journal of wound care JWC
VOLUME 26. NUMBER 11. NOVEMBER 2017

Topical oxygen therapy promotes the healing of chronic diabetic foot ulcers: a pilot study

***P.D. Hayes**,[1] MD FRCS(Ed), Consultant Vascular Surgeon;
N. Alzuhir,[1] MB ChB, Clinical Research Fellow;
G. Curran,[1] MB ChB, Clinical Research Fellow;
I.M. Loftus,[2] MB ChB, Consultant Vascular Surgeon

***Corresponding author email:** paul.hayes@addenbrookes.nhs.co.uk

1 Department of Vascular Surgery, Cambridge University Hospitals NHS Trust, Addenbrooke's Hospital, UK.
2 St George's Vascular Unit, St George's Healthcare NHS Trust, Tooting, London, UK.

Topical oxygen therapy promotes the healing of chronic diabetic foot ulcers: a pilot study

Objective: Interventions that can heal or reduce diabetic foot ulcer (DFU) size may reduce the incidence of infection and amputation, and reduce associated social and economic costs. Many chronic wounds exhibit a degree of hypoxia and this leads to a reduction in healing processes including cell division and differentiation, angiogenesis, infection prevention, and collagen production. The aim of this pilot study was to assess the effects of a device supplying continuous oxygen ambulatory therapy on healing in chronic DFUs.
Method: Patients with chronic DFUs from two tertiary referral hospitals in the UK received treatment with the device. Data were prospectively obtained on wound size using standardised digital images measured by a clinician blinded to the study. Data on device satisfaction and pain were also obtained.
Results: We recruited 10 patients, with a mean ulcer duration of 43 weeks (median: 43 weeks) before treatment. By week eight, mean ulcer size had decreased by 51% (median: 53%). Seven of the 10 ulcers were in a healing trajectory, one ulcer present for 56 weeks healed completely, a two-year old ulcer was reduced by more than 50%, and a third, present for 88 weeks, was down to 10% of its original size by the end of the eight-week study. There was also a non-significant trend towards reduction in pain and the device was extremely well tolerated.
Conclusion: The ambulatory topical oxygen delivery device showed a significant beneficial effect on wound size. This poses practical advantages over currently existing oxygen-based wound therapies such as hyperbaric oxygen therapy due to its continuous oxygen delivery, ease of use, safety and lower cost. The results of this study warrant further review of the device in comparison to standard wound therapies.
Declaration of interest: PH undertakes consultancy work for Inotec. The study was wholly funded through an NHS contract under the Small Business Research Initiative scheme, administered by Health Enterprise East.

diabetic • foot ulcer • oxygen • wound healing

In 2012 the cost of diabetic foot ulcers (DFUs) and related amputations in the UK was between £600–700 million per year, with most of the costs associated with type 2 diabetes due to hospitalisation.[1] Furthermore, patients with diabetes are more likely to be admitted with a foot ulcer than any other complication of the disease.[2] Interventions that can potentially heal or reduce the size of DFUs may reduce the incidence of infection and amputation rates in this patient group, leading to lower associated costs for healthcare providers.

For a wound to heal, overall body metabolism must increase energy production by around 20% for clean wounds and 50% for infected wounds,[3] and local cellular metabolism at the wound bed must increase by around 500%. This energy is necessary for the cellular processes required for cell division, angiogenesis and collagen production, all of which are essential for wound healing. As such, wound healing is most efficient when cells have sufficient energy to reproduce, manufacture proteins, and fight infection. When oxygen levels in a wound are low, one molecule of oxygen generates just two molecules of energy, adenosine triphosphate (ATP). However, with plentiful local oxygen, the process is 18 times more efficient, with each oxygen molecule generating 36 molecules of ATP (energy). As such, by creating an oxygen-rich environment, wound healing is improved.

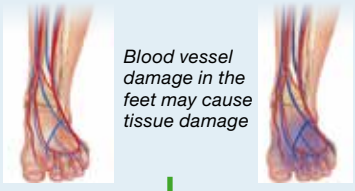
Wound hypoxia occurs in patients with diabetes for a number of reasons, including macrovascular and microvascular disease, and local oedema (Fig 1). Despite the fact that tissue oxygenation is achieved by several means, the central area of a wound in a patient with diabetes can be as low as 0–10mmHg,[4] well below that required to heal wounds, especially given that wounds in this setting have a higher metabolic demand than wounds in non-diabetic patients.[5] Even in patients with diabetes and foot pulses, there can be a failure of oxygen delivery to the capillary bed, and therefore the tissues, because of arterio-venous shunting. Furthermore, there

***P.D. Hayes**,[1] MD FRCS(Ed), Consultant Vascular Surgeon; **N. Alzuhir**,[1] MB ChB, Clinical Research Fellow; **G. Curran**,[1] MB ChB, Clinical Research Fellow; **I.M. Loftus**,[2] MB ChB, Consultant Vascular Surgeon
***Corresponding author email:** paul.hayes@addenbrookes.nhs.co.uk
1 Department of Vascular Surgery, Cambridge University Hospitals NHS Trust, Addenbrooke's Hospital, UK. **2** St George's Vascular Unit, St George's Healthcare NHS Trust, Tooting, London, UK.

Fig 1. Most wounds exhibit a degree of hypoxia, low oxygen levels lead to reduced rates of wound healing

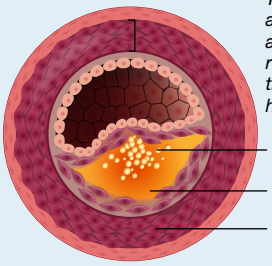
Possible causes of low oxygen levels

Diabetes



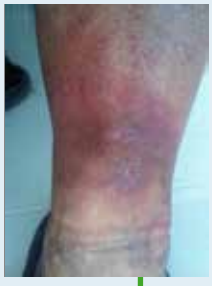
Blood vessel damage in the feet may cause tissue damage

Atherosclerosis



The thickening of the artery wall seen in atherosclerosis, reduces oxygen transfer from haemoglobin

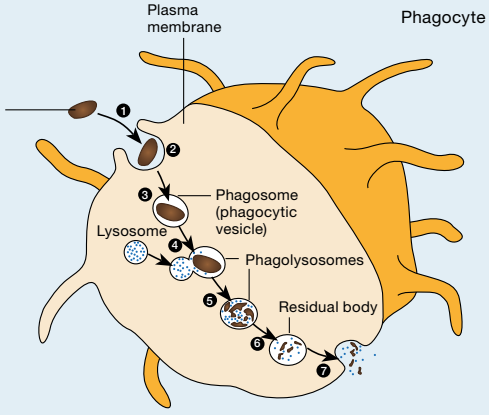
Venous skin damage



The thickening of the tissues seen with chronic venous skin damage prevents oxygen transfer to the cells trying to heal the wound

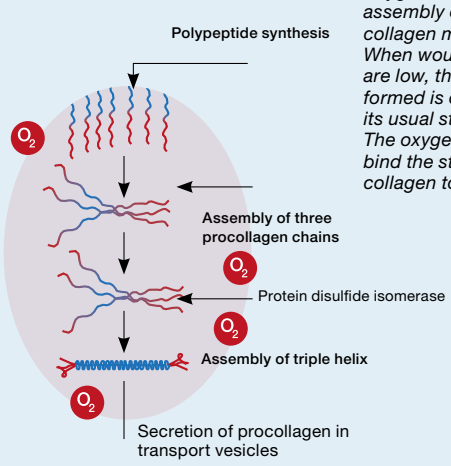
L O W W O U N D O X Y G E N C A N L E A D T O

1. Failure to fight infection leading to wound deterioration



Neutrophils and macrophages are key for clearing infection from wounds. During this process their oxygen demands increase 50-fold. The oxygen is used to generate potent antibacterial superoxide molecules

2. Poor quality tissue with high wound recurrence rates



Oxygen is key to the assembly of a strong collagen matrix. When wound oxygen levels are low, the collagen formed is only one-third of its usual strength. The oxygen is used to bind the strands of collagen together

3. Inability to produce new skin cells that spread and cover the wound

Epithelial migration is very energy dependent as a large number of processes need to occur. Energy production in the presence of adequate oxygen is 18-times more efficient than in a hypoxic wound

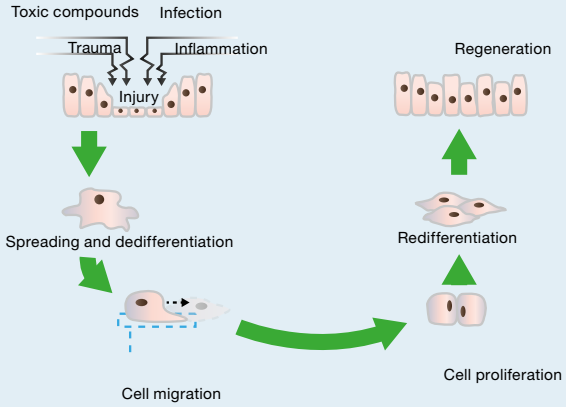


Fig 2. A portable oxygen delivery system used in the study

is considerable evidence to support the importance of oxygen for efficient wound healing from studies that have shown that hypoxia inhibits the crucial cellular mechanisms that promote and underlie tissue healing,[3,6] and that inferior clinical outcomes of healing are associated with low transcutaneous partial pressure of oxygen ($TcPO_2$).[7] Processes such as collagen synthesis and cross linking, long-term angiogenesis, the respiratory burst for bacterial killing and epithelialisation are all reduced in hypoxic tissue.[8]

As such, it is now generally accepted that correcting wound hypoxia increases the healing response,[9] and this has been the subject of various modes of intervention in recent years. The concept of increasing the availability of oxygen to facilitate wound healing was developed originally with systemic hyperbaric oxygen therapy (HBOT). However, this treatment modality has shown limited success in wound healing because it can only be used for very short periods of the week (approximately 5%), which limits its efficacy in raising oxygen levels in wounds for a prolonged period.[10] In addition, access to the treatment is limited, patients must be confined to the chamber for the duration of the treatment, and it is costly.[11]

Although systemic HBOT has been shown to potentially reduce the rate of major amputation in people with chronic DFUs[12,13] as well as improve healing in the short term,[14] current guidelines are inconclusive with respect to incorporating this mode of therapy into standard treatment on grounds of insufficient evidence.[15,16] Adverse effects arising from barotrauma and oxygen toxicity have also negatively impacted on its widespread applicability, along with practical limitations such as accessibility and cost of treatment.[17]

Local HBOT employs an entirely different route of delivery that circumvents systemic exposure to supra-atmospheric air pressures and supra-physiologic oxygen levels. Acceleration in healing with local hyperbaric oxygen therapy has been demonstrated[18] although, again, there is a paucity of level 1 or 2 evidence to support its routine use. A common difficulty with both treatment modalities is that the administration of oxygen is intermittent due to the restrictive nature of the chamber or device by which it is provided.

Topical continuous diffusion of oxygen is a mode of oxygen therapy that has been revisited in the past decade. The delivery of oxygen is achieved in either a gaseous or dissolved form. Gaseous oxygen is administered by a device consisting of a small battery-powered electrochemical oxygen generator that electrolyses atmospheric water vapour to produce pure humidified oxygen. The oxygen is transported down a fine bore tube and delivered onto the surface of the wound, creating a high concentration of oxygen under the dressing, and allowing for oxygen to be diffused down the concentration gradient into the wound. While the topical route of delivery is similar to that of local HBOT, a major distinction is that the compact nature of the device allows the patient to be completely ambulatory, and therefore undergo continuous 24/7 treatment while the device is *in situ* (Fig 2). From a practical standpoint, this method's relative low costs and simplicity of use create the potential for it to be a widely available treatment

Fig 3. Effect of topical oxygen therapy on a failed transmetatarsal amputation. The patient had been offered a below-knee amputation before starting topical oxygen therapy (**a**), after eight weeks the wound had reduced by 72% and was ultimately salvaged (**b**)

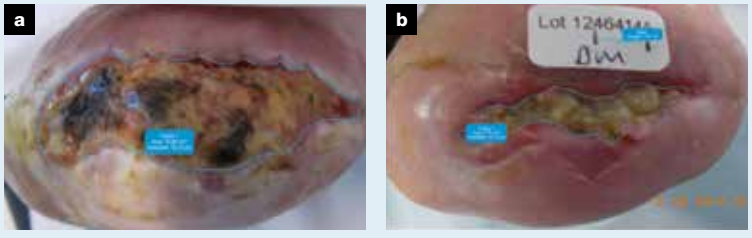
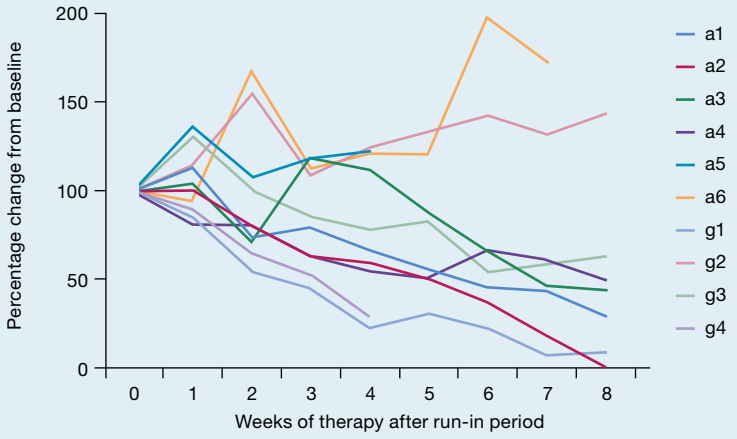
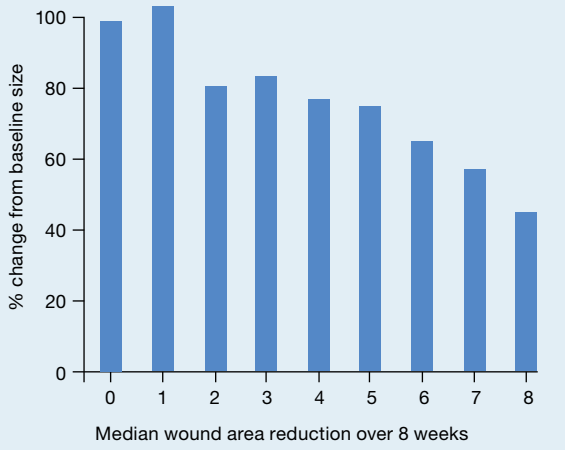


Fig 4. Individual healing curves, showing percent change over time in wound size relative to baseline. Note the initial increase in size in some wounds before going on to improve



a—Addenbrooke's; g—St George's

Fig 5. Mean wound area reduction over the eight-week trial period for the 10 chronic, previously non-healing, diabetic foot ulcers studied. Even with the limited sample size the therapy resulted in a statistically significant reduction in wound size over time when tested with repeated measures ANOVA (p=0.015)



adjunct in hospital and community settings if evidence supports its efficacy in healing DFUs and reducing associated morbidity and mortality.

There are a number of ways of increasing oxygen delivery to tissues, and these are summarised in a recent European Wound Management Association (EWMA) document 'Use of oxygen therapies in wound healing: focus on topical and hyperbaric oxygen'.[19] The effectiveness of topical oxygen in diabetic foot wounds remains largely unverified due to the relatively recent development of the therapy. This phase I study aims to examine the efficacy and safety of topical continuous diffusion of oxygen in diabetic foot wounds, and to detect and describe any potential adverse effects.

The ambulatory topical oxygen delivery device[20] used in this study delivers continuous oxygen to the wound bed through an oxygen distribution system, or diffuser that sits on the wound surface and is connected to the generator by a fine bore tube. The generator employs a small, battery-powered electrochemical 'oxygen generator' that produces oxygen from water molecules in the atmosphere at a concentration of around 98%, and a rate of approximately 15ml per hour. The oxygen distribution system is held in place, overlying the wound bed by a conventional dressing, and the oxygen generator is worn by the patient in a holster on the waist or above the calf, or can be placed in a trouser pocket, therefore enabling the patient to enjoy normal mobility whilst receiving continuous oxygen treatment.

The aim of this pilot study was to assess the effects of an ambulatory topical oxygen delivery device on healing in chronic DFU.

Method

The study was conducted jointly at Addenbrooke's Hospital in Cambridge, UK and St Georges Hospital in London, UK over a six month period. The use of the device in 10 patients with chronic DFUs was studied over an eight-week period. Patients with chronic, non-healing DFUs were selected across the two sites, and all had previously undergone a full diabetic and arterial assessment. Where appropriate, they were maintained in offloading footwear and had their arterial inflow optimised where possible.

The criteria for inclusion in the study were as follows:

- No significant ulcer size reduction (<20%) seen despite using best practice care for a minimum of four weeks in the tertiary care centre
- There was no minimum ankle-brachial pressure index (ABPI) level and patients were not required to have this performed
- Patients with evidence of acute, invasive infection were excluded, but chronic osteomyelitis was allowable
- Ability of patient to change and charge the battery in the device.

Each patient was followed up in clinic for eight weeks; this matched current standard follow-up practice in the two centres. As this was our first pilot study, for ethical reasons, we chose to only treat the patients for eight weeks as the effect of the therapy was unknown at that time. All data were collected prospectively for this period, but not beyond as our Research Ethics Committee permission was for an eight-week study.

Secondary overlying dressings were chosen from each hospital's wound care formulary. In each patient, the disposable oxygen delivery system dressing was placed directly on to the wound bed, and the wound was then dressed with what was felt to be standard care for each particular wound. Changes of dressing types were allowable throughout the study period.

Patients were reviewed in clinic every week and assessed between these visits by community nurses. Wounds were measured and digitally photographed at each review visit, and all relevant consents and permissions were obtained. The images were measured by a single observer using a commercially available software system (https://www.klonk.dk). An analogue scoring system was used to evaluate patients' pain scores, and also satisfaction with the use of the device.

Results

We recruited 10 patients across both sites. Before treatment with the ambulatory topical oxygen delivery device, the mean duration of ulceration was 43 weeks, indicating that these were chronic, non-healing wounds. In addition, half of the patients studied also had previously documented peripheral arterial disease. The mean age was 64, and 80% of the participants were male. There was a good variation in ulcer types: three plantar, two heel, two over metatarsal heads, two toes, and one failed trans-metatarsal amputation.

By week eight of the study, the median ulcer size had decreased by 53% (mean: 51%) and 7/10 ulcers were on a healing trajectory with a documented decrease in size. Complete healing was seen in one heel ulcer that had been present for 56 weeks, and a further ulcer that had been present for two years reduced by more than 50% during the eight-week study period. A third ulcer that had been present for 88 weeks had reduced to 10% of its original by the end of the study.

The first patient included in the study had already been offered an amputation, after a failed transmetatarsal amputation, but by the end of the eight-week period, his ulcer had decreased to 30% of its initial size (Fig 3).

The results of the study are summarised graphically in Figs 4 and 5. It is of note that by week six, there appears to be a clear delineation between those ulcers that responded positively to the oxygen therapy and those that failed to do so. Of further note is the fact that 6/10 ulcers actually increased in size over the first two weeks, before four of these six then had significant decreases in size.

There was also a non-significant trend towards a reduction in pain scores. Across the baseline and week 1, 39% of patients recorded pain scores of 5/10 or above (7/18), but by weeks seven and eight only 7% of pain scores were above five (1/13; p=0.05).

Despite the novel nature of the therapy, it was well tolerated, and no patient stopped the treatment through personal choice. Patient feedback was wholly positive and several patients reported enjoying having an active role in the management of their treatment with the device. This was echoed by three members of the healthcare teams involved who felt that the patients were empowered by their participation in the care of their wounds.

Further follow-up of the patient group has shown persistent benefit from the use of the device; there have been no recurrent ulcers and several of the ulcers have gone on to heal completely. Two patients who subsequently developed new ulcers at other sites requested the device as first line treatment.

Discussion

To date, there is a paucity of animal[21] and human[22] studies of wound closure rates with continuous topical gaseous oxygen therapy, but there is evidence from those that have been undertaken that it may be a promising adjunct therapy in chronic refractory wounds. The phase I study reported here describes the potential applicability of continuous topical oxygen therapy for initiating healing in chronic DFUs. Moreover, the absence of any reported adverse effects related to the use of this particular device confirms its safety. The compactness of the device, convenient application and ease of use mean that patients can remain mobile and be treated in the wider community setting. This is an important practical milestone for oxygen-based therapies which have previously been difficult to universally administer due to accessibility, patient inconvenience and high costs. Concordance for patients with DFUs has been relatively poor with many conventional therapies, such as total contact casts, thus reducing their overall efficacy. High concordance such as seen in this study, is likely to aide the therapy in closing the wound.

An additional advantage of this therapy is the continuous nature of the treatment it provides. A typical regimen for systemic HBOT consists of a maximum of two-hour sessions, five times a week,[23] and for local hyperbaric oxygen therapy, three hours twice per day.[24] Studies have shown that $TcPO_2$ remains elevated for a few hours after treatment,[10] but nevertheless, this still comprises only a small fraction of the 24-hour day, throughout which a topical application can continuously provide oxygen therapy.[25]

Many DFUs remain refractory despite the use of current best practice, multidisciplinary care pathways, including pressure offloading, revascularisation, blood glucose control, infection management and appropriate debridement and dressings. The patients included in this study were recruited from two tertiary centres in the UK that provide such a service, yet their wounds were very chronic with a median duration of 43 weeks, giving them a poor prognosis and high likelihood of progressing to amputation. The success achieved in this difficult-to-heal group demonstrates promise for the use of continuous topical oxygen therapy in tipping such ulcers in to a pro-healing phase, even when currently available treatment options have been exhausted.

The effectiveness of hyperbaric oxygen therapy has been shown to be predicted by the $TcPO_2$ of the adjacent tissue that is achieved in response to treatment.[26] This study reinforces the therapeutic effect of correcting wound hypoxia, but it can also be argued that certain characteristics of the DFUs and the patients' physiology reduce the systemic delivery of oxygen to it. Inspired oxygen must overcome several barriers before it is delivered to distal sites, including the wound bed of a DFU, and these include factors related to cardiopulmonary status and the macrovascular and microvascular disease caused by diabetes. The delivery of topically applied oxygen is independent of such factors. It involves the diffusion of gaseous oxygen down its concentration gradient and through to the interstitial solution to the metabolically active cells. Recent *in vivo* studies have shown that the penetration of oxygen across the skin surface can occur to a depth up to 700um.[27] This validates the fundamental basis of topical oxygen delivery. It also highlights the role of local wound conditions in influencing the effectiveness of topical oxygen therapy. For example, the presence of slough on the wound surface may reduce oxygen diffusion and therefore, the effectiveness of the therapy, and this underlines the importance of thorough debridement throughout the therapy cycle. Accordingly, the protocol in this study mandated regular debridement of the ulcer as per standard diabetic ulcer management, and this is a key factor in optimising oxygen delivery. By the same principle, reducing oedema by elevation of the leg may also help reduce diffusion distance.

The hypoxia of wounds may also be further exacerbated by the choice of overlying dressings. Since the study by Winter et al. in the 1960s, the focus of wound dressings has shifted towards providing a moist environment as this was deemed the most preferred environment for wound healing.[28] However, retaining moisture within the dressings may also inadvertently reduce the availability of atmospheric oxygen to the wound bed.[29] Such local dressing-induced hypoxia is not desirable for wound healing but by providing humidified oxygen directly to the wound surface, the wounds can potentially be kept moist and sufficiently oxygenated to optimise healing.[30]

An interesting fact that was noted in this early trial, and has been anecdotally confirmed by other clinical teams using this topical oxygen delivery system, is the initial increase in the size of the wound. Six of the 10 wounds increased in size initially, with four of these then reducing after a couple of weeks. It is well known that neutrophils and macrophages are less active in hypoxic environments, and that reversal of the hypoxia leads to an increase in their debriding and scavenging capabilities.[9] Good clinical practice would dictate that we regularly debride our wounds, although in reality we may not all be as good at that as we think. Effectively debrided wounds often heal well. It is possible that the increase in oxygen tensions have led to neutrophils and macrophages debriding the wound edges, and then allowing it to heal.

Limiatations

Several limitations to the study are inherent in the sample size, the absence of a control, and the low numbers of complete wound closure during the eight-week follow-up period.

A larger, blinded, randomised controlled trial over a longer follow-up is clearly necessary in determining the true effect of the therapy over the standard management of the DFU. By studying the effect of the therapy on a larger patient cohort, insight may be gained into the subgroups of patients who will most benefit from treatment and at what stage in the disease. An 18-centre double-blinded, placebo-controlled trial of the device is currently underway in the UK, along with the creation of a new registry of patients with DFUs of more than six months' duration. Preliminary results are expected to be reported early in 2018.

Conclusion

In conclusion, this phase I study has demonstrated the safety and efficacy of topical oxygen therapy in the treatment of diabetic foot ulcers. The dramatic reduction in the sizes of such refractory wounds warrants attention and further investigation.

Almost half of foot care expenditure is in the primary and outpatient sector. An inpatient with a DFU is, on average, likely to spend 13 days longer in hospital than without.[2] The ambulatory topical oxygen delivery device studied showed a significant beneficial effect on wound size in patients with diabetes. It has practical advantages over existing oxygen-based wound therapies such as HBOT in that it delivers oxygen continuously, it is easy to use, and it is accessible. Its suitability for use in the community could prove cost-effective. Its application is very straightforward and no complicated training is required. **JWC**

References

1 NHS Diabetes. Foot care for people with diabetes: the economic case for change. Patient safety resource centre 2013. https://tinyurl.com/y9ogzwgs (accessed 31 October 2017).
2 Diabetes UK. Diabetes in the UK 2012 (April 2012). https://tinyurl.com/y9nocdeg (accessed 31 October 2017)
3 Jonsson K, Jensen JA, Goodson WH et al. Tissue oxygenation, anemia, and perfusion in relation to wound healing in surgical patients. Ann Surg 1991; 214(5):605–613. https://doi.org/10.1097/00000658-199111000-00011
4 Silver IA. Tissue PO2 changes in acute inflammation. Adv Exp Med Biol 1977; 94:769–774
5 Ruangsetakit C, Chinsakchai K, Mahawongkajit P et al. Transcutaneous oxygen tension: a useful predictor of ulcer healing in critical limb ischaemia. J Wound Care 2010; 19(5):202–206. https://doi.org/10.12968/jowc.2010.19.5.48048
6 Wu L, Xia YP, Roth SI et al. Transforming growth factor-beta1 fails to stimulate wound healing and impairs its signal transduction in an aged ischemic ulcer model: importance of oxygen and age. Am J Pathol 1999; 154(1):301–309. https://doi.org/10.1016/S0002-9440(10)65276-5
7 Wyss CR, Harrington RM, Burgess EM, Matsen FA 3rd. Transcutaneous oxygen tension as a predictor of success after an amputation. J Bone Joint Surg Am 1988; 70(2):203–207. https://tinyurl.com/yazlytez
8 Tandara AA, Mustoe TA. Oxygen in wound healing—more than a nutrient. World J Surg. 2004; 28(3):294–300. https://doi.org/10.1007/s00268-003-7400-2
9 Sen CK. Wound healing essentials: let there be oxygen. Wound Repair Regen 2009; 17(1):1–18. https://doi.org/10.1111/j.1524-475X.2008.00436.x
10 Hodges ANH, Delaney JS, Lecomte JM et al. Effect of hyperbaric oxygen on oxygen uptake and measurements in the blood and tissues in a normobaric environment. Br J Sports Med 2003; 37:516–520.
11 Healthcare Finance. Medicare flags overuse of hyperbaric therapy for diabetics due to questionable value. June 28 2017. https://tinyurl.com/yawl4dvx (accessed 31 October 2017).
12 Game FL, Hinchliffe RJ, Apelqvist J et al. A systematic review of interventions to enhance the healing of chronic ulcers of the foot in diabetes. Diabetes Metab Res Rev 2012; 28 Suppl 1:119–141. https://doi.org/10.1002/dmrr.2246
13 Abidia A, Laden G, Kuhan G et al. The role of hyperbaric oxygen therapy in ischaemic diabetic lower extremity ulcers: a double-blind randomised-controlled trial. Eur J Vasc Endovasc Surg 2003; 25(6):513–518. https://doi.org/10.1053/ejvs.2002.1911
14 Löndahl M, Katzman P, Nilsson A, Hammarlund C. Hyperbaric oxygen therapy facilitates healing of chronic foot ulcers in patients with diabetes. Diabetes Care 2010; 33(5):998–1003. https://doi.org/10.2337/dc09-1754
15 Kranke P, Bennett MH, Martyn-St James M et al. Hyperbaric oxygen therapy for chronic wounds. Cochrane Database Syst Rev 2012; 4(4):CD004123.
16 Gottrup F, Apelqvist J. Present and new techniques and devices in the treatment of DFU: a critical review of evidence. Diabetes Metab Res Rev 2012; 28 Suppl 1:64–71. https://doi.org/10.1002/dmrr.2242
17 Thom SR. Hyperbaric oxygen: its mechanisms and efficacy. Plast Reconstr Surg 2011; 127 Suppl 1:131S–141S. https://doi.org/10.1097/PRS.0b013e3181fbe2bf
18 Blackman E, Moore C, Hyatt J et al. Topical wound oxygen therapy in the treatment of severe diabetic foot ulcers: a prospective controlled study. Ostomy Wound Manage 2010; 56(6):24–31.
19 Gottrup F, Dissemond J, Baines C et al. Use of oxygen therapies in wound healing: focus on topical and hyperbaric oxygen treatment. J Wound Care 2017; 26(Sup5):S1-S43. https://doi.org/10.12968/jowc.2017.26.Sup5.S1.
20 NATROX Oxygen Wound Therapy. Inotec AMD Ltd, UK. https://tinyurl.com/y9mj838a (accessed 31 October 2017).

21 Said HK, Hijjawi J, Roy N et al. Transdermal sustained-delivery oxygen improves epithelial healing in a rabbit ear wound model. Arch Surg 2005; 140(10):998–1004. https://doi.org/10.1001/archsurg.140.10.998
22 Woo KY, Coutts PM, Sibbald RG. Continuous topical oxygen for the treatment of chronic wounds: a pilot study. Adv Skin Wound Care 2012; 25(12):543–547. https://doi.org/10.1097/01.ASW.0000423439.62789.90
23 Löndahl M, Katzman P, Nilsson A, Hammarlund C. Hyperbaric oxygen therapy facilitates healing of chronic foot ulcers in patients with diabetes. Diabetes Care 2010; 33(5):998–1003. https://doi.org/10.2337/dc09-1754
24 Tawfick WA, Sultan S. Technical and clinical outcome of topical wound oxygen in comparison to conventional compression dressings in the management of refractory nonhealing venous ulcers. Vasc Endovascular Surg 2013; 47(1):30–37. https://doi.org/10.1177/1538574412467684
25 Siddiqui A, Davidson JD, Mustoe TA. Ischemic tissue oxygen capacitance after hyperbaric oxygen therapy: a new physiologic concept. Plast Reconstr Surg 1997; 99(1):148–155. https://doi.org/10.1097/00006534-199701000-00023
26 Fife CE, Buyukcakir C, Otto GH et al. The predictive value of transcutaneous oxygen tension measurement in diabetic lower extremity ulcers treated with hyperbaric oxygen therapy: a retrospective analysis of 1144 patients. Wound Repair Regen 2002; 10(4):198–207. https://doi.org/10.1046/j.1524-475X.2002.10402.x
27 Roe DF, Gibbins BL, Ladizinsky DA. Topical dissolved oxygen penetrates skin: model and method. J Surg Res 2010; 159(1):e29–e36. https://doi.org/10.1016/j.jss.2009.10.039
28 Winter GD. Formation of the scab and the rate of epithelization of superficial wounds in the skin of the young domestic pig. Nature 1962; 193(4812):293–294. https://doi.org/10.1038/193293a0
29 Larry M Sirvio. The effect of gas permeability of film dressings on wound environment and healing. J Invest Dermatol 1989; 93(4):528–531.
30 Stücker M, Struk A, Altmeyer P et al. The cutaneous uptake of atmospheric oxygen contributes significantly to the oxygen supply of human dermis and epidermis. J Physiol 2002; 538(3):985–994. https://doi.org/10.1113/jphysiol.2001.013067

Reflective questions

- Describe the facets of wounds healing that are affected by low oxygen levels?
- What proportion of the wounds I treat might have sub optimal amounts of oxygen present?
- How would my patients manage using a topical oxygen therapy device?
- In my practice, how could topical oxygen therapy affect local expenditure on chronic wounds?