



Getting to the Bottom of the Diabetic Foot

By John Embil, MD, FRCPC

Case

Mr. JF presented to the emergency department (ED) after having been unable to work for the past five days. He has felt weak and thinks he has a fever alternating with chills. His wife became concerned when she detected a foul odor arising from his right foot. When she removed his sock, she became concerned and brought him to the ED.

He recalls having recently purchased new work boots and notes that he had developed a blister on the dorsum of the foot where the steel toe ended. In the ED, he appeared toxic and his random blood glucose was 22 mmol/L. The emergency physician told him he has diabetes. A surgeon was called to evaluate him further as he has a limb threatening infection (Figure 1).

The term “diabetic foot” is somewhat misleading as it implies that only the foot suffers from diabetes. In reality, diabetes mellitus (DM), is a multi-system disease resulting from altered glycemic control, either from the complete absence of insulin production or from relative insulin resistance. Regardless of whether diabetes has its onset during childhood or in the adult years, it is associated with a multitude of end organ complications which may have devastating consequences.¹

In this article:

1. How do foot problems develop in people with diabetes?
2. How to examine and treat an infected foot.
3. What therapies are used for mild, moderate and severe foot infections?
4. How to interpret the microbiology report.
5. What are the implications of foot complication in diabetes?



Figure 1. Limb threatening infection characterised by a large amount of devitalised tissue and a purulent foul smelling discharge was present.

Diabetic Foot

Why do foot problems develop in diabetes?

DM results in vasculopathy, nephropathy, retinopathy and neuropathy. In the lower extremity, complications arising from ischemia and/or neuropathy may include pain, discomfort, deformity (*i.e.*, Charcot foot, claw toes, prominent metatarsal heads), ulcers, infection and may ultimately result in the amputation of a digit(s), forefoot, or an entire lower extremity. Peripheral neuropathy increases the risk of plantar ulcerations sevenfold.² Without the presence of periph-



Dr. Embil is associate professor, department of medicine, section of infectious diseases, University of Manitoba, and director, infection control, Health Sciences Centre, Winnipeg, Manitoba.

eral neuropathy, it is unlikely that a person with diabetes will develop a plantar ulceration. Important contributing factors for the development of plantar ulcerations include peripheral vascular disease, infection, and extensive or repetitive trauma.³

Table 1

Antibiotic Therapy for the Infected Diabetic Foot

Type of Infection	Medication
<p>Mild Infections</p> <ul style="list-style-type: none"> Deemed to be neither a limb nor life threatening processes. They are usually associated with cellulitis surrounding an ulceration. A small amount of purulent material may be present at the base of the ulcer. The most likely pathogens are aerobic gram-positive cocci (<i>S. aureus</i>, <i>Streptococcus</i> spp). Patients with these infections can frequently be treated as outpatients with oral antimicrobial therapy. 	<p>Cloxacillin Cephalexin Trimethoprim-sulfamethoxazole (Tmp/Smx) Clindamycin Amoxicillin-clavulanic Acid</p>
<p>Moderate Infections</p> <ul style="list-style-type: none"> These infections are more significant and may be associated with plantar abscesses. The selected antimicrobial regimens should be effective for: <i>staphylococci</i>, <i>streptococci</i>, <i>anaerobes</i> and the gram-negatives. Patients who are not toxic may be treated with oral antimicrobial therapy while those with more significant infections require parenteral therapy and are best managed using the agents summarised below for severe infections. 	<p>Tmp/Smx and metronidazole Tmp/Smx and clindamycin Ciprofloxacin and clindamycin Amoxicillin-clavulanic</p>
<p>Severe Infections</p> <ul style="list-style-type: none"> Patients with these processes have limb or life threatening infections requiring immediate hospitalisation, parenteral antimicrobial therapy, and consultation with a surgeon. 	<p>Clindamycin and gentamicin Clindamycin and ciprofloxacin Cefotetan Piperacillin/tazobactam Clindamycin and ceftriaxone Imipenem/cilastatin Meropenem</p>

What are the implications?

Approximately 15% of people with diabetes will develop a foot ulcer in their lifetime and between 6% to 20% of all hospitalised people with diabetes have a complication related to a foot ulcer.⁴ Individuals with a diabetic foot ulcer also have an increased mortality. Non-healing plantar ulcers are an instigator for most (84%) lower extremity amputations in persons with diabetes.³ Approximately 20% of persons with diabetes and plantar ulcers eventually undergo an ipsilateral lower extremity amputation.⁴ There is an increased mortality associated with foot complications in persons with diabetes.⁵

Approximately 15% of diabetics will develop a foot ulcer in their lifetime.

How should one examine the foot?

Inspection

The absence of hair may be indicative, albeit not pathognomic, of suboptimal circulation. Previously amputated toes suggest profound neuropathy, previous infection and possibly suboptimal circulation. The presence of ulcerations may serve as a portal of entry for micro-organisms.

Footwear should be inspected. The status of wear, foreign bodies in the shoe, penetrating objects through the sole, and ill fitting footwear may all lead to foot complications.

How do foot problems develop in diabetics?

As noted above, diabetes can lead to end organ complications, specifically peripheral neuropathy. The absence of protective sensation predisposes diabetics to foot trauma, such as blisters which break down leaving denuded deeper tissues. Punctures, lacerations, and blunt trauma may also serve as portals of entry for micro-organisms. Altered leukocyte function, peripheral vascular disease and repetitive unappreciated trauma may lead to an infection and/or ulceration which does not heal and progresses to deeper tissues.



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Diabetic Foot



Figure 2. Mild Infection: The ulcer has a clean base, however, there is limited surrounding cellulitis.

The morphology of the foot should be examined. Charcot changes, other deformities, and amputations may result in bony prominences and altered biomechanics of ambulation leading to ulcerations. Trophic nails may be an indicator of suboptimal circulation. Long and unkempt nails may traumatise surrounding digits. Tight shiny skin may be compatible with suboptimal circulation. Joint mobility should be examined as rigid digits, as a consequence of trauma and previous septic arthritis, may predispose to trauma.

Palpation

Check the patient's pulses and temperature. A cool, red, foot is more likely to be dependent rubor than cellulitis. The crepitus should be compatible with air in the soft tissues. The patient's sensation should be examined. The inability to appreciate the 10 g monofilament is indicative of loss of protective sensation indicating a "high risk" foot.

Are all diabetic foot ulcers infected?

No. Most ulcerations are merely superficial abrasions on the skin which may be colonised with



Figure 3. Moderate Infection: A bulging abscess is noted with associated erythema and heat. The patient refused admission to hospital and was managed with incision and drainage of the abscess and oral antimicrobial therapy.

micro-organisms. A swab obtained for culture may yield multiple micro-organisms, but unless there is surrounding erythema, heat, purulence and pain, even in the presence of peripheral neuropathy, an infection is likely not present.

How are infections classified and managed?

Skin and soft tissue infections can be divided into mild, moderate and severe classifications (Table 1).⁶ A mild infection is one that could be managed with oral antibiotic therapy and does not jeopardise the limb or life of the patient (Figure 2). A moderate infection is a deeper infection which may have abscess formation and may require surgical intervention and parenteral antimicrobial therapy (Figure 3). A severe infection is one which threatens the patient's life and limb, requires admission to hospital, surgical debridement and parenteral antimicrobial therapy (Figure 4).

Osteomyelitis may occur as a consequence of hematogenous spread, however, in the person with diabetes and the neuropathic limb, osteomyelitis is invariably due to contiguous spread from the ulceration. Unlike skin and soft tissue infections where, at the end of antimicrobial therapy, the

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infection is deemed cured, osteomyelitis may relapse at a later date and, therefore, not unlike a neoplasm, osteomyelitis can be deemed to be “in remission” versus “cured.”

What bacteria can be found?

Initially, aerobic gram-positive bacteria, such as *Staphylococcus aureus* and *Streptococcus pyogenes* or *Streptococcus agalactiae* are the most frequently isolated micro-organisms. As the ulceration or infection persists, more necrotic tissue is present and gram-negative and anerobic bacteria will predominate in the wound.

What is the best specimen to obtain?

Specimens for culture are best obtained from infected tissue that does not communicate with the skin's surface. The ideal specimen for culture assessment of infection is a curettage specimen from the base of the ulcer or bone biopsy specimens if osteomyelitis is suspected. If such specimens are not available, cultures of purulent exudate from within the ulcer base or sinuses may be an alternative.

What additional issues must be considered?

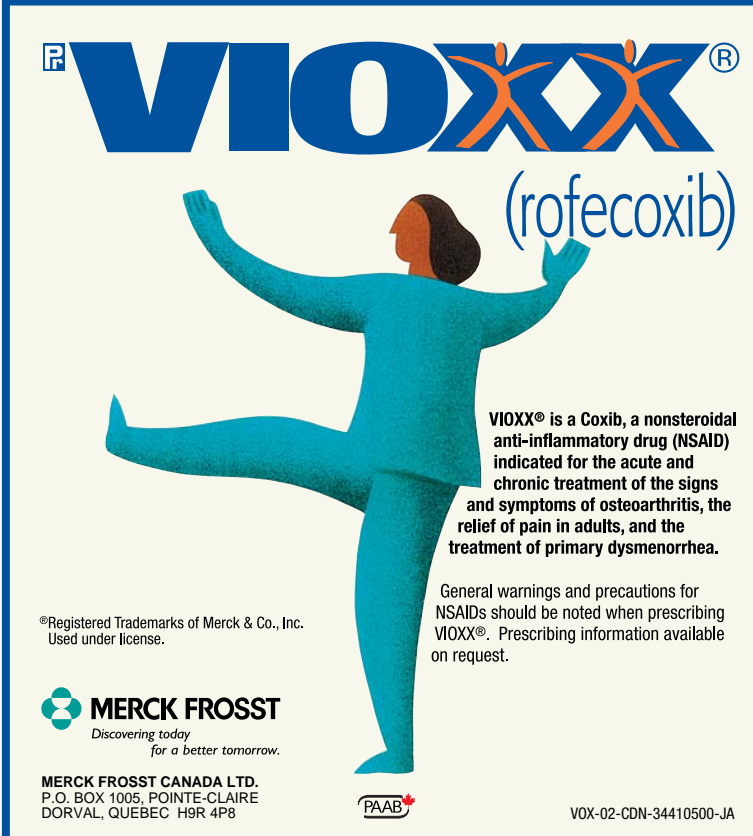
An erythematous cool foot may be deceiving as it may mimic cellulitis but may actually be dependent rubor.

For resolution of infection and promotion of wound healing, adequate cir-



Figure 4. Severe Infection: This patient presented with constitutional symptoms and a foul smelling erythematous and painful foot.

ulation is necessary and is usually most easily assessed by palpating distal pulses. If pulses are not palpable in the lower extremity, it is important to obtain an estimate of the adequacy of circulation. The ankle brachial blood pressure index (ABI), is an effective non-invasive method of comparing the dorsalis pedis or posterior tibial



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Table 2

Investigations for a patient with a diabetic foot

1. Complete blood count and blood cultures.
2. Serum biochemistry and measure of renal function: "Tight glycemic control" is important for resolution of infections and wound healing.^{13,14}
3. Radiograph of the foot: It is important to exclude a foreign body, such as glass; pieces of metal, such as an insulin needle; or pebbles which may act as ongoing nidi for infection. The plain radiograph will also demonstrate gas in the soft tissues which may indicate a more significant underlying infection. Osteomyelitis will also be demonstrated on the plain radiograph. The plain radiograph will only demonstrate bony abnormalities related to osteomyelitis 10–20 days after the bone infection has occurred and 40%–70% of bone has been resorbed.¹⁵ Serial radiographs may be of benefit to diagnose and follow osteomyelitis.
4. Probing the wound: Probing the wound with a sterile swab or steel probe is helpful to determine whether bone is palpable. Palpable bone is highly correlated with an underlying osteomyelitis.
5. Erythrocyte sedimentation rate (ESR): This is a non-specific technique which can be used to monitor inflammation and the resolution there over time. The ESR will be elevated during acute inflammatory events, such as fractures, skin and soft infection, as well as osteomyelitis.
6. Ankle brachial indexes < 0.5 indicate significant reduction in large blood vessel flow, corresponding to severe peripheral vascular disease.¹⁶ Ratios of < 0.3 are associated with rest pain and limb-threatening ischemia.¹⁷

blood pressure to the brachial artery blood pressure. For a list of the investigations, see Table 2.

What is the duration of therapy?

It is difficult to predict precisely how long skin, soft tissue, and bone infections should be treated with antimicrobial therapy. A general rule is that mild skin and soft tissue infections will resolve with 10 to 14 days of oral antimicrobial therapy. Moderate to severe infections may require adjunctive surgery to drain abscesses and debride non-viable tissue. The parenteral antimicrobial therapy is usually provided until clinical resolution of the infection is observed

and a switch to culture-directed oral antimicrobial therapy is warranted. Therapy duration varies according to the clinical response.

The management of osteomyelitis is less well defined as bone debridement may be necessary in conjunction with adjunctive antimicrobial therapy. Traditionally, six weeks of culture-directed parenteral antimicrobial therapy has been used, however, numer-

Caution is urged in the interpretation of lab results as they are only meaningful in the context of the clinical scenario.

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Figure 5. Callus paring with a scalpel is an effective method for reducing skin prominences which may lead to undermining of the underlying tissue.

ous reports suggest that prolonged (three to six months) culture driven oral antimicrobial therapy may be as effective and less inconvenient for the patient.^{7,8,9}

How do I interpret the microbiology report?

This is a frequently encountered dilemma. A swab is obtained and multiple micro-organisms are recovered. Which micro-organism is the true pathogen and which micro-organisms can be ignored? This is a difficult question to answer as it clearly depends upon the clinical scenario; a swab obtained from a clean, non-erythematous, non-purulent, non-painful ulceration is likely unnecessary and will yield meaningless results as clinical evidence of infection is absent. A swab obtained from the base of an erythematous, purulent and edematous wound with surrounding cellulitis, is more likely to yield meaningful results as clinical evidence of an infection is present. These results must, of course, be interpreted with caution as superficial colonisation with other micro-organisms may occur.

The recovery of micro-organisms, such as *Staphylococcus aureus* and *Streptococcus pyogenes* (group A streptococcus), *Streptococcus agalactiae* (group B streptococcus) are usually true pathogens while *Enterococcus* spp, coagulase negative staphylococci (e.g. *Staphylococcus epidermidis*), and the diphtheroids are usually colonising the wound. Caution is urged in the interpretation of laboratory results as the results are only meaningful in the context of the clinical scenario. The exact role of the anaerobes remains unclear as some have speculated that adequate treatment of the micro-organisms more frequently associated with a diabetic foot infection precludes the need for targeting therapy at the anaerobes.¹⁰ This, of course, must be interpreted in the context of the clinical scenario, particularly if the infection has been ongoing for a prolonged period and the process is foul smelling. The gram-negatives may be considered pathogens, however, *Pseudomonas* spp must be interpreted with cau-

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tion, particularly if the patient has been soaking his or her foot or using a wet dressing, as colonisation with *Pseudomonas* spp may have occurred.

What empiric therapy can be started for an acute diabetic foot infection?

There is no definite answer to this question as nothing can specifically replace clinical acumen and knowledge of local epidemiology in terms of antimicrobial susceptibility profiles. If the infection has arisen in an area where the skin is intact, cefazolin is often a reasonable first choice, particularly, as *S. aureus* or *Streptococcus* spp are the most likely culprits. The only drawback is that cefazolin must be administered three times a day, however, there is a body of evidence suggesting that parenteral cefazolin 2 g administered once a day in conjunction with 1 g of oral probenecid is as effective as once daily ceftriaxone.^{11,12}

It is important to note, however, that probenecid may interfere with the excretion of other drugs the patient may be taking and, therefore, must be used with caution. It may be prudent to check with the pharmacy staff for potential drug interactions.

What adjunctive measures exist?

Appropriately fitted footwear is critical for the person with diabetes and peripheral neuropathy as it will serve to protect the foot. In those with peripheral neuropathy, an orthotic is of benefit to assist in displacing pressure from bony prominences. Regular footcare consisting of callus paring and nail cutting, can minimise potential complications (Figure 5). Thick calluses can lead to undue pressure and undermining of the underlying skin. Long and poorly maintained nails may

traumatise the surrounding soft tissues leading to potential portals of entry for infection.

In addition to controlling of infection, optimal weight displacement from any open lesions must occur. If weight is not removed from the affected area, ongoing destruction and erosion into the deeper tissues will occur. This weight displacement can be undertaken using total contact casts, removable orthopedic walking boots and healing sandals. Although a multitude of different dressings and topical therapies exist, few have been subjected to rigorous clinical trials evaluating them against a suitable comparator and, therefore, reference to these products has been deliberately omitted. CME

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Take-home message

What to do if your patient suffers from a diabetic foot:

1. Perform a thorough history and physical examination.
 2. Treat the infections according to severity. Mild infections can often be managed with oral antimicrobial therapy. Moderate to severe infections frequently require parenteral antimicrobial therapy and may require surgical interventions.
 3. Adequate perfusion to the lower extremity is critical for resolution of infection and wound healing.
 4. Should a foot ulcer be present, optimal weight displacement using a healing sandal, an orthopedic walking boot, a total contact cast, and/or crutches is critical.
 5. Even seemingly minor infections may have significant sequelae and small vessel thrombosis may occur as a consequence of the infection. Always warn patients to monitor their feet during the management and convalescence period of their infections.
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Glycemic control is essential for resolution of infection and improving chances of wound healing.

Should a foot ulcer be present, optimal weight displacement using a healing sandal, an orthopedic walking boot, a total contact cast, and/or crutches is critical.

Even seemingly minor infections may have significant sequelae and small vessel thrombosis may occur as a consequence of the infection. Always warn patients to monitor their feet during the management and convalescence period of their infections.

Shouldn't the first depression
be the last depression?



Getting to the bottom of The Diabetic Foot

1. Why does diabetes cause foot problems?

Diabetes can lead to damage of the nerves and blood vessels. People with diabetes often have poor or no feeling in their feet and poor circulation. Minor injuries may occur and go unnoticed because of the lack of feeling. The poor circulation prevents healing of any open sores.

2. How are infections managed?

A mild infection is one that could be managed with oral antibiotic therapy and does not jeopardise the limb or life of the patient.

A moderate infection is a deeper infection which may have abscess formation and may require surgical intervention and parenteral antimicrobial therapy.

A severe infection is one which threatens the patient's life and limb, requires admission to hospital, surgical debridement and parenteral antimicrobial therapy.

As presented at the University of Manitoba

Presented at University of Manitoba CME Program, November 1, 2002

By John M. Embil, MD, FRCPC

3. What are the implications of foot problems?

Individuals with a diabetic foot ulcer also have an increased mortality. Non-healing plantar ulcers are an instigator for most (84%) lower extremity amputations in persons with diabetes.

About 20% of people with diabetes and plantar ulcers eventually undergo an ipsilateral lower extremity amputation. There is an increased mortality associated with foot complications in people with diabetes.

4. Are all diabetic foot ulcers infected?

No. Most ulcerations are merely superficial abrasions on the skin which may be colonised with micro-organisms. A swab obtained for culture may yield multiple microorganisms, but unless there is surrounding erythema, heat, purulence and pain, even in the presence of peripheral neuropathy, an infection is likely not present.

For an in-depth article on the Diabetic Foot, please go to page 93.