

The Pathway to Foot Ulceration in Diabetes

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KEYWORDS

- Diabetic foot ulceration • Diabetic neuropathy • Peripheral vascular disease
- Foot pressures • Risk factors

KEY POINTS

- Risk factors for foot lesions include peripheral and autonomic neuropathy, peripheral vascular disease, history of ulceration or amputation, other microvascular complications (particularly end-stage renal disease on dialysis), foot deformity, and abnormalities of foot pressures.
- Peripheral neuropathy, foot deformity, and trauma (often from ill-fitting footwear) represent the commonest causal pathway to foot ulceration.
- All patients with diabetes require an annual foot screen, and those found to be at risk require specialist foot care and preventive foot-care education.
- Recent developments in foot screening include the Ipswich Touch Test, the Vibratip, and the Neuropad. An understanding of the implications of the loss of protective sensation is essential if we are to succeed in reducing the all too high incidence of foot problems in diabetes.

INTRODUCTION

*“Coming events cast their shadow before”
—Thomas Campbell.*

Foot ulcers in diabetic patients are common but eminently preventable, and occur in both main types of diabetes. From a global perspective, although diabetic foot ulcers (DFU) are seen in every race and country, the pathways resulting in foot lesions do vary according to the geographic location. It has been estimated that the lifetime risk of a patient with diabetes developing a foot ulcer may be as high as 25%,¹ and at any one time in Western countries 2% to 3% of diabetic patients are likely to have active foot ulceration.^{2,3} It has also been estimated that up to 80% of all amputations in diabetes are preceded by DFU, therefore any success in reducing the incidence of DFU will also

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have some impact on amputation rates. A thorough understanding of the pathways leading to foot ulceration is therefore vital if any reduction in the incidence of these feared complications is to be achieved. The words of Campbell, although clearly not referring to foot ulceration or amputation, can be applied to the etiopathogenesis of foot ulceration. There are many “shadows” or signs that may be detected in patients with diabetes that would suggest they may be at increased risk of developing foot lesions. DFU rarely occur spontaneously, so it is a combination of several contributory factors that ultimately result in the development of an ulcer. Foot ulceration invariably occurs as a consequence of an interaction of specific abnormalities in the lower extremity acting in conjunction with environmental hazards. Lower extremity problems are one of the commonest precipitants of hospitalization in diabetic patients, and there are therefore potential economic benefits to be gained by preventive strategies. The cost of DFU has been reviewed,⁴ and the potential economic benefits of prevention strategies have been calculated.⁵

Several contributory factors that are important in the pathogenesis of DFU are considered in this review, followed by a description of the pathways that might result in ulceration. The value of screening for patients with diabetes for risk factors for foot ulceration and potential preventive strategies are then discussed; finally, the challenges of living with sensory loss are explained.

ETIOPATHOGENESIS OF DIABETIC FOOT ULCERATION

As already noted, DFU rarely result from a single pathologic factor; the large number of potential contributory factors that might result in breakdown of the high-risk foot are discussed in this section (Fig. 1). The breakdown of the diabetic foot was traditionally considered to result from an interaction between peripheral vascular disease (PVD), distal symmetric polyneuropathy, and infection. However, whereas both PVD and

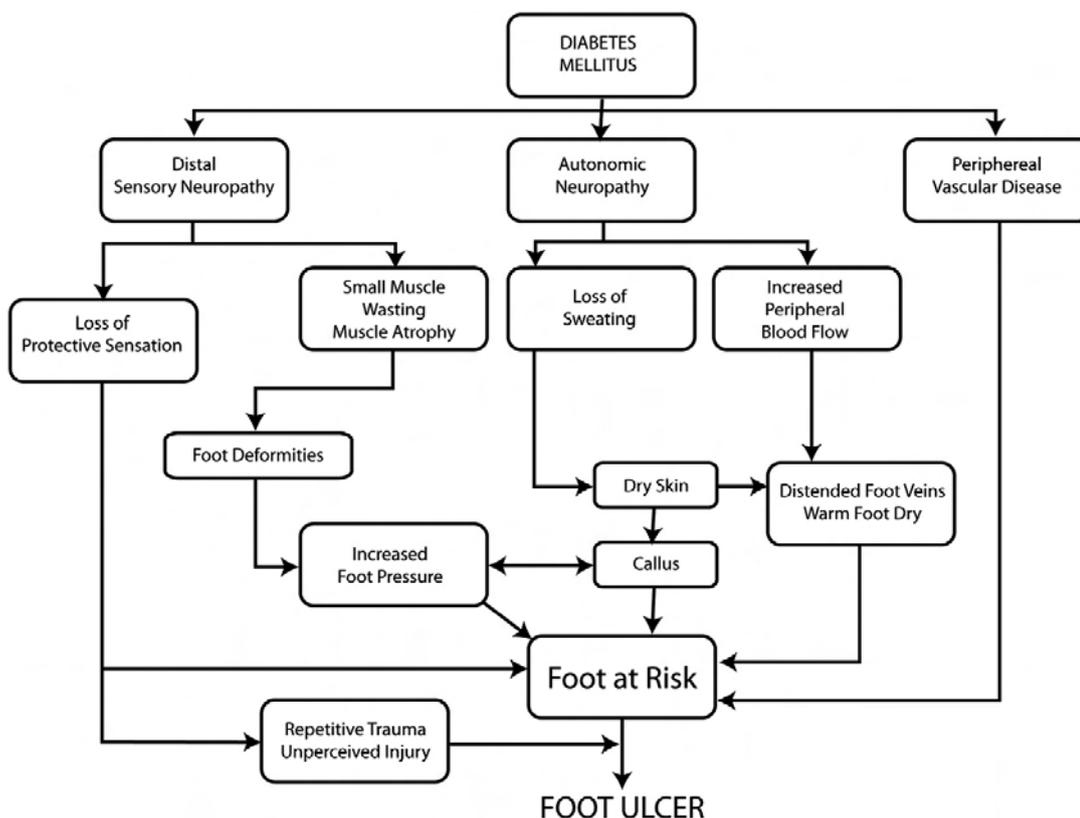


Fig. 1. Potential pathways to diabetic foot ulceration.

neuropathy are confirmed risk factors for foot ulceration, there is no evidence that infection is a contributory factor; rather, infection occurs as a result of ulceration. Thus, the question of infection in the diabetic foot, discussed in detail articles elsewhere in this issue, are not further described in this article.

Peripheral Vascular Disease

That PVD is common in patients with diabetes has been confirmed by large epidemiologic studies.⁶⁻⁸ The DARTS Study from Scotland confirmed the enormous burden of macrovascular disease in type 2 diabetes, and showed that the incidence rates of peripheral vascular disease per 1000 patients in this population-based study were 5.5 for type 1 diabetes and 13.6 for type 2 diabetes.⁶ The large National Health and Nutrition Examination Survey reported the prevalence of PVD in the general population of the United States to be 4.3%, and having diabetes was positively associated with prevalent PVD (odds ratio 2.8).⁷ In the Fremantle Diabetes Study, a population-based study of peripheral arterial disease in type 2 diabetes in Australia, the reported prevalence for PVD in this population was 13.6%. In a 5-year follow-up, the incidence of new PVD was 3.7 per 100 patient-years.⁸ Prevalent and incident PVD were both strongly and independently associated with other factors such as total serum cholesterol and smoking. In the Fremantle Study, PVD was also shown to predict cardiac death.⁸ In most studies of PVD in diabetes, simple screening techniques such as foot pulse evaluation and using a handheld Doppler stethoscope to calculate the ankle brachial index (ABI) have frequently been used.⁹ However, peripheral arteries in the diabetic patient frequently have medial and intimal calcification, resulting in higher ankle pressures and falsely elevated ABIs (**Fig. 2**). Therefore, measurement of toe pressures may be more reliable.⁹

In the pathogenesis of ulceration, PVD in isolation is rarely a cause of ulceration: as with neuropathy, a combination of risk factors with minor trauma more commonly leads to ulceration. A frequent scenario is a minor injury and subsequent infection, both of which go unnoticed because of coexistent neuropathy that increases the demand for blood supply beyond the circulatory capacity; neuroischemic or ischemic ulceration, and the risk of amputation, follow. In the last 2 decades there has been a change in the patterns of ulceration seen in Western countries, with the previously predominant neuropathic ulcer having been replaced by the neuroischemic ulcer as the most frequently seen in many clinics.¹⁰ In the Eurodiale Study, more than 1000 consecutive patients presenting to specialist foot clinics in 14 European hospitals in 10 countries were investigated. PVD was present in nearly half of all subjects, with infection in more than half, and more than one-third had both PVD and infection. This finding suggests that ischemia is increasingly common in the pathogenesis of diabetic foot ulcers, often in combination with neuropathy.¹⁰ In a follow-up of the Eurodiale Study, the presence of infection and peripheral arterial disease (PAD) emerged as a predictor of nonhealing.¹¹ This finding led the investigators to propose that DFU with or without concomitant PVD should be defined as 2 separate disease states. When assessing determinants of minor amputations in diabetes, PAD, as well as ulcer depth and male sex, was a significant predictor of amputation, suggesting that early referral of patients to a diabetic foot clinic is indicated in those with PVD and infection.¹²

In summary, PVD is a common contributory factor to the genesis of DFU in diabetic patients. Although the role of blood glucose in the genesis of macrovascular disease is controversial, there is no doubt that educational strategies aimed at the cessation of smoking and control of hypercholesterolemia remain extremely important in the prevention of PVD in diabetes.



Fig. 2. Radiograph of the foot of a neuropathic diabetic patient showing extensive medial arterial calcification down to the digital vessels. Such calcification is also present in larger proximal vessels, and will lead to false elevation of the ankle brachial index.

Diabetic Peripheral Neuropathy

The diabetic neuropathies are among the commonest of all the long-term diabetic complications, and may present with diverse clinical manifestations.¹³ One of the important functions of the sensory peripheral nervous system is to protect the extremities from injury: small afferent nerve fibers carry the sense of pain and temperature, whereas larger fibers conduct sensory abnormalities including vibration and sensation of joint position. Chronic sensorimotor diabetic peripheral neuropathy (DPN) is the commonest of all the neuropathies and this, together with peripheral autonomic sympathetic neuropathy, plays an important part in the development of foot ulceration. Much about the pathogenesis and management of insensitive foot lesions has been learned from the writings of Paul Brand, a surgeon working with leprosy patients in South India in the last century. It was Brand who described pain as “God’s greatest gift to mankind.” Although the pathologic causes of sensory loss in leprosy in diabetes are very different, the end results are the same, namely the insensitive high-risk foot. Sympathetic autonomic neuropathy affecting the lower extremities leads to reduced sweating, resulting in dry skin that is prone to crack or fissure but also to increased blood flow (in the absence of PVD) caused by the release of sympathetic controlled vasoconstriction. That both DPN and peripheral sympathetic neuropathy are important in the genesis of foot ulcers in diabetes has been recognized for many years,¹⁴ and each is now described in further detail.

Chronic Sensorimotor Diabetic Peripheral Neuropathy

The frequency of DPN in the diabetic population is well described in both clinic-based¹⁵ and population-based¹⁶ studies, which report a prevalence varying from approximately 25% to 35%. It can be safely assumed that at least half of older type 2 diabetic patients have significant sensory loss.^{13,17} The diagnosis must never be made without a careful clinical examination of the lower limbs, as absence of symptoms can never be equated with absence of signs.¹³

DPN is of gradual or insidious onset, and up to 50% of patients may never experience any typical neuropathic symptoms.¹³ For those who do experience symptoms, the commonest include altered temperature perception (feet feel on fire, burning, or freezing), sharp stabbing electrical-type sensations, paresthesias, and hyperesthesias, all of which are prone to nocturnal exacerbation. Clinical examination typically reveals a sensory deficit in a stocking distribution with signs of motor dysfunction, including small-muscle wasting and absence of ankle reflexes. A well-recognized situation originally described by Ward is the “painful-painless leg,” in which patients experience severe neuropathic symptomatology, but on examination there is loss of sensation to all modalities. Such patients are at high risk of insensitive injury. The explanation for this observation is that there is severe distal loss of nerve fibers, but that electrical (“neuroma”-like) activity proximally is interpreted by the patient as originating from where the peripheral nerve used to innervate.¹⁸

The threshold of sensation that protects normal feet from injury is difficult to define. As described by Brand,¹⁹ the purpose of pain sensation is not to cause discomfort but to enable the body to use its strength to the maximum, short of damage. A person with reduced sensation therefore has not totally lost the ability to perceive pain, but simply feels the discomfort at a higher level of stimulation. It thus requires more pressure or temperature, or more prolonged ischemia, before the residual nerve fibers are activated to warn higher centers. It is therefore important to realize that neuropathic ulceration may occur in patients who still have some ability to perceive stimuli to various modalities. As it is extremely difficult to define a “significant loss of sensation,” or at what level sensory loss becomes “critical,” it is usual therefore to set levels of sensory loss for the purpose of screening conservatively, as it is preferable to have more false positives (ie, those who are identified as being at risk because of sensory loss but in fact have sufficient protective sensation) than false negatives.

DPN is a sensorimotor neuropathy and, although the symptoms are predominantly sensory, motor dysfunction commonly occurs in this condition and is important in the genesis of foot ulceration. A long-term follow-up study of type 1 diabetic patients confirmed that muscular atrophy in DPN occurs early in the feet and progresses steadily, potentially leading to weakness at the ankle.²⁰ Using quantitative tests for the assessment of muscle function, patients with both type 1 and type 2 diabetes have been detected to have weakness at the ankle and even the knee. This motor dysfunction leads to an increased risk of developing foot ulcers, owing to secondary alterations in the biomechanics of the feet caused by muscle atrophy.²¹

Peripheral Sympathetic Autonomic Neuropathy

DPN is typically accompanied by distal sympathetic autonomic neuropathy, signs of which are often found on examination. These signs include dryness of the skin with a propensity to callus formation under high-pressure areas, and a warm foot in the absence of large-vessel PVD. The warm, insensitive, and dry foot that results from a combination of somatic and autonomic dysfunction may provide the patient with a

false sense of security, as most patients have a “vascular model,” believing that most problems in the lower limb occur as a consequence of PVD.

Neuropathy in the Pathway to Ulceration

Although it has been stated for more than 200 years that loss of sensation results in foot ulceration, it is only in the last 2 decades that prospective studies have confirmed that this is indeed the case. The first single-center prospective study to confirm neuropathy as a risk factor for foot ulcers assessed vibration perception threshold (VPT) as measured by the biothesiometer (Biomedical Instrument Co, Newbury, OH, USA) in a population of diabetic patients with no history of ulcers. In a 4-year prospective study, those patients with a baseline threshold above 25 V were 7 times more likely to develop foot ulcers.²² These observations were subsequently confirmed in a larger multicenter study that showed a significant increase in risk with each volt increase of VPT over 25 V.²³ A large study in northern United Kingdom (the North West Diabetes Foot Care Study) followed a cohort of 10,000 patients for 2 years and confirmed, using a simple neuropathy disability score (NDS), that those with an NDS of 6 or more had a 6% annual incidence of first ulcers, compared with 1% in those with a baseline NDS of less than 6.²³ Other prospective trials have confirmed the key role of both large-fiber (proprioceptive/vibration deficits) and small-fiber (loss of pain and temperature sensation) neurologic deficits in the pathogenesis of ulceration.^{13,24}

OTHER RISK FACTORS FOR DIABETIC FOOT ULCERATION

Demographics

1. *Age.* The risk of ulcers and amputations increases with age and duration of diabetes.^{1–3,17} The average age of patients presenting with new foot ulcers tends to be on average 10 years more than in those presenting with new Charcot neuroarthropathy.²⁵
2. *Gender.* The male sex has been associated with a 1.6-fold increased risk of ulcers in most,^{3,4,10,26} but not all² studies from Western countries. Amputation rates also appear to be higher in the male sex²⁶; mechanisms by which the male sex is at greater risk of these lower extremity complications have yet to be explained.
3. *Ethnicity.* Within Europe, it appears that diabetic patients of European origin have higher risks of both foot ulcers and amputations than those patients with Indian subcontinent, Asian, or African-Caribbean ancestry.²⁷ Explanations for these differences, particularly in the Asian population, probably relate to several factors including better foot care in certain religious groups, reduced foot pressures, and the fact that diabetic neuropathy appears to be less prevalent in this population.^{27,28}

Similar data exist in United States populations, with ulceration and amputation more common in Hispanic Americans and Native Americans than in non-Hispanic whites.²⁹ Similarly, amputation rates are higher in African Americans.

History of Foot Ulceration or Amputation

Patients with a history of foot ulcers or amputations are at the highest risk of recurrent foot ulcer. In some series, the annual recurrence rate is as high as 50%. Certainly in the North West Diabetes Foot Care Study, a history of ulcers was the strongest predictor of development of new ulceration.³ A recent systematic review has confirmed the importance of previous ulcer or lower extremity amputation as predictors of future risk of foot problems.³⁰

Other Diabetic Microvascular Complications

1. *Retinopathy*. Not surprisingly, poor vision, mainly as a consequence of diabetic retinopathy, was shown to be a significant predictor of the risk of foot ulceration in the Seattle Diabetic Foot Study (**Box 1**).³¹
2. *Nephropathy*. It has been known for many years that patients at all stages of diabetic nephropathy, even microalbuminuria, appear to have an increased risk of foot ulceration.³² However, the very high risk of ulceration and amputation among patients with end-stage renal disease has recently been the focus of several studies. Game and colleagues³³ first showed a temporal association between the initiation of dialysis treatment in diabetic patients and the increased incidence of foot ulceration. In subsequent collaborative studies between the United Kingdom and the United States, dialysis has been shown to be an independent risk factor for foot ulceration in diabetic patients,³⁴ and the same group also confirmed that the ethnic protection from neuropathy and risk of foot ulcer is lost when diabetic patients of Asian origin are on long-term dialysis therapy.³⁵ Of note, even nondiabetic patients in dialysis units have observed the high risk of foot ulcers and amputations in the dialysis unit: Carey wrote "throughout dialysis, patients suddenly appear with amputations: very often with heavily managed feet rapidly followed by crutches and then wheelchairs."³⁶ Thus diabetic patients on dialysis must be regarded as being at extremely high risk of lower extremity complications, and warrant regular foot-care education and podiatry.

Peripheral edema

The presence of peripheral edema, presumably because of impairment of local blood flow, has been associated with an increased risk of ulceration.³⁷

Callus

The presence of plantar callus, as already noted, a consequence of peripheral sympathetic dysfunction in the neuropathic foot, is strongly associated with risk of ulceration.

Box 1

Risk factors for foot ulceration

- Diabetic neuropathy
 - Distal sensorimotor neuropathy
 - Peripheral sympathetic neuropathy
- Peripheral vascular disease
- Foot deformity
- Callus under weight-bearing areas
- History of foot ulceration
- Previous amputation
- Other microvascular complications
 - Proliferative retinopathy/visual impairment
 - End-stage renal disease
 - Any dialysis treatment
 - Postrenal transplant
- Poor glycemic control
- Smoking

In one prospective study ulceration only occurred at sites of callus, representing an infinite increase in risk.³⁸

Deformity

Deformities are frequently present in the neuropathic foot in diabetes, and may occur as a consequence of an imbalance between flexor and extensor muscles, giving rise to prominence of the metatarsal heads and clawing of the toes.²¹ In the neuropathic foot, Charcot prominences are a not infrequent cause of ulceration, and the presence of other potentially nonrelated abnormalities such as hallux valgus will increase the risk of breakdown in the insensate foot. Prospective follow-up in the North West Diabetes Foot Care Study showed that foot deformities were independently related to the risk of new ulcers.³

THE PATHWAY TO FOOT ULCERATION

As described earlier, a single pathologic factor, such as insensitive feet secondary to diabetic neuropathy, does not itself result in ulceration. It is therefore a combination of risk factors that ultimately results in the pathway to skin breakdown. Pecoraro and colleagues³⁹ and then later Reiber and colleagues³⁷ used the Rothman model for causation, and applied this first to amputation and later to foot ulceration in diabetes. The model used is the concept that a single component cause (eg, neuropathy or foot deformity) is not sufficient on its own to result in ulceration; when several component causes act together, this combines to form a sufficient cause that inevitably will lead to ulceration. In the first study on amputation, 5 component causes were described to lead to amputation: neuropathy, minor trauma, ulceration, faulty healing, and gangrene.³⁹ When applied to the pathogenesis of DFU, several causal pathways were identified, with several component causes working together to result in ulceration. In this particular study, 3 component causes working together (neuropathy, deformity, and trauma) were present in nearly 2 out of every 3 incident cases of ulceration. Most of the other risk factors for foot ulceration (see **Box 1**) also featured as component causes in this observational study.³⁷

Simple examples of a 2-component pathway would be the patient with an insensitive foot that ulcerates after placing his or her foot, which is perceived to be cold, against a radiator (component causes: neuropathy plus thermal injury). An example of a 3-component pathway would be a patient with insensitive feet and clawing of the toes who wears a shoe with an insufficiently deep toe-box and develops dorsal ulcers in the interphalangeal area of the toes (component causes: neuropathy plus deformity plus trauma).

Abnormalities of pressures and loads under the diabetic foot have been recognized for many years,^{1,14} and these may form a component cause on the pathway to ulceration. Pressure ulcers on the plantar surface of the foot are the consequence of pressure that would not normally cause ulceration, but which, because of intrinsic abnormalities of the neuropathic foot, leads to plantar ulceration when repetitively applied. Thus, the combination of insensitivity, abnormally high foot pressures, and repetitive stress from, for example, walking, may lead to breakdown under high-pressure areas such as the metatarsal head region. Autonomic neuropathy leading to dry skin and callus build up at such sites, and can also be regarded as a component cause. A prospective study by Veves and colleagues⁴⁰ observed a 28% incidence of ulceration in neuropathic feet with high plantar pressures during a 2.5-year follow-up period. By contrast, no ulcers developed in patients with normal pressure. Therefore biomechanics, the branch of science concerned with the consequences of forces applied to living tissue, is clearly

relevant to diabetic foot disease because many neuropathic foot ulcers result from repetitive stress that is not perceived by the patient.

Several methodologies that may be useful in research studies are available to assess plantar pressures.⁴¹ Simple, semiquantitative estimation of pressure distribution under the foot can be used in clinical practice. The Pressure Stat or Podotrack is a simple, inexpensive, semiquantitative footprint mat that was validated by comparing with the then gold standard, the optical pedobarograph.⁴² Such a simple, inexpensive, semiquantitative footprint mat has the potential for use as a screening tool for high pressures in clinical practice. The same group described the potential of reducing plantar pressures in patients with active foot ulcers using a pressure-relieving dressing⁴³; no such dressing is yet available for therapeutic use, but the technology could be applied in the future.

Using the Rothman model for causation has provided a better understanding of factors that result in incident ulcers, and suggests the possibility of prevention of foot ulcers by identifying potential component causes and preventing them occurring together in any one patient. Thus, for example, regular podiatry with removal of callus could reduce high foot pressures and remove that single component cause.³⁸ Similarly, use of appropriate orthotics in appropriate footwear can reduce foot pressures.

IDENTIFICATION OF THE FOOT AT RISK OF ULCERATION

“The trouble with doctors is not that they do not know enough, but that they do not see enough”

—Sir Dominic Corrigan.

The words of Corrigan, best known for his description of the collapsing pulse in aortic valve disease, can be usefully applied to the identification of the foot at risk of ulceration in diabetic patients. Brand later observed that the most important step in reducing amputations in diabetes is that every time a patient with diabetes is seen by the physician, the shoes and socks should be removed and the feet examined carefully.¹⁹ It is likely that many patients' feet are not examined because they have no specific complaints; as already noted, up to 50% of patients with diabetic neuropathy may have no symptoms of the condition whatsoever. Again, it was Brand who described that the insensitive foot is not only painless, but often feels as if it does not belong to the individual. Screening for “at-risk feet” is the job of all of those caring for people with diabetes. Every diabetic patient warrants an annual review whereby symptoms and signs suggestive of the development of the late complications of diabetes are assessed. A Taskforce of the American Diabetes Association (ADA) reported in 2008 on what the central components of the Comprehensive Diabetic Foot Examination (CDFE) should be.⁴⁴ The main attributes of the CDFE are now summarized, and recommendations for screening according to the level of care are provided in **Table 1**.

History

Although the medical history is a pivotal component of any risk assessment, a careful examination of the foot remains the key component of the foot check in the diabetic patient.

1. Any history of past or present neuropathic symptoms?
2. History of ulcer or minor/major amputation?
3. Other diabetic complications, especially visual impairment or end-stage renal failure (on dialysis or posttransplant)
4. History of any lower extremity vascular problem (intermittent claudication/rest pain/history of bypass surgery or angioplasty)
5. Social factors (living alone? blood glucose control? cigarette smoking?)

	Primary Care	Secondary Care	Clinical Research
History (eg, past ulcer, neuropathy, peripheral vascular disease)	+++	+++	+++
Clinical examination	+++	+++	+++
Monofilament	+++	++	+
Vibration perception	++	++	+++
Ipswich Touch Test	+++	+	–
Vibratip	++	++	–
Quantitative sensory tests	–	+	++
Neuropad	++	++	+
Electrophysiology	–	–	++
Pressure mat (eg, Pressure Stat)	++	++	++
Quantitative foot pressure	–	+	++

Key: +++, recommended; ++, useful if available; +, occasionally required, –, not indicated.

Clinical Examination: An Essential Component of the Annual Check

1. Inspection after shoes and socks removed
 - a. Skin status: color, thickness, callus, dryness, cracking?
 - b. Normal sweating?
 - c. Any signs of bacterial/fungal infection? Always check between toes
 - d. Any breaks in skin/ulceration?
 - e. Foot deformities: check for Charcot changes/clawing of the toes/prominent metatarsal heads, and so forth
 - f. Foot shape
 - g. Small muscle wasting?
 - h. Skin temperature? Compare both feet. A unilateral warm swollen foot with intact skin should be considered to be an acute Charcot neuroarthropathy until proven otherwise
 - i. Check patients' footwear for suitability
2. Neurologic assessment

The **CDFE report by the ADA⁴⁴** recommends the use of 2 simple tests to identify the patient with loss of protective sensation (LOPS). One of these should be pressure perception using a 10-gauge monofilament, which has been shown in several prospective studies to be a useful predictor of foot ulceration.^{44,45} The recommended sites for assessment of pressure perception are the first, third, and fifth metatarsal heads, and the plantar surface of the distal hallux. The patient should be asked if he or she perceives the sensation of pressure when the monofilament buckles. Failure to detect the perception of pressure at 1 or more sites in each foot would be considered to be an abnormal response.

The result of the monofilament pressure perception test should then be confirmed by using 1 of the following for simple tests of sensory perception:

1. *Vibrating 128-Hz tuning fork*. This vibration should be tested over the apex of the hallux bilaterally, and an abnormal response would occur when the patient fails to perceive vibration.

2. *Pin-prick sensation*. The inability of a patient to detect pin-prick sensation can be tested using a disposal pin, again over the apex of the halluces. An abnormal result would be failure to perceive pin-prick sensation on either tested site.
3. *Ankle reflexes*. Absence of ankle reflexes in either leg would be regarded as an abnormal response.
4. *Vibration perception threshold*. As many Centers in North America and Europe possess a biothesiometer or similar vibration detection instrument, it was agreed that this could be 1 of the 4 other tests required to confirm the monofilament test. Again, this is tested over the apex of the hallux: an abnormal result would be a VPT of 25 V or more as determined by previous studies.^{22,23}
5. *Vascular assessment*. A vascular examination would normally comprise palpation of the posterior tibial and dorsalis pedis pulses: the pulses should be described as being either “present” or “absent”; assessing a pulse as “reduced” is notoriously inaccurate.

Bedside assessment of the circulation using a Doppler ultrasound probe can be useful, although it is recognized that because of arterial calcification as noted earlier, the ABI is less accurate; waveform analysis and toe pressures are likely to be more effective.⁴⁶

Other Assessments

Quantitative sensory testing

Detailed quantitative sensory testing (QST) is not indicated for the annual screen of diabetic patients.⁴⁴ However, vibration perception using the biothesiometer may be helpful if available. Other detailed QST and electrophysiology are generally indicated only in clinical research studies, although they may occasionally be useful in the secondary care (hospital) setting.

Foot-pressure studies

Use of devices such as the Pressure Stat, which is a simple, inexpensive, semiquantitative footprint mat that takes a minute or two to measure plantar pressures, may be helpful in identifying specific high-risk areas under the diabetic foot, but these may also be used as an educational tool.⁴²

Recently Described Screening Tests

Several potentially useful screening tests have been described since the publication of the 2008 ADA CDFE Guidelines, and these are briefly described here.

1. *Ipswich Touch Test (IpTT)*. The simplest of all screening tests, the IpTT was developed to promote more foot screening of inpatients with diabetes. The IpTT simplifies sensory testing to lightly touching the tips of the first, third, and fifth toes of each foot. This simple procedure has been validated by comparing its results with well-validated tests such as the monofilament. On direct comparison, the agreement between the IpTT and the monofilament was virtually perfect ($\kappa = 0.88$; $P < .0001$).⁴⁷ This test may be particularly useful in developing countries where availability of any equipment is limited, and also has the advantage of having no cost whatsoever.
2. **Vibratip (Fig. 3)**. The Vibratip is a pocket-sized disposal device for testing the integrity of the sensory nervous system, and has been specifically designed to overcome barriers associated with other methods such as the high cost for purchase and replacement as well as the requirement for training. A recent study validated

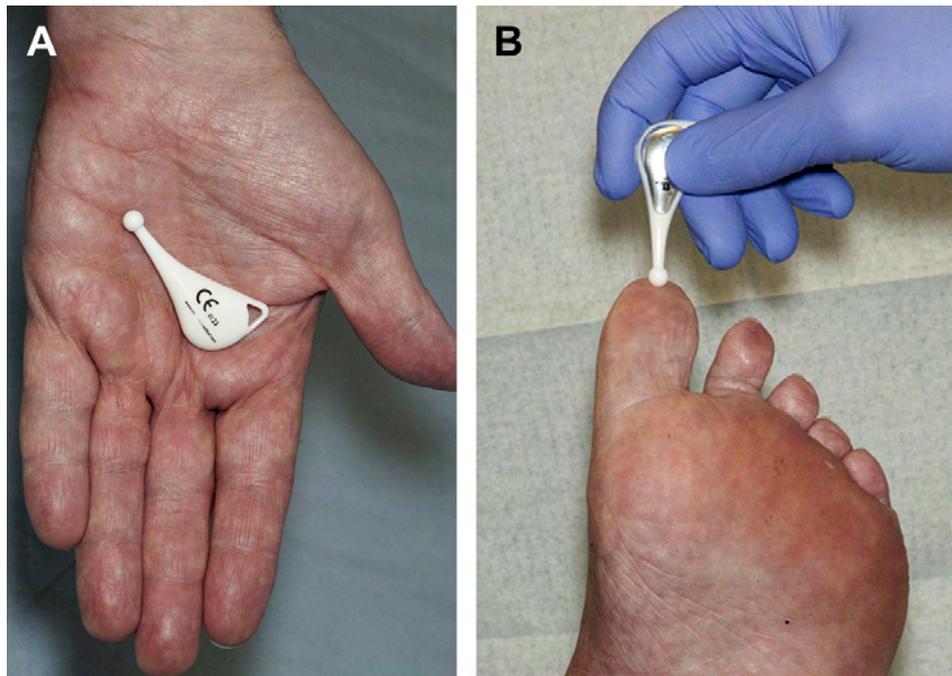


Fig. 3. **The Vibratip**, a new handheld disposal device for testing vibration perception. This battery-operated disposal device is shown in (A). In (B) it is shown being tested on a patient's hallux: Squeezing the top of the device leads to vibration in the tip, which is then reported by the patient. The test is reported as positive (ie, complete loss of vibration perception) or normal (normal vibration perception).

this device by comparing it with gold-standard tests including the monofilament, the NDS, and VPT using the biothesiometer. Again, almost perfect agreement was found when comparing the Vibratip and its ability to predict the risk of ulcers with the other standard tests.⁴⁸

3. **Neuropad.** The Neuropad⁴⁹ is a simple, noninvasive indicator test that has been developed for the assessment of sweating and, hence, autonomic innervation of the diabetic foot. This plaster-like device is applied to the plantar surface of the foot; with normal sweating, callus changes from blue to pink. Absence of sweating results in no color change. The diagnostic ability of Neuropad to identify absent sweating has been shown to have excellent reproducibility, with high sensitivity and negative predictive value. In a study comparing the Neuropad assessment with quantitative sensory and autonomic function testing as well as intraepidermal nerve-fiber density in foot skin biopsies, this test was confirmed to be sensitive in detecting clinical neuropathy.⁵⁰

In summary, there are several well validated tests that can be used in the screening of diabetic patients for evaluation of their risk of foot ulceration. Whereas the simpler tests summarized in the **CDFE**⁴⁴ are entirely appropriate for screening patients in the community, the more sophisticated tests described here might be used in hospital care and in clinical research settings.

SUMMARY

It should now be possible to achieve a reduction in the incidence of foot ulceration and amputations as knowledge about pathways that result in both these events increases.⁵¹ However, despite the universal use of patient education and the hope of reducing the incidence of ulcers in high-risk patients, there are no appropriately

designed large, randomized controlled trials actually confirming that education works. It has been recognized for some years that education as part of a multidisciplinary approach to care of the diabetic foot can help to reduce the incidence of amputations in certain settings.^{52–54} Ultimately, however, a reduction in neuropathic foot problems will only be achieved if we remember that the patients with neuropathic feet have lost their prime warning signal—pain—that ordinarily brings patients to their doctor. Very little training is offered to health care professionals as to how to deal with such patients. Much can be learned about the management of such patients from the treatment of individuals with leprosy¹⁹: if we are to succeed, we must realize that with loss of pain there is also diminished motivation in the healing of and prevention of injury.

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