

# The diabetic foot

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## Abstract

Foot disease is a common complication of type-1 and type-2 diabetes. The term 'diabetic foot' refers to a spectrum of disease that includes the foot at risk of ulceration, the ulcerated foot, and the Charcot foot. Risk of ulceration is conferred by peripheral neuropathy and peripheral vascular disease. The ulcerated foot can be classified as neuropathic, neuroischaemic or ischaemic. The principles of ulcer management include diagnosis and treatment of infection, establishment and treatment of vascular insufficiency, off-loading and optimization of the wound environment. The Charcot foot is a rare complication of the neuropathic foot and off-loading in the acute phase is important to prevent destruction of joint architecture. Long-established multidisciplinary foot clinics have achieved up to 50% reductions in major amputations in the UK.

**Keywords** Charcot; diabetic foot; diabetic ulcer; neuroischaemic foot; neuropathic foot

## Classification

Foot disease is a common complication of Type 1 and Type 2 diabetes mellitus. The term 'diabetic foot' refers to a spectrum of disease.

**The foot at risk of ulceration** – the risk of ulceration is conferred by the diabetic microvascular complication of peripheral neuropathy, and the macrovascular complication of peripheral vascular disease.

**The ulcerated foot** can be neuropathic, neuroischaemic or ischaemic.

**The Charcot foot** is rare in the UK, but can lead to significant bony destruction, deformity and ulceration.

## Prevalence

About 20–40% of patients with diabetes have neuropathy, and 50% will develop symptomatic peripheral vascular disease within 20 years of diagnosis. The lifetime prevalence of foot ulceration in people with diabetes is about 15%. Ulceration with

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infection can lead to tissue necrosis and amputation. Diabetes is the leading non-traumatic cause of major amputation of the lower limbs.

## Pathophysiology

### Neuropathy

Nerve damage due to disease of the vasa nervorum results in a 'glove and stocking' sensorimotor peripheral neuropathy that may progress proximally. The motor component results in denervation of the small muscles of the foot, leading to:

- hyperextension at the metatarsophalangeal joints
- hyperflexion at the interphalangeal joints
- cavus deformity of the arch of the foot.

These features produce the classical 'claw foot' deformity (Figure 1). The neuropathic posture puts increased pressure on the plantar aspects of the metatarsal heads, leading to callus formation. Sensory neuropathy results in loss of the protective sensations of pain, heat and pressure, making the patient unaware of actual or incipient ulceration. Autonomic neuropathy leads to vasomotor denervation and arteriovenous shunting, compromising the ability to direct blood flow into capillary beds. The paradox of bounding peripheral pulses in the presence of reduced microvascular flow may mask tissue ischaemia. Autonomic denervation of sweat glands leads to dry skin and fissuring, which may provide a portal for microbial invasion.

### Ischaemia

Ischaemia can be due to large- or small-vessel disease.

**Large-vessel disease** is due to accelerated atherosclerosis, usually in the femoral, popliteal and tibial arteries.

**Small-vessel disease** is due to structural and functional abnormalities of the microvascular endothelium. The skin of the foot is red, dry and thin, and susceptible to breakdown on minimal trauma.



**Figure 1** The classical 'claw foot' deformity in diabetic neuropathy. There is hyperextension at the metatarsophalangeal joint and hyperflexion at the interphalangeal joints. The arch of the foot has a cavus deformity.

### Contributory factors

In addition to neurovascular disease in the foot, a combination of factors may contribute to the onset of ulceration in diabetic patients, including:

- poor vision
- limited mobility in the joints
- cerebrovascular disease
- peripheral oedema due to coronary heart disease.

### The foot at-risk

#### Clinical assessment

The diabetic foot should be assessed for neuropathy and peripheral vascular disease.

**Neuropathy** is detected by:

- testing vibration with a biothesiometer or tuning fork
- discriminatory touch using a 10-g monofilament (highly reproducible)
- assessing the ankle jerks.

**Vascular examination** should include palpation for femoral, popliteal, posterior tibial and dorsalis pedis pulses. Skin colour and temperature, strength of pulsation, and the presence of abdominal and femoral bruits should be documented. Dependent rubor is seen in severe peripheral vascular disease (which may be mistaken for cellulitis).

**Clinical assessment** should include glycaemic control, duration of diabetes, renal disease, cigarette smoking and poor social circumstances; these are independent risk factors for complications of the diabetic foot.

#### Management

Monitoring and self-care are key aspects of management. There are no data concerning the optimal frequency of specialist review, although 3–6-monthly review is probably adequate. Patient education includes washing, inspection, care of corns and calluses, toenail cutting and wearing suitable footwear.

### The ulcerated foot

There may be intrinsic defects in ulcer healing in diabetic patients, including impaired fibroblast function, deficiency in growth factors, and abnormalities of the extracellular matrix. Delayed wound healing and prolonged hospital admissions are therefore common. A prospective study of 314 consecutive diabetic patients with foot ulcers referred to a multidisciplinary team in a teaching hospital in Sweden reported that healing was achieved in 62% of patients, amputations were necessary in 25%, while 13% died with unhealed ulcers.

#### Clinical assessment

Neuropathic ulcers are associated with callus, which typically develops on the plantar aspects of the metatarsal heads (Figure 2). Neuroischaemic ulcers occur on the margins of the foot (Figure 3). Infection is divided into local and superficial; spreading soft tissue infection and cellulitis; and osteomyelitis. The signs of inflammation and early infection may be difficult to detect in the presence of peripheral vascular disease. The ability to pass a probe directly onto underlying bone is a sensitive marker of osteomyelitis.



**Figure 2** A neuropathic ulcer in a diabetic patient. The breakdown of skin has occurred at the site of maximum pressure – under the head of the first metatarsal joint.

**Diagnosis and treatment of infection:** deep wound swabs often show the presence of several bacteria, including Gram-positive, Gram-negative, aerobic and anaerobic organisms. A positive swab may indicate colonization or invasive infection. It is unknown whether superficial ulcers that do not appear infected but which have positive swabs should be treated with antibiotics; some advocate the use of antibiotics more readily in the neuroischaemic than the neuropathic foot because the former can rapidly lead to necrosis, gangrene and amputation.

**Osteomyelitis** is a common sequela of diabetic foot ulceration, and is usually caused by *Staphylococcus aureus*. The incidence of methicillin-resistant *Staphylococcus aureus* in UK hospitals has more than doubled since 2001.

Plain radiographs should be performed on all patients with diabetic foot ulcers, with more sophisticated imaging if osteomyelitis is suspected; MRI and leukocyte scans have equivalent sensitivity (although MRI provides more detailed anatomical information



**Figure 3** A neuroischaemic ulcer in a diabetic patient. The skin is necrotic and has developed in an area of relative pressure. Neuroischaemic ulcers are common on the margins of the foot.

and greater specificity). Some groups advocate image-guided bone biopsy.

Although surgical intervention is often necessary, conservative approaches may be effective. The authors' policy is to use MRI to diagnose and assess the extent of osteomyelitis and to give a 3-month course of appropriate oral antibiotics (initially intravenous only if cellulitis or systemic signs of infection are present). MRI is then used to reassess at 3 months:

- stop antibiotics if the wound has healed and there has been improvement or resolution of signal change on MRI
- repeat the 3-month cycle of antibiotics if the wound is not yet healed and signal change on MRI is improved but persists
- intervention is needed if at any point there is clinical or radiological deterioration – revascularization if possible, otherwise definitive amputation.

The choice of antibiotics is governed by the anticipated or proven spectrum of organisms. The regimen of the authors' unit for emergency management before microbial identification is shown in Table 1.

**Assessment and treatment of vascular insufficiency:** all patients with diabetic ulcers should undergo non-invasive vascular testing because clinical evaluation may underestimate the extent of disease. The ratio of blood pressure at the ankle to pressure in the arm produces the ankle-brachial pressure index. A value of <0.9 indicates significant arterial disease. Arterial calcification (common in diabetes) may lead to a falsely elevated value. A low value is therefore significant, but normal values can be consistent with significant disease.

Waveforms measured by Doppler flow and pulse volume recording are also helpful. A normal waveform is narrow and triphasic: a tall systolic peak, dicrotic notch and rapid run-off. With increasing disease, the waveform becomes wider and flatter, and the dicrotic notch is lost, leading to a biphasic (and eventually monophasic) pattern. Duplex sonography permits assessment of the anatomy of the vessel and haemodynamic flow. The technique is operator-dependent at the level of the tibial arteries and below.

Revascularization with angioplasty or surgery should be considered if arterial insufficiency is present. Occlusive vascular disease in diabetes involves medium-sized arteries, primarily at the popliteal trifurcation. Distal pedal vessels are often spared occlusive lesions and can be amenable to bypass grafting. Anatomical evaluation using digital subtraction angiography is necessary if

revascularization is planned. Pre-hydration and treatment with N-acetylcysteine is recommended because intravenous contrast is nephrotoxic. Magnetic resonance angiography can be superior to conventional angiography and is a useful alternative in renal impairment.

**Off-loading:** the insensate diabetic foot ulcerates as a result of minor trauma from poorly fitting shoes and abnormal biomechanics. High pressures must be reduced and redistributed in order to optimize wound healing.

The first-line treatment in the UK is total-contact casting, which is minimally padded, moulded to the foot, and allows for mobility while the ulcer heals. Disadvantages include lack of access for wound inspection and dressing, impracticality, and unsuitability in the presence of ischaemia. Alternative strategies include removable cast walkers (e.g. Aircast walker™, Scotch cast boots™ (fibreglass removable casts), 'half-shoes').

**Optimization of wound environment:** the goal of preparation of the wound bed is to create non-infected, well-vascularized granulation tissue.

**Debridement** prepares the wound bed for healing and improves outcome by removing necrotic tissue that often carries the heaviest bacterial load. Surgical debridement is recommended, although enzymatic debriding agents may also be used. Sterile larvae of the greenbottle fly (maggots) are effective in cleaning the wound bed, but may be unacceptable to patients. Silver- and iodine-containing solutions are used as topical anti-septics, although efficacy data are lacking.

**Other measures – after debridement,** tissues should be kept warm and moist to prevent the formation of necrotic material. Various topical dressings (e.g. alginates, foam, hydrogels, hydrocolloids) that absorb wound exudates and promote hydration are available in the UK. Hyperbaric oxygen has been used to counteract ischaemia, and there is now evidence for the beneficial use of vacuum-assisted closure devices.

Cultured skin dermis (e.g. Dermagraft™) and growth factors may be considered, but are expensive and should be used only when conventional approaches fail. Cultured skin dermis consists of neonatal dermal fibroblasts cultured *in vitro* onto a bioabsorbable mesh to produce metabolically active dermal tissue. Weekly application improves wound healing. Synthetic growth factors stimulate formation of granulation tissue and enhance epithelialization. Preliminary clinical trials using platelet-derived growth factor and granulocyte colony stimulation factor have been encouraging.

**Emergency management of the infected diabetic foot ulcer before microbial identification**

**Antibiotic regime**

<i>First line</i>	Augmentin 625 mg tds
<i>Penicillin allergic</i>	Clindamycin 300 mg qds
	Ciprofloxacin 500 mg bd
<i>Known MRSA carriage</i>	*Rifampicin 300 mg bd
	*Doxycycline 100 mg bd

\*assuming previously identified MRSA was sensitive.

**The Charcot foot**

**Clinical features**

The Charcot foot, originally described in association with tabes dorsalis, affects about 0.2% of patients with diabetes and is commonly seen in specialist diabetic foot clinics. Four factors are permissive for the onset of Charcot deformity:

- peripheral neuropathy
- autonomic neuropathy
- localized osteopenia due to the hyperdynamic flow associated with autonomic neuropathy and resulting in susceptibility to fracture or dislocation
- trauma (significant or minor).

**Table 1**

Some orthopaedic surgeons suggest doubling the period of immobilization in diabetic patients with peripheral neuropathy who have a fractured tarsal or metatarsal bone in order to avoid Charcot deformity. The initial insult (which may go unnoticed) results in fracture or dislocation.

**The acute phase** is characterized by a red, swollen, oedematous and often painful foot. Foot pulses are bounding. This phase is often misdiagnosed as cellulitis, deep vein thrombosis, gout or an ankle sprain. Due to the sensory neuropathy, continued weight bearing may lead to gross destruction and distortion of the joint. The mid-foot is usually involved (Figure 4). The acute phase may last for months or even years, but eventually results in increased bone formation, sclerosis and arthrodesis. In about 20% of cases, the contralateral limb is affected within several years. The self-limiting nature of the acute phase (and the association with minor trauma) bears similarities to reflex sympathetic dystrophy. Both conditions may respond to bisphosphonates given intravenously, possibly through local inhibition of cytokine release.

The mainstay of treatment in the acute phase is immobilization of the joint to prevent further bone destruction and deformity, ideally by total contact casting. The optimum duration of immobilization is not known. The authors have found that a minimum 6-month immobilization is necessary.

**Quiescent phase:** custom-made footwear can be used. There is a role for reconstructive orthopaedic surgery. Identifying concurrent osteomyelitis (particularly if an area of high pressure has resulted in ulceration) can be particularly difficult, even with



**Figure 4** Acute Charcot changes in the left mid-foot. The mid-foot is swollen, hot and deformed. The pathophysiology is complex, but probably involves neuropathy, bone weakening and undetected trauma.

MRI. A Charcot foot complicated by ulceration and infection is at high risk of major amputation. ◆

#### FURTHER READING

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