The diabetic foot

Andrew JM Boulton

Abstract

Foot ulceration in diabetes mellitus is common. Foot problems remain the most common cause of hospital admission among patients with diabetes mellitus in developed countries. The lifetime risk of a patient with diabetes developing an ulcer may be as high as 30%, and up to 85% of all lower limb amputations in diabetes are preceded by foot ulcers. Up to 50% of older patients with type 2 diabetes have risk factors for foot problems, and regular screening by careful clinical examination is essential; those found to be at risk should attend more regular follow-up, with education in foot self-care. The key to management of diabetic neuropathic foot ulceration is aggressive debridement with removal of callus and dead tissue, followed by application of some form of cast to offload the ulcer area. Most ulcers heal if pressure is removed from the ulcer site, arterial circulation is sufficient, and infection is managed and treated aggressively. Patients with a warm swollen foot without ulceration should be presumed to have acute Charcot neuro-arthropathy until proven otherwise. The optimal approach to reducing ulceration requires regular screening, patient education and a team approach to management, both in the community and in hospital.

Keywords Amputation; Charcot neuro-arthropathy; diabetic neuropathy; foot ulceration; infection; MRCP; osteomyelitis; peripheral arterial disease

Key points

- Every time you see a person with diabetes mellitus in the clinic, always inspect their feet, with their shoes and socks removed
- All diabetic patients on dialysis must be considered to be at risk of foot problems
- If a foot infection is suspected on clinical grounds, deep tissue cultures, and not superficial wound swabs, should be taken
- Any patient with diabetes without neuropathy who presents with a unilateral warm swollen foot should be considered to have Charcot neuro-arthropathy until proven otherwise
- Diabetic patients with a history of renal or simultaneous pancreas–kidney transplantation must be regarded as having a particularly high risk of developing foot ulceration and Charcot neuro-arthropathy

Definitions and epidemiology

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

Foot problems account for more hospital admissions than any other long-term complications seen in patients with diabetes mellitus. Understanding 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 diabetes can be prevented by effective identification and education.

Foot problems occur in both type 1 and type 2 diabetes and it has been estimated that the lifetime risk of a patient developing a foot ulcer may be as high as 30%.[1,2] Ulcers are more common in men and in patients >60 years of age. A large population-based study of >10,000 diabetic patients in north-west England reported that 5% had past or present foot ulceration, and almost 67% had one or more risk factors; the annual incidence of ulceration in these diabetic patients was 2.2%. Foot ulcers are more common in white individuals than Asian or African-Caribbean patients. Foot ulceration also appears to be associated with social deprivation.

Foot lesions can be the presenting feature of type 2 diabetes, so any patient with a foot ulcer of undetermined cause should be screened for diabetes.

Pathogenesis of foot ulceration

Foot ulceration occurs as a result of trauma (often unperceived) in the presence of neuropathy and/or peripheral arterial disease (PAD) (Figure 1). Contrary to popular belief, infection is not a primary cause of foot ulcers, but is a secondary phenomenon after ulceration of the protective epidermis.

Advanced somatic neuropathy results in insensitivity, facilitating trauma and altered proprioception and small-muscle wasting. This, in the presence of limited mobility in the subtalar and mid-foot joints, can lead to altered loading under the foot on standing and walking.

This combination of insensitivity and high pressures applied to the foot places the patient at great risk of neuropathic ulceration. Such patients usually have peripheral autonomic dysfunction, which, in the absence of PAD, 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 repetitive high pressure leads to the formation of callus tissue beneath weight-bearing areas. Research has shown that the presence of callus in an insensitive foot is highly predictive of subsequent foot ulceration.

PAD is more common in individuals 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 neuro-ischaemic problems has increased, and neuro-ischaemic ulcers are now the most common lesions seen in most UK diabetic foot clinics. Similarly, in Europe, PAD is present in 49% of foot ulcers, with infection present in 58%.

Andrew JM Boulton *MD DSc FRCP is a Professor of Medicine at the University of Manchester, UK and the University of Miami, USA, and Consultant Physician at Manchester Royal Infirmary, UK. Competing interests: none declared.*

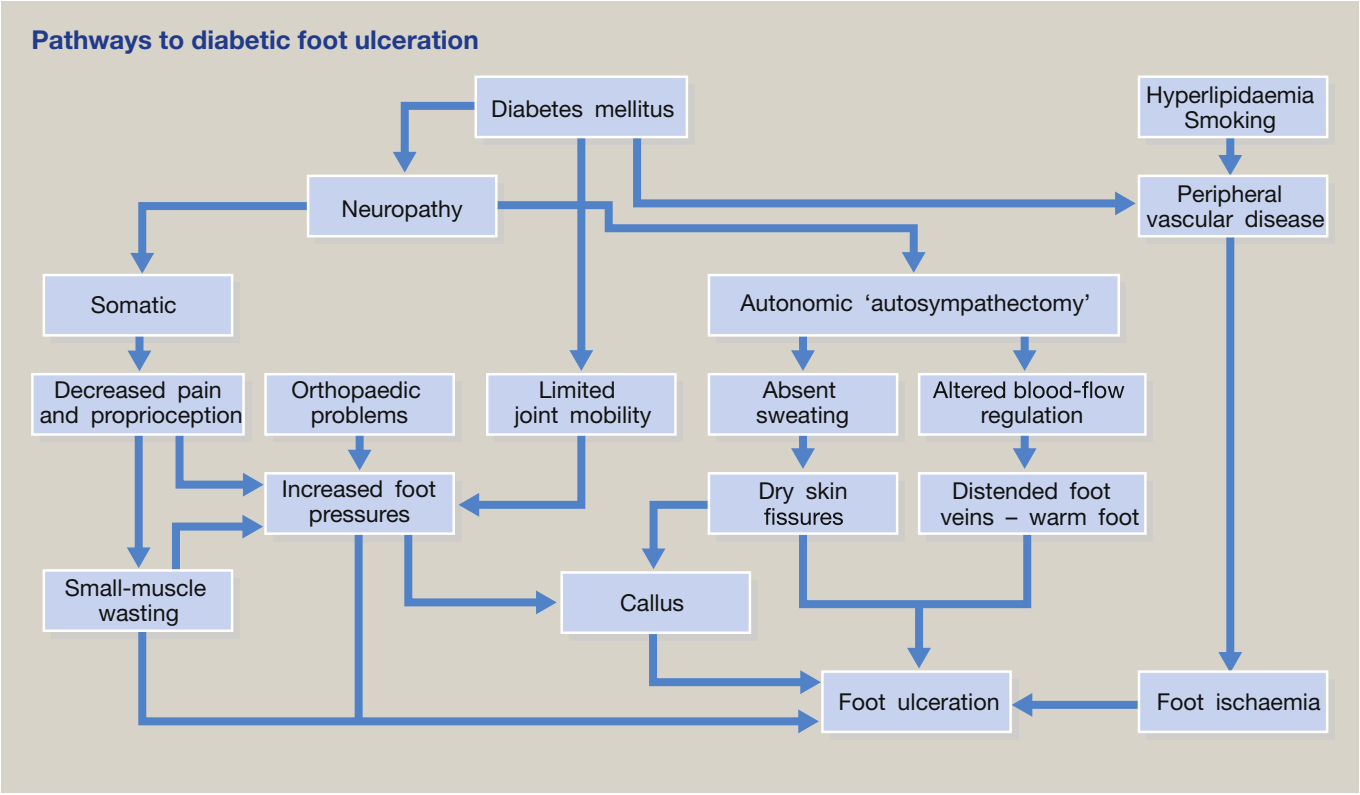

Figure 1

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 expect. 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 (patients with restricted vision can injure their feet when attempting self-care)
- end-stage renal disease – especially in those who are on dialysis or have undergone transplantation
- poor social circumstances (e.g. elderly people, particularly those living alone).

Signs of neuropathy include dry skin, callus formation, distended dorsal foot veins (autonomic dysfunction) and small-muscle wasting (somatic neuropathy). The American Diabetes Association has proposed that the annual screening for sensory loss should use a 10 g monofilament (a nylon fibre that, when applied to the skin until it buckles, applies a pressure of 10 g) to assess the pressure perception threshold. Sensory loss should be confirmed using an alternative test to detect absence of, for example, pinprick sensation, vibration perception using a 128 Hz tuning fork, temperature perception using hot and cold rods, or vibration perception threshold using a biothesiometer (if available).[3] Recently, two even simpler screening tests have been validated:

- In the Ipswich touch test, the examiner touches the apices of the first, third and fifth toes and asks if the patient can perceive the touch: this test has proved equally as accurate as the 10 g monofilament in diagnosing the 'high-risk' foot.
- A simple pocket-sized disposable device is available to test the integrity of vibration sensation; this has been shown to have almost perfect agreement with the vibration perception threshold and the neuropathy disability score.[3]

Skin temperature and peripheral pulses should also be assessed.

Prevention of foot problems

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

Patients with any risk factor should be reviewed more frequently and 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 and formation of callus
- always have their feet measured when purchasing shoes
- avoid walking barefoot
- avoid thermal injury (e.g. from hot-water bottles, fires)
- seek medical attention for any foot injury or discomfort, however trivial it seems

- avoid the temptation to attempt self-treatment of corns, calluses and other disorders.

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

The foot tends to lie 'between specialties', and many centres have developed diabetes foot-care teams that can include a diabetologist, surgeon (vascular and/or orthopaedic), podiatrist, specialist nurse and shoe-fitter. A primary role of the team is foot-care education, which is often provided by the podiatrist 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, practice nurse and chiropodist, and education for at-risk patients is often provided in this setting. The introduction of multidisciplinary teamwork to the community has been shown to result in a significant reduction in the number of amputations.[3]

Diabetic foot ulceration

Despite preventive measures, patients can still develop ulcers, so a system of classification is important. In recent years, many new ulcer classification systems have been proposed; one of the most commonly used was devised at the University of Texas (UT) (Table 1). 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.[1–3]

UT diabetic wound classification system

Stage	Grade 0	Grade 1	Grade 2	Grade 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

Table 1

Grade 0

A UT grade 0 foot has no open lesions but is at risk. The patient may have a history of foot ulcers or pre-ulcer lesions, such as callus and 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, the podiatrist should see patients with callus formation in order to trim the callus and/or remove it by paring. These patients can usefully be followed in the diabetic foot clinic.

Grade 1

These ulcers are superficial, but there is full-thickness skin loss. They tend to be predominantly neuropathic, without (UT 1A) or with (UT 1B) infection. Such ulcers commonly occur under high-pressure areas (e.g. 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. Key management steps are as follows.

- Callus should be removed with a scalpel to expose the ulcer floor.
- Superficial swabs are of little value in assessing infection: if there is clinical suggestion of infection, deep tissue specimens should be taken from the ulcer base after adequate debridement.[3]
- Radiographs should be obtained to exclude bony infection (if this is found, the ulcer should be considered grade 3).
- Local infections can be treated on an outpatient basis with broad-spectrum antibiotics (e.g. co-amoxiclav 375 or 625 mg orally 8-hourly or clindamycin 300 or 450 mg orally 6-hourly). A particularly useful combination for chronically infected neuropathic foot ulcers is clindamycin (which has good bone penetration) and ciprofloxacin, which provides broad-spectrum antibacterial cover for most commonly found organisms. Unfortunately, there are few robust randomized controlled trials to guide the prescriber in choosing the most efficacious antibiotic in diabetic foot infections.
- 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 can be achieved using a plaster cast (below-knee) or a Scotchcast™ boot (a lightweight, removable, ankle-length cast), which permits mobility but prevents application of pressure over the ulcer area. The gold standard, confirmed in controlled trials, remains total-contact casting, but this should be used only in clinics with sufficient experience of casting insensitive limbs. More recently, use of an 'instant total-contact cast' (a removable cast walker rendered irremovable by wrapping with one layer of casting material) was shown to be as efficacious as the more traditional total-contact cast. Such an offloading device could be used in most clinics, even if no casting technician were available.
- Blood glucose control should be assessed and directed towards normoglycaemia. Insulin is temporarily required in some individuals with type 2 diabetes.

Grade 2

Ulcers are deeper lesions that often penetrate subcutaneous tissue, reaching tendon and/or capsule. Local infection is often present (UT 2B or 2D), but by definition there is no bony involvement. These lesions can be typically neuropathic if located on the plantar surface of the forefoot. Heel ulcers tend to be predominantly neuro-ischaemic (UT 2C or 2D) (Figure 2).

Infection with bacteria (e.g. staphylococci, streptococci, anaerobic bacteria) is common, and isolates are almost always

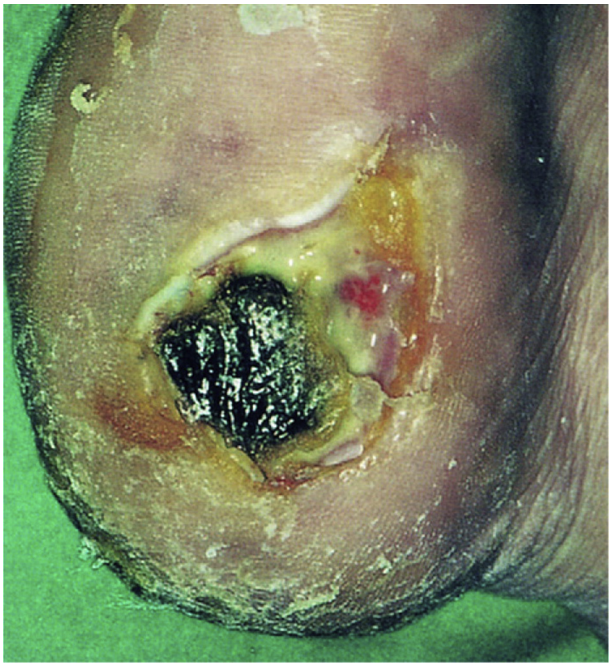

Figure 2 Neuro-ischaemic ulcer (UT grade 2D) on the lateral area of the left heel. This partially painful ulcer was caused by inappropriate footwear. Examination revealed absence of pain sensation, a cool foot and absence of pulses. Doppler studies suggested a proximal obstructive lesion, which was confirmed 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.

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 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

These ulcers (Figure 3) 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 if indicated in moderate to severe cases
- 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. amoxicillin: 500 mg 6-hourly plus flucloxacillin, 500 mg 6-hourly plus metronidazole, or 400 mg 8-hourly; OR clindamycin, 300–450 mg 6-hourly plus ciprofloxacin, or 500 mg -750 mg 12-hourly) is often given initially
- non-invasive assessment of peripheral circulation, using Doppler ultrasonography
- radiology of the foot

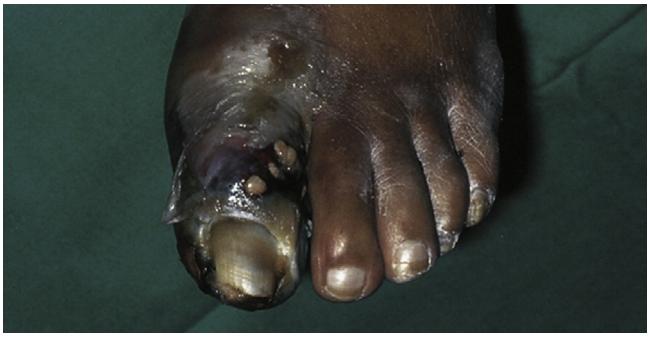

Figure 3 Osteomyelitis of the great toe. Osteomyelitis was confirmed on a radiograph, and it was possible to probe to bone. This ulcer is therefore UT grade 3B and, because of involvement of both proximal and distal phalanges with a septic arthritis of the interphalangeal joint, the toe was amputated.

- surgical opinion – if arterial inflow is satisfactory, local surgery with removal of infected bone (e.g. ray excision for osteomyelitis of a metatarsal head) may be indicated (see below); if there is proximal arterial disease, angioplasty or bypass surgery may be indicated before radical local surgery can be attempted
- care of the other foot to avoid pressure ulcers on the heel.

There is increasing evidence that UT grade 3B lesions (i.e. without vascular disease) can respond to long-term antibiotic treatment without the need for surgery or hospital admission.[4] A recent randomized comparative trial of antibiotics versus conservative surgery for localized diabetic foot osteomyelitis showed similar outcomes in the two groups.[3] An accompanying review suggests that, in selected cases, antibiotic therapy alone can be curative, but this should currently be restricted to individuals without necrotizing soft tissue infections or peripheral arterial disease, and probably to those with only forefoot involvement. Further studies in this area are clearly indicated.

Readers are referred to a recent review on the conservative management of diabetic foot osteomyelitis:[4] many cases of localized disease can be managed with oral antibiotics for a period of 6–8 weeks, together with appropriate offloading if indicated, and standard wound care.[4] There is also no evidence to suggest that parenteral (intravenous) antibiotics are superior to oral therapy.

Peripheral arterial disease and gangrene

Whereas there is no doubt that PAD is more common in patients with diabetes, screening methods effective in non-diabetic patients are less reliable in diabetes, particularly in the presence of neuropathy. Qualitative Doppler waveform analysis and toe-pressure measurement have been shown to be the best measures.

PAD in diabetes is more severe, is more likely to affect distal vessels and is associated with a poorer outcome than in non-diabetic patients. However, any patient with PAD associated with worsening claudication, rest pain or ischaemic ulceration should undergo angiography with a view to angioplasty or bypass surgery. Distal bypass surgery can safely be undertaken in patients with diabetes and is associated with a high likelihood of saving the limb. However, in younger patients (<40 years), long-term graft survival and life expectancy are poor, particularly in the presence of renal disease.

Gangrene (Figure 2) often results from ischaemia in combination with neuropathy, giving rise to a neuro-ischaemic foot. The principles of management are similar to those of the lesions described above, but urgent assessment of the peripheral circulation and the opinion of a vascular surgeon are indicated. Angioplasty or bypass surgery can be required if arteriography reveals a suitable stenotic lesion. Once the peripheral circulation is adequate, local surgery to remove gangrenous areas may be attempted, although 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 neuro-ischaemic 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.

Aftercare

It is essential to remember that hospitalized patients with diabetes are at potential risk of further insensitive ulceration, particularly if bed rest is prolonged. Protection of the heels and other pressure points is of paramount importance, and 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 (CN)

CN is non-infective arthropathy in a well-perfused, insensitive foot. It is a progressive condition characterized by joint dislocations, pathological fractures and debilitating deformities. It results in progressive destruction of bone and soft tissues and, in its most severe form, can cause significant disruption of the bony architecture and result in amputation.

Recent advances have increased understanding of the mechanisms involved in the pathogenesis of osteopenia and osteoporosis, and the central role of the receptor activator of nuclear factor κB/osteoprotegerin (RANKL/OPG) signalling system. This has led to the suggestion that acute CN might be triggered in a susceptible individual by an event that leads to localized inflammation in the affected foot, resulting in a vicious cycle with increasing bone breakdown. The neuro-arthropathy is usually precipitated by minor trauma in the presence of insensitivity, peripheral sympathetic dysfunction and an adequate arterial inflow. The patient with acute CN 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 urgently assessed.

There is increasing evidence that patients who have undergone pancreas or simultaneous pancreas–kidney transplants are at high risk of developing foot problems, particularly CN. Regular screening of these high-risk individuals is therefore indicated.

Investigation

Early radiographs can be normal. Later changes include fractures, osteolysis, fragmentation, new bone formation and disorganized joints. During the active (destructive), phase, which can last for several months, CN can be difficult to distinguish from osteomyelitis, which has similar radiographic features. An indium-labelled white blood cell scan or magnetic resonance imaging of the foot is very helpful in distinguishing infective from neuro-arthropathic causes.

Management

In the acute phase, there is evidence that offloading 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 be started immediately, and be continued until the swelling and hyperaemia have resolved and the skin temperature differential is 1°C or less. Custom-moulded shoes with insoles are subsequently indicated.

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

The foot in remission

Unfortunately, recurrence is common even after resolution of a foot ulcer or acute CN.[1] Recurrence rates after ulcer healing can be as high as 40% after 1 year and 65% after 5 years. Individuals with CN have up to a 50% chance of developing the same problem in the contralateral foot, and are also at very high risk of ulceration in either foot. Thus, the concept of 'remission' may be preferable to 'healing'.[1] Analogous with cancer, remission alerts the patient to the possibility or even likelihood of a subsequent ulcer developing.

The future

Extensions of 21st-century technology may help in the prevention of ulcers, especially recurrent ones. It is well known that a preulcerative neuropathic foot heats before it ulcerates, as a consequence of inflammation.[1,5] Thus, a novel remote foot-temperature monitoring system (in the form of a wireless daily-use thermometric foot mat) has been shown to predict impending foot ulcers. Using an asymmetry of 2.2°C, the system correctly identified 97% of observed ulcers.[5] In-shoe pressure and/or temperature sensors may help to identify impending ulceration. Similarly, 'smart socks' have been developed that can warn the patient of impending foot lesions. This rapidly expanding area has thus opened up new opportunities in preventive foot care.[5] ◆

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

A 45-year-old man presented with a 5-day history of progressive painless swelling of his left foot. He had a 32-year history of type 1 diabetes. He worked as a postman and had a 3-mile delivery round each day. On clinical examination, he had a hot, swollen foot with loss of sensation of pain, temperature and vibration in both feet and ankles. The swelling extended just above the malleolar level. He walked without a limp and he could not recall a history of injury.

What is the first step in his management?

A Arrange for venous Doppler studies to exclude a deep vein thrombosis
B Arrange for a plain X-ray of his left foot and ankle
C Provide him with a removable offloading device
D Check his erythrocyte sedimentation rate and C-reactive protein concentration
E Request an urgent magnetic resonance scan of the left lower leg

Question 2

A 64-year-old woman presented with a 5-day history of an ulcer on the plantar surface of her right hallux. She had a 10-year history of type 2 diabetes. Although she was experiencing no pain, she complained of a malodorous discharge.

On clinical examination, she had a swollen, warm sausage-shaped hallux with erythema, and a distal plantar ulcer surrounded by thick callus and discharging yellow pus. There was also some swelling of the dorsum of the foot. She had a dense neuropathy, and the dorsalis pedis pulse could not be palpated. The posterior tibial pulse was present. It was possible, using a metal probe, to probe the distal phalanx.

What is the most likely diagnosis?

A Acute Charcot neuro-arthropathy with an infected neuropathic ulcer
B Osteomyelitis in a neuropathic foot
C Gout
D A neuro-ischaemic infected ulcer
E Osteomyelitis in a neuro-ischaemic foot