BMJ Best Practice

Diabetic foot complications

The right clinical information, right where it's needed

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Summary

- Diabetic foot complications, including ulcers and infections, are a common and costly complication of diabetes mellitus.
- The majority of diabetic foot ulcers are caused by repetitive trauma sustained during activity on a structurally abnormal, insensate foot.
- Ulcers act as a portal of entry for bacterial infections. Preventing and/or healing ulcers helps prevent infections and thereby minimise limb loss risk.
- Initial evaluation and early management may be by general practitioners; however, there should be a low threshold to refer to a interdisciplinary diabetic foot care clinic or inpatient unit. This is particularly true if there is any loss of sensation or signs of peripheral artery disease.
- Leg amputation should be avoidable in the majority of cases and is rarely the first-choice option for ambulatory patients.

Definition

The term diabetic foot complications encompasses the conditions of diabetic foot ulcer (i.e., a full-thickness epithelial defect below/distal to the ankle),[1] and diabetic foot infections (i.e., any soft-tissue or bone infection occurring in the diabetic foot, including osteomyelitis).

Epidemiology

Diabetes mellitus is one of the most common chronic diseases in the UK. There were almost 2.9 million people diagnosed with the disease in 2013, an increase of approximately 53% from 2006.[6] It is estimated that 10% of people with diabetes will have a diabetic foot ulcer at some point in their lives. Diabetes is the most common cause of non-traumatic limb amputation, with foot ulcers preceding more than 80% of amputations.[6]

The prevalence of diabetes mellitus in adults in the US increased from 3.7% to 9.1% from 1991 to 2011, and approximately 22 million adults currently live with diabetes.[7] Among adults aged older than 65 years, the prevalence rates of diabetes and peripheral artery disease reach 20% and 12% respectively.[7] [8] Approximately 113,000 diabetic foot ulcers occurred in patients with diabetes in 2009 and 68,000 non-traumatic limb amputations were performed.[7]

Unfortunately, significant treatment variability has been identified both in Europe and the US. Only 27% of patients who had an ulcer for 3 or more months in duration were referred for specialty care in the multicentre, prospective EuroDIALE study, and only 40% of those with peripheral artery disease were referred for vascular imaging or revascularisation.[9]

Aetiology

Various factors increase the risk of developing a diabetic foot ulcer.[2] These factors fall into 3 main categories:

- Abnormal distribution of plantar pressures due to structural/biomechanical abnormalities (e.g., bunions, hammer or mallet toes, Charcot's mid-foot deformities), impaired joint mobility, gait abnormalities, and motor neuropathies
- Impaired protective mechanisms (e.g., dry skin, immune system abnormalities, peripheral artery disease)
- Impaired recognition due to sensory neuropathy and/or visual impairments.

In most patients, epithelial ulceration results from repetitive trauma from the shoe contacting various prominent skin surfaces of the foot during ambulation. This in addition to various combinations of the above factors lead to a portal of entry for bacterial inoculation into the foot. Moreover, puncture wounds, along with these various risk factors, may also lead to bacterial inoculation and subsequent infection.

Pathophysiology

A healthy, intact visco-elastic and supple epithelium is the most important protection against foot infection. When various combinations of risk factors are present, ulceration or puncture injuries occur and may elude recognition. The longer the duration a wound has been present, the higher the risk of both soft-

tissue and bone infection. Infection often spreads along anatomic planes in the foot and will often cause hyperglycaemia. Chronic hyperglycaemia may lead to sensory neuropathy and immune system dysfunction, but hyperglycaemia does not directly affect the development of foot infections.

Untreated macrovascular (typically popliteal- and tibial-level) atherosclerotic disease poses a higher risk for foot infections among those with unhealed foot ulcers and increases the risk for amputation.[9] [10]

Although microvascular abnormalities (including abnormal arteriovenous shunting and basement membrane thickening) are often present in patients with diabetes mellitus, there has been no evidence that occlusive phenomena in the microvasculature of the foot (i.e., small-vessel disease) contributes significantly to ulcer development, infection, or poor healing. Indeed, it was pointed out decades ago that a belief in the concept of small-vessel disease often leads to inappropriate pessimism towards the treatment of diabetic foot infections.[11]

Classification

American Diabetes Association (ADA): risk classification[2]

The ADA has produced a classification scheme that categorises the risk of developing a foot ulcer in patients with diabetes mellitus. The classification is not appropriate for active (unhealed) ulcers, or for patients with a wound, tissue loss, or an infection.

High risk (diabetic foot in remission):

- History of previous toe, partial foot, or leg amputation, or history of previous foot ulcer but no active foot ulcer currently
- The annual incidence of ulcers in this group is 50%.[3]

Moderate risk:

- Peripheral artery disease with or without sensory neuropathy but no active foot ulcer currently
- The annual incidence of ulcers in this group is 14%.[3]

Low risk:

- Sensory neuropathy but no active foot ulcer currently
- The annual incidence of ulcers in this group is 4.5%.[3]

Normal risk:

- None of the above and no active foot ulcer currently
- The annual incidence of ulcers in this group is 2%.[3]

An active ulcer immediately connotes a greater sense of urgency and should be classified according to the degree of tissue loss, the presence/degree of ischaemia, and the presence/degree of infection. The key factors associated with occurrence or recurrence include the presence of sensory neuropathy (loss of protective sensation), the presence of vascular disease and/or a past history of an ulcer, Charcot's arthropathy, or amputation. These three factors can easily be screened without complex equipment.[4]

International Working Group on the Diabetic Foot (IWGDF): risk classification[5]

At risk for ulceration:

- A patient with diabetes who does not have an active foot ulcer but who has peripheral neuropathy, with or without the presence of foot deformity or peripheral artery disease, or a history of foot ulcer(s) or amputation of (or part of) the foot or leg.

In general, patients without any of these risk factors do not appear to be at risk for ulceration.

Primary prevention

In the UK, the National Institute for Health and Care Excellence (NICE) guidelines recommend assessing the risk of foot problems in patients with diabetes:

- At time of diagnosis of diabetes, and then at least annually
- When any foot problems arise
- On any admission to hospital, and if there is any change in the patient's status in hospital.

Patients aged 12 to 17 years with diabetes should have their feet assessed annually.

When the feet are examined in a patient with diabetes, shoes, socks, bandages, and dressings should be removed, and both feet should be examined for evidence of:

- Neuropathy
- Limb ischaemia
- Callus formation
- Infection and/or inflammation
- Deformity
- Gangrene
- Charcot's arthropathy.

Likewise, the American Diabetes Association recommends an annual, comprehensive foot examination in all patients with diabetes mellitus to identify risk factors that are predictive of ulcers and amputations. The examination should include:[13]

- A general inspection of the skin integrity and any musculoskeletal deformities and to identify the presence of ulcers
- Inspection and assessment of pedal pulses
- Assessment for sensory neuropathy with monofilament testing.

Patients should be urged to completely abstain from tobacco use. Optimal medical therapy should include modification of risk factors (including glucose control, hypertension, and hypercholesterolemia) to within recommended treatment goals.[13]

Screening

Screening for foot complications in diabetic patients should be done at least once yearly. The screening examination identifies risk factors and may help reduce the risk of limb loss. This assessment can be done without any specialised equipment and can be completed in as little as 3 minutes.[14]

Inspecting for skin integrity and foot deformities should be done twice yearly in all patients with diabetes mellitus. All skin surfaces below the ankle should be inspected for structural deformities (e.g., hammer toes, bunions, calluses, blisters, and ulcers).[13]

Monofilament testing for sensory neuropathy should be done once yearly in all patients with diabetes. The test is considered positive (i.e., insensate or lack of protective sensation) if monofilament is not detected in any of the 4 tested areas in the forefoot. The identification of sensory loss is important for risk stratification and the initiation of prevention efforts (e.g., diabetic footwear, foot-care education).[13] 1[C]Evidence

A pulse examination should be done once yearly in all patients with diabetes. Similar to sensory neuropathy, the absence of palpable pedal pulses suggests an elevated risk for the development of foot ulcers, and preventive efforts should be initiated.

In the UK, the National Institute for Health and Care Excellence (NICE) guidelines recommend that a resting ankle-brachial index (ABI) is required in patients with suspected peripheral artery disease.[6] Current guidelines from the American College of Cardiology Foundation and American Heart Association state that a resting ABI is indicated in patients who have non-healing foot ulcers, as well as patients with exertional leg symptoms, patients aged 50 years or older with diabetes or a history of smoking, and all other patients aged 65 years and older, in order to establish a diagnosis of lower extremity peripheral artery disease.[17]

NICE guidelines also recommend assessing the risk of foot problems in patients with diabetes:[6]

- At time of diagnosis of diabetes, and then at least annually
- When any foot problems arise
- On any admission to hospital, and if there is any change in the patient's status in hospital.

Patients aged 12 to 17 years with diabetes should have their feet assessed annually.

When the feet are examined in a patient with diabetes, shoes, socks, bandages, and dressings should be removed, and both feet should be examined for evidence of:

- Neuropathy
- Limb ischaemia
- Callus formation
- Infection and/or inflammation
- Deformity
- Gangrene
- Charcot's arthropathy.

Secondary prevention

Patients should habituate themselves to examining their feet on a daily basis. The integrity of the skin on all areas of the foot should be examined for calluses, bunions, blisters, ulcers, or other changes. Socks should be visually inspected before wearing to identify any fabric defects. The inside and outside of shoes should be examined for the integrity of the insole, as well as the presence of any foreign bodies. Patients who cannot see the plantar aspects of their feet because of body shape, poor strength, or poor range of motion can inspect this area by placing a hand mirror on the floor. Those with poor vision should enlist the help of family members or neighbours for frequent visual inspections.

Patients should ally themselves with a primary care provider to prevent progression of diabetes mellitus and/or peripheral artery disease. Such efforts should include monitoring blood pressure and blood glucose, quitting or avoiding tobacco products, and maintaining a heart-healthy diabetic diet.

Daily foot thermography has been demonstrated to significantly reduce the recurrence of neuropathic foot ulcers. This consists of using specialised thermometers to check the cutaneous temperature of the skin of the foot for areas significantly warmer than surrounding skin.

Surveillance duplex ultrasound examinations may also be important in optimising the long-term patency of surgical bypasses. Patients should be made aware of the institutional schedule of when these examinations should take place.

The use of specialised therapeutic footwear is recommended for high-risk patients with diabetes, such as those with severe peripheral neuropathy, foot deformities, or a history of amputation.[22] There are no data to support specialised orthotics in average-risk patients.[23]

Case history

Case history #1

A 62-year-old man with diabetes mellitus presents with a 3-day history of progressive left foot swelling, redness, and malaise. He reports noticing a blister on his forefoot several months ago after he started wearing work boots for a new job. He has dressed the area daily with bandages; however, the area has not healed. He also has a history of sensory neuropathy, chronic kidney disease (stage 2), and hypertension. He is a smoker (1 pack per day). Physical examination is notable for fever (38.1°C [100.6°F]) and mild tachycardia (pulse rate of 105 bpm). There is a malodorous left foot ulcer overlying the first metatarsophalangeal joint. Fluctuance and blanching erythema extends 4 cm beyond the ulcer border. The remaining areas of the foot and ankle are notable for moderate pitting oedema. The dorsalis paedis pulse is palpable.

Case history #2

A 70-year-old man presents with a 3-month history of a non-healing foot ulcer. He is unsure how it began. He reports seeing a podiatrist once in the past, but failed to return for follow-up care. His medical history is notable for diabetes mellitus, remote stroke without residual neurological defect, laser photocoagulation for retinopathy, and two previous percutaneous coronary interventions following myocardial infarcts. He stopped smoking cigarettes 3 years ago. Physical examination is notable for a plantar forefoot ulcer beneath the second metatarsal head. There is no associated erythema, swelling, or foul odour. No pedal pulses are palpable.

Other presentations

Patients with Charcot's arthropathy (mid-foot collapse) may develop ulcers and infections in the mid-foot that are associated with structural abnormalities there. Heel ulcers occur less frequently in ambulatory patients, and are often due to decubitus pressure in non-ambulatory patients debilitated by previous stroke. Leg/calf ulcers (occurring between the knee and the malleoli at the ankle) are generally due to chronic venous insufficiency. Occasionally, infections are initiated by a puncture wound rather than ulceration from repetitive trauma.
[Fig-1]

Step-by-step diagnostic approach

General practitioners are generally on the front line of care for patients with foot complications of diabetes mellitus. As such, most of the initial evaluation and management is done through primary care clinics. Endocrinologists and other medical specialists may also be involved in the evaluation and management of these patients.

The main goals of the initial evaluation include:

- Identifying the presence of any foot ulcers
- Assessing for any clinical symptoms or signs of infection

- Assessing for the presence of sensory neuropathy
- Documenting pedal pulses.

This should be done in patients with diabetes, even in the absence of any suspicion of diabetic foot complications.

An active ulcer immediately connotes a greater sense of urgency and should be classified according to the degree of tissue loss, the presence/degree of ischaemia, and the presence/degree of infection. The key factors associated with occurrence or recurrence include the presence of sensory neuropathy (loss of protective sensation), the presence of vascular disease and/or a past history of an ulcer, Charcot's arthropathy, or amputation. These three factors can easily be screened without complex equipment.[4]

The American Diabetes Association's Comprehensive Diabetic Foot Exam (CDFE) has been condensed into a 3-minute foot examination designed to retain the above key factors whilst dramatically reducing time for a clinician to perform a thorough assessment.[14] [Journal of Family Practice: How to do a 3-minute diabetic foot exam]

History

Strong risk factors for diabetic foot include: sensory neuropathy; previous history of foot ulcer, infection, or partial amputation; chronic kidney disease (including end-stage renal disease), and Charcot's mid-foot deformity (i.e., mid-foot collapse). Lack of protective sensation is most often due to diabetes but can occasionally be due to other causes (e.g., alcohol abuse).

A foot ulcer is defined as a full-thickness epithelial defect below/distal to the malleoli that has persisted for ≥2 weeks.[15] Most patients who develop foot ulcers have at least some degree of sensory neuropathy. However, it is common for patients to note the onset of foot pain in a previously insensate area when an infection is present. The presence of fever, chills, malaise, or anorexia is suggestive of an infection.

Physical examination

The physician should examine the skin integrity of the foot and any muscular deformities in a well-lit room. The majority of non-healing foot ulcers and foot infections occur in the forefoot, the portion of the foot distal to the tarsometatarsal (Lisfranc) joint, and result from repetitive trauma during ambulation on an insensate, structurally abnormal foot.
[Fig-2]

Patients with Charcot's arthropathy (mid-foot collapse) may develop ulcers and infections in the mid-foot that are associated with structural abnormalities there.
[Fig-1]

Heel ulcers occur less frequently in ambulatory patients and are often due to decubitus pressure in non-ambulatory patients debilitated by previous stroke. Leg/calf ulcers (occurring between the knee and the malleoli at the ankle) are generally due to chronic venous insufficiency.

Oedema and localised warmth of the foot, ankle, or calf is suggestive of infection.
[Fig-3]

Erythema is suggestive of cellulitis, with or without a deep soft-tissue infection (i.e., abscess). Fluctuance is also suggestive of an abscess. Occasionally, infections are initiated by a puncture wound rather than ulceration from repetitive trauma.

It is worth noting that because of the impaired immune response and abnormal arteriovenous shunting present in the neuropathic foot, clinical signs of infection in diabetic patients may be more subtle than in non-diabetic patients.

Pedal pulse examination

Pulse examination is the most accessible modality for evaluating arterial blood flow to the foot; however, even when performed by an experienced physician such as a vascular surgeon, inter-observer agreement is modest. The examination can be further impaired by the foot and ankle oedema that is common in the setting of a foot infection. Nevertheless, the ability to palpate normal pedal pulses indicates adequate arterial perfusion to the foot. Absent or weak pulses should prompt referral for evaluation and non-invasive testing in a vascular specialty clinic. Augmenting the examination with a handheld continuous-wave Doppler probe provides additional information when properly performed and interpreted; however, while monophasic signals do suggest significant peripheral artery disease, biphasic signals do not exclude significant peripheral artery disease.

Investigations

Initial investigations in all patients should include a FBC, blood glucose level, and an x-ray of the foot. Leukocytosis may suggest the presence of an infection; however, this test has medium sensitivity/specificity.[16]

X-rays are ordered to screen for osteomyelitis, fractures, joint stability, and other deformities. Weight-bearing films should be considered whenever feasible, especially in patients with Charcot's arthropathy.

Non-invasive vascular testing (ankle/toe pressures) can aid the diagnosis of peripheral artery disease and should be ordered in patients with a diabetic foot ulcer when the physical examination finds anything other than clearly palpable pulses (e.g., weak pulses, examination limited by oedema). However, angiography is considered to be the best test for diagnosing peripheral artery disease and shows haemodynamically significant (i.e., >50%) stenosis or occlusions between the aorta and the foot.

The National Institute for Health and Care Excellence (NICE) recommend that a resting ankle-brachial index (ABI) is required in patients with suspected peripheral artery disease.[6] Current guidelines from the American College of Cardiology Foundation and American Heart Association state that a resting ABI is indicated in patients who have non-healing foot ulcers, as well as patients with exertional leg symptoms, patients aged 50 years or older with diabetes or a history of smoking, and all other patients aged 65 years and older, in order to establish a diagnosis of lower extremity peripheral artery disease.[17]

An MRI of the foot is considered the best imaging test for the diagnosis of osteomyelitis. It may be more accurate in the setting of adequate arterial perfusion (i.e., without peripheral artery disease or after revascularisation). It is also useful for the diagnosis of soft-tissue infection if diagnosis is not evident from the physical examination.

Renal function tests are not needed for the diagnosis of foot infection, but can be helpful in determining the feasibility of giving iodinated contrast for arterial imaging (if necessary).

ESR and CRP may be elevated in the presence of an infection; however, these tests are still considered to be emerging tests for this indication and are not routinely ordered. CT angiography can also be used to diagnose peripheral artery disease; however, it has poorer diagnostic accuracy compared with angiography due to the perigeniculate/infrageniculate distribution of atherosclerotic lesions common in

patients with diabetes and foot ulcers (because of inferior spatial resolution) and vessel wall calcification. Therefore, it is still considered to be an emerging test.

Risk factors

Strong

sensory neuropathy

- Aside from a previous history of ulcer or amputation, sensory neuropathy is the single most influential factor associated with the risk of foot ulcers (and subsequent infection or limb loss).[12] It blunts or obviates the nociceptive feedback that usually signals an injury sustained during ambulation or via a puncture wound.

previous history of foot ulcer

- It is estimated that 10% of people with diabetes will have a diabetic foot ulcer at some point in their lives.[6] The annual incidence of foot ulcers in patients with diabetes mellitus who have a previous history of a foot ulcer is 30%.[3]

previous history of partial foot (toe) amputation

- Leg amputation elevates the risk of ulceration in the contralateral foot through gait abnormalities and increased plantar pressures.[2] [3]

Charcot's mid-foot deformity

- Charcot's mid-foot deformity (i.e., mid-foot collapse) is uncommon, but when present it can represent a significant challenge. Mid-foot ulcers associated with Charcot's deformity are difficult to offload and heal.
  [Fig-1]

  Osteomyelitis in the mid-foot is more difficult to address with surgery without jeopardising the foot stability.

chronic kidney disease

- Although the precise mechanism is not known, chronic kidney disease (including end-stage renal disease) has a significant impact on the development of foot ulcers and the ability to heal foot ulcers.

Weak

structural forefoot deformities

- Various structural forefoot abnormalities pose a risk by leading to improper distribution of pressure across the foot during ambulation. These include hallux valgus (medial deviation of the first metatarsophalangeal joint, also known as bunion), hammer toes, and/or mallet toes.

limited ankle joint mobility (ankle equinus)

- Joint immobility in patients with diabetes mellitus is thought to be the result of deposition of advanced glycosylation end-products.
- Stiffness of the Achilles' tendon and/or gastrocnemius muscle may reduce ankle dorsiflexion, thereby increasing pressure in the forefoot during the push-off phase of gait. An inability to passively dorsiflex

the ankle past neutral (i.e., to passively achieve an angle of <90° between the plantar foot and the calf) is considered abnormal.

- There is some evidence that addressing ankle equinus via orthopaedic/podiatric lengthening procedures may help the healing of forefoot ulcers and may reduce their recurrence.

peripheral artery disease

- The presence of peripheral artery disease somewhat increases the risk of foot ulcer development. In the overwhelming majority of these cases, the chronic impairment in arterial blood flow to the foot is not the direct cause of the foot ulcer; rather, peripheral artery disease of varying severity impairs the normal inflammatory response to foot trauma and, therefore, mainly represents an impediment to healing once an epithelial defect is already present.

visual impairment

- In addition to hindering ability to visually inspect one's feet, visual impairment in the setting of diabetes mellitus is often a marker of microvascular complications.

poor glucose control

- There is a very clear causal relationship between poor glucose control and the development of sensory neuropathy (among other microvascular complications). However, after adjusting for the presence or absence of sensory neuropathy, glucose control itself has a weaker causal association with the development of foot ulcers.[12]

History & examination factors

Key diagnostic factors

presence of risk factors (common)

- Key risk factors include sensory neuropathy, previous history of foot ulcer, previous history of partial foot (toe) amputation, Charcot's mid-foot deformity, and chronic kidney disease.

history of diabetes mellitus (common)

- Present in the majority of patients presenting with a foot ulcer or foot infection, and in all patients with diabetic foot complications.

foot ulcer (common)

- A full-thickness epithelial defect that has been present for ≥2 weeks. Most occur in the forefoot, the portion of the foot distal to the tarsometatarsal (Lisfranc) joint.
- Patients with Charcot's arthropathy (mid-foot collapse) may develop ulcers in the mid-foot that are associated with structural abnormalities there.
- Heel ulcers are often due to decubitus pressure in non-ambulatory patients debilitated by previous stroke.

[Fig-2]

[Fig-1]

foot pain (common)

- Most patients who develop foot ulcers have at least some degree of sensory neuropathy. However, it is common for patients to note the onset of foot pain in a previously insensate area when an infection is present.

fever or chills (uncommon)

- Suggests infection.

Other diagnostic factors

malaise (common)

- Suggests infection.

anorexia (common)

- Suggests infection.

foot erythema (common)

- Suggests cellulitis, with or without deep soft-tissue infection (i.e., abscess). [Fig-3]

oedema of foot, ankle, or calf (common)

- Suggests infection.

absent pedal pulses (common)

- Consistent with the presence of peripheral artery disease.
- Ability to palpate normal pedal pulses indicates adequate arterial perfusion to the foot. Absent or weak pulses should prompt referral for evaluation and non-invasive testing in a vascular specialty clinic.
- Augmenting the examination with a handheld continuous-wave Doppler probe provides additional information when properly performed and interpreted. However, while monophasic signals do suggest significant peripheral artery disease, biphasic signals do not exclude significant peripheral artery disease.

fluctuance (uncommon)

- Suggests a deep soft-tissue infection (i.e., abscess). [Fig-3]

Diagnostic tests

1st test to order

Test	Result
FBC • Ordered in all patients with diabetic foot complications. May suggest the presence of an infection; however, test has poor sensitivity.[16]	**may show leukocytosis with left-shift**
blood glucose level • Ordered in all patients with diabetic foot complications. Often elevated in the presence of infection.	**may be elevated**

Test	Result
x-ray foot • Ordered in all patients with diabetic foot complications to screen for osteomyelitis, fractures, joint stability, and other deformities. • Weight-bearing films should be considered whenever feasible, especially in patients with Charcot's arthropathy.	**may show hypolucencies, cortical destruction/ osteolysis, and/or joint subluxation**

Other tests to consider

Test	Result
renal function • Not needed for the diagnosis of foot infection, but can be helpful in determining the feasibility of giving iodinated contrast for arterial imaging (if necessary).	**variable**
ankle/toe pressures • Should be ordered in patients with a diabetic foot ulcer when the physical examination finds anything other than clearly palpable pulses (e.g., weak pulses, examination limited by oedema). • Ankle pressures may be spuriously elevated because of arterial calcification and, thus, should be augmented by toe pressures or transcutaneous oximetry (TCpO2) measurements. • The National Institute for Health and Care Excellence (NICE) recommend that a resting ankle-brachial index (ABI) is required in patients with suspected peripheral artery disease.[6] • Current guidelines from the American College of Cardiology Foundation and American Heart Association state that a resting ABI is indicated in patients who have non-healing foot ulcers, as well as patients with exertional leg symptoms, patients aged 50 years or older with diabetes or a history of smoking, and all other patients aged 65 years and older, in order to establish a diagnosis of lower extremity peripheral artery disease.[17]	**elevated (if peripheral artery disease present)**
angiography • Considered to be the best test for diagnosing peripheral artery disease. • May also provide the opportunity for endovascular intervention.	**haemodynamically significant (i.e., >50%) stenosis or occlusions between the aorta and the foot (if peripheral artery disease present)**
MRI foot • Considered the best imaging test for diagnosing osteomyelitis. • May be more accurate in setting of adequate arterial perfusion (i.e., without peripheral artery disease or after revascularisation). • Also useful for diagnosis of soft-tissue infection if diagnosis is not evident from physical examination.	**hypo-intense areas of bone on T1 sequences; hyper-intense areas of bone on T2 sequences; soft-tissue fluid collections (if osteomyelitis present)**

Emerging tests

Test	Result
CT angiography • Poorer diagnostic accuracy compared with angiography due to the perigeniculate/infrageniculate distribution of atherosclerotic lesions common in patients with diabetes mellitus and foot ulcers (because of inferior spatial resolution) and vessel wall calcification.	**haemodynamically significant (i.e., >50%) stenosis or occlusions between the aorta and the foot (if peripheral artery disease present)**
ESR • Suggestive of an infection; however, has medium sensitivity/ specificity.[16]	**elevated**
CRP • Suggestive of an infection; however, has medium sensitivity/ specificity.[16]	**elevated**

Differential diagnosis

Condition	Differentiating signs / symptoms	Differentiating tests
Venous leg ulcer	• Generally occurs in the gaiter area of the leg (i.e., below the knee, above the malleoli), and rarely occurs on the dorsum of the foot. • May have surrounding lipodermatosclerosis (i.e., skin thickening and discoloration due to inflammation, scarring, and haemosiderin deposition).	• Ultrasound or venous plethysmography: can confirm venous incompetence, which makes this diagnosis more likely; however, venous leg ulcers can occasionally occur in the setting of a competent superficial venous system.
Gout	• May be associated with pain, swelling, and erythema in the forefoot, but is not generally adjacent to a foot ulcer. May occur in the setting of previous history of gout.	• Plain x-ray of foot: shows radiographic signs of gout (i.e., joint space narrowing, scattered bony erosions, tophaceous arthritis).
Acute Charcot's arthropathy	• May cause pain, erythema, and swelling. • May not be associated with a foot ulcer. • Generally occurs in the midfoot (i.e., between proximal metatarsals to calcaneus).	• MRI foot: shows midfoot subchondral bone marrow edema (subcutaneous tissues are not typically involved).

Diagnostic criteria

The Society for Vascular Surgery lower extremity threatened limb classification system: risk stratification based on wound, ischaemia, and foot infection (WIfI)[18] [19]

Wound (W):

- 0: no ulcer or gangrene
- 1: mild - small, shallow ulcer(s) on distal leg or foot; no exposed bone (unless limited to distal phalanx); no gangrene
- 2: moderate - deeper ulcer with exposed bone, joint, or tendon; generally not involving the heel; shallow heel ulcer without calcaneal involvement; gangrenous changes limited to digits
- 3: severe - extensive, deep ulcer involving forefoot and/or midfoot; deep, full thickness heel ulcer ± calcaneal involvement; extensive gangrene involving forefoot and/or midfoot; full thickness heel necrosis ± calcaneal involvement.

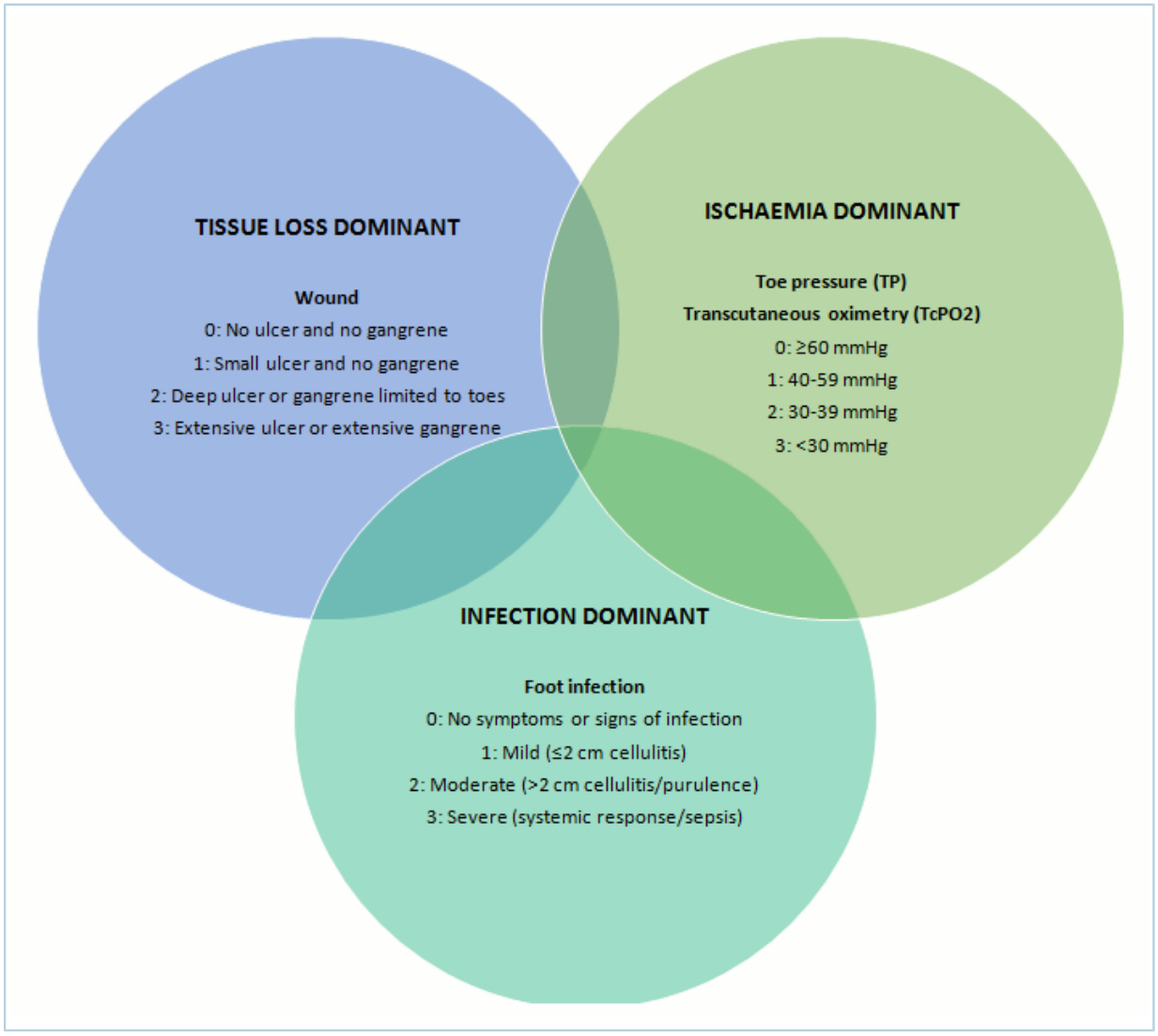
Ischaemia (I):

- 0: ankle-brachial index (ABI) ≥0.80; ankle systolic pressure >100 mmHg; toe pressure (TP)/ transcutaneous oximetry (TcPO2) ≥60 mmHg
- 1: mild - ABI 0.6 to 0.79; ankle systolic pressure 70 to 100 mmHg; TP/TcPO2 40 to 59 mmHg
- 2: moderate - ABI 0.4 to 0.59; ankle systolic pressure 50 to 70 mmHg; TP/TcPO2 30 to 39 mmHg
- 3: severe - ABI ≤0.39; ankle systolic pressure <50 mmHg; TP/TcPO2 <30 mmHg.

Foot infection (FI):

- 0: no symptoms or signs of infection
- 1: mild - infection present, as defined by the presence of at least 2 of the following:
    - Local swelling or induration
    - Erythema >0.5 cm to ≤2 cm around ulcer
    - Local tenderness or pain
    - Local warmth
    - Purulent discharge.
- 2: moderate - local infection (as described above) with erythema >2 cm, or involving structures deeper than skin and subcutaneous tissues (e.g., abscess, osteomyelitis, septic arthritis, fasciitis); no systemic inflammatory response signs
- 3: severe (limb and/or life-threatening) - local infection (as described above) with signs of systemic inflammatory response syndrome as manifested by at least 2 of the following:
    - Temperature >38°C (100.5°F) or <36°C (96.8°F)
    - Heart rate >90 bpm
    - Respiratory rate >20 breaths/minute or PaCO2 <32 mmHg
    - WBC count >12x10^9/litre or <4x10^9/litre or 10% immature (band) forms.

A simple Venn diagram has been designed to assist clinicians in defining what specific factor is dominant.



Diabetic foot problems can be related to the presence of a wound, ischaemia, or infection (WIfI). Which of these parameters is dominant can vary, and a flexible long-term management approach is needed. The Venn diagram shows intersecting rings of dominance for these three parameters, with gradings listed for each. The shaded areas represent combinations of these parameters of dominance.
From the collection of Dr David G. Armstrong and Dr Joseph L. Mills Sr; used with permission

University of Texas: diabetic wound classification[3]

Stages:

- A: no infection or ischaemia present
- B: infection present
- C: ischaemia present
- D: infection and ischaemia present.

Grades:

- 0: epithelialised (healed) ulcer
- 1: superficial ulcer (epithelium with or without dermis)
- 2: ulcer penetrates to tendon or capsule
- 3: ulcer penetrates to bone or joint.

International working group for the diabetic foot (IWGDF): osteomyelitis classification[20]

Possible osteomyelitis:

- Cortical destruction on x-ray
- Bone oedema on MRI
- Ulcer probes to bone or visible bone
- ESR >70 mm/hour with no other plausible explanation
- Non-healing wound despite adequate offloading and perfusion for >6 weeks duration
- Ulcer with clinical evidence of infection for >2 weeks duration.

Probable osteomyelitis:

- Visible cancellous bone in ulcer
- MRI showing bone oedema and other signs of osteomyelitis
- Bone sample with positive culture but negative or absent histology
- Bone sample with positive histology but negative or absent culture
- Any 2 possible criteria (above).

Definite osteomyelitis:

- Bone sample with positive culture and positive histology
- Purulent bone found at surgery
- A traumatically detached bone fragment removed from ulcer
- MRI shows intra-osseous abscess
- Any 4 possible criteria, or 2 probable criteria, or 1 probable and 2 possible criteria (above).

Step-by-step treatment approach

General practitioners are generally on the front line of care for patients with foot complications of diabetes mellitus. As such, most of the initial evaluation and management is done through primary care clinics.

Endocrinologists and other medical specialists may also be involved in the evaluation and management of these patients. Management involves infection management (if present), wound care, nutrition, and the use of offloading footwear (therapeutic shoes that provide pressure redistribution).

Inpatient versus outpatient care

Mild infections can usually be treated in an outpatient setting. Moderate infections may be treated in an outpatient or inpatient setting, depending on the clinical circumstances. Patients with severe infections should be admitted for inpatient care. Indications for immediate transfer to an acute care setting include:

- Presence of systemic symptoms/signs (e.g., fever, nausea/vomiting, tachycardia, hypotension, uncontrolled hyperglycaemia)
- Traumatic or puncture wounds.

Wound care

Dressings that maintain a moist environment, including non-adherent dressings covered with a layer of gauze or other absorptive material, are generally best for wound healing. Wounds with tunnelling (i.e., the presence of deep sinus tracts), copious exudate, or a significant amount of overlying eschar (i.e., dried/desiccated material) should be referred to an interdisciplinary foot clinic for debridement.2[C]Evidence An interdisciplinary team will usually include a podiatrist, wound care nurse, and specialist (e.g., endocrine, vascular surgeon, orthopaedic, infectious diseases, dermatological, prosthetist/orthotist), as well as other allied health professionals who work together to optimise patient care. Surrounding callus should be debrided (usually by a podiatrist) to optimise offloading of the ulcer periphery and facilitate re-epithelialisation.

Split-thickness skin grafting is a helpful option for achieving wound healing in patients with a large epithelial defect that has a tissue bed with healthy granulation. The success rate for autologous skin grafting is high; however, their use over high-pressure areas (namely, the heel and the plantar forefoot overlying the metatarsal heads) may be limited.

There are also several skin substitutes (i.e., non-autologous xenogenic or allogenic tissues) that have been approved for use on diabetic foot wounds. In contrast to autologous skin grafts, several applications of the skin substitute are generally needed at 1- to 2-week intervals to achieve complete re-epithelialisation. There is currently little evidence to support the use of skin substitutes for diabetic foot wounds.

Offloading footwear

Repetitive trauma sustained during ambulation is the most common cause of foot ulcers in diabetic patients. Therefore, minimising or avoiding this repetitive trauma is essential in order to achieve ulcer healing. Total contact casts3[A]Evidence and non-removable cast-walkers are the most effective options for offloading footwear, although removable cast-walkers and modified footwear4[C]Evidence can also be considered if wound care needs require more frequent access to the wound than non-removable options would allow. [21]

The use of specialised therapeutic footwear is recommended for high-risk patients with diabetes, such as those with severe peripheral neuropathy, foot deformities, or a history of amputation.[22] There are no data to support specialised orthotics in average-risk patients.[23]

Nutrition

Malnutrition, including sarcopenia, is very common in diabetic patients and may impair wound healing. Therefore, it should be addressed with dietary counselling and supplementation as needed. Dietary supplementation with arginine, glutamine, and beta-hydroxy-beta-methylbutyrate (a metabolite of the amino acid leucine) has been shown to improve foot ulcer healing in patients with low albumin (i.e., <40 g/L) or peripheral artery disease (i.e., ankle brachial index <0.9).[24]

Antibiotic therapy

Superficial swabs should not be obtained and should not be used to guide antibiotic therapy. This is because organisms obtained from the surface of an ulcer often represent colonising organisms, and superficial swab results have poor correlation with deep operative culture results.[25] In patients with moderate-to-severe infections, it is recommended that a surgeon be consulted to obtain a deep wound culture specimen.[25] Some guidelines recommend sending a soft tissue or bone sample from the base of the debrided wound for microbiological examination.[6]

Antibiotics are not recommended if there are no signs or symptoms of infection (e.g., erythema, oedema, pain).[25] An empiric antibiotic regimen is recommended when there are signs of infection and should be based on the severity of the infection and the likely aetiological agents.

Mild infection:

- Defined as limited erythema ≤2 cm beyond the ulcer border and/or localised swelling, warmth, or pain[18]
- Should be treated with oral antibiotics. A fluoroquinolone (e.g., ciprofloxacin, levofloxacin) plus clindamycin is an example of an empiric regimen that provides good cover.[26] Other options include clindamycin or levofloxacin alone, cephalexin, amoxicillin/clavulanic acid, doxycycline (if MRSA suspected), or trimethoprim/sulfamethoxazole (if MRSA suspected).[25]

Moderate infection:

- Defined as erythema >2 cm beyond the ulcer border or deep soft-tissue infection (e.g., abscess, osteomyelitis)[18]
- May be treated with oral or parenteral, broad-spectrum, empiric antibiotics. Examples of oral options include clindamycin or trimethoprim/sulfamethoxazole plus either ciprofloxacin or amoxicillin/clavulanic acid. Examples of intravenous options include vancomycin plus: a carbapenem (e.g., ertapenem, imipenem/cilastatin); ampicillin/sulbactam; or a quinolone and metronidazole
- Should be promptly referred to an established interdisciplinary diabetic foot clinic for further management.

Severe infection:

- Defined as a foot infection that is associated with ≥2 signs of the systemic inflammatory response syndrome (i.e., temperature >38°C [100.5°F]; heart rate >90 bpm; respiratory rate >20 breaths/

minute or PaCO2 <32 mmHg; WBC count >12x10^9/litre or <4x10^9/litre, or 10% immature (band) forms)[18]

- Usually treated as an inpatient with parenteral, broad-spectrum, empiric antibiotics. Examples of intravenous options include vancomycin plus1 of 3 choices: a carbapenem (e.g., ertapenem, imipenem/cilastatin); ampicillin/sulbactam; or a quinolone and metronidazole.
- Should be promptly referred to an established interdisciplinary diabetic foot clinic for further management.

Definitive therapy should be based on culture results and clinical response to the empiric regimen. Therapy should be continued until there is a resolution in the signs of infection (usually 1-2 weeks for mild infections and 2-3 weeks for moderate-to-severe infections).[25]

It is worth noting that because of the impaired immune response and abnormal arteriovenous shunting present in the neuropathic foot, clinical signs of infection in diabetic patients may be more subtle than in non-diabetic patients. As such, the threshold for referral to specialty units should be low.

Surgery

Surgery should be considered in moderate-to-severe infections to drain/debride any ongoing deep soft-tissue infection (e.g., drain an abscess or infected joint space, debride fasciitis/myonecrosis/necrotic bone).

Endovascular intervention (usually balloon angioplasty with or without stent placement) and/or surgical bypass (usually femorotibial or femoropedal bypass) may be necessary to establish adequate arterial perfusion to the foot. This is generally done after the soft-tissue infection has been controlled or at least addressed. Endovascular intervention appears to be as effective as bypass surgery for limb preservation (i.e., avoiding above-ankle amputation). Repeat endovascular intervention is required in 35% to 65% of patients to treat recurrent stenosis or occlusions occurring after angioplasty alone or to treat in-stent re-stenosis occurring after stent placement.[27]

Minor amputations (i.e., toe or partial foot resections) may be performed on areas with irreversible gangrene. Major amputations are generally reserved for 2 situations:

- Infection or gangrene that is so extensive that reconstruction either is not possible or will not preserve meaningful function in the affected limb
- Patients who have very little or no function in the limb (excluding previous history of stroke or paralysis).

Follow-up and referral

Non-healing foot ulcers and foot infections have the potential to progress suddenly, with few warning signs. The patient should be followed up every 1 to 2 weeks to assess for resolution of infection and check for wound healing. A wound that has not healed or decreased in area by ≥50% within 2 to 4 weeks should be referred to a diabetic foot clinic or inpatient unit.

General practitioners should provide basic clinical care at an initial visit for a new diabetic foot ulcer, but they should also have a low threshold to refer to interdisciplinary foot clinics or inpatient units for more focused care. Lack of recognition of ischaemia and infection are two major, but avoidable, pitfalls that lead to delayed referral.[28] Interdisciplinary care – usually including at least a podiatrist and vascular surgeon with experience and interest in diabetic foot complications, perhaps with orthopaedic, infectious disease,

dermatological, and prosthetist/orthotist input – has repeatedly been demonstrated to significantly lower leg amputation rates.[29] [30] [31] [32]

Indications for referral to a interdisciplinary diabetic foot clinic generally include the following:

- Wound remains incompletely healed after 2 to 4 weeks of basic care (e.g., offloading footwear, wound care)
- Local signs of infection (e.g., erythema, oedema, fluctuance, purulent drainage, foul odour) without systemic signs or symptoms
- Ulcer associated with known or suspected peripheral artery disease
- Plain x-ray demonstrating signs suggestive of osteomyelitis.

It is important to remember the need for proper follow-up of the diabetes itself (e.g., regular check-ups, maintenance of target blood glucose levels, blood pressure and lipid management) according to current guidelines. These goals do not change in the presence or absence of diabetic foot complications.

In the UK, the National Institute for Health and Care Excellence (NICE) guidelines recommend that a patient with a limb-threatening or life-threatening diabetic foot problem should be referred immediately to acute services.[6] The interdisciplinary foot care service should be informed so the patient can be assessed and an individualised treatment plan put in place. Examples of limb-threatening and life-threatening diabetic foot problems include the following:

- Ulceration with fever or any signs of sepsis
- Ulceration with limb ischaemia
- Clinical concern that there is a deep-seated soft tissue or bone infection (with or without ulceration)
- Gangrene (with or without ulceration).

Patients with other active diabetic foot problems should also be referred, within 1 working day, to the interdisciplinary foot care service or foot protection service.

Treatment details overview

Consult your local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing. (see Disclaimer)

Acute (summary)

Patient group	Tx line	Treatment
at initial presentation	**1st**	**wound care**
	adjunct	**hospital admission**
	plus	**offloading footwear**
	plus	**dietary advice and supplements**
▪ **with mild infection**	**plus**	**oral antibiotic therapy**
▪ **with moderate-to-severe infection**	**plus**	**oral or intravenous antibiotic therapy**

Acute (summary)

with moderate-to-severe infection	adjunct	drainage and/or debridement

Ongoing (summary)

Patient group	Tx line	Treatment
after initial definitive treatment	1st	follow-up and continuing diabetic care ± referral
	adjunct	surgical bypass and/or endovascular intervention
	adjunct	amputation

Treatment options

Acute

Patient group	Tx line	Treatment
at initial presentation	**1st**	**wound care**
		» Dressings that maintain a moist environment, including non-adherent dressings covered with a layer of gauze or other absorptive material, are generally best for wound healing.
		» Wounds with tunnelling (i.e., the presence of deep sinus tracts), copious exudate, or a significant amount of overlying eschar (i.e., dried/desiccated material) should be referred to an interdisciplinary foot clinic for debridement.2[C]Evidence An interdisciplinary team will usually include a podiatrist, wound care nurse, and specialist (e.g., endocrine, vascular surgeon, orthopaedic, infectious diseases, dermatological, prosthetist/orthotist), as well as other allied health professionals who work together to optimise patient care. Surrounding callus should be debrided (usually by a podiatrist) to optimise offloading of the ulcer periphery and facilitate re-epithelialisation.
		» Split-thickness skin grafting is a helpful option for achieving wound healing in patients with a large epithelial defect that has a tissue bed with healthy granulation. The success rate for autologous skin grafting is high; however, their use over high-pressure areas (namely, the heel and the plantar forefoot overlying the metatarsal heads) may be limited.
		» There are also several skin substitutes (i.e., non-autologous xenogenic or allogenic tissues) that have been approved for use on diabetic foot wounds. In contrast to autologous skin grafts, several applications of the skin substitute are generally needed at 1- to 2-week intervals to achieve complete re-epithelialisation. There is currently little evidence to support the use of skin substitutes for diabetic foot wounds.
	adjunct	**hospital admission**
		» Mild infections can usually be treated in an outpatient setting.
		» Moderate infections may be treated in an outpatient or inpatient setting, depending on the clinical circumstances.

Acute

Patient group	Tx line	Treatment
		» Severe infections should be treated in hospital. Indications for immediate transfer to an acute care setting include: (1) presence of systemic symptoms/signs (e.g., fever, nausea/vomiting, tachycardia, hypotension, uncontrolled hyperglycaemia); and/or (2) traumatic or puncture wounds.[33]
	plus	**offloading footwear**
		» Repetitive trauma sustained during ambulation is the most common cause of foot ulcers in diabetic patients. Therefore, minimising or avoiding this repetitive trauma is essential in order to achieve ulcer healing.
		» Total contact casts3[A]Evidence and non-removable cast-walkers are the most effective options for offloading footwear, although removable cast-walkers and modified footwear4[C]Evidence can also be considered if wound care needs require more frequent access to the wound than non-removable options would allow.[21]
	plus	**dietary advice and supplements**
		» Malnutrition, including sarcopenia, is very common in diabetic patients and may impair wound healing. Therefore, it should be addressed with dietary counselling and supplementation as needed.
		» Dietary supplementation with arginine, glutamine, and beta-hydroxy-beta-methylbutyrate (a metabolite of the amino acid leucine) has been shown to improve foot ulcer healing in patients with low albumin (i.e., <40 g/L) or peripheral artery disease (i.e., ankle brachial index <0.9).[24]
with mild infection	**plus**	**oral antibiotic therapy**
		» Defined as limited erythema ≤2 cm beyond the ulcer border and/or localised swelling, warmth, or pain.[18]
		» Treat with a suitable oral empiric antibiotic regimen. A fluoroquinolone (e.g., ciprofloxacin, levofloxacin) plus clindamycin provides good cover.[26] Other options include clindamycin or levofloxacin alone, cephalexin, amoxicillin/clavulanic acid, doxycycline (if MRSA suspected), or trimethoprim/sulfamethoxazole (if MRSA suspected).[25]

Acute

Patient group	Tx line	Treatment
with moderate-to-severe infection	**plus**	**oral or intravenous antibiotic therapy**

» Definitive therapy should be based on culture results and clinical response to the empiric regimen.

» Therapy should be continued until there is a resolution in the signs of infection (usually 1-2 weeks).[25]

Primary options

» ciprofloxacin: 500-750 mg orally twice daily
-or-
» levofloxacin: 500 mg orally once daily
--AND--
» clindamycin: 300-450 mg orally three to four times daily

OR

Secondary options

» clindamycin: 300-450 mg orally three to four times daily

OR

Secondary options

» levofloxacin: 500 mg orally once daily

OR

Secondary options

» cephalexin: 500 mg orally twice daily

OR

Secondary options

» amoxicillin/clavulanic acid: 250 mg orally three times daily, or 500 mg orally twice daily
Dose refers to amoxicillin component.

OR

Secondary options

» doxycycline: 100 mg orally twice daily

OR

Secondary options

» trimethoprim/sulfamethoxazole: 160/800 mg orally twice daily

TREATMENT

Acute

Patient group	Tx line	Treatment

» Should be promptly referred to an established interdisciplinary diabetic foot clinic for further management.

» Moderate infection: defined as erythema >2 cm beyond the ulcer border or deep soft-tissue infection (e.g., abscess, osteomyelitis).[18]

» Severe infection: defined as a foot infection that is associated with ≥2 signs of the systemic inflammatory response syndrome (i.e., temperature >38°C [100.5°F]; heart rate >90 bpm; respiratory rate >20 breaths/minute or PaCO2 <32 mmHg; WBC count >12x10^9/litre or <4x10^9/litre, or 10% immature (band) forms).[18]

» Moderate infections may be treated with oral or parenteral, broad-spectrum, empiric antibiotics. Examples of oral options include clindamycin or trimethoprim/sulfamethoxazole plus either ciprofloxacin or amoxicillin/clavulanic acid. Examples of intravenous options include vancomycin plus: a carbapenem (e.g., ertapenem, imipenem/cilastatin); ampicillin/sulbactam; or a quinolone and metronidazole.

» Severe infections are usually treated with parenteral, broad-spectrum, empiric antibiotics. Examples include vancomycin plus one of three choices: a carbapenem (e.g., ertapenem, imipenem/cilastatin); ampicillin/sulbactam; or a quinolone and metronidazole.

» Definitive therapy should be based on culture results and clinical response to the empiric regimen.

» Therapy should be continued until there is a resolution in the signs of infection (usually 2-3 weeks).[25]

Primary options

» clindamycin: 300-450 mg orally three to four times daily
-or-
» trimethoprim/sulfamethoxazole: 160/800 mg orally twice daily

--AND--

» ciprofloxacin: 500-750 mg orally twice daily
-or-
» amoxicillin/clavulanic acid: 250 mg orally three times daily, or 500 mg orally twice daily
Dose refers to amoxicillin component.

TREATMENT

Acute

Patient group	Tx line	Treatment
		OR **Primary options** » vancomycin: 500 mg intravenously every 6 hours, or 1000 mg intravenously every 12 hours **--AND--** » ertapenem: 1 g intravenously every 24 hours **-or-** » imipenem/cilastatin: 500 mg intravenously every 6 hours, or 1000 mg intravenously every 8 hours Dose refers to imipenem component. **OR** **Primary options** » vancomycin: 500 mg intravenously every 6 hours, or 1000 mg intravenously every 12 hours **-and-** » ampicillin/sulbactam: 1.5 to 3 g intravenously every 6 hours Dose consists of 1 g of ampicillin plus 0.5 g of sulbactam (1.5 g); or 2 g of ampicillin plus 1 g sulbactam (3 g). **OR** **Primary options** » vancomycin: 500 mg intravenously every 6 hours, or 1000 mg intravenously every 12 hours **-and-** » ciprofloxacin: 400 mg intravenously every 12 hours **-and-** » metronidazole: 15 mg/kg intravenously as a loading dose, followed by 7.5 mg/kg intravenously every 6 hours
with moderate-to-severe infection	**adjunct**	**drainage and/or debridement** » Surgery should be considered in moderate-to-severe infections to drain/debride any ongoing deep soft-tissue infection (e.g., drain an abscess or infected joint space, debride fasciitis/myonecrosis/necrotic bone). » In patients with moderate-to-severe infections, it is recommended that a deep wound culture specimen be obtained.[25] Some guidelines recommend sending a soft tissue or bone

Acute

Patient group	Tx line	Treatment
		sample from the base of the debrided wound for microbiological examination.[6]

Ongoing

Patient group	Tx line	Treatment
after initial definitive treatment	**1st**	**follow-up and continuing diabetic care ± referral** » Patient should be followed up every 1 to 2 weeks to assess for resolution of infection and check for wound healing. A wound that has not healed or decreased in area by ≥50% within 2 to 4 weeks should be referred to a diabetic foot clinic or inpatient unit. » General practitioners should have a low threshold to refer to interdisciplinary foot clinics or inpatient units for more focused care.[28] Interdisciplinary care has repeatedly been demonstrated to significantly lower leg amputation rates.[24] [29] [30] [31] Indications for referral to a interdisciplinary diabetic foot clinic generally include the following: (1) wound remains incompletely healed after 2 to 4 weeks of basic care (e.g., offloading footwear, wound care); (2) local signs of infection (e.g., erythema, oedema, fluctuance, purulent drainage, foul odour) without systemic signs or symptoms; (3) ulcer associated with known or suspected peripheral artery disease; (4) plain x-ray demonstrating signs suggestive of osteomyelitis. » Diabetes itself should be followed up (e.g., regular check-ups, maintenance of target blood glucose levels, blood pressure and lipid management) according to current guidelines. » In the UK, National Institute for Health and Care Excellence (NICE) guidelines recommend that a patient with a limb-threatening or life-threatening diabetic foot problem should be referred immediately to acute services.[6] The interdisciplinary foot care service should be informed, so the patient can be assessed and an individualised treatment plan put in place. Examples of limb-threatening and life-threatening diabetic foot problems include the following: (a) ulceration with fever or any signs of sepsis; (b) ulceration with limb ischaemia; (c) clinical concern that there is a deep-seated

Ongoing

Patient group	Tx line	Treatment
		soft tissue or bone infection (with or without ulceration); (d) gangrene (with or without ulceration). Patients with other active diabetic foot problems should also be referred, within 1 working day, to the interdisciplinary foot care service or foot protection service.
	adjunct	**surgical bypass and/or endovascular intervention** » Endovascular intervention (usually balloon angioplasty with or without stent placement) and/or surgical bypass (usually femorotibial or femoropedal bypass) may be necessary to establish adequate arterial perfusion to the foot. This is generally done after the soft-tissue infection has been controlled or at least addressed. » Endovascular intervention appears to be as effective as bypass surgery for limb preservation (i.e., avoiding above-ankle amputation). Repeat endovascular intervention is required in 35% to 65% of patients to treat recurrent stenosis or occlusions occurring after angioplasty alone or to treat in-stent restenosis occurring after stent placement.[27]
	adjunct	**amputation** » Minor amputations (i.e., toe or partial-foot resections) may be performed on areas with irreversible gangrene. » Major amputations are generally reserved for 2 situations: (1) infection or gangrene that is so extensive that reconstruction either is not possible or will not preserve meaningful function in the affected limb; and (2) patients who have very little or no function in the limb (excluding previous history of stroke or paralysis).

Emerging

Local/rotational soft-tissue flaps and skin grafting

Many advanced soft-tissue and/or bone reconstruction options have been described for patients with large foot wounds; however, they are not commonly used in clinical practice. The goal of these options is to achieve an intact skin surface in a functional, weight-bearing surface on the residual foot, thereby avoiding major (above-ankle) amputation. The outcomes of these procedures can be excellent. Patients should be referred to an interdisciplinary diabetic foot clinic for evaluation for these procedures. The use of split-thickness skin grafting for defects, particularly in concert with surgery designed to reduce stress over an area, should also be strongly considered in an effort to move toward wound closure surgery.[34] [35]

Gene therapy

Several randomised trials have looked at various gene therapy options for non-reconstructible peripheral artery disease. Although results are promising, gene therapy is not currently a standard component of treatment for patients with foot ulcers and/or peripheral artery disease outside of centres participating in ongoing investigation of these treatment options.

Recommendations

Monitoring

Once- or twice-weekly follow-up is appropriate until a durable and 100% intact skin surface has been achieved. When wound healing is complete, follow-up frequency can be gradually decreased to twice per year. Once healed, patients are at very high risk for recurrence. For this reason the term diabetic foot remission, rather than healing, is often used to communicate this risk to both patients and caregivers.[39] [40]

Patient instructions

Adherence to any offloading restrictions is the single most important instruction to reiterate to patients. Specifically, the need to wear any protective offloading footwear or removable cast-walkers for any steps taken (even within the home) should be emphasised.

Patients should habituate themselves to examining their feet on a daily basis. The integrity of the skin on all areas of the foot should be examined for calluses, bunions, blisters, ulcers, or other changes. Socks should be visually inspected before wearing to identify any fabric defects. Ideally, socks should have no seams to minimise local trauma to the toes. White fabric may allow for blood or drainage from blisters to be identified more readily than dark fabric. The inside and outside of shoes should be examined for the integrity of the insole, as well as the presence of any foreign bodies. Patients who cannot see the plantar aspects of their feet because of body shape, poor strength, or poor range of motion can inspect this area by placing a hand mirror on the floor. Those with poor vision should enlist the help of family members or neighbours for frequent visual inspections.

Patients should ally themselves with a general practitioner to prevent progression of diabetes mellitus and/or peripheral artery disease. Such efforts should include monitoring blood pressure and blood glucose, quitting or avoiding tobacco products, and maintaining a heart-healthy diabetic diet.

Unless an autologous skin graft or biologic skin substitute has been recently placed, foot and leg wounds should be left open (uncovered) when showering. Local wound care instructions should be provided verbally and in writing.

In the UK, National Institute for Health and Care Excellence (NICE) guidelines recommend that each patient with a diabetic foot problem should be provided with oral and written information and clear explanations as part of the individualised treatment plan.[6] Information should include:

- A clear explanation of the patient's foot problem
- Pictures of diabetic foot problems
- Care of the other foot and leg
- Prevention and management of diabetic foot problems
- Foot emergencies and whom to contact
- Footwear advice
- Wound care
- General information about diabetes and the importance of blood glucose control.

[Diabetes UK: Putting feet first]

[Diabetes Australia: Foot care]

[American Podiatric Medical Association: Diabetic wound care]

[American Diabetes Association: Foot care]

Complications

Complications	Timeframe	Likelihood
delayed wound healing	**short term**	**medium**
The desired healing rate is at least a 50% wound area reduction within 4 weeks. The most common reasons for delayed wound healing are subtle infection (especially osteomyelitis), inadequate arterial perfusion, and inadequate offloading. Clinicians should consider further evaluation for these aetiologies using tests with higher sensitivity (e.g., MRI or bone biopsy if plain x-ray alone does not suggest osteomyelitis; diagnostic angiogram if non-invasive testing does not suggest arterial insufficiency; non-removable offloading footwear such as a total contact cast or non-removable cast-walker in patients previously provided removable footwear such as an orthopaedic shoe).		
osteomyelitis	**long term**	**medium**
Osteomyelitis (infection of the cortical and/or trabecular bone) may occur when chronic ulcers allow for the entry of bacteria into bone. Most cases are polymicrobial, and involvement of gram-positive and -negative organisms is common. Management generally consists of surgical resection of the bone, but oral or parenteral antibiotics alone may be appropriate in select patients. Six weeks of antimicrobial therapy appears to be as effective as 12 weeks.[36] Furthermore, oral antimicrobial therapy may also be considered for non-surgical treatment of osteomyelitis in low-resource communities or in patients with a functioning gut.		
ulcer recurrence	**long term**	**low**
Should be identified by the patient (during daily foot exams) or the provider (during clinic follow-up). Recurrence in the location of a previous ulcer that had completely healed is often due to suboptimal foot biomechanics (i.e., an improper distribution of pressure across the weight-bearing surfaces of the foot). Management should be similar to that of an initial foot ulcer.		
Charcot's arthropathy	**long term**	**low**
Neuro-inflammatory condition that occurs in a minority of patients with diabetes, and may lead to collapse of the longitudinal and transverse arches of the foot.[37] Pain, erythema, and redness may appear acutely, mimicking a foot infection. Chronic deformation may lead to repetitive trauma of the mid-foot (arch) during walking, leading to ulceration in this area. [Fig-1] Management is challenging and may require specialised orthopaedic reconstruction to prevent or treat limb-threatening foot infections.		
graft stenosis or thrombosis	**variable**	**low**

Complications	Timeframe	Likelihood
Stenosis requiring endovascular or surgical intervention occurs in about 20% of vein graft bypasses within the first 2 years after creation.[38] Most vascular surgeons will perform routine ultrasound surveillance to identify such stenosis. Although graft thrombosis is often asymptomatic, it may occasionally cause obvious signs of ischaemia, including delayed wound healing, ischaemic rest pains, clinical signs of acute limb ischaemia such as acute-onset weakness, paraesthesias, or limb pain (especially if the vascular reconstruction was done with a prosthetic vascular graft). Incidence may be as high as 10% to 15% during the first year after revascularisation and <5% per year during subsequent years.[38]		

Prognosis

Outcomes, including the avoidance of leg amputation, can be quite favourable, especially in healthcare settings with interdisciplinary teams that have experience and interest in managing diabetic foot complications. The recurrence of foot ulcers or foot infection is uncommon if complete wound healing is achieved.

Neuropathic foot ulcer

Typically requires 2 to 3 months for complete wound healing. Patients should anticipate the need to minimise weight-bearing on the affected foot, adhere to offloading instructions, and wear offloading footwear or cast-walkers for this period of time. Follow-up may occur on a weekly or twice-weekly frequency.

Non-healing foot ulcer associated with severe peripheral artery disease

Typically requires approximately 6 months for complete wound healing. Endovascular interventions may be performed on an outpatient or short-stay basis. Surgical revascularisation in this setting may require hospitalisation for about 1 week. Subsequent foot debridement or reconstructive procedures are common and often done on an outpatient basis.

Foot infection

May require 3 to 4 months for complete wound healing in patients with no peripheral artery disease, or 6 to 12 months in patients with peripheral artery disease.

Amputation

Mortality rates after amputation have been found to be high, with up to 70% of patients dying within 5 years of having an amputation. The high rate is thought to be associated with cardiovascular disease.

Diagnostic guidelines

North America

Standards of medical care in diabetes - 2017

Published by: American Diabetes Association **Last published:** 2017

Summary: Includes information about assessment of risk for diabetes-related foot problems.

Clinical practice guideline for the diagnosis and treatment of diabetic foot infections

Published by: Infectious Disease Society of America **Last published:** 2012

Treatment guidelines

Europe

Diabetic foot problems: prevention and management

Published by: National Institute for Health and Care Excellence **Last published:** 2016

International

IWGDF guidance on footwear and offloading interventions to prevent and heal foot ulcers in patients with diabetes

Published by: International Working Group on the Diabetic Foot **Last published:** 2015

Summary: Guidance on the prevention and treatment of foot ulcers.

IWGDF guidance on the prevention and management of foot problems in diabetes

Published by: International Working Group on the Diabetic Foot **Last published:** 2015

IWGDF guidance on use of interventions to enhance the healing of chronic ulcers of the foot in diabetes

Published by: International Working Group on the Diabetic Foot **Last published:** 2015

IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes

Published by: International Working Group on the Diabetic Foot **Last published:** 2015

IWGDF guidance on the diagnosis, prognosis and management of peripheral artery disease in patients with foot ulcers in diabetes

Published by: International Working Group on the Diabetic Foot **Last published:** 2015

North America

Standards of medical care in diabetes - 2017

Published by: American Diabetes Association **Last published:** 2017

Summary: Includes information about the treatment and prevention of diabetes-related foot problems.

Microvascular complications and foot care

Published by: American Diabetes Association **Last published:** 2017

The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine

Published by: Society for Vascular Surgery; American Podiatric Medical Association; Society for Vascular Medicine **Last published:** 2016

Summary: This guideline provides evidence-based guidance on the management of diabetic foot.

Inpatient management of diabetic foot disorders: a clinical guide

Published by: American Diabetes Association **Last published:** 2013

Management of patients with peripheral artery disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Published by: American College of Cardiology Foundation; American Heart Association **Last published:** 2013

Clinical practice guidelines: 32 Foot care

Published by: Canadian Diabetes Association **Last published:** 2013

Clinical practice guideline for the diagnosis and treatment of diabetic foot infections

Published by: Infectious Disease Society of America **Last published:** 2012

Oceania

National evidence-based guideline: prevention, identification and management of foot complications in diabetes

Published by: Australian Government National Health and Medical Research Council; Baker IDI Heart & Diabetes Institute **Last published:** 2011

Online resources

1. Journal of Family Practice: How to do a 3-minute diabetic foot exam *(external link)*
2. Diabetes UK: Putting feet first *(external link)*
3. Diabetes Australia: Foot care *(external link)*
4. American Podiatric Medical Association: Diabetic wound care *(external link)*
5. American Diabetes Association: Foot care *(external link)*

Evidence scores

1. Ulcer development: low-quality evidence suggests that it is unknown whether patient education is more effective than usual care at reducing the risk of developing foot ulcers.
Evidence level C: Poor quality observational (cohort) studies or methodologically flawed randomized controlled trials (RCTs) of <200 participants.

2. Ulcer healing rate: low-quality evidence suggests that debridement with hydrogel may be more effective than standard care at increasing ulcer healing rates after 12 weeks.
Evidence level C: Poor quality observational (cohort) studies or methodologically flawed randomized controlled trials (RCTs) of <200 participants.

3. Ulcer healing rate: there is good-quality evidence that pressure off-loading with total-contact casting is more effective at increasing ulcer healing rates compared with traditional dressing changes.
Evidence level A: Systematic reviews (SRs) or randomized controlled trials (RCTs) of >200 participants.

4. Ulcer incidence: low-quality evidence suggests that it is unknown whether therapeutic footwear is more effective than usual footwear at reducing the incidence of foot ulcers in patients without severe foot deformity after 1 to 2 years.
Evidence level C: Poor quality observational (cohort) studies or methodologically flawed randomized controlled trials (RCTs) of <200 participants.

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Images

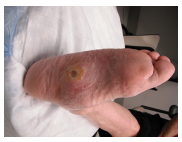

Figure 1: Mid-foot ulcer in a patient with Charcot's arthropathy (mid-foot collapse)

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Figure 2: Uninfected foot ulcer overlying the plantar aspect of the first metatarsophalangeal joint. Note the hyperkeratotic skin (callus) surrounding the wound edge

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Figure 3: A foot infection originating from a gangrenous third toe. Note the erythema and fluctuance in the mid-foot. An abscess cavity was found tracking under the longitudinal section of macerated skin

From the collection of Dr Neal R. Barshes; used with permission

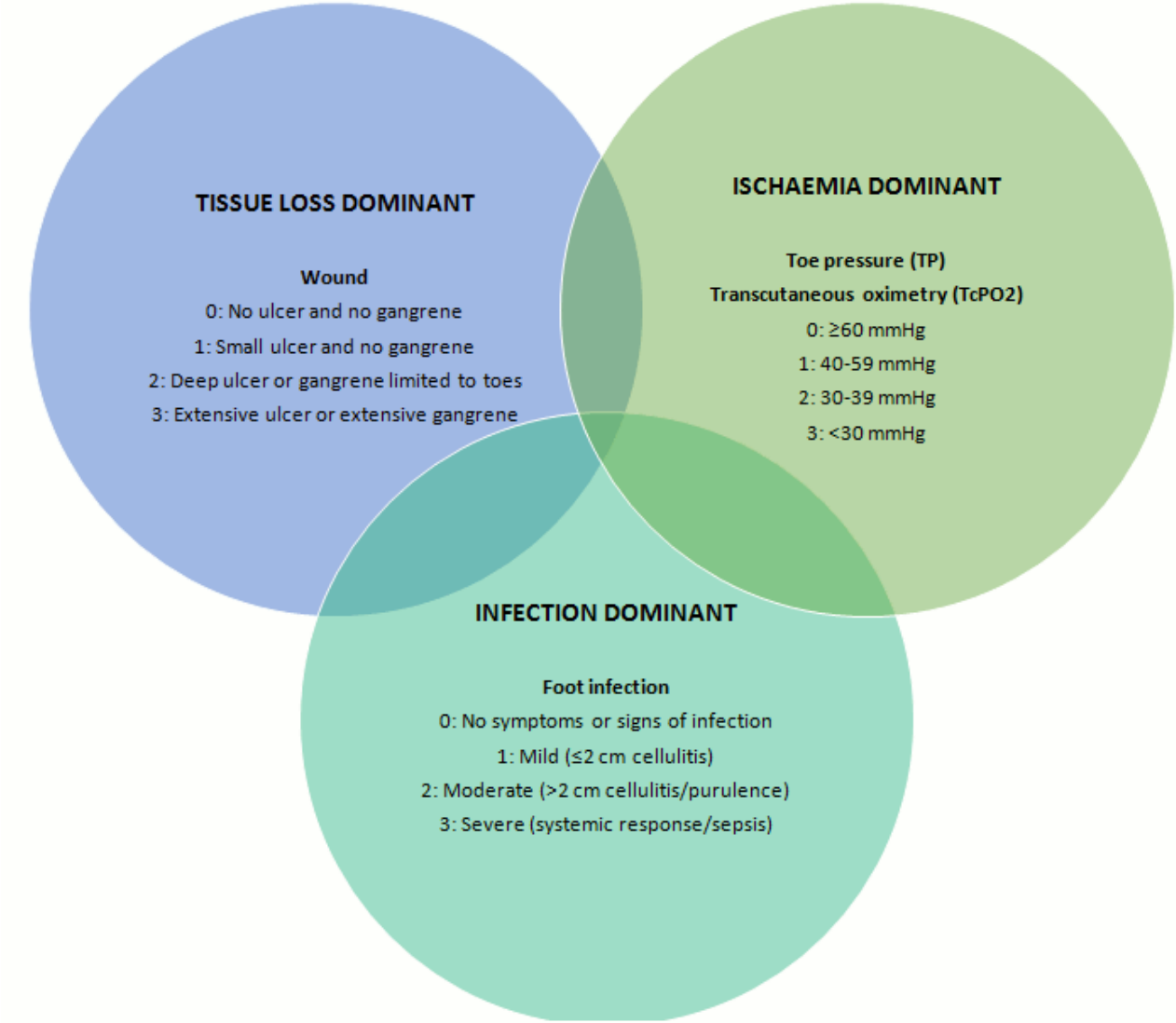

Figure 4: Diabetic foot problems can be related to the presence of a wound, ischaemia, or infection (WIfI). Which of these parameters is dominant can vary, and a flexible long-term management approach is needed. The Venn diagram shows intersecting rings of dominance for these three parameters, with gradings listed for each. The shaded areas represent combinations of these parameters of dominance.

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