Nails in diabetes

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We all have our hobbies. Dr William B Bean studied his fingernails for at least 35 years.1 A little unusual perhaps, but our nails have much to teach us.

Nails are made of keratin and grow lifelong. The nail plates protect the nail bed. The nail matrix – the living tissue which produces the nails – is visible as the lunula, the white crescent at the base of the nail. Fingernails grow about 3mm/month or 0.1mm/day; toenails about 1mm/month. Keratin is a strong protein that forms an extensively folded mesh linked by very stable disulphide bonds. It is hard and resistant to injury. There are skin folds at both sides of the nail plate, and at the base where the fold extends into the dead skin cells of the cuticle.2

Infection

Paronychia

This infection of the nail fold can be acute or chronic. In the latter, damage to the cuticle may result in distortion of underlying nail tissues causing spaces that can readily be infected. Infecting organisms include Staphylococcus aureus, Escherichia coli, Proteus vulgaris, and Pseudomonas aeruginosa (which may turn the nail blue-black), as well as yeasts or fungi such as Candida albicans or Candida parapsilosis.3 Over-zealous manicuring may cause injury and a portal for infection, especially in neuropathic fingers.

Fungal nail infections (onychomycosis)

Nail infections with yeasts or fungi are common among people with diabetes – usually affecting toenails.4 White/yellow/greenish discolouration and thickening at the end of the nail spreads gradually to involve the whole nail which may be thick and brittle. The distorted nail can become sharp or break off, and can dig into neighbouring toes. Onychomycosis is a significant predictor of diabetic foot ulcer; hazard ratio 1.58 (1.16–2.16).5 Treatment is lengthy and challenging. Seek early signs to allow prompt treatment.

Circulation

People with diabetes may have some redness around the nails, and, if sought, periungual telangiectasia. It can be difficult to decide if the erythema is simply circulatory or due to paronychia (see above).

The nail folds (the skin from which the cuticle derives) are a window onto the microcirculation via capillaroscopy. People with advanced diabetes show dilated capillaries, although changes may not be seen early in diabetes. In hypertension there is reduced capillary density.6 One study demonstrated reduced microvascular reactivity in patients with later onset type 1 diabetes.7

Infrared fluorescence videomicroscopy showed nail-fold capillary aneurysms in 3/17 healthy controls; and in 7/14 people with type 1 diabetes without retinal microaneurysms and in 10/17 of those with retinal microaneurysms.8

Like other tissues, the nail needs a viable blood supply. Even in early vascular disease, reduced circulation to the nail matrix can cause thin, brittle nails that break and split and then separate from the nail bed (onycholysis). This allows dirt and moisture to get under the nail and facilitates infection. The nail may show longitudinal ridges, koilonychia (see below), general or punctate whitening (leukonychia), and Beau’s line (see below). The nail plate may separate completely, or become distorted (onychogryphosis) leading to very misshapen toenails. Impaired circulation may also cause localised hypertrophy of the nail plate. People with diabetes can also get periungual blisters, haemorrhage and ulceration. They may also show splinter haemorrhages if there have been arterial emboli – but injury is a more common cause.9 With absent circulation, the nail dies like the rest of the tissue.

Neuropathy

Nerve damage can impair nail growth. A man with long-standing diabetes and multiple complications had mono-neuritis multiplex, including bilateral ulnar involvement. The nails of the ring and little fingers on both hands were shortened, yellowish, and fragile.9

Abnormal foot posture and gait secondary to neuropathy or previous surgery may cause toes and toenails to wedge against shoes or each other and become damaged or distorted. In people with sensory neuropathy, toes may be injured during toenail cutting, or subsequently if sharp corners or edges are left. Ingrowing toenails can also cause unsuspected injury and infection.

Terry’s nails

‘Fully developed white nails exhibit a ground-glass-like opacity of almost the entire nail bed. It extends from the base of the nail, where the lunula is indistinguishable, to within one or two millimetres of the distal border of the nail bed, leaving a distal zone of normal pink. The condition is bilaterally symmetrical, with a tendency to be more marked in the thumb and forefinger.’10

Among American hospital inpatients, 129/512 (25.2%) had Terry’s nails: 45% of those with ‘adult-onset’ diabetes; 75% of those with cirrhosis, and 44.7% of those with congestive cardiac failure. Older patients were more likely to have Terry’s nails but ‘the risk of cirrhosis, congestive cardiac failure or diabetes was still 2.69 times greater in patients of any age with Terry’s nails than in those without. The relative risk rose to 5.28% for patients of 50 years or younger.’ Longitudinal nail biopsies in three patients showed telangiectasia in the upper dermis at the site of the distal band.11 It is
difficult to disentangle the effects of diabetes, and its circulatory, renal and hepatic complications.

Other nail changes
Beau’s lines are horizontal ridges in the nails thought to be due to temporary disturbance of the nail matrix – which can include injury, an episode of paronychia or systemic illness, such as infection, and many chronic illnesses, including diabetes. They may first appear about a month after an acute event and remain visible for five to six months in thumbnails and two years in big toenails.

It has been suggested that advanced glycosylation end products are responsible for the yellowing of the nails sometimes seen in people with diabetes. Many other conditions can cause yellow nails, including yellow-nail syndrome which is not linked with diabetes.

Koilonychia or spoon-like nails are usually thought to be a sign of iron deficiency anaemia. However, they may be found early in haemochromatosis – in which diabetes also occurs – and in vascular insufficiency (see above).

Red lunulae can be found in some or all finger and toenails in people with diabetes, and in many other conditions such as cardiovascular disease and thyroid problems. The cause is unclear.

Biochemical measurements in nails
Glycosylation
An early study found higher glycosylation of nail protein in people with diabetes than in those without. Among people with diabetes, there was a significant correlation between glycosylated nail protein and glycosylated haemoglobin; and also between nail protein glycosylation and fasting blood glucose. Glycation of nail protein can take six to nine months. Nail fructosamine analysis (using a method adapted for nails) showed that the highest levels were found in the deep layers of nail clippings, not in superficial layers. Nail fructosamine correlated with glycated eye lens protein and with glycosylated haemoglobin. The authors suggest that glycated nail protein might be a way of diagnosing diabetes in areas where obtaining and transporting blood samples is very difficult, as nail samples are simpler to collect and more robust.

Mercury and selenium levels
It has been suggested that methylmercury exposure (for example accumulated from eating fish) could cause pancreatic β-cell dysfunction. Americans aged 20–32 years without diabetes were followed between 1987 and 2005. Baseline and interval toenail mercury levels were measured. During that time 288/3875 were diagnosed with diabetes. In complex multi-variate analysis (including selenium) higher toenail mercury concentrations were associated with greater risk of diabetes (highest vs lowest quintiles hazard ratio 1.65 [1.07–2.56]). People with greater baseline toenail mercury levels had reduced β-cell function as calculated by homeostasis model assessment (HOMA).

Another study included 142 550 person-years of follow up with 780 new diagnoses of type 2 diabetes and found that the risk of developing this was lower with higher toenail selenium levels.

Summary
People with diabetes are vulnerable to infections in and around the nails, including Gram-negative bacteria or fungi. Neuropathy and glycaemia increase the risk, as does damage to the nail or adjacent skin, for example by distorted or sharp-edged nails. It is vital to have good nail care in both hands and feet.

Nails are signposts to general or digital health. The nail matrix needs a good supply of blood containing oxygen and other nutrients, and a normal nerve supply. Interruptions to this, for example by vascular disease, can cause temporary or permanent changes in nail shape, contour or colour. Such changes are more frequent in diabetes than is recognised. Patients may end up with missing or grossly distorted nails.

Nail proteins are glycosylated and this correlates with glycaemia. Nail clippings might be a way of diagnosing diabetes in locations without prompt access to laboratory facilities or personnel.

Look at your patients’ nails – you may be surprised by what you find!

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References