What is the diabetic foot?

The rising prevalence of diabetes worldwide will mean an increasing prevalence of complications such as those of the extremities.

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In 2007 the International Diabetes Federation estimated that worldwide approximately 246 million people or 5.9% of the 20 - 79 age group had diabetes. This estimate is expected to increase to 380 million or 7.1% of the population by 2025. About 80% of these diabetics live in developing countries. Type 2 diabetes accounts for 85 - 90% of cases in developed countries, and an even higher proportion in developing countries.[1] We can expect to see a massive increase in the complications related to diabetes as a result of this increasing prevalence, which is coupled with an ageing population that are living longer.

The American Diabetes Association defines the diabetic foot as the anatomical area below the malleoli in a person with diabetes mellitus. The diabetic foot may be defined as a group of syndromes in which neuropathy, ischaemia and infection lead to tissue breakdown, resulting in morbidity and possible amputation (World Health Organization, 1995).[2]

Foot complications (Table I) account for more hospital admissions than any other diabetic complication. The major adverse outcomes of foot complications are foot ulcers and amputations. It is estimated that 15% of diabetics develop a foot ulcer within their lifetime and that up to 70% of all non-traumatic amputations in the world occur in diabetics.[3] Many of these amputations are preventable as 85% are preceded by a foot ulcer.

Table I. Foot complications in diabetes[2]

Peripheral neuropathy	20 - 40% of patients with diabetes
Peripheral vascular disease	20 - 40% of patients with diabetes
Foot ulceration	5% of patients/year
Foot infection and osteomyelitis	22 - 66% of foot ulcers
Amputation	0.5% of patients with diabetes/year
Charcot's neuroarthropathy	0.1 - 0.4% patients with diabetes/year

Leg amputations are associated with an increased mortality in patients with diabetes. There is a 10% perioperative mortality rate, while 30% die within 1 year, 50% within 3 years and up to 70% within 5 years.[1] This is usually due to the severe cardiovascular and renal co-morbidities that exist in diabetics requiring an amputation.

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Pathogenesis of diabetic foot ulcers

A number of contributory factors work together to cause foot ulceration in patients with diabetes (Fig. 1). These include peripheral neuropathy, peripheral vascular disease, foot deformities, external trauma and peripheral oedema. With the exception of trauma, it is usually a combination of problems rather than a single risk factor that causes ulceration. One of the commonest combinations causing ulceration is peripheral neuropathy, foot deformity and trauma. The commonest cause of trauma in Western countries is inappropriate footwear (Fig. 2).[5]

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Peripheral neuropathy

Of longstanding diabetic patients, 20 - 40% develop peripheral neuropathy. This is related to hyperglycaemia-induced metabolic abnormalities. There is an accumulation of intracellular sorbitol and fructose, resulting in a reduction in the production of nerve cell myo-inositol, required for normal nerve conduction. There is also a decrease in the nicotinamide adenine dinucleotide phosphate stores necessary for deactivation of reactive oxygen species and production of nitric oxide. This results in increased oxidative stress and vasoconstriction, resulting in ischaemia and further nerve dysfunction.[6]

Neuropathy in diabetic patients affects the sensory, motor and autonomic components of the nervous system.

Sensory symptoms vary from patient to patient but common complaints are numbness, paraesthesiae, hyperaesthesia, tingling and pain beginning in the toes and soles of the feet and progressing over months or years to involve the whole foot, ankle and lower shins. Sensory symptoms are often worse at night and patients commonly find that moving, standing or walking alleviates the pain.[7] Loss of sensation is one of the strongest risk factors for ulceration. Patients are unable to detect trauma or discomfort and as a result wounds often go unnoticed and progressively deteriorate as the area is subjected to repetitive pressure and shear forces from walking and weight bearing.[6]

Damage to the **motor** nerves to the intrinsic muscles of the foot results in an imbalance between flexion and extension. This causes foot deformities that result in abnormal pressure areas that gradually cause skin breakdown and ulceration. A common example is the claw toe deformity, which is caused by the constant flexion of the toes.

Autonomic neuropathy causes decreased function of the sebaceous glands of the foot resulting in decreased oil and sweat secretions. As a consequence the foot loses its ability to moisturise the skin and becomes dry and susceptible to cracks and subsequent infection. Autonomic nerve dysfunction also affects local blood flow regulation by abnormally dilating the arteriovenous (AV) shunts (which are located in the soles, but not in the dorsum of the feet). These AV shunts, which are usually kept tightly shut, dilate in cold weather to direct blood away from the surface of the skin back toward the central (core) part of the body. With autonomic dysfunction, the shunts dilate and blood bypasses the surface of the skin, causing a decrease in the integrity of the skin and aiding its becoming dry. The combination of poor natural lubrication and reduction in blood flow to the soles of the feet allows the skin to become dry and cracked, form fissures and become hard.[7] The clinical features of a neuropathic foot are shown in Fig. 3.

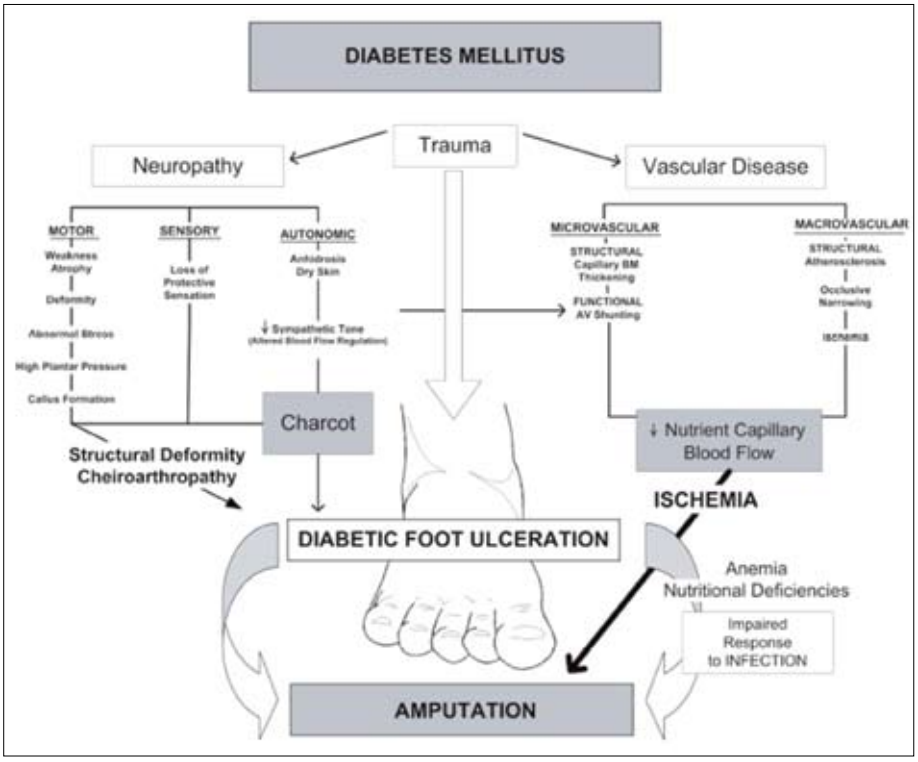

Fig. 1. Common pathway to foot ulceration and amputation. (Reprinted from Frykberg RG, et al. J Foot Ankle Surg *2006; 45(5): S1-S8, with permission from Elsevier.)*

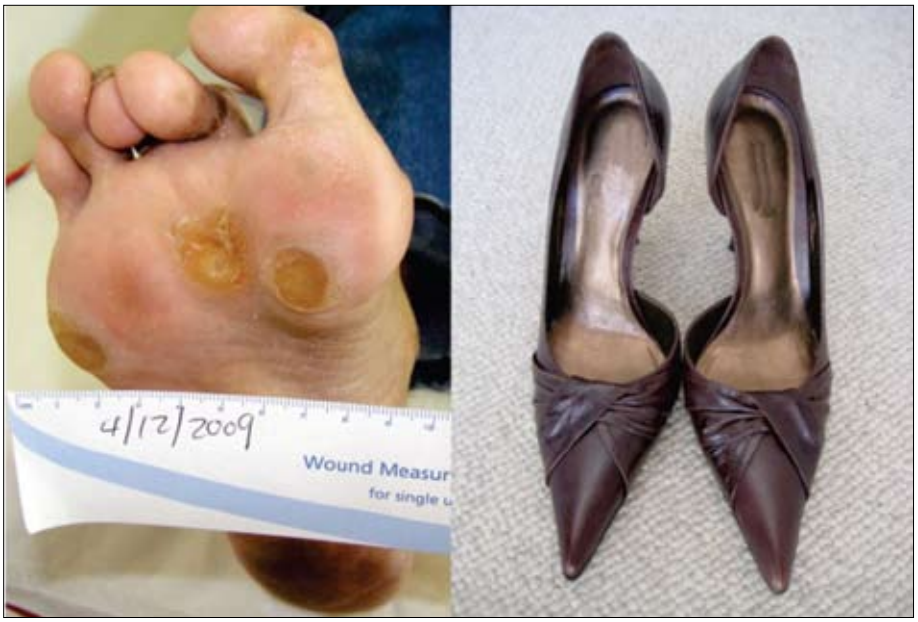

Fig. 2. Naughty and not-no-nice: inappropriate footwear for a neuropathic diabetic foot.

Peripheral vascular disease (PVD)[1]

The arteries in a diabetic are affected by two disease processes, namely atherosclerosis and (Monckenberg's) medial sclerosis. Atherosclerosis causes ischaemia by narrowing and blocking the arteries. Medial sclerosis is calcification of the media of the artery and causes rigid vessels without narrowing the lumen. It does not cause ischaemia, but does interfere with the measurement of Doppler pressures as it results in falsely high readings.

As many as 20 - 40% of patients with diabetes have peripheral vascular disease and up to 50% of patients with a foot ulcer have signs of PVD. Ischaemia secondary to peripheral vascular disease is the most important factor related to the outcome of a diabetic foot ulcer. There are no atherosclerotic lesions specific to diabetes, although the pattern of atherosclerosis is slightly different. The most noticeable differences compared with non-diabetics are:

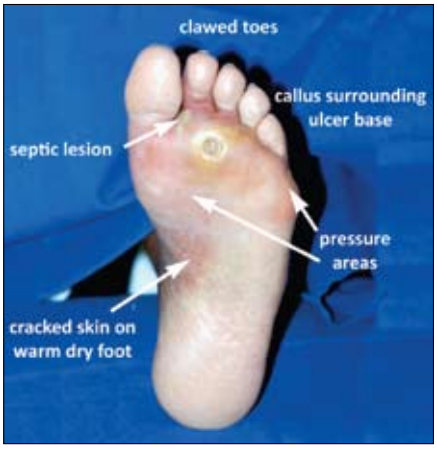

Fig. 3. Clinical features of a neuropathic foot.

- it affects younger patients
- it tends to affect smaller vessels below the knee with relative sparing of aorto-iliac segments
- it is more aggressive
- its progression is faster
- there is no sex difference.

The presence of peripheral vascular disease in diabetics is related to the traditional vascular risk factors, which include smoking, hypertension, older age and hyperlipidaemia. The level of glycaemic control has also been shown to play a role, with a 26% increase in the risk of PVD for every 1% increase in HbA_{1c}.[2] End-stage renal disease is also a risk factor.

Neuropathy in diabetic patients affects the sensory, motor and autonomic components of the nervous system.

The majority of patients with clinically detectable PVD are asymptomatic. Less than 25% with significant disease report intermittent claudication. End-stage symptoms are ischaemic rest pain (especially at night) and ulceration/gangrene. Many of these patients, however, may not experience any pain despite extensive tissue loss because of sensory loss due to their peripheral neuropathy.

Soft-tissue infection and osteomyelitis

Soft-tissue infection in the foot of a diabetic almost always represents a complication of a breach in the integrity of the skin rather than a primary process. When infection complicates an existing wound it often triggers deterioration in the wound, which may be slow or rapidly progressive. Although most infections stay superficial, they can spread to muscle, joints and bone. Unchecked infection can precipitate tissue necrosis and gangrene, especially in an

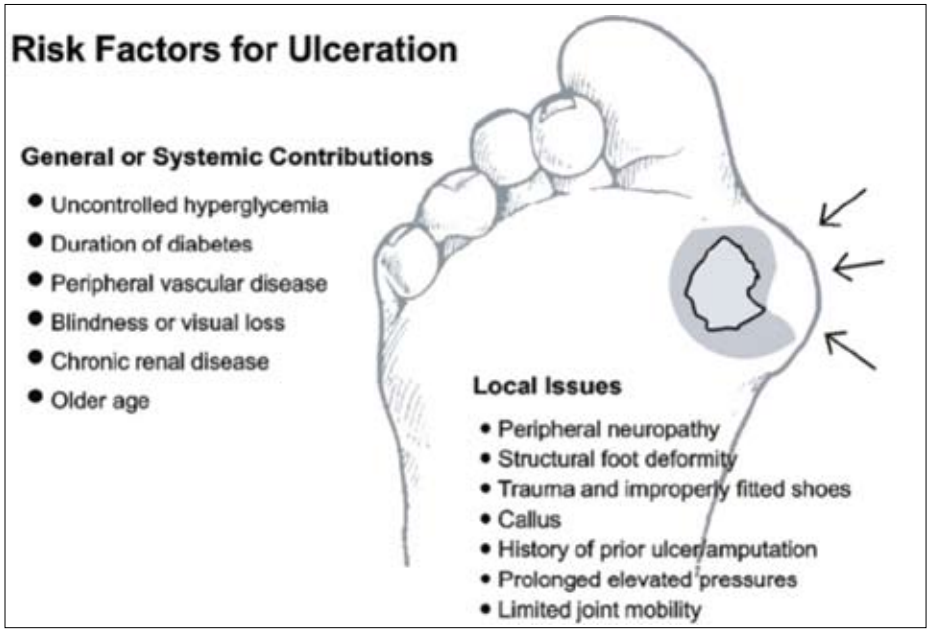

Fig. 4. Risk factors for foot ulceration.(Reprinted from Frykberg RG, et al. J Foot Ankle Surg ***2006; 45(5): S1-S8, with permission from Elsevier.)***

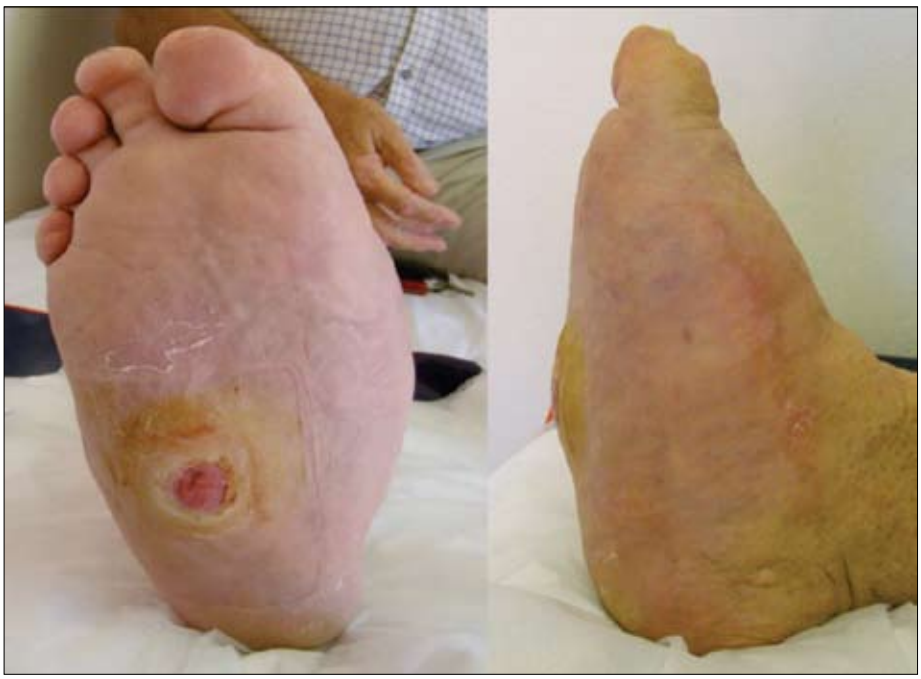

Fig. 5. Charcot's foot with rocker-bottom foot deformity and plantar ulcer (picture courtesy of Sr Anne Berzen).

ischaemic limb. Although infection does not cause ulceration, it can impair healing and lead to further tissue loss and is a major precipitating factor leading to limb loss.[8]

Thus, when faced with a foot ulcer, a major priority is to diagnose or exclude bacterial infection and institute appropriate antibiotic treatment when indicated. The diagnosis of infection is made clinically, based on signs of inflammation, and is not a microbiological diagnosis. A wound is infected when there are systemic signs of infection (fever, leukocytosis, raised inflammatory markers), or pus, or 2 or more signs of local inflammation (erythema, warmth, swelling, induration, pain, tenderness).[9] The purpose of obtaining a wound culture is to identify sensitivity to antibiotics of possible infecting organisms, rather than diagnosis. Wound samples should ideally be from curettage or wound biopsy as superficial swabs are often contaminated by colonising flora and fail to identify infecting organisms.[8]

The possibility of underlying **osteomyelitis** should be considered when underlying bone is exposed or can be palpated with a blunt probe or in any chronic non-healing wound. Bone is infected in up to 20% of patients with foot ulcers who present to specialised wound clinics. The majority of cases are due to contiguous spread from an adjacent soft-tissue infection. The diagnosis of osteomyelitis can be difficult, especially when trying to differentiate it from an acute Charcot's foot. Diagnosis is generally based on the combination of clinical signs of infection with evidence of underlying bone disruption or inflammation on specific imaging tests. Wound swabs are not useful for demonstrating underlying bone infection – pus or bone samples need to be obtained. Although plain X-ray is the first line of imaging, characteristic changes of bone destruction can take 2 weeks or longer to develop and do not occur until 30 - 50% of bone has been destroyed.[10] Nuclear medicine scans such as technetium bone scan or indium-labelled leukocyte scans are more sensitive than plain radiology but are nonspecific and less accurate than MRI, which can demonstrate soft-tissue inflammation and bone marrow oedema.

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Foot ulceration

A number of systemic and local risk factors have been identified that increase the risk of ulceration (Fig. 4).

Approximately 50% of people with diabetes who present at dedicated foot clinics have neuropathic feet and approximately 50% have neuro-ischaemic feet.

Although infection does not cause ulceration, it can impair healing and lead to further tissue loss and is a major precipitating factor leading to limb loss.

Neuropathic feet have good circulation and are warm, numb, dry, usually painless and have palpable pulses. Neuropathic ulcers, mainly on the soles of feet, and neuropathic (or Charcot) joints are the two main complications that may result.[2]

Neuro-ischaemic feet are cool and pulses are absent. Ischaemic rest pain, ulceration at the edges of the foot from localised pressure damage, and gangrene may occur in addition to neuropathic complications.[2]

Charcot's foot

Charcot's foot (neuropathic osteoarthropathy) is a rare condition that complicates diabetic neuropathy. It is a progressive condition characterised by joint dislocation, pathological fractures and severe disruption of foot architecture. This leads to debilitating foot deformity, increased risk of ulceration and even amputation (Fig. 5). Both sensory and autonomic peripheral neuropathy are believed to be prerequisites for the development of Charcot's foot: sensory neuropathy allows repeated insensate injury to go unnoticed and autonomic dysfunction in the absence of proximal arterial disease results in increased blood flow to bone with AV shunting and increased bone resorption.[5]

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The acute phase of the Charcot's foot is often precipitated by minor trauma. It is characterised by mild pain, swelling, local heat, erythema, joint effusion and bone resorption. The clinical picture may be nonspecific and difficult to distinguish from acute gouty arthritis, osteoarthritis, cellulitis and septic arthritis.[7] It is important to differentiate from infection, which may be suggested by an increase in ESR and CRP. If not treated promptly, osteolysis, osteopenia and ligament laxity occur, resulting in gradual remodelling, chronic deformity and fusion of bones in abnormal positions.[10] Early diagnosis, offloading and joint immobilisation may prevent chronic complications.

Conclusion

Disease of the foot remains a major and common complication of diabetes. It is difficult and expensive to treat and is associated with potentially devastating medical, social and psychological consequences. The rising epidemic of diabetes in the world, especially in the developing world, will ensure that the incidence of foot complications will continue to increase in the diabetic population. Early detection of the at-risk foot and prevention of complications that may lead to an amputation is the key to future management.

References available at www.cmej.org.za

In a nutshell

- The diabetic foot may be defined as a group of syndromes in which neuropathy, ischaemia and infection lead to tissue breakdown.
- Diabetic foot problems are the commonest cause of hospitalisation in diabetics.
- Diabetes is the commonest cause of non-traumatic amputations in the world: many are preventable if the at-risk foot is identified and treated early.
- With the exception of trauma, it is usually a combination rather than any single risk factor that causes ulceration.
- Neuropathy in diabetic patients affects the sensory, motor and autonomic components of the nervous system.
- The majority of patients with clinically detectable peripheral vascular disease are asymptomatic.
- Ischaemia secondary to peripheral vascular disease is the most important factor determining the outcome of a diabetic foot ulcer.
- The diagnosis of infection is made clinically, based on signs of inflammation, and is not a microbiological diagnosis.
- Osteomyelitis may be difficult to differentiate from the acute Charcot's foot.
- Early diagnosis, offloading and joint immobilisation of the acute Charcot's foot may prevent chronic complications.

Single suture

Dead is dead

One clinical examination should be enough to establish whether a person has no brain activity. A second test is not only unnecessary, but also makes organ donation less likely.

So says Eelco Wijdicks of the Mayo Clinic in Rochester, Minnesota, whose study is challenging guidelines for diagnosing brain death in certain US states. New York, for example, recommends using two clinical exams 6 hours apart.

Wijdicks and colleagues reviewed the cases of 1 311 people diagnosed as brain-dead at 100 New York hospitals. Each person had two examinations with an average time interval of 19 hours.

No brain function returned, and viable organ donors fell from 57% to 45% as the time between the exams increased. Organ donation was no longer an option in about 12% of cases because of cardiac arrests between or after the exams. During this time, family opposition to donation increased from 23% to 36%.

The researchers think that refusal to allow donation could be a result of stress and sense of uncertainty that families experience when having to wait for multiple diagnoses.

The American Academy of Neurology has updated its guidelines on brain death, developed in 1995, to recommend only one examination.

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