema)
Switch to PO antibiotics
Treat x 10-14 days total (IV+PO)
Persistent swelling/ fever
Consider possibility of…
- underlying abscess
- underlying osteomyelitis
- ? resistant organism
- non-infectious etiology
(check MRI and culture results)
Osteomyelitis
Long-standing
Deep ulcer/Can probe to bone
Radiograph: osteomyelitis
MRI or Bone scan: + bone involvement
Ceftriaxone (2 gm IV q24 hr) +
Metronidazole (500 mg PO Q 8hr)
OR
Ciprofloxaxin + clindamycin
(penicillin-allergy)
OR
Pip/taz 4.475 gm IV q 8hr +
Vancomycin (1 gm IV Q 12 hr)
(Septic or hypotensive pt only!)
Reevaluate patient at 3-10 days…
Good response
(afebrile, minimal drainage)
Consider PO antibiotics
Fair response
(continued swelling/discomfort)
Consider additional 4 weeks of
home IV antibiotics
Poorly compliant pt: continued in-hospital IV Rx
(transfer to SNF)

Diabetic Foot Infection for the Houseofficer

Appendix

Diabetic foot infection—10 common outpatient scenarios

1. **How to manage "simple" cellulitis:** This is the patient that has "mild' limited cellulitis with minimal fever and *absence* of signs of "toxicity" (e.g. fever, severe pain, gangrene). On examination, the patient has erythema, but typically doesn't have a visible abscess or purulent cellulitis (see below).

   - ✓ Most of these cases are due to streptococci (grp A, grp B, viridans streptococci) and/or staphylococci
   - ✓ Treat with oral cephalexin (500 mg Q 6hr) or amoxicillin/clavulanic acid (875 mg BID)
   - ✓ Administer clindamycin or levofloxacin in those with significant penicillin allergy,
   - ✓ Instruct the patient to call or return in 48 hours if they are not beginning to improve.

2. **Purulent cellulitis and/or "abscess":** When there is clear evidence of a focal infection (e.g. abscess) or 'purulent" cellulitis, *Staph aureus* is the more likely pathogen and you need to consider the possibility of MRSA (methicillin resistant *Staph aureus*).

   - ✓ Always culture these lesions if purulent drainage is present. Approximately 50% of community-acquired staphylococcal isolates are MRSA (although the incidence in diabetic foot infection is somewhat lower).
   - ✓ In addition to treatment with cephalexin, consider adding TMP/SMX (1 DS tablet BID) or doxycycline (100 mg BID) for MRSA coverage.
   - ✓ Clindamycin is an alternative agent which doesn't require co-administration of cephalexin
   - ✓ Linezolid has good gram-positive coverage but is expensive ($50-$100 per day) and often requires a high copay or insurance approval.

3. **Foul smelling drainage:** The presence of "foul smelling" drainage from a foot ulcer often suggests the presence of anaerobic bacteria which are found in up to 50% of diabetic foot infections.

   - ✓ Culture any drainage and request *both* aerobic and anaerobic cultures
   - ✓ Use an antibiotic with activity against "anaerobes" including any of the following…
     - ➢ Amoxicillin/clavulanic acid (875 mg BID)
     - ➢ Clindamycin: Also has activity against gram positives including MRSA
     - ➢ Metronidazole (500 mg BID): Active against "strict" anaerobes—need to combine with drug active against streptococci (e.g. amoxicillin or cephalexin or levofloxacin)

4. **"I stepped on a nail":** As outlined previously (see Chapter 9), these wounds are usually infected with staphylococci or streptococci. Nevertheless, many specialists will recommend concomitant treatment with a quinolone (e.g. ciprofloxacin; levofloxacin) because of the higher risk of *Pseudomonas* infection. If the surgeon plans to explore the wound (? Foreign body), it might be best to delay therapy till immediately after you obtain cultures.

5. **"Dog licked my foot":** Not all that uncommon a history (if you take the time to ask about pets such as dogs and cats) and an important marker for infection with *Pasteurella* species—organisms that can cause rapid-onset severe cellulitis with associated bacteremia. *Pasteurella* is typically resistant to first generation cephalosporins (e.g. cephalexin) and macrolides (e.g. erythromycin)—if you suspect this organism, treat with oral amoxicillin (or amoxicillin/clavulanic acid), doxycycline or quinolone (e.g. ciprofloxacin; levofloxacin).

6. **Penicillin allergy:** If you obtain a history of "penicillin allergy", ask about the nature of the reaction—if the patient had a true IgE mediated reaction (e.g. anaphylaxis; hives; difficulty breathing), avoid penicillin and other B-lactams such as cephalosporins. If there was "just a rash" (after 5-10 days of therapy), the patient most likely had a cell-mediated reaction to penicillin and may well be able to take a cephalosporin. If in doubt about the history, it is better to go with agents from a different class (e.g. clindamycin, doxycycline; levofloxacin).

7. **Black toe (dry gangrene):** On examination, you see a "black toe" with minimal erythema or drainage—this is the classic definition of "dry gangrene" and the toe may well auto-amputate without any surgical intervention. Nevertheless, clinicians are divided as to the need for "empiric" antibiotics in this situation—some experts believe that it represents a risk for further cellulitis/infection and treat the patient with prophylactic oral antibiotic (e.g. cephalexin or amoxicillin/clavulanic acid). Other experts avoid prophylactic antibiotics (e.g. they

are worried about potential side effects and the possibility for encouraging "resistant" bacteria) and only treat the patient if they develop clinical cellulitis or "wet" gangrene.

8. **Patient taking warfarin:** This is an increasingly common issue as patients are aggressively treated for underlying conditions such as atrial fibrillation and TIAs. What follows is a quick list of the common oral antibiotics and the effect they have on warfarin metabolism:

Drug	Effect on PT*	Action*
Amoxicillin	No effect	No dose adjustment
Amox/clavulanic acid	No effect	No dose adjustment
Cephalexin†	No effect	No dose adjustment
Ciprofloxacin	↑ **INR**	**Avoid/use alternative**
Clindamycin	No effect	No dose adjustment
Dicloxacillin	↓ **INR**	**Avoid/use alternative**
Doxycycline	↑ **INR**	**Monitor/modify therapy**
Linezolid	No effect	No dose adjustment
Levofloxacin	↑ **INR**	**Avoid/use alternative**
Metronidazole	↑ **INR**	**Avoid/use alternative**
TMP/SMX	↑ **INR**	**Avoid/use alternative**
Rifampin	↓ **INR**	**Monitor/modify Rx**

* Based on Epocrates accessed on 12/29/14
† Other cephalosporins including cefadroxil (Duricef), cefpodoxime (Vantin), cefixime (Suprax), cefuroxme and cefdinir (Omnicef) also appear to have minimal effect on INR.

With regard to warfarin (Coumadin), several things need to be kept in mind…

- ✓ Always review your patients list of medications and ask about warfarin, especially if you plan to prescribe a drug that might have an effect on the INR.
- ✓ Most β-lactam antibiotics (except for dicloxacillin) appear to have little effect on the INR and can be co-administered safely with warfarin.
- ✓ Some drugs (e.g. doxycycline; rifampin) should be avoided but can be given with proper monitoring of the INR (may need to alter dose of warfarin).
- ✓ Some drugs (e.g. quinolones; sulfa drugs; metronidazole) increase INR and are best avoided in patients taking warfarin. If you need to use these agents, talk with the patient's internist about dose-reducing the warfarin or considering a switch to an alternative form of anti-coagulation (e.g. subcutaneous heparin).
- ✓ Even if a drug has "no effect" on INR, it might be best to check an INR within a few days to make sure there are no unanticipated effects on anticoagulation.

9. **How long to treat?:** Most patients with "simple" cellulitis should respond to 10-14 days of treatment—patients with a "deep" infection (e.g. deep ulcer; + probe-to-bone test) may well have osteomyelitis and generally require more prolonged treatment (8-12 weeks). If you suspect osteomyelitis, always obtain a radiograph and sedimentation rate (an ESR > 75 suggests underlying osteomyelitis).

10. **A word of caution!** Even when they appear relatively "benign" (e.g. patient afebrile, minimal pain/inflammation), never underestimate the power of these "simple" infections to progress rapidly, leading to foot loss or mortality. When choosing to treat with oral antibiotics, always give the patient explicit instructions to call you—or return to the emergency room—if the infection appears to be progressing (e.g. increased pain; high fever; worsening cellulitis) within 48 to 72 hours. If in doubt, consider admitting the patient (for parenteral antibiotics) or giving an initial dose of IV ceftriaxone in order to "cover" patients while waiting for culture results.

ID Checklist: The diabetic foot—the next "step" in clinic

You're in ID clinic and have just picked up a chart on a diabetic patient with a foot infection. In most cases, it will be a patient who is already on antibiotics, possibly from a recent hospitalization. Here is a checklist to help you determine if the patient is getting better and guide you in the next "step" of management:

❑ Did the patient have cellulitis or osteomyelitis?

Almost by definition, most of the patients in ID clinic have osteomyelitis—otherwise, they wouldn't get past the clinic screener! Nevertheless, as you are seeing them, it's a good idea to see if they met any of the following criteria for osteomyelitis since this generally implies a longer course of therapy…

√ **Ability to probe to bone** (or visible bone at the base of the ulcer)
√ **Bone abnormality** on plain film, bone scan or MRI
√ **Elevated ESR or CRP** (the higher the ESR [>50]…the more likely underlying osteomyelitis)

❑ Is the patient clinically improving?

Hopefully the patient is clinically improving. With proper therapy, you should see decreased pain, erythema and swelling. If the patient has a wound, look for presence of good granulation tissue (red) and gradual closure of the wound. Measure the ulcer (document this in the chart) and compare it with previous measurements or pictures in the medical record.

❑ What did the initial cultures show?

Review culture results at the start of therapy. Compared with a superficial swab of the ulcer, cultures obtained following a good deep debridement are likely to be more predictive of the true pathogen. If there is continued purulence, consider obtaining another culture to make sure the patient does not have antibiotic resistant pathogens.

❑ Is the ESR (CRP) improving?

When first diagnosed, we recommend obtaining a baseline ESR and C-reactive protein—in most patients, clinical improvement is heralded by a steady decrease in serum levels. Despite clinical improvement, the ESR may remain elevated—some investigators believe that the CRP is a more sensitive to clinical response and prefer to follow this parameter. In general, a worsening sedimentation rate or CRP is a poor sign and raises the possibility of ultimate treatment failure.

❑ What about radiographic studies?

Look back on the initial diagnosis—how was the diagnosis of osteomyelitis made? In the presence of infection (erythema, swelling, pus), evidence of bone destruction on a plain film is a clear indication of osteomyelitis. For those with "negative" plain films, an MRI (or bone scan) can suggest underlying osteomyelitis; however, these tests can be overly sensitive and sometimes are false positive. If the initial plain films are negative, consider repeating the film after 2-4 weeks of therapy—the appearance of bone destruction pretty much clinches the diagnosis of osteomyelitis and is a harbinger of a poor outcome.

❑ What antibiotics are they receiving?

Patients recently discharged from the hospital are often on parenteral antibiotics—check the previous culture results and make sure they are receiving the correct therapy. Make sure they are actually taking the medications (not always guaranteed!) and ask about any potential side effects (nausea, diarrhea, rash, fever). Understandably, compliance is less common in patients with side effects, extremely frequent dosing (TID or QID) or poor social circumstances.

❑ Can you switch to oral therapy?

The exact timing of this switch is unclear—anywhere after 2, 4 and 6 weeks of parenteral treatment, depending upon the patient's clinical response and appearance of the ulcer. Recommended oral regimens are often quite effective—in some cases (quinolones, metronidazole) serum levels following oral administration reach levels equivalent to those obtained following parenteral administration. After checking previous culture results, choose one (or more) of the following agents:

Choose oral therapy based on culture results and likely pathogens:		
Oral therapy regimens	**Dose***	**Comment**
Amoxicillin	500 mg TID	Good for strep and enterococcus
Amox/clav (Augmentin)	875 mg BID	Use in mixed (aerobe + anaerobe) infection
Cephalexin	500 mg q 6 hr	Good for uncomplicated cellulitis (Grp A strep or *S. aureus*)
Ciprofloxacin	500-750 mg BID	Use for GNR infection
Clindamycin	450-600 mg q 6 hr	Good for strep, staph (MRSA) and anaerobes: Use in combination with cipro for mixed infection
Dicloxacillin	500 mg QID	Good activity against MSSA
Minocycline	100 mg BID	Good for MRSA; do not take with milk or calcium
Metronidazole	500 mg q 12 hr	Use in combination with cipro or cephalexin for mixed infection
Rifampin	600 mg q day	Use in combination with cipro for tmp/smx for *S. aureus*
TMP/SMX (Bactrim DS)	2 tabs BID	Use in combo with rifampin for MRSA infection
* Dosing for 70 kg pt with normal renal function		

❑ How long to treat?

Again, there is no hard and fast rule for this but most experts prefer somewhere between 8-12 weeks of treatment, counting both parenteral and oral therapy. I tend to go on the longer side (12 weeks +) if the patient had a particularly nasty infection or if there is still an open wound. In patients with slow healing and definite osteomyelitis, we may go longer (6-12 months) if relapse is highly probable.

❑ How do you know if the patient is cured?

This is an especially difficult question—even with full clinical response (healed wound, low ESR, pain absent), some experts believe that clinical relapse always remains a distinct possibility. In my experience, patients with clear evidence of osteomyelitis (+ plain films) almost always suffer a relapse, despite prolonged antibiotic therapy.

❑ My patient is not getting better—what's wrong?

If the patient is not clinically improving, one of the following situations could be present:

1. **Wrong bug:** Your treating the wrong bug (Review previous cultures and consider a repeat)
2. **Poor antibiotic absorption:** The patient is not taking (or absorbing) their medications. Review the regimen and barriers to compliance (e.g. side effects; too frequent dosing; social circumstances).
3. **Improper wound care:** Make sure the patient is dressing the wound properly (Need to maintain a "moist" wound environment. Off-loading the wound (e.g. using crutches, wheel chair or special boots) is critical—a wound won't heal if the patient continues to walk on it!
4. **Vascular obstruction:** The medication may not be getting to the site of infection. Check pulses, review the vascular studies (Ankle-brachial index) and consider a vascular evaluation if the physical exam or ABI (< 0.9) suggest vascular disease.
5. **Surgery needed:** In patients with clear evidence of osteomyelitis or devitalized tissue (gangrene), more aggressive surgery may be required. Refer the patient back to podiatry.
6. **Wrong diagnosis:** Not all foot inflammation is infection—keep in mind the possibility of cellulitis "mimics" such as gout, vascular gangrene, calciphylaxis (in ESRD) and Charcot osteolysis (Charcot foot).

Diabetic foot infection—Oral antibiotic pocket card

As a clinician seeing patients with diabetic foot infection, you will be commonly called upon to prescribe oral antibiotics. This handout gives an overview of the most common antibiotics, including antimicrobial "spectrum", dosing and potential side effects. This is by no means encyclopedic—we have tried to keep it simple by sticking to the most common drugs and have included a set of "guidelines" for when oral (versus parenteral) antibiotics are most appropriate. In general, we rely on oral therapy in several situations:

- **"Mild" illness:** If a patient is severely ill or requires hospital admission, they probably should receive parenteral antibiotics till cultures are available and the severity of illness clear.
- **"Step down" therapy:** After patients have received a course of parenteral treatment, we usually "step down" to an oral regimen to finish out treatment, especially in patients with osteomyelitis who typically require a total of 8-12 weeks of therapy.
- **Post-amputation:** Even if the wound looks clean—and the surgeon is confident that they "got all the disease"—we often recommend several days of additional treatment "just to make sure".

The "top" 14 oral antibiotics for diabetic foot infection

What follows is a brief review of the most common oral antibiotics along with some specific features that any physician "needs to know" about the agents:

Drug	Antimicrobial spectrum	Abs (%)	Dose	Side effects
Cephalexin	*Staph* species (not MRSA) Streptococci *E. coli* (80% isolates)	99	250-500 mg QID	Allergy: Occasional rash Rare anaphylaxis
Cefuroxime	Same + *H. influenzae*	52	500 q12hr	More expensive but less frequent dosing Take with food for best absorption

- Cephalexin is appropriate agent for "simple" cellulitis in patient with mild illness.
- If MRSA is a consideration (e.g. "purulent" cellulitis; focal abscess), consider adding TMP/SMX or using alternative agent (e.g. doxycycline; clindamycin; linezolid).
- Cefuroxime has similar spectrum to cephalexin with less frequent dosing (BID vs QID) but is more expensive

Amoxicillin	Streptococci; enterococcus	90	500 mg Q 8hr	Allergy (Anaphylaxis; rash)
Amox/clav acid (Augmentin)	Strep; staph (MSSA); E. coli; *Klebsiella*;anaerobes	90/60	875/125 Q BID	Allergy (Anaphylaxis; rash) GI upset (N/V; diarrhea; abdominal pain)
Dicloxacillin	*Staph aureus* (MSSA)	50	500 mg Q 6 hr	Allergy (Anaphylaxis; rash)

- Amoxicillin/clavulanic acid has "broad" coverage including strep, staph (not MRSA), GNRs and anaerobes. Although generally well-tolerated, it can have significant (~10% incidence) GI side effects such as nausea, vomiting and diarrhea.
- Dicloxacillin is drug of choice for patients with documented MSSA

Ciprofloxacin	GNRs including *Pseudomonas aeruginosa*	70	500-750 q 12 hr	GI upset ; arthropathy; tendon rupture CNS side effects (anxiety; insomnia; rare seizures)
Levofloxacin	Same but with better streptococcal coverage	99	500-750 Q 24 hr	

- The quinolones (Cipro; levo) have excellent absorption along with good *Pseudomonas* coverage (50% isolates).
- Levofloxacin is more expensive than ciprofloxacin but has better streptococcal coverage and only requires Qday dosing.

Doxycycline	*Staph aureus* (MSSA/MRSA) Less optimal strep coverage	93	100 mg BID (200 mg load)	Good activity against most strains of *Staph aureus*, including MRSA
Minocycline	Same		100 mg BID (200 mg load)	Slightly better MICs for MRSA More frequent dizziness and rare lupus-like reactions

- In DFI, the tetracyclines are primarily used for treatment of staphylococcal infection, especially community-acquired MRSA
- These drugs have excellent oral absorption and good bone penetration; a good choice for staphyloccous osteomyelitis

Clindamycin	Gram positives (strep; staph including MRSA);anaerobes	90	300-600 mg Q 8hr	Rash; *C. difficile* colitis
Metronidazole	"Strict" anaerobes: *Bacteroides,* anaerobic strep; *Clostridia*	90	500 mg Q12 hr	Often combined c agent with strep activity (e.g. amoxicillin; levofloxacin) N/V; GI upset; neuropathy
TMP/SMX (Bactrim)	Staphylococci(MSSA/MRSA)	98	1 DS tab BID	Sulfa rash; anemia; leukopenia: Occasional elevated creatinine/K^+
Linezolid	Gram positives: strep; MSSA; MRSA; enterococcus	100	600 mg Q 12 hr	Expensive drug (100$ per day!) "Serotonin rxn" in pts on SSRI Low platelet counts
Rifampin	Staphylococci; streptococci	95	600 mg Q 24 hr	Multiple CY450 drug interactions

- Clindamycin good for "mixed" gram positive + anaerobic infection; however, does not have gram negative activity
- Metronidazole is usually combined with agent that has streptococcal activity such as amoxicillin, cephalexin or levofloxacin
- TMP/SMX good agent when community-acquired MRSA is likely
- Rifampin should not be used alone—resistance develops rapidly (usually combine c quinolone for susceptible staph infection).

Tables based on material from Cunha BA, Antibiotic Essentials, Physicians Press 2002
Abbrev: Abs: Absorption; MSSA: methicillin susceptible *Staph aureus*; MRSA: methicillin resistant *Staph aureus*; TMP/SMX: trimethoprim/sulfamethoxazole

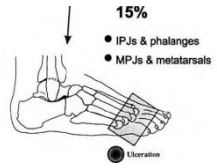
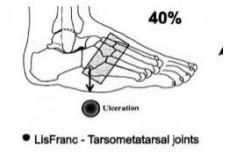
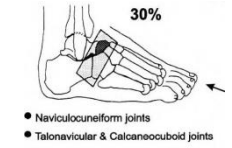
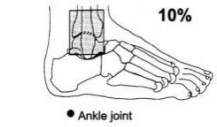
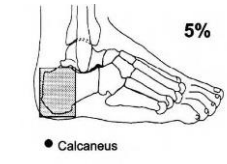
Rules of oral antibiotic therapy: When confronted by the above situations, there are a couple of additional "rules" of oral antibiotic therapy that should be followed …

- **Check susceptibilities:** While we rely on empiric therapy at initial presentation, whenever possible obtain cultures (or look at previous cultures) to see what bacteria are growing—though not foolproof, this will give you a general idea if the drug you plan to use is a reasonable choice.
- **? Nausea/vomiting:** The presence of serious nausea and vomiting is a general contraindication to oral therapy—in this situation, parenteral treatment is generally much better until you've been able to control the underlying GI problem. Keep in mind that some oral agents (e.g.amoxicillin/clavulanic acid) often have nausea and GI upset as a common side effect.
- **Ask about allergy!** Before you prescribe any drug, ask about previous allergies—although any drug may be associated with anaphylaxis, B-lactams (penicillins; cephalosporins) and sulfa drugs are most commonly associated with drug-induced allergies.
- **Look out for drug interactions:** Review the medical record and ask the patient about other medications—drug interactions can sometimes have an unexpected effect on subsequent therapy, decreasing efficacy (lower antibiotic levels) or increasing the risk of side effects. Interactions with warfarin (Coumadin) are especially problematic.
- **Stress compliance:** Antibiotics won't work if they are not taken—adherence can be difficult if a drug requires frequent dosing (e.g. QID) or specialized dietary requirements. This doesn't mean you shouldn't prescribe the drug, only that you need to "know your patient" and stress the importance of medication compliance.

Know the score—classification of Charcot foot

There are several schemes available to "classify" Charcot osteoarthropathy, either based on the progression of the process (Eichenholz classification) or the pattern involvement (Sanders and Frykberg Classification). The Frykberg classification (see below) outlines the multiplicity of patterns that might occur. Most commonly, patients with Charcot arthropathy present with midfoot (Type 2 or Type 3 pattern); however, they may also develop forefoot involvement (Type 1), involvement of the ankle (Type 4) or calcaneus (Type 5). The importance of these less common presentations is that they may also mimic osteomyelitis or infection—before you commit the patient to long term antibiotics, always consider the possibility that the clinical or radiologic process might be secondary to a Charcot's process.

Table 1: Sanders-Frykberg classification of Charcot foot

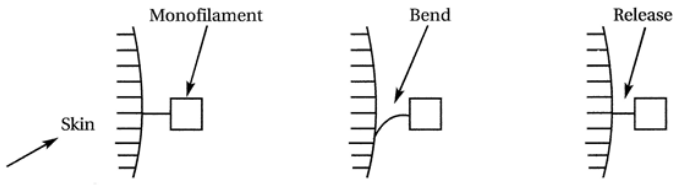
Pattern	Comments
Pattern 1 	**Pattern I** involves the forefoot joints, mimicking the radiographic appearance most commonly involved in diabetic osteomyelitis. Common radiographic changes include osteopenia, osteolysis, juxta-articular cortical bone defects, subluxation and destruction.
Pattern 2 	**Pattern II** involves the tarsometatarsal joints including the metatarsal bases, cuneiforms and cuboid. Involvement at this location may present as subluxation or fracture/ dislocation, and it frequently results in the classic rocker bottom foot deformity.
Pattern 3 	**Pattern III** involves Chopart's joint or the naviculocuneiform joints. Radiographic changes typically show osteolysis of naviculocuneiform joints with fragmentation and osseous debris dorsally and plantarly.
Pattern 4 	**Pattern IV** involves the ankle with or without subtalar joint involvement. Radiographs reveal erosion of bone and cartilage with extensive destructive of the joint, which may result in complete collapse of the joint and dislocation. Typically, this pattern of involvement results in a severe unstable deformity.
Pattern 5 	**Pattern V** is isolated to the calcaneus and usually results from an avulsion of the Achilles tendon off the posterior tubercle.
	http://heidimates.blogspot.com/2014/04/diabetic-charcot-neuroarthropathy.html **(accessed 1/28/15)**

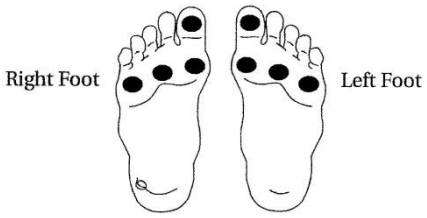
Use of the Semmes-Weinstein Monofilament

Directions for use of Semmes- Weinstein Monofilament

1. Assess integrity of monofilament (no bends/breaks).
2. Show the monofilament to the patient. Place the end of the monofilament on his/her hand or arm to show that the testing procedure will not hurt.
3. Ask the patient to turn his/her head and close his/her eyes or look at the ceiling.
4. Hold the monofilament perpendicular to the skin.
5. Place the end of the monofilament on the sole of the foot. Ask the patient to say 'yes' when he/she feels you touching his/her foot with the monofilament. DO NOT ASK THE PATIENT "did you feel that?" If the patient does not say "yes" when you touch a given testing site, continue on to another site. When youhave completed the sequence RETEST the area(s) where the patient did not feel monofilament.
6. Push the monofilament until it bends, then hold for 1-3 seconds.
7. Lift the monofilament from the skin. Do not brush or slide along the skin.
8. Repeat the sequence randomly at each testing site on the foot (see pictures below).

Loss of protective sensation = absent sensation at one or more sites





Sites on the sole of the foot for monofilament testing

Notes

Apply only to intact skin. Avoid calluses, ulcerated or scarred areas. DO NOT use a rapid or tapping movement.

■ If the monofilament accidentally slides along the skin, retest that area later in the testing sequence.

■ Store the monofilament according to the manufacturer's instructions.

■ Clean the monofilament according to agency infection control protocols.

Reference: Registered Nurses' Association of Ontario (2004). *Reducing Foot Complications for People with Diabetes.* Toronto,

Canada: Registered Nurses' Association of Ontario. *Nursing Best Practice Guideline Source:* Website: www.rnao.org/bestpractices accessed: 4/14/13