Back to Basics: understanding Charcot neuroarthropathy

KEY WORDS
- Charcot neuroarthropathy
- Diabetes mellitus
- Diabetic foot ulceration
- Diabetic peripheral neuropathy
- Rocker-bottom foot deformity

'Active' Charcot neuroarthropathy (CN) is characterised by non-infectious inflammation in the presence of peripheral neuropathy (van Netten et al, 2019). The area of the foot most commonly affected is the mid-foot and this is associated with classic 'rocker-bottom foot' deformity (Botek et al, 2010; Mumoli et al, 2012; Dissanayake et al, 2012). While this condition is frequently associated with deformity, this may be prevented if caught early. Without timely recognition and offloading of the affected limb, progressive bone and joint destruction may, however, lead to significant deformity, ulceration, amputation and a vastly reduced quality of life (Caputo et al, 1998; Cates et al, 2019).

TRUDIE YOUNG
Director of Education and Training, Welsh Wound Innovation Centre

BENJAMIN BULLEN
Programme Director / Lecturer in Podiatry, Wales Centre for Podiatric Studies, Cardiff Metropolitan University

The condition known today as Charcot foot or CN bears the name of the French pathologist, former Salpêtrière Hospital Medical Director and 'Father of Neurology,' Jean-Martin Charcot (1825–1893). Charcot first described this neuropathic arthropathy in 1868 among individuals with Tabes Dorsalis (myelopathy due to tertiary syphilis) (Caputo et al, 1998; Rosskopf et al, 2019). Charcot subsequently established CN as a distinct pathological condition in his 1881 'Demonstration of arthropathic affectations of locomotor ataxy' lecture at the 7th International Medical Congress (Kucera et al, 2016).

During his esteemed career, Charcot further described a butterfly-shaped ulcer occurring over the sacrum. Patients' that developed these ulcers usually died shortly thereafter and consequently he labelled them 'Decubitus Ominosus.' Today these wounds would be described as pressure ulcers occurring at the end of life (Sibbald, 2009; Young, 2017). Ulcerated CN may too be considered ominous, having been associated with significantly increased morbidity and mortality (*Figure 1*).

While CN has been associated with a 15% major amputation rate, this may sharply increase to between one- and two-thirds of individuals initially presenting with ulceration (Pinzur, 1999; Pakarinen et al, 2009; Sohn et al, 2010; Game et al, 2012). A mortality rate exceeding 25% within five years of diagnosis also increases in the presence of foot ulceration (Dissanayake et al, 2012; Nobrega et al, 2015; Kucera et al, 2016).

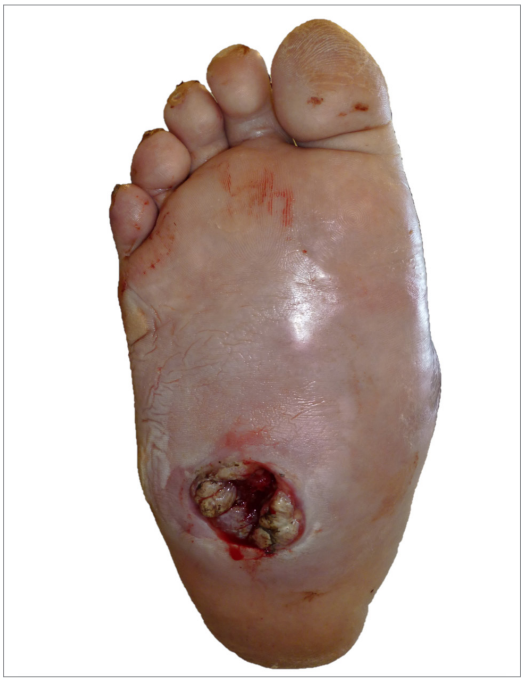

Figure 1: Charcot neuroarthropathy with 'rocker-bottom' foot deformity and ulceration.

CAUSE

In the Western world, CN is most commonly associated with diabetes mellitus (DM). No predilection has been demonstrated for either type one or two DM; however, DM duration exceeding

a decade is typical (Leung et al, 2009; Pakarinen et al, 2009; Christensen et al, 2010; Pakarinen et al, 2011; Moura-Neto et al, 2012; Sämann et al, 2012; Ergen et al, 2013). People developing CN tend to be in their fifth or sixth decades of life, with diabetic peripheral neuropathy but intact peripheral circulation (Rosskopf et al, 2019).

This condition is not exclusively seen in people with DM and may occur with a variety of peripheral and central neuropathies, such as leprosy, poliomyelitis, alcoholic neuropathy, syringomyelia, rheumatoid arthritis, multiple sclerosis, congenital neuropathy and spinal injury (Papanas et al, 2013; Sono et al, 2019; Botek et al, 2010; Alavi et al, 2014; Yousaf et al, 2018).

While traumatic injury or repetitive damage have been implicated in the development of CN, a history of trauma may be absent or rather, unrecognised, due to sensory loss (Alavi et al, 2014; Chapman et al, 2014). The types of traumatic injury that may precipitate CN range from relatively minor, such as a slip, trip or fall, or local surgery. An intervention to improve the vascular supply to the foot may also trigger CN (Caputo et al, 1998; Kaynak et al, 2013; Kucera et al, 2016; Goldsmith et al, 2019; Botek et al, 2010; Schaper et al, 2019). The precise aetiology and true prevalence remain unknown (Dissanayake et al, 2012; Holmes et al, 2019).

PATHOPHYSIOLOGY

Charcot initially theorised CN developed centrally, due to irritation of the vasomotor nerve centres, leading to altered bone and joint nutrition (Kaynak et al, 2013). This hypothesis would later develop into the 'Neurovascular Theory,' associating osteopenia with autonomic effects such as arteriovenous shunting and resultant increased peripheral vascularity (Soin et al, 2016). Sensory neuropathy was later implicated and may be considered the 'sine qua non' for development of CN (Jude et al, 2001; Jostel and Jude, 2008). The later 'Neurotraumatic Theory' of Volkman and Virchow associated characteristic osteopaenia with repeated and unrecognised microtrauma, precipitating traumatic bone resorption (Papanas et al, 2013, Sono et al, 2019).

Motor neuropathy has also been proposed to play a role in CN development, due to muscular imbalance and overloading (Pinzur, 2018). An unregulated inflammatory response has further been described, associating osteopenia and osteolysis with pro-inflammatory cytokine activity (Dissanayake et al, 2012; Alavi et al, 2014; Soin et al, 2016; Pinzur, 2016; Holmes et al, 2019).

Not all individuals with DM will develop CN due to the fact that it only affects limbs that are able to mount an inflammatory response and this can vary due to the type and degree of neuropathy present (Kaynak et al, 2013). While the precise pathogenesis of CN remains 'a bone of contention' (Durgia et al, 2018, p. 116), it is, perhaps easier to consider a typical CN presentation here.

In the absence of pain and prescribed rest, an individual with osteopaenic bones (regardless of causation) and insensitivity to pain may not reduce their weight-bearing activity. Unbridled walking, for example, may continue to stress the bones and joints of the vulnerable foot, resulting in fractures, subluxation or complete dislocation and ultimately, permanent foot deformity (Dissanayake et al, 2012; Alavi et al, 2014).

CLINICAL PRESENTATION

Due to the progressive, destructive nature of CN, early diagnosis is essential and once made it is recognised as a medical emergency that requires immediate immobilisation (Yousaf et al, 2018). Clinical signs of 'Active' CN include unilateral erythema, swelling and increased foot temperature. A two degrees Celsius warmer foot (measured with an infrared thermometer) compared with the contralateral limb is considered indicative of 'active' disease (Caputo et al, 1998; Botek et al, 2010; Alavi et al, 2014; Cates et al, 2019).

Bilateral CN has been reported in the literature, which makes the comparison of foot temperature difficult to achieve (Fauzi and Yang, 2013; Loupa et al, 2019). The high incidence of major amputation may further prevent comparison with a contralateral limb. Symptomatology may range from entirely painless to extremely painful, depending on the type and severity of neuropathy present (Paez et al, 2013; Chapman et al, 2014). An absence of pain has been implicated in contributing to delayed presentation to health professionals in the early (inflammatory) stages of this disease (Botek et al, 2010).

CLASSIFICATION

Radiological classification of CN may be achieved using the modified Eichenholtz classification (Rosskopf et al, 2019). This classification scheme describes disease progression from the initial inflammatory 'prodromal' and 'development' phases through 'coalescence,' where bone fragments are reabsorbed and ultimately 'reconstruction' and 'reconstitution,' characterised by final bone repair and remodelling (Yousaf et al, 2018). For the purpose of this article, however, pragmatic classification is adopted and advised for routine clinical practice, describing CN as either 'Active' or 'in Remission' (Bullen et al, 2019; 2020).

DIAGNOSIS

Unfortunately, there are no laboratory criteria or specific haematological markers to aid diagnosis of CN. Nevertheless, they can help to eliminate the differential diagnoses (Dissanayake et al, 2012). As stated earlier, CN is frequently under-diagnosed. This is because in the 'active' phase it can mimic cellulitis, deep vein thrombosis, gout, ankle sprains and osteomyelitis (Caputo et al, 1998; Hartemann-Heurtier et al, 2002; Botek et al, 2010; Dissanayake et al, 2012). In ulcerated CN, coexisting osteomyelitis may further complicate and confuse the diagnostic process (Goldsmith et al, 2019).

Misdiagnosis may occur in up to 95% of cases (Chantelau, 2005; Wukich et al, 2011; Hingsammer et al, 2016), possibly be due to a lack of knowledge. An American survey identified that 67% of primary care doctors and internal medicine specialists had little or no knowledge of CN (Schmidt et al, 2017). The delay in diagnosis is not helped by the lack of radiological confirmation of the changes in the foot in the 'prodromal' phase (first two to three weeks) when X-rays may be unremarkable. Therefore, if initial radiographic findings show no damage, weekly serial X-rays may be of assistance until radiographic changes are apparent (Caputo et al, 1998; Chapman et al, 2014; Goldsmith et al, 2019).

Magnetic Resonance Imaging (MRI) has the highest diagnostic accuracy, sensitivity and specificity in early CN (Botek et al, 2010; Dissanayake et al, 2012). This imaging modality demonstrates the nature of the bony damage along with evidence of inflammation in the bone, specifically bone marrow oedema, as well as fluid in the adjacent soft tissues (Paez et al, 2013; Schaper et al, 2019). However, it must be recognised that MRI assessment is not available to all health professionals and a high proportion rely on successive plain X-ray images (Rastogi et al, 2019).

CONSERVATIVE TREATMENT

The goal of treatment is to maintain or achieve structural stability, preserve the shape of the foot and lower limb and prevent ulceration. To achieve this, immobilisation involves application of a non-removable below-knee offloading device, the gold standard being total contact cast (TCC). This is normally required for several months at least and during this time progress can be monitored through temperature assessment and serial imaging.

The TCC will require changing in the first few days if fluctuant oedema has reduced and then subsequently every two weeks or more often if an ulcer is present. Once consolidation is achieved, a change to a removable offloading device may be considered (Rosskopf et al, 2019). Following CN remission, modular or bespoke footwear may be required if the foot can no longer be accommodated in high street footwear (Glaser et al, 2017; Yousaf et al 2018).

SURGICAL TREATMENT

Reconstructive surgery may be performed to create a plantigrade foot, regain foot stability and improve function, thus decreasing the future risk of ulceration and amputation (Cates et al, 2019). Surgical intervention may be particularly indicated for unstable rear-foot and ankle deformities (Dissanayake et al, 2012; Kim et al, 2019). The typical 'rocker-bottom' foot deformity may benefit from a plantar-based mid-foot wedge osteotomy and resection to achieve a plantigrade foot (Persky et al, 2019).

Less invasive surgery may be also used to remove or reduce the impact of any abnormal bony prominence on the foot. Negative pressure wound therapy has also been used alongside surgical intervention, e.g. post ulcer debridement, post reconstruction and amputation and to stabilise closed surgical incisions (Ramanujam et al, 2013).

Definition

Osteopaenia is the term used for low bone density or thinning of the bones resulting in fragility and a high propensity for subsequent fracture.

PATIENT EDUCATION

Our advice for health professionals is to remain vigilant for the early 'danger signs' of CN, namely an unexplained erythematous, hot and swollen foot in a person with neuropathy. Throughout 'Active' management, advice to avoid weight-bearing through the vulnerable limb should be reinforced. Podiatry and/or physician-lead diabetes or 'high-risk' foot services should be the first port of call in the event of clinical suspicion. On developing CN, there is an increased risk of subsequent recurrence. Life-long surveillance is therefore advised, including patient education and shared responsibility between the health professional and the individual. Self-management supported by informal carers is one way of achieving self-care in this vulnerable population (Messenger et al, 2019). There is support for individuals available via social media; Charcot foot research and support group *https://www.facebook.com/groups/496881060O5/* .

CONCLUSION

CN is a difficult and complex disease to diagnose and manage. Early recognition is key, given preventive care may not be possible (Dissanayake et al, 2012). The precise cause of the condition has not been unequivocally established, although characterised by a non-infectious and unregulated inflammatory response coexisting in individuals with peripheral neuropathy. Frequent misdiagnosis of CN occurs due to low clinician awareness of the condition combined with the presence of alternative diagnoses such as cellulitis or gout.

Without early intervention to limit mobility, destruction of the architecture of the foot will occur, resulting in foot deformity with the potential for amputation. Once diagnosed, care should be directed by podiatry and/or physician-lead diabetic 'high-risk' foot services. Such services monitor individuals during the 'Active' and 'in Remission' stages of the condition, with recurrence being a potential future event. WUK

REFERENCES

Alavi A, Sibbald RG, Mayer D et al (2014) Diabetic foot ulcers. *J Am Acad Dermatol* 70(1):e1–18. https://doi.org/10.1016/j.jaad.2013.06.055

Botek G, Anderson M, Taylor R (2010) Charcot neuroarthropathy: An often overlooked complication of diabetes. *Cleveland Clinic Journal of Medicine* 77 (9):593–9. https://doi.org/10.3949/ccjm.77a.09163

Bullen B (2020) Understanding what it means to be "Charcot foot health literate". *iWoundsnews* 3:11. https://tinyurl.com/y2xklsho (accessed 12 August 2020)

Bullen B, Young M, Mcardle C, Ellis, M (2019) It's time we talked about Charcot foot: results of a podiatry patient education questionnaire. *The Diabetic Foot Journal* 22(3,):12–7. https://tinyurl.com/y5fl8ov8 (accessed 12 August 2020)

Caputo GM, Ulbrecht J, Cavanagh PR, Juliano P (1998) The Charcot foot in diabetes: Six key points. *Am Fam Physician* 57 (1): 2707–10

Cates NK, Elmarsafi T, Bunka T J et al (2019) Peripheral vascular disease diagnostic related outcomes in diabetic charcot reconstruction. *J Foot Ankle Surg* 58(6):1058–63. https://doi.org/10.1053/j.jfas.2019.06.002

Chantelau E (2005) The perils of procrastination: effects of early vs. delayed detection and treatment of incipient Charcot fracture. *Diabetic Med* 22(12):1707–12. https://doi.org/10.1111/j.1464-5491.2005.01677.x

Chapman Z, Matthew C, Shuttleworth J, Huber JW (2014) High levels of anxiety and depression in diabetic patients with Charcot foot. *J Foot Ankle Res* 7(22):1–8. https://doi.org/10.1186/1757-1146-7-22

Christenson TM, Bulouw J, Simonsen L et al (2010) Bone mineral density in diabetes mellitus patients with and without a Charcot foot. *Clin Physiol Funct Imaging* 30(2):130–4 https://doi.org/10.1111/j.1475-097x.2009.00915.x 4

Dissanayake SU, Bowling FL, Jude EB (2012) The diabetic charcot foot. *Current Diabetes Reviews* 8(3):191–4. https://doi.org/10.2174/157339912800563981

Durgia H, Sahoo J, Kamalanathan S et al (2018) Role of bisphosphonates in the management of acute Charcot foot. *World J Diabetes* 9(7):115–26. https://doi.org/10.4239/wjd.v9.i7.115

Ergen FB, Sanverdi SE, Oznur A (2013) Charcot foot in diabetes and an update on imaging. *Diabet Foot Ankle* 4 (1): 10.3402/dfa.v4i0.21884. https://dx.doi.org/10.3402%2Fdfa.v4i0.21884

Fauzi AA, Yang CT (2013) Bilateral diabetic Charcot foot. *Aust Fam Physician* 42(1–2): 55–6

Game FL, Catlow R, Jones GR et al (2012) Audit of acute Charcot's disease in the UK: the CDUK study. *Diabetologia* 55 (1): 32–5. https://doi.org/10.1007/s00125-011-2354-7

Glaser ES, Fleming D, Glaser B (2017) Charcot foot management using MASS posture foot orthotics: A case study. Foot & Ankle Online Journal 10(3):4. https://doi.org/10.3827/faoj.2017.1003.0004

Goldsmith L, Barlow M, Evans PJ, Srinivas-Shankar U (2019) Acute hot foot: Charcot neuroarthropathy or osteomyelitis? Untangling a diagnostic web. *BMJ Case Rep* 12:e228597 http://dx.doi.org/10.1136/bcr-2018-228597

Hartemann-Heurtier A, Van GH, Grimaldi A (2002) Nov 30. The Charcot foot: Case review. *Lancet* 360(9347):1776–9. https://doi.org/10.1016/S0140-6736(02)11671-0

Hingsammer AM, Bauer D, Renner N (2016) Correlation of systemic inflammatory markers with radiographic stages of Charcot osteoarthropathy. *Foot Ankle Int* 37(9):924–8. https://doi.org/10.1177/1071100716649173

Holmes CM, Munson ME, Rothenberg GM, Schmidt BM (2019) Charcot foot: Why have we not made progress? *The Diabetic Foot Journal* 22(4):8–11

Jostel A, Jude EB (2008) Medical treatment of Charcot neurooosteoarthropathy. *Clin Podiatr Med Surg* 25(1): 63–9. https://doi.org/10.1016/j.cpm.2007.09.001

Jude EB et al (2001) Matrix metalloproteinase and tissue inhibitor of metalloproteinase expression in diabetic and venous ulcers. *Diabetologia* 44:A1–A325. https://doi.org/10.1007/BF03180172

Kaynak G, Birsel O, Guven MF, Ogut, T (2013) An overview of the Charcot foot pathophysiology. *Diabet Foot Ankle* 4. https://doi.org/10.3402/dfa.v4i0.21117

Kim YK, Lee HS, Seo SG et al (2019) Results of simple conservative treatment of midfoot charcot arthropathy. *Clin Orthop Surg* 11(4):459–65. https://doi.org/10.4055/cios.2019.11.4.459

Kucera T, Haikh HH, Sponder P (2016) Charcot neuropathic arthropathy of the foot: A literature review and single-center experience. *J Diabetes Res* 2016:3207043. https://doi.org/10.1155/2016/3207043

Leung HB (2009) Charcot foot in a Hong Kong Chinese diabetic population. *Hong Kong Med J* 15(3):191–5

Loupa CV, Meimeti E, Kokas A et al (2019) An atypical and bilateral presentation of Charcot foot disease. *BMC Endocr Disord* 19(1):96. https://doi.org/10.1186/s12902-019-0422-z

Messenger G, Taha N, Sabau S et al (2019) Is there a role for informal car-

egivers in the management of diabetic foot ulcers? a narrative review. *Diabetes Ther* 10(6):2025–33. https://doi.org/10.1007/s13300-019-00694-z

Moura-Neto A, Fernandes TD, Zantut-Wittmann DE (2012) Charcot foot: Skin temperature as a good clinical parameter for predicting disease outcome. *Diabetes Res Clin Pract* 96(2):e11-4. https://doi.org/10.1016/j.diabres.2011.12.029

Mumoli N, Camait A (2012) Charcot foot. CMAJ 184(12): 1392. https://doi.org/10.1503/cmaj.111972

Nobrega MBDM, Aras R Netto EM (2015) Risk factors for Charcot foot. *Arch Endocrinol Metab* 59(3): 226–30. https://doi.org/10.1590/2359-3997000000042

Paez FG, Sutto SET, Gonzales SP et al (2013) New insights on treatment. The Diabetic Charcot Foot (Online Book) Chapter 13. https://tinyurl.com/yyurpasn (accessed 12 August 2020)

Pakarinen TK, Laine HJ, Maenpaa H et al (2009) Long-term outcome and quality of life in patients with Charcot foot. *Foot Ankle Surg* 15(4):187–91. https://doi.org/10.1016/j.fas.2009.02.005

Pakarinen TK, Laine HJ, Maenpaa H et al (2011) The effect of zoledronic acid on the clinical resolution of Charcot neuroarthropathy: A pilot randomized controlled trial. *Diabetes Care* 34(7): 1514–6. https://doi.org/10.2337/dc11-0396 6

Papanas N, Maltezos E (2013) Etiology, pathophysiology and classifications of the diabetic Charcot foot. *Diabet Foot Ankle* 4. https://doi.org/10.3402/dfa.v4i0.20872

Persky JD, Langan T, Smith CN, Burns PR (2019) Plantar Approach for Midfoot Wedge Resection to Reconstruct the Rocker Bottom Foot. *J Foot Ankle Surg* 58(5):1030–1035. https://doi.org/10.1053/j.jfas.2019.01.004

Pinzur MS (2016) Surgical treatment of the Charcot foot. *Diabetes Metab Res Rev* 32(1): 287–91. https://doi.org/10.1002/dmrr.2750

Pinzur MS (1999) Benchmark analysis of diabetic patients with neuropathic (charcot) foot deformity. *Foot Ankle Int* 20(9): 564–7 https://doi.org/10.1177/107110079902000905

Pinzur MS (2018) An evidence-based introduction to charcot foot arthropathy. *Foot & Ankle Orthopaedics* 3(3). https://doi.org/10.1177%2F2473011418774269

Ramanujam CL, Stapleton JJ, Thomas Zgonis (2013) Negative-pressure wound therapy in the management of diabetic Charcot foot and ankle wounds. *Diabet Foot Ankle* 4: 10.3402/dfa.v4i0.20878. https://dx.doi.org/10.3402%2Fdfa.v4i0.20878

Rastogi A, Prakash M, Bhansali A (2019) Varied presentations and outcomes of Charcot neuroarthropathy in patients with diabetes mellitus. *International Journal of Diabetes in Developing Countries* 39(3): 513–22

Rosskopf AB, Loupatatzis C, Pfirrmann CWA et al (2019) The Charcot foot: a pictorial review. *Insights Imaging* 10:77. https://dx.doi.org/10.1186%2Fs13244-019-0768-9

Samann A, Pofahl S, Lehmann T (2012) Diabetic nephropathy but not HbA1c is predictive for frequent complications of Charcot feet–long-term follow-up of 164 consecutive patients with 195 acute Charcot feet Exp Clin *Endocrinol Diabetes* 120(6):335–9. https://doi.org/10.1055/s-0031-1299705

Schaper NC, Van Netten JJ, Apelquist J et al (2019) IWGDF Guidelines on the Prevention and Management of Diabetic Foot Disease. IWGDF Practical Guidelines

Schmidt BM, Wrobel JS, Holmes CM (2017) Physician knowledge of a rare foot condition – influence of diabetic patient population on self-described knowledge and treatment. *Clinical Diabetes and Endocrinology* 3:2. https://tinyurl.com/y4jx5gx4 (accessed 12 August 2020)

Sibbald RG, Krasner DL, Lutz J (2010) SCALE: Skin Changes at Life's End: Final Consensus Statement: 2009, October 1. *Adv Skin Wound Care* 2(5): 225–36. https://tinyurl.com/yxg5oa5k (accessed 12 August 2020)

Sohn MW, Stuck RM, Pinzur M et al (2010) Lower-extremity amputation risk after charcot arthropathy and diabetic foot ulcer. *Diabetes Care* 33(1): 98–100. https://doi.org/10.2337/dc09-1497

Soin SP, Hunter JG, Kates SL Pathophysiology of diabetes and Charcot neuroarthropathy. In: Herscovici Jr D (ed) *The Surgical Management of the Diabetic Foot and Ankle*. Springer, 2016

Sono T, Meyers CA, Miller D et al (2019) Overlapping features of rapidly progressive osteoarthrosis and Charcot arthropathy. *J Orthop* 16(3):260–4. https://doi.org/10.1016/j.jor.2019.02.015

van Netten JJ et Bus S, Apelqvist J al (2019) Definitions and criteria for diabetic foot disease. *Diabetes/Metabolism Research and Reviews* 36(S1):e3268. https://doi.org/10.1002/dmrr.3268

Wukich DK, Sung W, Wipfe SAM, Armstrong DG (2011) The consequences of complacency: managing the effects of unrecognized Charcot feet. *Diabet Med* 28(2):195–8. https://doi.org/10.1111/j.1464-5491.2010.03141.x

Young T (2017) Caring for patients with malignant and end-of-life wounds. *Wounds UK* April: 20-9 https://tinyurl.com/y2s5z4qt (accessed 12 August 2020)

Yousaf S, Dawe EJC, Saleh A et al (2018) The acute Charcot foot in diabetics: Diagnosis and management. *EFORT Open Reviews* 3(10): 568–73. https://doi.org/10.1302/2058-5241.3.180003