That's shocking news

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Welcome to another *Diabetes Digest* commentary. There is a selection of paper abstracts that are perhaps worth considering taking a closer look at. The paper that I have chosen to bring to your attention and expand upon is one that I feel has some exciting evidence that is not just applicable to diabetic foot wounds but potentially other soft tissue pathologies and maybe acute Charcot neuroarthropathy. This research paper is from Quebec, Canada, and published in *Biology*. It is an experimental *in-vitro* study, thus *in-vivo* investigations and studies are required.

It is well known that diabetic foot ulcers are difficult to heal and some of this is due to delayed or abnormal fibroblast activity and quality. It has been shown that fibroblasts from chronic wounds (such as diabetic ulcers) display abnormalities e.g., decreased proliferation, altered patterns of cytokine release, early senescence and abnormal metalloproteinase activity. As a result, allogenic fibroblasts grafted to a bi-layered skin substitute have been used to support local dysfunctional fibroblasts, however, these do not persist indefinitely but do serve as a source of growth factors and cytokines. There is some evidence that electrical stimulation (ES) in non-diabetes-related skin can increase the growth of fibroblasts.

Furthermore, fibroblasts exposed to ES have also been shown to secrete higher levels of cytokines and growth factors, compared to non-exposed cells. This study evaluated the effect of ES on diabetic human skin fibroblasts (DHSF). The investigators examined DHSF adhesion, growth, the secretion of cytokines and growth factors compared with an experimental control group. The control group were exactly the same as the test group but without ES.

The authors also investigated the long-term effects of ES on DHSF shape and growth. The DHSF were harvested and isolated from skin tissues collected from patients with diabetes (61 to 80 years old) following leg amputation surgery. These were seeded (5×104 cells/cm^2) on the membranes in the electrical cell culture device and cultured for 24 hours at 37°C in a 5% CO^2 humid atmosphere. ES at various intensities of 100, 80, 60, 40 and 20 mV/mm were then applied or not to the cells for 6 or 24 hours. Following each stimulation period, the culture medium was refreshed and the cells were cultured for an additional 48 hours. The effect of ES on fibroblast adhesion and growth was evaluated using Hoechst staining, MTT and trypan blue exclusion assays. The secretion of cytokine and growth factor was assessed by cytokine array and ELISA assay.

This study reports that ES at 20 and 40 mV/mm promoted DHSF cell adhesion, viability and growth. It also demonstrated that ES decreased the secretion of pro-inflammatory cytokines IL-6 and IL-8 yet promoted growth factor FGF7 secretion during 48 hours after ES. Additionally, it also showed that the effect of ES DHSF growth was maintained up to 5 days after ES.

This paper is not the easiest to read but the study design is good and it is worth reading. As always, nothing replaces the fundamental triad of diabetic ulcer healing — in/outflow, infection control and offloading — but ES may be a worthwhile adjunct therapy. ■

Abedin-Do A, Zhang Z, Douville Y et al (2021) Effect of electrical stimulation on diabetic human skin fibroblast growth and the secretion of cytokines and growth factors involved in wound healing. *Biology (Basel)* 10(7): 641

J Wound Care

People living with diabetes are unaware of their foot risk status or why they are referred to a multidisciplinary foot team

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 The study investigated the self-reported understanding of patients' foot risk status and the underlying reasons for their referral to a multidisciplinary foot team. They conducted a 7-month service evaluation, including consecutive newly referred patients.

2 Two-hundred-and-two patients were asked about their understanding of their foot-risk status, their pathway of care pre-presentation and about their interest in diabetes-related foot education, as well as their preferred learning style.

3 Eighty-six percent of the participants had type 2 diabetes, 65% were male, the mean age was 64±15 years (mean±standard deviation), 86% had type 2 diabetes, and the mean HbA_{1c} was 65±23mmol/mol (8.3±3.7%).

4 Just 4% of participants expressed knowledge of their current foot risk status, while 52% could not explain why their care had been escalated to a multidisciplinary foot clinic. Those with type 2 diabetes more readily expressed an interest in further foot education compared with participants with type 1 diabetes (70% versus 29%, P=0.001).

5 These findings suggest possible communication and educational barriers between patients and clinicians, which may be contributing factors as to why individuals are less aware of their foot risk status and why engagement may be suboptimal.

Walton DV, Edmonds ME, Bates M et al (2021) People living with diabetes are unaware of their foot risk status or why they are referred to a multidisciplinary foot team. *J Wound Care* 30(8): 598–603

BMC Infect Dis

The microbiology of diabetic foot infections: a meta-analysis

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓

1 Although diabetic foot ulcers are a common complication of poorly controlled diabetes, often becoming infected, there has been no meta-analysis providing a global overview of data pertaining to the microbiology of diabetic foot infection.

2 The authors carried out a meta-analysis to investigate the prevalence of bacteria isolated from DFIs. Studies of any design were analysed, which reported diabetic foot infection culture results.

3 Numerous electronic databases were all searched for studies containing microbiological culture results from at least 10 diabetic foot infection patients, that were published up to and including 2019. One-hundred-and-twelve studies were included in this study, including 16,159 patients from which 22,198 microbial isolates were taken.

4 *Staphylococcus aureus* was the organism most commonly identified in the study with 18.0% being MRSA (95% CI 13.8-22.6%; I2 = 93.8% [93.0-94.5%]). *Pseudomonas spp.*, *E. coli* and *Enterococcus spp.* were other highly prevalent organisms. A correlation was found between Gross National Income and the prevalence of Gram-positive or negative organisms present in diabetic foot infections, which may suggest differences in healthcare provision and sanitation.

Macdonald KE, Boeckh S, Stacey HJ, Jones JD (2021) The microbiology of diabetic foot infections: a meta-analysis. *BMC Infect Dis* 21(1): 770

Clin Biomech

Changes in sub-calcaneal fat pad composition and their association with dynamic plantar foot pressure in people with diabetic neuropathy

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓

1 Diabetic foot disease is linked with physiological and biomechanical abnormalities in the foot that increase ulceration risk. This study assessed MRI changes in the composition of sub-calcaneal fat pad tissue and its association with plantar pressure during walking.

2 This study assessed barefoot plantar pressure distribution during walking of 14 people with diabetes and peripheral neuropathy, as well as five age-matched healthy controls. All subjects underwent T1-weighted sagittal plane spin-echo Dixon MRI of the rearfoot. Fat-only and water-only images were created by Dixon Chemical Shift Imaging.

3 The mean ± SD fat signal fraction was found to be significantly lower in the neuropathic subjects than the healthy controls (0.55 ± 0.11 vs. 0.72 ± 0.03, $P<0.005$). Fat signal fraction and peak pressure were significantly inversely correlated (r=-0.59, $P<0.01$). The lower mean ± SD fat signal fraction was put down to a lowering in fat signal (R2 0.87), rather than an increase in water signal (R2 0.32).

4 The MRI presented a reduced fat signal fraction in sub-calcaneal fat pad tissue in those with diabetic neuropathy. Fat pad function also appeared compromised, indicated by an associated increase in peak plantar pressures, which may increase foot ulceration risk.

Bus S, Akkerman EM, Maas M (2021) Changes in sub-calcaneal fat pad composition and their association with dynamic plantar foot pressure in people with diabetic neuropathy. *Clin Biomech (Bristol, Avon)* 88: 105441

J Wound Care

Peripheral arterial disease in patients with renal diabetic foot ulcers

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 The authors set out to describe the angiographic characteristics of peripheral arterial disease in individuals with diabetic foot ulcers on dialysis treatment using a retrospective analysis of patients with diabetic foot ulcers and peripheral arterial diseasewho had been referred to the authors' diabetic foot clinic.

2 A pre-set limb salvage protocol was used to manage all patients and arterial lesions (stenosis between 50–99% and occlusions) were retrospectively evaluated using angiogram analysis. A total of 239 patients were split into two groups: renal-diabetic foot and diabetic foot, according to the presence or otherwise of dialysis.

3 The mean age was 71.8 years, 72.4% were male and 87.4% had type 2 diabetes. The mean duration of diabetes was 21.4 years. A higher number of vessels was affected in the renal-diabetic foot group compared with the diabetic foot group (n=5±1.6 versus 3.9±1.5, respectively, $P<0.0001$). In addition, the renal-diabetic foot group showed a higher rate of revascularisation failure in comparison to diabetic foot patients (43.9% versus 15.3%, respectively, $P<0.0001$).

4 In conclusion, renal-diabetic foot patients showed a widespread distribution of arterial lesions with a higher involvement of foot arteries when compared with diabetic foot patients.

Meloni M, Izzo V, Giurato L et al (2021) Peripheral arterial disease in patients with renal diabetic foot ulcers. *J Wound Care* 30(8): 660–4

"Nothing replaces the fundamental triad of diabetic ulcer healing — in/outflow, infection control and offloading — but electrical stimulation may be a worthwhile adjunct therapy."