

### End-stage renal failure – the uraemia phase

Diabetes should not exclude patients from renal replacement therapy programmes. The mode of therapy (dialysis or transplantation) depends on clinical judgement and local facilities and resources. Good glycaemic control is important for patients' well-being before and during renal replacement therapy, and is associated with a lower mortality. In specialized centres, combined kidney and pancreas transplantation may be considered, to maintain euglycaemia and prevent recurrence of glomerulopathy in the transplanted kidney.

During the uraemic phase, interpretation of HbA<sub>1c</sub> and, particularly, fructosamine (and therefore their use as monitoring indices for diabetic control) may be less reliable. HbA<sub>1c</sub> is probably preferable to fructosamine, but should be interpreted with caution.

Recent data suggest that careful cardiovascular assessment (including coronary angiography and correction of significant coronary lesions) may confer improved life expectancy, particularly in patients undergoing transplantation. However, the outcome of renal replacement therapy remains poorer in patients with diabetic chronic renal failure than in those with non-diabetic renal disease. Furthermore, the associated vascular, neuropathic and infective complications increase the socioeconomic costs of renal replacement therapy in those with diabetes.

### Pregnancy and proteinuria

Development of microalbuminuria or macroalbuminuria in a pregnant woman with diabetes should alert the physician to the risk of pre-eclampsia. Pregnancy is no longer contraindicated in women with diabetic proteinuria; however, proteinuria may rise and the risk of eclampsia is increased. Diabetes in pregnancy is discussed further on page 58. ♦

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## The Diabetic Foot

Andrew J M Boulton

Foot problems account for more hospital admissions of diabetic patients than any of the other long-term complications. An understanding of the causes of these problems enables early recognition of patients at high risk. It has been shown that up to 50% of amputations and foot ulcers in diabetic patients can be prevented by effective identification and education.

In this contribution, the term 'diabetic foot' includes any pathology that results directly from diabetes or its long-term complications.

### Epidemiology

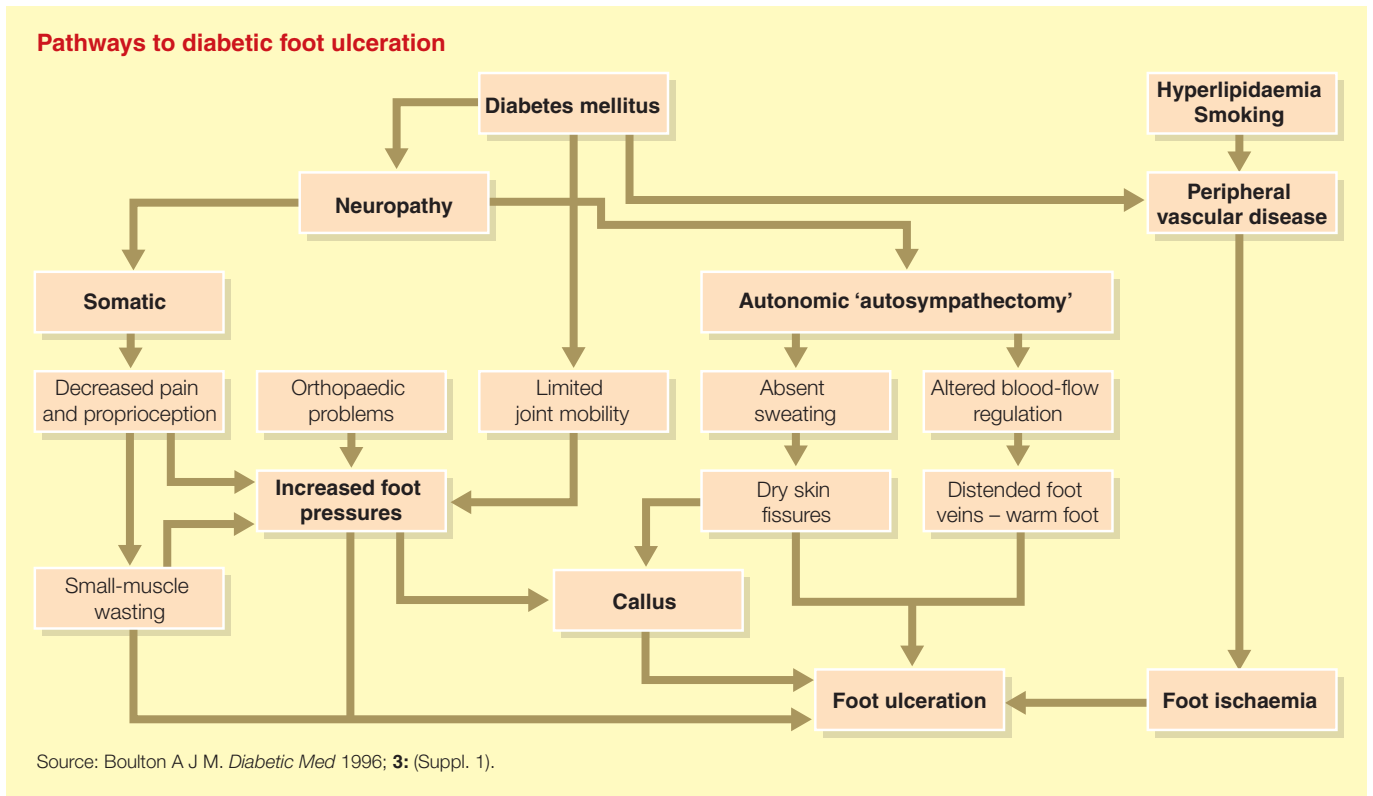
Diabetic foot problems occur in both type 1 and type 2 diabetes. They are more common in men, and in patients over 60 years of age. A recent population-based study of more than 10,000 patients in the North West of England reported that 5% had past or present foot ulceration and almost 67% had one or more risk factors. Foot ulcers are more common in Caucasians than in Asian and Afro-Caribbean patients; foot ulceration also appears to be associated with social deprivation.

Foot lesions may be the presenting feature of type 2 diabetes. Therefore, any patient with a foot ulcer of undetermined aetiology should be screened for diabetes.

### Pathogenesis of foot ulcers

Foot ulceration occurs as a result of trauma (often unperceived) in the presence of neuropathy and/or peripheral vascular disease (Figure 1). Contrary to popular belief, infec-

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tion is not a primary cause of foot ulcers, but is a secondary phenomenon following ulceration of the protective epidermis.

Advanced somatic neuropathy results in:

- insensitivity, facilitating trauma
- altered proprioception and small-muscle wasting (in the presence of limited mobility in the subtalar and mid-foot joints, this leads to altered loading under the foot during standing and walking).

This combination of insensitivity and high pressures applied to the foot puts the patient at great risk of neuropathic ulceration. Such patients usually have peripheral autonomic dysfunction which, in the absence of peripheral vascular disease, results in increased resting blood flow; it should be noted that warm, insensitive feet are very much at risk. This 'auto-sympathectomy' also leads to dry skin that cracks and fissures, and, as a result of repetitive high pressure, callus tissue forms under weight-bearing areas. Recent research has shown that the presence of callus in an insensitive foot is highly predictive of subsequent foot ulceration.

Peripheral vascular disease is more common in patients with diabetes and is a major factor in the aetiology of ulceration. Pure ischaemic ulcers probably represent only 10% of diabetic foot lesions; 90% are caused by neuropathy, alone or with ischaemia. In recent years, the incidence of neuroischaemic problems has increased, and neuroischaemic ulcer is now the most common lesion seen in most UK diabetic foot clinics.

### Identification of the at-risk foot

Careful inspection and examination of the foot is an integral part of the annual medical review that all patients with diabetes should receive. The clinician should never rely on symptoms alone to identify high-risk patients – 50% of patients with insensitive feet have no previous history of neuropathic symptoms, and claudication may not be prominent in those with ischaemic feet. Patients at greatest risk of ulceration are those with:

- evidence of neuropathy
- evidence of ischaemia
- foot deformity (e.g. claw toes, Charcot changes)
- callus at pressure areas
- previous history of foot ulcers
- impairment of sight (neuropathy is more common in patients with retinopathy, and patients with restricted vision may injure their feet when attempting self-care)
- neuropathy
- poor social circumstances (e.g. the elderly, particularly those living alone).

Signs of neuropathy include dry skin, callus formation, distended dorsal foot veins (autonomic dysfunction) and small-muscle wasting (somatic neuropathy). Evidence of sensory loss should be established using a pin, a 128 Hz tuning fork and, if available, monofilaments to assess the pressure perception threshold. (Monofilaments are nylon fibres of various

diameters that exert a fixed pressure when applied to the surface of the skin. Inability to perceive the pressure from a 10 g monofilament has been shown to be a sensitive but simple means of identifying an 'at-risk' foot.) Skin temperature and peripheral pulses should also be assessed.

### Prevention of foot problems

Patients without risk factors who have healthy feet should receive general advice on foot hygiene, nail care and purchase of footwear. Their risk status should be reviewed annually.

Patients with any risk factor should be reviewed more frequently, and should be educated about preventive foot care. High-risk patients should be advised to:

- wash and inspect their feet daily
- use creams or lotions to prevent dry skin/callus formation
- always have their feet measured when purchasing shoes
- avoid walking barefoot and avoid thermal injury (e.g. from hot water bottles, fires)
- seek medical attention for any injury/discomfort, however trivial it may seem
- avoid the temptation to attempt self-treatment of corns, calluses and other disorders.

These simple steps have been shown to significantly reduce the incidence of foot ulceration.

The foot tends to lie 'between specialties', and therefore many centres have developed diabetes foot care teams. Such teams may include a diabetologist, a surgeon (vascular and/or orthopaedic), a chiropodist, a specialist nurse and a shoe-fitter. A primary role of the team is foot care education, which is often provided by the chiropodist or nurse. Much of the screening and primary health education of patients with diabetes is undertaken in primary care. A community foot care team might comprise a general practitioner, a practice nurse and a chiropodist, and education for at-risk patients is often provided in this setting.

### Diabetic foot ulceration

Despite preventive measures, patients may still develop ulcers, and a system of classification is therefore important. In recent years, many new ulcer classification systems have been proposed; one of the most commonly used is that de-

vised at the University of Texas (Figure 2). In this system, grades refer to the depth of the wound, and each grade has four stages depending on the presence or absence of infection and/or ischaemia.

**Grade 0:** a grade 0 foot has no open lesions, but is at risk. The patient may have a past history of foot ulcers or pre-ulcer lesions such as the presence of callus or deformity, often with insensitivity. The presence of callus under weight-bearing areas is particularly dangerous, because this can act as a foreign body and cause ulceration of the underlying skin. Thus, patients with any callus formation should be seen by the podiatrist and the callus trimmed and/or removed by paring. These patients can usefully be followed in the diabetic foot clinic.

**Grade 1** ulcers are superficial, but there is full-thickness skin loss. Such ulcers tend to be predominantly neuropathic with (1B) or without (1A) infection. Such ulcers commonly occur under high-pressure areas (e.g. the metatarsal heads, toes). A classical appearance is a 'punched-out' ulcer surrounded by a rim of callus. Management involves removal of direct pressure from the ulcer and treatment of any infection. The presence of ischaemia should be confirmed by clinical examination and, if necessary, non-invasive assessments.

- Callus should be removed with a scalpel to expose the ulcer floor.
- Deep swabs may be taken from the ulcer base.
- Radiographs should be obtained to exclude unsuspected bony infection (if this is found, the ulcer should be considered a grade 3 lesion).
- Local infections can be treated on an out-patient basis with broad-spectrum antibiotics (e.g. co-amoxiclav, 375 mg t.d.s., clindamycin, 150 mg q.d.s.). A particularly useful combination for chronically infected neuropathic foot ulcers is clindamycin and ciprofloxacin. This combination provides broad-spectrum antibacterial cover for most commonly found organisms; furthermore, clindamycin has good bone penetration. However, there is no evidence to suggest that long-term use is beneficial.
- Wounds should be kept clean with a dressing, but pressure relief is of paramount importance, because patients can continue to weight-bear in the absence of pain. This may be

#### University of Texas diabetic wound classification system

Stage	Grade			
	0	1	2	3
A	Pre-ulcerative or post-ulcerative lesion, completely epithelialized	Superficial wound, not involving tendon, capsule or bone	Wound penetrating to tendon or capsule	Wound penetrating to bone or joint
B	With infection	With infection	With infection	With infection
C	With ischaemia	With ischaemia	With ischaemia	With ischaemia
D	With infection and Ischaemia	With infection and ischaemia	With infection and ischaemia	With infection and ischaemia

achieved using a plaster cast (below-knee) or a Scotch-cast boot (a light-weight, removable, ankle-length cast), which permits mobility but prevents application of pressure over the ulcer area. The gold standard, as recently confirmed in a controlled trial, remains total-contact casting, but this should be used only in clinics with sufficient experience of casting insensitive limbs.

- Blood glucose control should be assessed and directed towards normoglycaemia. Insulin may be required temporarily in some type 2 patients.

**Grade 2** ulcer is a deeper lesion that often penetrates subcutaneous tissue, reaching tendon and/or capsule. Local infection is often present (2B or 2D), but by definition there is no bony involvement. These lesions may be typically neuroischaemic if located on the plantar surface of the forefoot. Heel ulcers tend to be predominantly neuroischaemic (2C or 2D) (Figure 3). Infection with bacteria (e.g. staphylococci, streptococci, anaerobic bacteria) is common, and isolates are almost always polymicrobial. Assessment of infection is difficult, and unless deep wound swabs are taken directly to the laboratory in appropriate media (particularly for anaerobic bacteria), the results of cultures may not be truly representative. Local signs of infection include erythema, warmth, swelling and a



**3** Neuroischaemic ulcer (grade 2D) on the lateral left heel. This partially painful ulcer was precipitated by inappropriate footwear. Examination revealed absence of pain sensation, a cool foot and absence of pulses. Doppler studies suggested a proximal obstructive lesion, which was confirmed on arteriography. Successful proximal arterial bypass surgery was preceded by broad-spectrum antibiotics and followed by local debridement and protective heel care. Complete healing was achieved within a few weeks.

purulent, smelly discharge; pain is not a prominent complaint in patients with a neuropathic foot.

Management of grade 2 ulcers is similar to that of grade 1 ulcers.

**Grade 3** ulcers penetrate bone and/or joints. The ability to probe to bone has been shown to be a relatively sensitive means of identifying osteomyelitis, and therefore most ulcers are at least grade 3B. Traditional management of osteomyelitis includes:

- hospital admission
- initial debridement, with culture of the ulcer base and blood
- optimal glycaemic control (intravenous insulin may be required)
- broad-spectrum intravenous antibiotic therapy until sensitivities are known – multiple therapy (e.g. ampicillin, 500 mg q.d.s., plus cloxacillin, 500 mg q.d.s., plus metronidazole, 400 mg t.d.s., or clindamycin, 150 mg q.d.s., plus ciprofloxacin, 500 mg b.d.) is often given initially
- non-invasive assessment of peripheral circulation using Doppler ultrasonography
- radiology of the foot
- surgical opinion – if arterial inflow is satisfactory, local surgery with removal of infected bone (e.g. by ray excision for osteomyelitis of a metatarsal head) is indicated; in the presence of proximal arterial disease, angioplasty or bypass surgery might be indicated before radical local surgery can be attempted
- care of the other foot to avoid pressure ulcers on the heel.



**4** Osteomyelitis of the great toe. Osteomyelitis was confirmed on a radiograph, and it was possible to probe to bone. This ulcer is therefore grade 3B and, because of extensive destruction of the interphalangeal joint, the toe was amputated. The wound healed well because peripheral circulation was good.



There is recent evidence that grade 3B lesions (i.e. without vascular disease) occasionally respond to long-term antibiotic treatment, which may be given orally. Furthermore, there is anecdotal evidence that insertion of tobramycin-impregnated calcium sulphate beads might help in the local delivery of antibiotics to osteomyelitic bone.

**Gangrene** (Figure 4) is usually ischaemia in combination with neuropathy, giving rise to a neuroischaemic foot. The principles of management are similar to those of the lesions above, but urgent non-invasive assessment of the peripheral circulation and a vascular surgical opinion are indicated. Angioplasty or bypass surgery may be required if a suitable stenotic lesion is demonstrated by arteriography, and grafts to levels below the popliteal artery are being increasingly performed with successful results. Once the peripheral circulation is adequate, local surgery to remove gangrenous areas may be attempted, though single toes may be left to mummify and auto-amputate.

Larval therapy (using the ability of maggots to cleanse wounds, prevent infection and promote healing) is increasingly used successfully in neuroischaemic ulcers with necrotic slough tissue that is difficult to debride mechanically.

Patients with gangrene in the presence of diffuse distal arterial disease usually require major amputation; the likelihood of local healing is minimal.

**After-care:** it is essential to remember that hospitalized patients with diabetes are at potential risk of further insensitization, particularly if bed-rest is prolonged. Protection of the heels and other pressure points is of paramount importance; devices such as leg troughs are invaluable.

After discharge, all patients require education about foot care and careful follow-up, preferably by the foot care team, to prevent recurrent ulceration. Special footwear (e.g. extra-depth shoes with appropriate insoles) is necessary in many patients.

### Charcot neuro-arthropathy

Charcot neuro-arthropathy is non-infective arthropathy in a well-perfused, insensitive foot. The neuro-arthropathy is usually precipitated by minor trauma in the presence of insensitivity, peripheral sympathetic dysfunction and an adequate arterial inflow. The patient usually continues to walk and the foot becomes warm, swollen and occasionally painful. Any patient with neuropathy who complains of swelling or discomfort, with or without a history of injury, should be assessed urgently.

**Investigation:** early radiographs may be normal. Later changes include fractures, osteolysis, fragmentation, new bone formation and disorganized joints.

During the active (destructive), phase, which may last for several months, Charcot neuro-arthropathy may be difficult to distinguish from osteomyelitis, which has similar radiographic features. An indium-labelled WBC scan or MRI of the foot is most helpful in distinguishing infective and neuroarthropathic causes.

**Management:** in the acute phase, there is evidence that off-loading the affected foot using a plaster cast is most effective in reducing disease activity, which can be monitored by the difference in skin temperature between the active and the contralateral foot. Casting should continue until the swelling and hyperaemia have resolved and the skin temperature differential is 1°C or less, at which time custom-moulded shoes with appropriate insoles are indicated.

Bisphosphonates (pamidronate) have been shown to be useful in reducing disease activity by bone turnover markers in acute Charcot neuro-arthropathy. Further studies are required to determine whether oral bisphosphonates are equally useful.

Patients with a history of Charcot neuro-arthropathy are at high risk of future foot problems, and careful follow-up is mandatory. ♦

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