Effect of a surfactant-based gel on patient quality of life

Abstract: The characteristic clinical signs of chronic wounds, which remain in a state of prolonged inflammation, include increased production of devitalised tissue and exudate, pain and malodour. The presence of necrotic tissue, slough and copious exudate encourages microbial proliferation, potentially resulting in planktonic and/or biofilm infection. For patients, the consequences can include leakage of exudate, pain and reduced mobility, which can impair their ability to socialise and perform activities of daily living. This can severely reduce their quality of life and wellbeing. Concentrated surfactant-based gels (Plurogel and Plurogel SSD) are used in wound cleansing to help manage devitalised tissue. *In vitro* studies indicate they can sequester planktonic microbes and biofilm from the wound bed, although there is, limited clinical evidence to support this. A group of health professionals who have used this concentrated surfactant gel, in combination with standard care, in their clinical practice for several years recently met at a closed panel session. Here, they present case studies where topical application of these gels resulted in positive clinical outcomes in previously long-standing recalcitrant wounds. In all cases, the reduction in inflammation and bioburden alleviated symptoms that previously severely impaired health-related quality of life and wellbeing.

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biofilm • devitalised tissue • healing • health-related quality of life • inflammation • surfactant

At the 2018 European Wound Management Association (EWMA) meeting in Krakow, a closed panel discussion took place in which health professionals and basic scientists from the Australia, Canada, Switzerland, UK and US, and discussed the effects of Plurogel and Plurogel SSD (silver sulfadiazine) concentrated surfactant–based dressings for burns and wounds on patient health-related quality of life (HRQoL) and wellbeing. (Hereafter, these two devices are referred to as the Plurogel micelle matrix (PMM) and as PMM with 1% SSD.) Guided by that discussion, this article describes the effects of chronic wounds, specifically prolonged inflammation, cell salvage and wound biofilm, on patient wellbeing. It describes a treatment that, when used as part of standard care, manages devitalised tissue, softens, loosens and traps debris and planktonic microbes, and eradicates and prevents the reformation of biofilm, thereby helping to reduce inflammation and, in turn, the formation of slough, pain and discomfort. Although there are several *in vitro* studies on the efficacy of PMM, there is limited published clinical evidence of its use in practice. To address this gap, some of the panel members present case study evidence of their own clinical experience.

***Kevin Woo**,[1] PhD, RN, NSWOC, FAPWCA, Associate Professor; **Rosemary Hill**,[2] BSN, CWOCN, WOCC (C), Wound Ostomy Continence Clinician; **Kimberly LeBlanc**,[3] PhD, RN, NSWOC, WOCC(C), Chair, Wound Ostomy Continence Institute; **Steven L. Percival**,[4] PhD, CEO and Director; **Gregory Schultz**,[5] PhD, Researcher; **Dot Weir**,[6] RN, CWON, CWS; **Terry Swanson**,[7] MHSc, FAWMA, FMACNP, Nurse Practitioner; **Dieter O. Mayer**,[8] MD, FEBVS, Head of Vascular Surgery Unit and Wound Centre
Corresponding author email: kevin.woo@queensu.ca
1 Queen's University, Kingston, Canada. **2** Vancouver Coastal, Canada. **3** Canada. **4** Centre of Excellence in Biofilm Science and Technologies, Liverpool, UK. **5** Professor Ob/Gyn, Director Institute for Wound Research University of Florida, Gainesville, Florida, US. **6** Catholic Health Advanced Wound Healing Centres, Buffalo, New York, US. **7** Warrnambool, Australia. **8** Department of Surgery, HFR Fribourg — Cantonal Hospital, Fribourg, Switzerland

Effects of wounds on quality of life and wellbeing

The World Health Organization (WHO) originally defined quality of life (QoL) as 'Individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns'.[1] Living with a chronic non-healing wound can have a negative impact on an individual's wellbeing due to wound infection, pain, malodour and other related symptoms.[2]

Effects of biofilm and/or infection

In chronic wounds, healing is stalled due to many intrinsic and extrinsic factors that contribute to prolonged inflammation.[3] Release of pro-inflammatory cytokines and human and/or bacterial proteases cause tissue degradation, which, along with a concomitant increase in the microbial bioburden, accelerates the production of devitalised tissue, slough and exudate.[4] As microorganisms continue to proliferate, they can coaggregate to form microcolonies and develop into a highly organised entity (biofilm) that produces clinical signs and symptoms such as pain, malodour and healing that is delayed beyond expectation.[5,6]

Biofilm has a pro-inflammatory effect. For example, many of the components that make up the extracellular polymeric substances (EPS) of the biofilm cause an

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upregulation of pro-inflammatory cytokines associated with enhanced pain.[7] In addition, Hemmi et al. reported that a receptor expressed in immune system cells, the toll-like receptor 9 (TLR9), recognises and responds to bacterial but not human DNA sequences. As such, the human innate immune system is 'primed' to recognise sequences in bacterial DNA. This explains why patients with chronic wounds can experience a strong inflammatory response.[8]

Wound healing that has been delayed because of biofilms may develop into a subclinical infection and eventually become systemic.[9] Biofilms are ubiquitous, and are formed when microorgansims are encapsulated and protected by EPS. In this state, microbes are protected against host defences and become recalcitrant to antimicrobials.[10]

Effects of wound infection on quality of life

With prolonged inflammation, injured nerve fibres may become more excitable, leading to spontaneous firing and increased sensitivity to painful stimulation.[11]

Excessive exudate can also contribute to pain if exudate leaks into the periwound skin causing maceration and erosion. Patients with heavily exuding wounds face challenges in controlling the leakage. Leaking fluid emanates a pungent odour that can be perceived as unhygienic, contagious, unpleasant and embarrassing when other people are around, even if they are friends and family.[2] Subsequently, many patients reluctantly enter into self-isolation, curtailing social activities and interaction with other people, affecting their social, psychological and cultural domains of wellbeing.[12]

These symptoms can also reduce patients' ability to perform other activities of daily living (ADL), such as showering and bathing, getting dressed, climbing stairs and lifting, which will in turn have a profound effect on wellbeing.[13,14] This can increasingly lead to a loss of autonomy and a dependence on others, with the individual fearing that he or she has become a burden on those around them.[15] Meanwhile, regular home visits for dressing changes can interrupt daily routines.

Pain is consistently reported by patients as one of the worst aspects of living with chronic wounds, impacting on their HRQoL.[16,17] Painful wounds can limit mobility, affecting the individual's ability to perform ADL and engage in social or recreational pastimes that give them joy in life.[2] Persistent pain can be fatiguing: as many as 48.6% of people with chronic pain also report chronic insomnia.[18] Another possible consequence of pain is loss of appetite, which can eventually lead to malnutrition, which is a risk factor for impaired healing.

The psychological effects can be profound, particularly in the case of protracted indolent wounds. An open wound on the skin alters one's body image and patients are vulnerable to negative emotions/feelings ranging from self-consciousness and embarrassment, to shame, disgust and self-loathing, with an overall feeling of low self-esteem.[2] A Brazilian study found that, of a sample of 80 patients, most of those surveyed (80% of those with diabetic foot ulcers [DFUs] and 55% with venous leg ulcers [VLUs]) considered their chronic wounds to be a form of punishment.[15] Low mood or depression can lead to hopelessness and self-neglect.[19] Such feelings can also have a profound effect on personal relationships, exacerbated by the effect of an exuding, malodorous wound on physical intimacy. However, some older patients simply regard having a chronic wound as an inevitable part of old age.[20]

The pervasiveness of the impact of having a chronic wound is also evident in work environments. Wearing a wound dressing (potentially in combination with compression/offloading devices and shoes) can cause patients to feel conspicuous, particularly if it is bulky.[21] Regular follow-up visits with health professionals, often during working hours, can impair the individual's employment prospects.[22,23] The psychological effect can be devastating, due to the impact on the individual's self-image and their negative perception of how their family and societal roles have changed.[17] This can affect relationships both within the family and in broader social circles.[24]

The impact on wellbeing for carers should not be underestimated. Published case study evidence indicates that some carers give up their employment to care for a loved one with a chronic wound,[25] and this can affect their own self-image, with ensuing psychological effects on wellbeing. Living with someone who has a wound can disrupt the home and family life.[26,27] In addition, witnessing the effects of a chronic wound on a loved one's wellbeing can also be extremely upsetting.

Finally, even after a wound has healed, there can be a continued psychological effect, related to anxiety about the risk of recurrence and, for some wound types such as VLUs or DFUs, the need for life-long adherence to treatments such as compression stockings.[2]

Achieving patient-centred care

Patient-centred care recognises that the patient is placed at the centre of their own health care. The health-care providers are in the periphery to help define health goals that are realistic and achievable.[28] Although patient wellbeing is multidimensional, encompassing physical, psychological, social, cultural and even spiritual domains, many practitioners often focus on wound closure or reduction in wound size as the primary clinical objective. Wound healing is specific and measurable, and the progression towards this can be observed and documented at each follow-up visit.[20] In contrast, goals that are most relevant to patients are defined by the primary need to reduce pain and manage malodour and exudate strikethrough, given the effects of these symptoms on their ability to undertake ADL and interact with other people.[20,29]

The importance of holistic, patient-centred care is being emphasised, not only in terms of the need to assess the whole patient (not just the wound) to determine the aetiology but also to ensure, wherever

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possible, that the patient and practitioner work collaboratively as partners in care.[30] If the patient has some ownership over the treatment goals, which will then better reflect their individual needs, they are more likely to be adherent to treatment, increasing the likelihood of a better clinical outcome.[31] This will involve selecting different treatment outcomes from full healing, such as a reducing pain, which are closely related to wellbeing. Poor symptom management is demotivating and so more likely to lead to non-adherence to treatment.[2] In clinical terms, this demands a focus on treatments that target the causes of prolonged inflammation in the wound by removing biofilms and slough, as well as decreasing the production of pro-inflammatory cytokines and protease activity. Ease of application and the ability of treatments to accommodate the patient's lifestyle are other important considerations, as these can facilitate self-care, which will further encourage adherence with treatment.

The panel's perceptions on HRQoL and wellbeing

At the closed panel session, the participants discussed their perceptions of HRQoL and wellbeing in wound care, and how these influenced the treatment goals chosen for individual patients and thus product selection. There was a consensus that wellbeing is highly personal, and so can only be identified by the individual concerned: they recommended that, at referral, each patient should be asked to describe what their HRQoL of life/wellbeing was like before the wound developed and how it subsequently changed. This reflects Calman's hypothesis of how to determine HRQoL.[32] They stated that all of the domains of wellbeing should be considered during this discussion, including the socioeconomic effects of living with a chronic wound. The panel reiterated the need to consider whether the wound reduced the patient's autonomy and how it might be possible to empower the individual during treatment. They also advised health professionals not to overlook the carers, for whom caring for the patient and their wound can be time-consuming, demanding and frustrating, particularly when there is no clinical improvement. The pervasive effects of pain on HRQoL and wellbeing were acknowledged, and they emphasised that its treatment should be a clinical priority, bearing in mind that patients are likely to consider the alleviation or eradication of pain as a sign of progress. Finally, they advised practitioners to be realistic with patients when discussing treatment goals, as failure to achieve them can trigger feelings of distrust and hopelessness.

Surfactants in wound care

PMM and PMM with 1% SSD are poloxamer-based surfactants that can be used to cleanse the wound, manage devitalised tissue, disperse and break up biofilm, and sequester the dislodged biofilm. This will help to reduce inflammation and promote granulation tissue formation/epithelialisation.[33] The reduction in inflammation and associated propensity to localised infection should help to reduce pain, thereby increasing patient comfort and wellbeing.

The most common example of a surfactant is soap. When in aqueous solutions, surfactant molecules have distinct hydrophilic and hydrophobic zones. The surfactant molecules congregate to form spherical super-structures called micelles. The central core of these micelles is composed of the hydrophobic zones from individual surfactant molecules, and the outer area is hydrophilic, consisting of aggregated hydrophilic zones from many individual surfactant molecules.[33]

The surfactant micelles act as adaptors (devices that can connect two entities not designed to be joined) such as oil and water, or a solid and a liquid.[33] Taking oil and water as an example, the insoluble oil molecules are attracted to and trapped by the surfactant micelle's hydrophobic zone (core), while water molecules are attracted to the hydrophilic zone on the outside of the micelle. When used in wound care, insoluble proteins and aggregates, such as devitalised tissue and slough, planktonic microbes and biofilm, gravitate to the central hydrophobic zone, which entraps the insoluble substance. Any such wound debris, loose devitalised tissue, slough and/or biofilm that is trapped by the micelles is washed away when the micelles are removed by wiping or washing with any reasonable wound cleansing solution.[33]

In addition, as surfactants lower the surface tension between liquids and surfaces, products that contain surfactants can penetrate a surface more extensively. When used in wound care, this means that a cleansing fluid with surfactants will come into more intimate contact with the wound bed than one without,[34] thereby increasing its efficacy.

PMM is a water-soluble, highly concentrated poloxamer 188-based hydrogel. It has a liquid formulation when in ambient conditions, particularly when these are cooler, but forms a thick gel as it warms in contact with tissue. This differentiates it from other synthetic polymer surfactants, which are viscous when cooled and 'runny' when warmed.[35] Furthermore, as the micelles become more attracted to the water in the PMM gel as the ambient temperature decreases, the gel can be atraumatically washed away.[35]

It is also proposed that poloxamer 188 (the key ingredient of PMM) maintains blood flow in the arterioles and venules by helping to prevent the build-up blood clots and debris, thereby improving oxygenation of wounded tissue.[36]

Research indicates that PMM has anti-inflammatory properties in that it can help repair the damage to the cell membrane, potentially preventing cell death.[37] When chronic wounds are stuck in a phase of prolonged inflammation, the excess levels of reactive oxygen species (ROS) present can damage cell proteins and lipids, resulting in cell death. This will in turn further the inflammatory response, increasing the production of excess cytokines and proteases. Laboratory research

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indicates that PMM can 'plug' the holes that appear in the cell membrane during this process.[37] The cell membrane comprises a lipid bilayer that protects the internal part of the cell from the external environment. Large breaks in this membrane result in cell necrosis and death. It is thought that the poloxamer 188 within PMM is able to insert itself into the damaged cell membrane and stabilise portions of the lipid bilayer.[37,38] salvaging the cell's lipid membrane. When the new lipids are being synthesised, the PMM is 'squeezed out' of the cell membrane and excreted out of the body.[39,40,41] In this way, PMM can help promote cell survival and thus help address inflammation.

In addition, referring to the ability of the innate immune system to recognise unique DNA sequences in bacteria, as shown by Hemmi et al.,[8] it is proposed that the PMM gel not only kills bacteria, but removes the exopolymeric matrix from the wound as a result of its detergent/surfactant action.

Finally, it has also been suggested that PMM decreases inflammation in the wound by binding to bradykinins released by damaged cells.[35]

In terms of topical application, PMM gel can be applied either to gauze or a foam dressing, or directly to the wound in a 5–10mm layer. It can be washed away with water, with dressing changes ranging from daily to three times a week.

PMM gel can be safely applied until full healing has occurred. In some countries, PMM with 1% SSD is also available; the manufacturer states that this can be safely used on wounds with signs of localised infection until the signs have subsided. After this, the practitioner should switch to PMM for maintenance therapy. There have been no reported adverse effects for PMM with or without 1% SSD, regardless of the treatment duration.

In vitro and clinical evidence on PMM

In a comparative laboratory study, wiping mature *Pseudomonas aeruginosa* biofilms on pig skin implants with gauze and PMM resulted in complete eradication of the polymicrobial colony on day three, whereas they regrew back to baseline level on day three when wiped with gauze only.[10] The results for both PMM and PMM with 1% SSD were both statistically significant at day three, when compared with gauze alone (both p=0.003).

Ghatak et al. found that application of PMM to planktonic cultures of *Pseudomonas aeruginosa* and *Staphylococcus* in broth culture reduced proliferation of both species and inhibited virulence factor expression of the *Pseudomonas aeruginosa*, thereby disrupting its aggregation.[42] Additional tests on *Pseudomonas aeruginosa* and *Staphylococcus* biofilms showed that the application of PMM either alone or in combination with an antibiotic significantly reduced bacterial metabolism, whereas application of antibiotic alone had a similar effect to the control. The investigators concluded that PMM has a bactericidal effect, likely due to the antimicrobial preservatives present in the product version without silver tested here. It appears that this bactericidal effect is enhanced by the use of antibiotics.[42]

In another laboratory study, both PMM and PMM with 1% SSD were found to have an antimicrobial effect against *Pseudomonas aeruginosa*, *Enterococcus* spp., *Staphylococcus epidermidis*, *Staphylococcus aureus* and meticillin-resistant *Staphylococcus aureus* (MRSA) biofilms. PMM with 1% SSD completely killed all of these preformed bacterial biofilms. Contrary to expectation, PMM also demonstrated some antibiofilm activity, when tested using the MBEC model, with the highest log reduction values reported for MRSA (5.41±3.13) and the smallest for *Staphylococcus aureus* (4.41±3.13). PMM also eliminated *Pseudomonas aeruginosa* (but not the other biofilms) in the CDC biofilm reactor model test. Using confocal laser scanning microscopy, the investigators observed that PMM dispersed the biofilm within 10 minutes of treatment and then detached it.[9]

Finally, PMM was found to prevent biofilm formation on porcine skin explants incubated with *Staphylococcus aureus* and *Pseudomonas aeruginosa* planktonic bacteria, when compared with a saline-soaked gauze control.[43] In a separate test, PMM was unable to eliminate *Acinetobacter baumannii* biofilm with daily wiping with and gauze unless antibiotics were also used (PMM with 1% SSD was not used here). *Acinetobacter baumannii* has been shown to be highly resistant to antibiotics alone.[44]

Ongoing studies (Percival SL – personal communication) have demonstrated that the concentrated surfactant gel, preserved with antimicrobials, is not toxic to both L929 and HDFa cell lines. Furthermore, following treatment with a concentrated surfactant gel, preserved with antimicrobials, within a scratch test model cell movement to close the scratch gap was assessed at 24 and 48 hours. The results demonstrated that cells treated with the concentrated surfactant gel, preserved with antimicrobials, are able to decrease cell necrosis and improve cell resistance after a needle scratch. The concentrated surfactant gel, preserved with antimicrobials, has demonstrated an ability to accelerate wound closure by enhancing cell mobility. Furthermore, it also appears able to stabilise the plasma membrane and demonstrated a resealing ability and retain the plasma membrane integrity.

It is plausible that, in the clinical setting, the ability of the PMM to manage devitalised tissue and the wound microbiome will help reduce inflammation and thus

Box 1. Treatment protocol for the plurogel micelle matrix[33]

Ensure the PMM gel is applied using standard aseptic techniques
The gel can be applied either to a gauze or foam dressing, or directly to the wound
For adults, apply a 5–10mm layer of gel. For children, apply a 2–3mm layer. The gel can be applied to wounds of any size or location on the body
Dressing frequency can range from daily to three times a week, depending on the individual wound
Using a cold solution to wash away the gel will increase its viscosity, facilitating atraumatic removal

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pain, increasing patient comfort. Some clinical evidence for this comes in the form of a large European real-life multicentre evaluation involving 1036 patients with non-healing wounds of varying aetiologies that had not responded to the usual standard care (not defined) provided in the participating centres. Of the sample, 70% (n=678) achieved wound closure and 24% (n=234) a 'dramatic' progression towards healing. In this evaluation, progression towards healing was defined as >40% wound area reduction within four weeks. All 10 centres reported reduced patient pain, decreased inflammation in both wound site and periwound skin, decreased infection rates and decreased exudate. They also stated that dressing changes were quicker and easier for patients.[45].

Additional evidence is provided in the form of two case series evaluations. In 2016, Zölß and Cech found that use of PMM with 1% SSD was associated with full healing in 67% of 226 patients with non-healing wounds.[46] The sample comprised patients with chronic wounds (duration ≥8 weeks) of various aetiologies, mostly leg ulcers (74%). The treatment protocol comprised wound cleansing, mechanical debridement of necrotic tissue, if necessary, protection of the periwound skin, and application of the PMM with 1% SSD and a gauze or simple non-woven secondary dressing. In addition, foam dressings (n=49 cases) and systemic and/or local antibiotics (n=53) were also administered when necessary. Gold standard treatment, such as compression and pressure redistribution, was given when required. Of the total evaluation population, 42 (19%) were lost to follow-up, resulting in 184 being followed up. Of these, after 4 weeks, 124 (67%) healed, 25 (14%) showed a significant progression to healing (defined as a decrease in wound size of ≥75%) and 35 (19%) switched to another treatment regimen. In a subgroup of 74 patients whose wounds had not responded to standard care before entry, 72.7% healed within a median of 12 weeks.

More recently, Ratliff undertook a single-centre case series (n=18) involving patients with full-thickness chronic VLUs (n=7) or arterial leg ulcers (n=11). Baseline wound durations were ≥4 weeks and the exudate level was 'dry to minimal'.[47] The effectiveness of the PMM gel was assessed using PUSH scores, whose key parameters are wound size, exudate volume and tissue type in the wound bed. Total PUSH scores range from 0 to 17, with the lower the score, the greater the wound severity. After four weeks' treatment with PMM, all patients' total PUSH scores reduced, with the mean score falling from a baseline of 10.7 (range: 5–17) to 8.3 (range: 0–14). In terms of the individual parameters, the biggest reduction related to the wound size, where the mean score reduced from a baseline of 6.5 (range: 10–2, where the maximum score is 10) to an endpoint of 5.2 (range: 10–0). The investigator attributed this to a change in tissue type from slough/necrotic to red granulation, stating the PMM effectively cleansed the wound of slough and necrotic debris. However, she also acknowledged that its small sample and case series study design limits its generalisability.

The panel members elected to share examples of their clinical experiences of using the PMM gel. This is presented below, and starts with a small case series evaluation, followed by several case studies. The case series evaluation was provided by KW, and cases 1–3 by RH, 4 and 7 by DW and 5–6 by DM.

Case series evaluation

A small prospective evaluation was undertaken on five patients with chronic wounds in a large inpatient long-term care setting. All patients were aged ≥18 years and each had at least one wound measuring ≥1cm^2 with signs of localised infection but a good potential for healing, based on clinical assessment. The PMM gel was applied to the wound at each dressing change, which was undertaken 3–5 times per week over 4 weeks. The level of localised infection was assessed weekly using the upper and lower checklist (Table 1).[48]

At baseline, the mean surface area covered with slough was 88% (median: 100%; range: 50–100%). Wound surfaces reduced by 30% after 4 weeks of treatment (baseline mean surface areas: 60cm^2; range: 8–140cm^2).

In three patients, the production of slough was eliminated entirely, resulting in a clean granulating surface, and in the remaining two it reduced by 60% and 40% respectively. These two patients were followed up for a further two weeks, by which time the slough had disappeared. The mean wound infection score reduced from 3.6 at baseline to 0.8 at week four. Full details are given in Table 2. None of the wounds developed a deep wound infection requiring systemic antibiotics.

Following removal of devitalised tissue, there was a significant improvement in malodour and the volume of exudate from the wounds after the treatment with PMM. Frequency for dressing change was reduced and has a potential impact on nursing time and patients' comfort. Pictorial examples of outcomes achieved in one case are illustrated in Fig 1.

Case studies

Case 1

Following a traumatic injury, a male patient, aged 70 years, with venous insufficiency, confirmed by Doppler ankle brachial pressure index (ABPI), developed a long-standing wound on his lower leg. His comorbidities included type 2 diabetes and hypertension, both of which were controlled with medication, as well as a history of transient ischaemic attack (TIA) that led to a left-sided stroke that did not affect his mobility. The patient had no signs of neuropathy/peripheral arterial disease and no current or previous history of diabetic foot ulceration. He also had an anxiety disorder.

In the three years that followed the injury, the wound was treated with multiple dressings (a variety of silver

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Table 1. Clinical signs and symptoms of upper and lower wound infection[48]

UPPER wound compartment infection	Clinical signs and symptoms of localised infection in the upper wound compartment
U-unhealthy tissue	Presence of >50% of debris, red friable tissue or abnormal discoloration of granulation tissue
P-pain	Sudden increase in pain
P- poor healing	Wound size has reduced by 5–10% in past 7 days
E-exudate	Moderate to heavy exudate levels
R-reek	Malodour
LOWER wound compartment infection	**Signs and symptoms of localised bacterial infection in the lower or deeper wound compartment**
L-larger in size	Increase in wound size or new areas of satellite breakdown
O-osseous tissue	Wound that probes to bone
W-warmth	Increased periwound temperature of more than 30 fahrenheit (1–20C) compared with the contralateral limb
E-oedema	Mild to moderate oedema
R-redness	Spreading erythema (> 2cm) beyond wound margin

dressings, iodine, methylene blue and gentian violet) and cleansed with normal saline, but these resulted in only a minimal improvement. Initially, he did not wear compression, but latterly he was able to tolerate a light compression garment.

Unfortunately, after three years, and despite a recent course of antibiotics (cefazolin), the wound deteriorated and his pain increased. His pain relief comprised paracetamol (acetaminophen) and gabapentin 100mg tid. To relieve the pain, the patient tended to scratch his leg, resulting in additional superficial wounds.

In December 2016, the patient, who was now aged 70, was admitted to hospital for treatment of this recalcitrant wound. It was highly exuding and malodourous, with a friable, dark-red wound bed that felt exceedingly tender when touched (Fig 2a). The patient's self-reported pain score was 8/10 for when the wound was touched or cleansed, which made it almost impossible to perform conservative sharp debridement or apply Emla cream. No granulation tissue was present. On admission, he was prescribed intravenous (IV) cefazolin, piperacillin and tazobactam

Both standard imaging and fluorescence imaging (MolecuLight, Smith and Nephew)[49] were used to visualise the bacteria in the wound bed (Fig 2b). Areas that exhibit red fluorescence are presumed to have moderate/heavy bacterial contamination (≥10^4 CFU/g) and are swabbed. In this case, the culture grew multiple organisms, predominantly meticillin-susceptible *Staphylococcus aureus* (MSSA) and *Pseudomonas*.

It was decided to replace the previous unsuccessful treatments with the PMM gel. The patient consented to this as he was frustrated with the protracted nature of his wound, and the prospect of a new approach made him feel more hopeful. The wound ostomy continence nurse prescribed PMM, a silicone foam dressing and compression therapy, initially an elasticated tubular bandage and then a two-layer reduced compression bandage system. The wound was cleansed with normal saline. Daily dressing changes were required because of the large volume of exudate produced. PMM gel was used on an exuding wound to cleanse the wound bed of devitalised tissue, reduce inflammation and, in turn, the exudate volume. PMM with 1% SSD was not used as it is not available in the country (Canada).

Figs 2c and d shows the improvement in fluorescence imaging (bacteria) on days 1 and 8. The red fluorescence (circled) depicts the bacteria present on day 1, which

Table 2. Results of a small prospective evaluation involving five patients

	Wound aetiology	Wound duration	Percentage slough		Combined upper and lower infection score	
			Baseline	Week 4	Baseline	Week 4
Patient 1	Pressure ulcer	4 month	50	0	3	0
Patient 2	Venous leg ulcer	2 weeks	90	0	3	0
Patient 3	Pressure ulcer	3 weeks	100	40	3	1
Patient 4	Pressure ulcer	2 weeks	100	60	5	2
Patient 5	Pressure ulcer	4 weeks	100	0	4	1

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substantially reduced by day 4. The image taken on day 8 shows an island of epithelial tissue, which continued to expand over the days and weeks ahead. The patient was discharged in early January 2017, when it was possible to replace the IV antibiotics with oral ones. Due to the patient's anxiety disorder, he was always accompanied by a trained volunteer when he attended the wound clinic for assessment.

After 8 weeks, the wound size had decreased from a baseline of 39.70cm^2 (day 1) to 7.35cm^2. No periwound maceration occurred during treatment with the PMM gel. In addition, the patient did not report any pain when the gel was applied and after dressing changes. Antibiotics were used for a total of 6 weeks. As the wound continued to decrease in size, the patient became exceedingly pleased with its ongoing improvement and the reduction in pain, commenting that he was 'scratching' it much less. The PMM gel continued to be used for about 2 weeks, after which only compression and antimicrobial dressings were used. It closed in June 2017 and remains closed at the time of writing.

Case 2

An 85-year-old man was admitted to hospital with respiratory difficulties and a large wound on the lower limb. He had a history of hypertension, congestive heart failure, hypothyroidism, neurogenic bladder, dementia, non-insulin dependent diabetes mellitus and peripheral vascular disease.

He had lived at home, where he was cared for by his wife, who also undertook most of his wound care. Based on the ABPI results, a two-layer light compression system was prescribed, to be applied in strict accordance with guidelines. The wound was cleansed with normal saline. The community wound care clinician and home care nurses tried various advanced dressing products (a variety of silver and iodine dressings). As the wound failed to respond, they concluded there was insufficient perfusion and it was 'not healable'. The plan of care was thus changed to 'maintenance therapy', with his wife changing the dressing as needed. The recalcitrant nature of the wound had a profound effect on the patient's HRQoL, but more so on his wife's, who felt the burden of managing a wound that showed minimal signs of improvement. She worried that it was getting worse and felt somewhat responsible for this, fearing she could be doing more

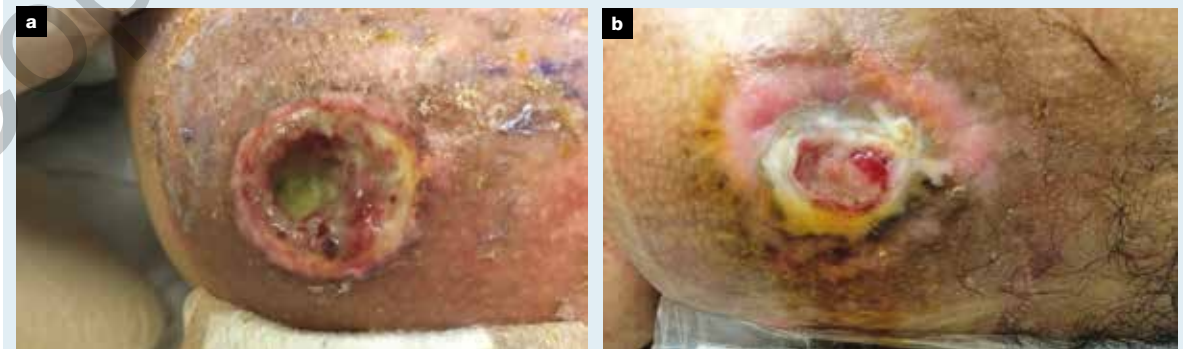
The attending physician referred the patient to the wound ostomy continence nurse. At presentation, the wound's surface area was 22.04cm^2 (Fig 3a). The wound bed was friable, slightly malodourous and felt extremely tender when touched. It was producing a moderate level of exudate and there was some periwound maceration. The patient's wife asked if a new treatment might make a difference. The PMM gel was therefore applied, along with light compression. No antibiotics were prescribed. After five days, the wound reduced to 15.60cm^2 (Fig 3b) and showed healthy granulation tissue. After eight days, it measured 14.47cm^2. The wound bed had a much healthier appearance, with granulation tissue. This was a great relief for the patient and his wife, who was delighted by the reduction in pain and hopeful of a good outcome. After one month, it had reduced to 11.99cm^2 (Fig 3c), decreasing further to 7.70cm^2 at 7 weeks (Fig 3d). Full healing was achieved after just over a 6-month period.

Case 3

A 75-year-old woman who had developed a hospital-acquired PU. This patient had incomplete L1 paraplegia secondary to a road traffic accident, several years earlier. She had a severe kyphotic back, for which Harrington rods had been inserted. As a result of the paraplegia, her lower extremities deteriorated rapidly and she developed urinary incontinence. She was malnourished and underweight. These factors increased her risk of PU.

The patient was admitted to hospital with pneumonia and diminishing mobility. In the first few days of her admission, she became exceeding short of breath. She chose to sit in the high Fowler's position. Her respiratory status deteriorated and to improve her oxygenation and achieve haemodynamic stability, she was intubated and taken to the intensive care unit. Unfortunately, due to her condition, there were periods of diminished

Fig 1. Case from case series evaluation: male patient, aged 57 years, with a spinal cord injury. He acquired a pressure ulcer in intensive care after a fall resulting in a c3 fracture. Week 0 (**a**). Week 3: following treatment with the PMM gel and iodine (**b**)



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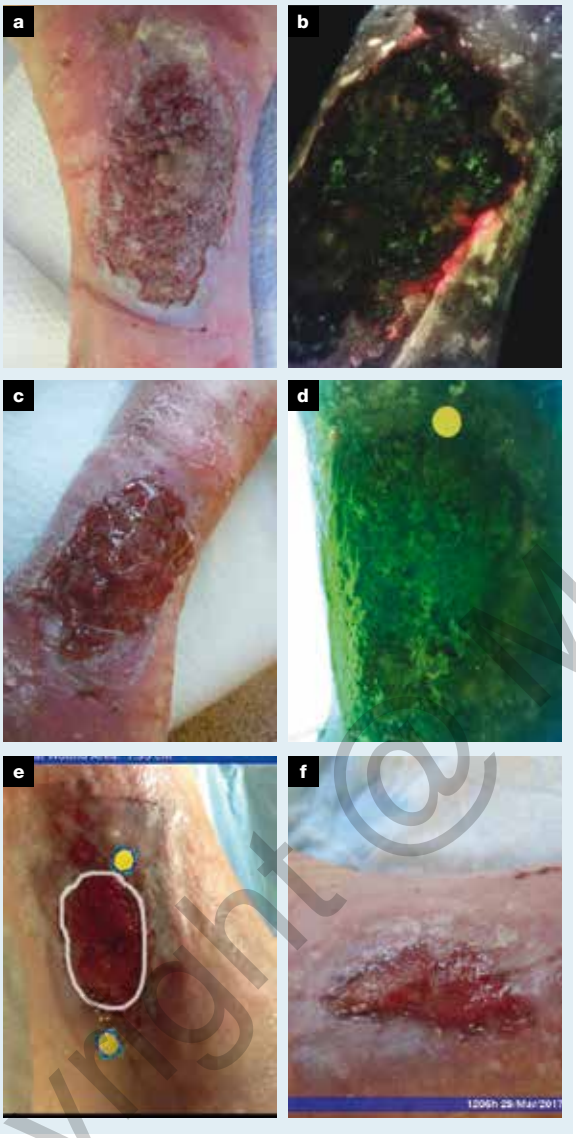

Fig 2. Case 1. 9 December 2016: the wound before treatment with PMM (**a**). Fluorecence imaging (before treatment) (**b**). 15 December: the wound following treatment with PMM (**c**). 19 December (day 8): fluorescence imaging (**d**). 23 February 2017: approximately 8 weeks later (**e**). The wound on 29 March 2017 (**f**)

movement, resulting in a PU. The wound, which was deemed unstageable, completely covered in soft, pale-yellow slough, was producing a moderate level of exudate and had demarcated edges. Multiple wound care regimens were used to reduce the eschar and slough: an amorphous hydrogel with occlusive dressing, a cadexomer iodine gel and an occlusive dressing, to help debride the slough.

Following a significant improvement in her respiratory status, the patient was moved to the rehabilitation unit, where she was treated with Hydrofera Blue Foam. No antibiotics were prescribed. Unfortunately, the PU continued to increase in size, measuring 12.08cm^2. The staff ensured pressure redistribution was in place, providing support surfaces for her wheelchair and bed, and referred her to the wound ostomy continence nurse clinician for specialist wound care advice. The condition of the wound bed and exudate level remained unchanged (Fig 4a); the wound was extremely painful, making only limited conservative debridement possible. It was swabbed for culture, but the results indicated that antibiotics were not required. As the previous treatments had not resulted in any improvement, it was considered reasonable to try the PMM gel to see if it would change or modify the wound bed slough.

The wound was cleansed with saline, and the PMM gel was covered with a foam dressing. After 4 days of treatment, buds of granulation tissue started to appear (Fig 4b). By day 6, approximately 25% of the slough had been removed from the periphery of the wound bed, indicating that the PMM gel was able to manage the devitalised tissue. Fig 4c shows the wound after 9 days of treatment. After 14 days, the central island of slough cleared to reveal a wound cavity and there was granulation tissue formation on the peripheral areas. The patient consented to surgical debridement and wound closure. She was exceedingly pleased that the wound had progressed to the extent that surgical closure was an option and was looking forward to being discharged. Sadly, several weeks later, the patient deteriorated for non-wound related reasons and died.

Case 4

This concerns a 29-year-old man with antiphospholipid syndrome, an autoimmune disease that can cause frequent clotting in the arteries and veins. The condition had developed while he was in college, but he continued to live a full and active life, which included playing football. He began to develop leg ulcers while in college and continued to have many in the following 10 years, as evidenced by the scars on his legs (Fig 5a). During this period, his medications included apixaban, clopidogrel and prednisone. Over the years, he was constantly treated with compression: stockings or socks when not ulcerated and multi-layer wraps when ulcerated. He was treated topically with close to every wound dressing category available, depending on his level of exudate, bioburden and pain level.

At one visit to the wound healing centre, he presented with two juxtaposed ulcers on his right anterior and anterolateral lower leg, in addition to multiple painful, highly exuding chronic ulcers on his posterior calf that needed daily dressing changes. Both wounds were almost completely covered with a very dark green moist, but densely adherent, devitalised tissue. As there were no clinical signs of infection, the wounds were not swabbed for culture.

To evaluate the best course of treatment, two different dressings were used: a pathogen-binding mesh on the anterolateral ulcer (Fig 5b) and the PMM gel on the anterior ulcer (Fig 5c). The patient was instructed to

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Fig 3. Case 2. The wound before treatment with the PMM gel (**a**). The wound after 5 days of treatment with the PMM gel (**b**). The wound after 31 days of treatment (**c**). The wound after 7 weeks of treatment (**d**)

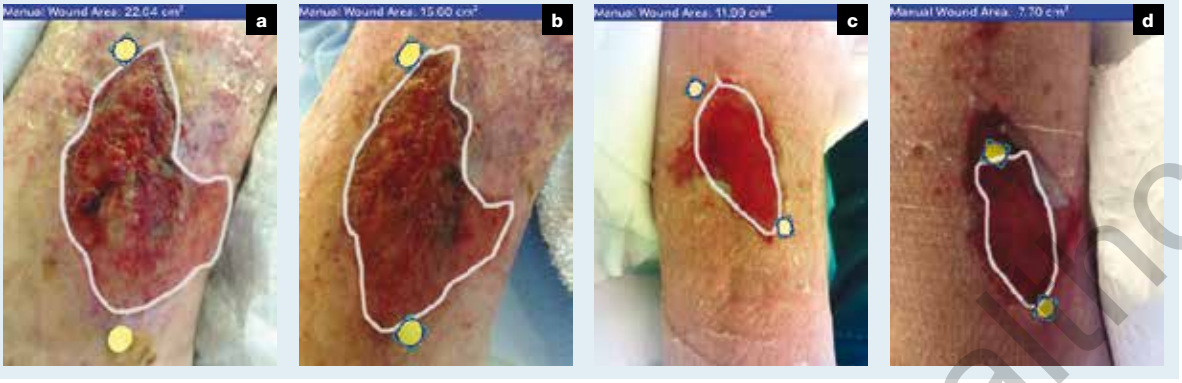


Fig 4. Case 3. The wound before treatment with the PMM gel (**a**). The wound after 4 days' treatment with the PMM gel (**b**). The wound after 9 days' treatment with the PMM gel (**c**)

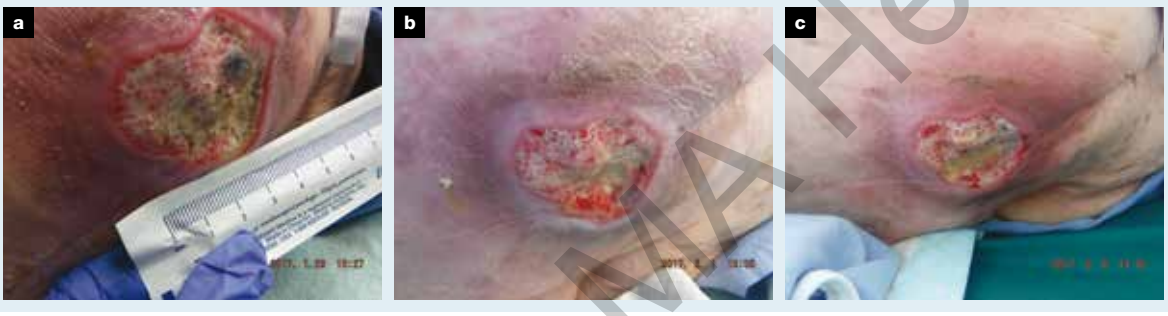
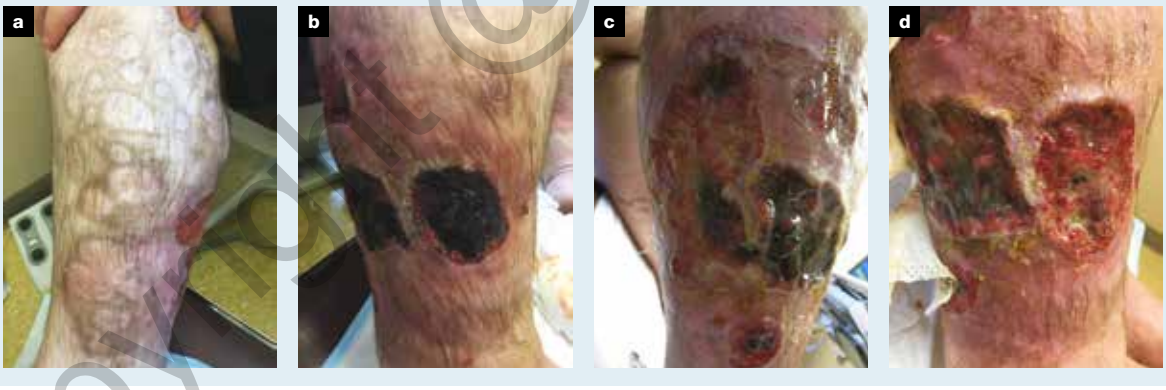


Fig 5. Case 4. Scars from a long history of ulceration (**a**). Wounds before the initiation of therapy with the PMM gel. Dark-green devitalised tissue is present (**b**). Posterior aspect of same leg, indicating reason for daily dressing change (**c**). Wound after treatment with the PMM gel; the wound bed on which the PMM had been used is much cleaner (**d**)



change the dressings daily due to the copious exudate from the other ulcers on the same leg (Fig 5c) and to return to the clinic the following week.

After six days, the mesh-treated wound had approximately 50% less devitalised tissue (Fig 5d, left) and the PMM-treated ulcer (Fig 5d, right) had approximately 95% less devitalised tissue, as well as evidence of granulation tissue formation, illustrating the remarkable ability of the gel to clean the wound and reduce the amount of bacteria present. Due to acquisition challenges, the PMM gel was only applied to this patient for this short time period, but the improvement in his wounds motivated the clinic team to undertake a larger evaluation of the PMM gel on other patients.

Case 5

This case study relates to an 82-year-old male patient with a non-healing venous ulcer. His comorbidities comprised an asymptomatic ischaemic and hypertensive cardiomyopathy and obesity.

Approximately 40 years previously, the patient underwent bilateral vein stripping. Three years ago, he presented at the wound clinic with a recurrent varicose ulcer due to recurrent varicose veins on his right leg, for which he was treated. He was prescribed compression

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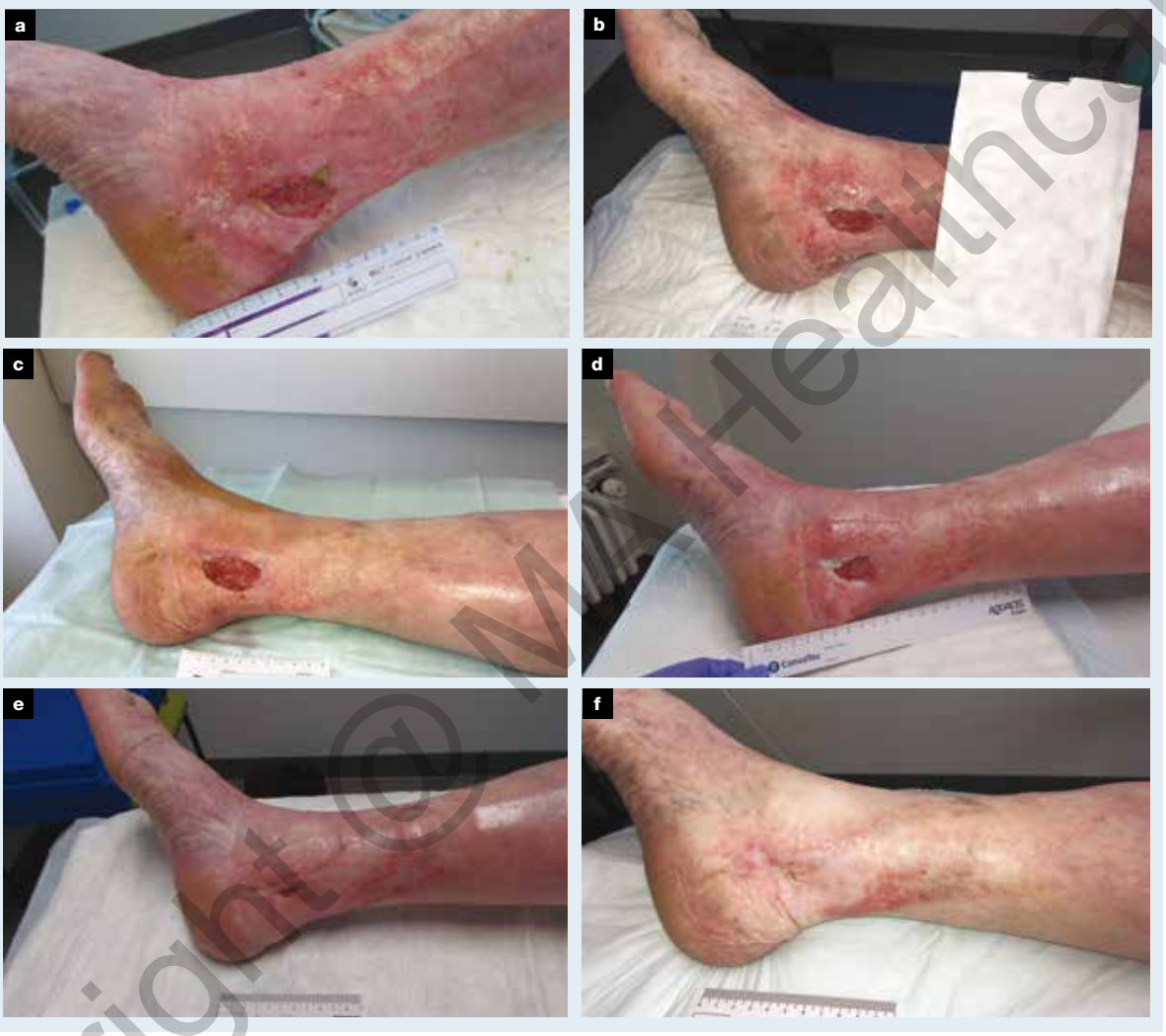
Fig 6. Case 5. The wound after 2 years of treatment with a variety of standard treatments (this picture was taken after debridement) (**a**). The wound after 5 weeks of treatment with the PMM gel with 1% SSD (**b**). The wound after 2 months' treatment with the PMM gel with 1% SSD. As signs of infection had resolved, it was decided to switch to pure PMM (**c**). The wound after 3 months' treatment with the PMM gel (5 months after initiation of treatment) (**d**). The wound after 7 months' treatment with the pure PMM gel (9 months after the initiation of treatment) (**e**). Full healing after 11 months with the pure PMM gel (or a total of 13 months' treatment) (**f**)



therapy, initially in the form of two-layer compression bandages and then class 2 compression stockings. His adherence to treatment was excellent. Local treatment spanned almost every modern wound dressing: antiseptic gels, hyaluronic acid, Hydrofiber dressings, alginates, various silver dressings, an oxidised regenerated cellulose (ORC) dressing, different foams with different adjuncts, superabsorbents, topical cortisone, to name a few. During this period, he also repeatedly received antibiotics for local infections.

Two years later, the wound had still not responded to compression therapy or topical treatment, and measured 40 x 20 x 5mm (Fig 6a). At presentation, the wound bed was filled with malodorous slough (which was debrided), the wound margins were macerated and inflamed and the periwound skin were fragile with signs of inflammations, as well as small satellite lesions. Over time, the patient had become desperate as his wound was not improving and he lost faith in his caregivers. He consented to treatment with PMM gel with 1% SSD. The wound was thoroughly sharp debrided and the gel, which was covered with a secondary gauze dressing, was applied three times weekly. No other active wound dressings or antibiotics were used. After 5 weeks of treatment, the wound depth had reduced by 2mm and the periwound inflammation had improved (Fig 6b). After 2 months, healthy granulation tissue had appeared (Fig 6c) and it was therefore decided to switch from PMM with 1% SSD to pure PMM.

After 5–9 months, there was a marked reduction in wound size (Fig 6d–e). The patient repeatedly reported at his visits how his life had changed since starting treatment

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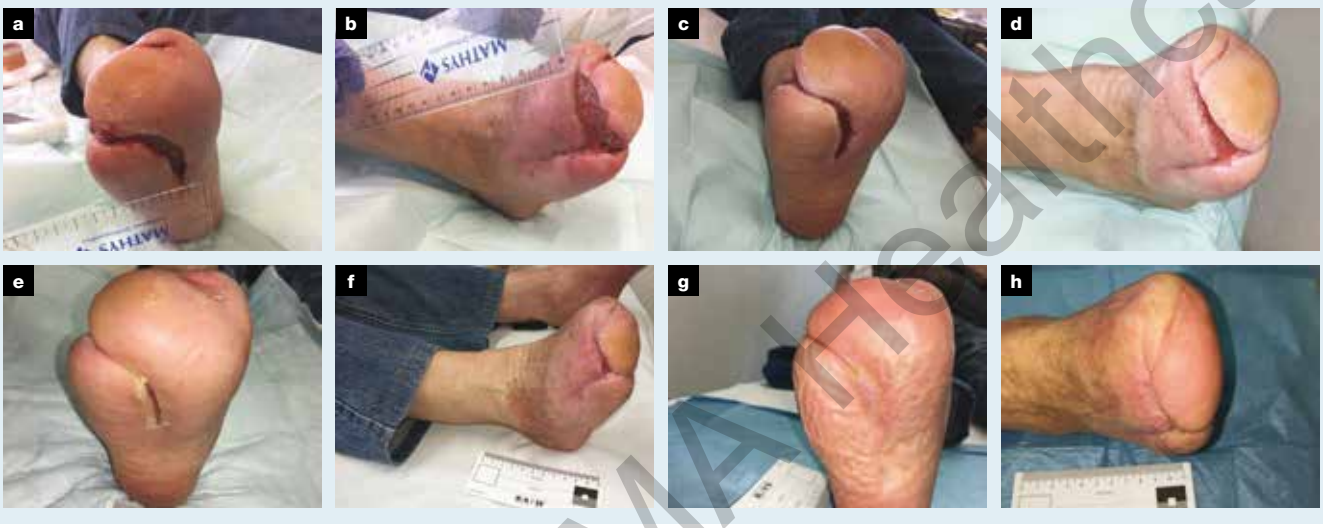
Fig 7. Case 6: Plantar aspect of the wound before treatment with the PMM gel with 1% SSD (**a**). Dorsal aspect of the wound before treatment. The small lesion on the anteromedial aspect was a fistula that extended to the first metatarsal bone, which had been debrided using a curette (**b**). Plantar aspect of the wound after 3 months' treatment with the PMM gel with 1% SSD. The wound bed, after debridement of fibrin, was showing good granulation tissue (**c**). Dorsal aspect of the wound after 3 months' treatment with PMM gel with 1% SSD (**d**). Plantar aspect of the wound after 6 months' treatment with the PMM gel with 1% SSD. Only a small fissure is evident, which had been cleaned with forceps. Hyperkeratosis of the wound margins were removed using a scalpel (**e**). Dorsal aspect of the wound after 6 months' treatment with the PMM gel with 1% SSD. After cleansing and debridement with forceps, a small triangular wound with nice granulation tissue is seen. The anteromedial fistula has almost closed (**f**). Plantar aspect of the wound after 14 months' treatment (8 months with PMM gel with 1% SSD and 6 months with the pure PMM gel (**g**). Dorsal aspect of the wound after 14 months' treatment (**h**)



with the PMM: the pain and malodour had disappeared, his clothes were not compromised by exudate anymore, and he had faith in his future once more.

Full healing occurred 13 months after the treatment was initiated (Fig 6f). The patient was finally able to care for his elderly wife, who needed his support.

Case 6

An 81-year-old male patient with a long-standing non-healing plantar ulcer on his right foot needed an urgent transmetatarsal amputation due to acute osteomyelitis of the third metatarsal head. Significant peripheral arterial occlusive disease was finally diagnosed and treated with angioplasty.

His postoperative recovery was complicated by deep vein thrombosis and, despite a long-term antibiotic regimen with co-amoxicillin (co-amoxiclav), several weeks after the primary amputation, the patient was scheduled for a below-knee amputation (Fig 7a-b). Additional comorbidities were coronary artery disease and chronic anaemia.

Despite documented well-restored blood flow to the foot, around the medial flap, there was a deep, postoperative non-healing wound, which was filled with slough and necrotic tissue. The wound was very painful (his visual analogue scale (VAS) ranged from 6 to 8 out of 10) and the moderate to heavy exudate levels had resulted in the various advanced dressings being changed several times daily. Significant oedema was also present. As a result, the patient had limited mobility. He became extremely depressed (low mood), stating that he was 'giving up on himself'.

The wound was surgically debrided, which revealed dehiscence and an inflamed wound bed. Treatment with PMM gel with 1% SSD was initiated while the patient was still in hospital. Gauze was applied as a secondary dressing. The patient received no other wound treatments. He refused all offloading devices and was therefore instructed how to walk on his heel on crutches. The wound was initially sharp debrided weekly and then, following his discharge to a nursing home 2 months later, three to four times weekly. At the nursing home, offloading comprised a simple forefoot offloading shoe and crutches; he received no other adjunctive treatment.

Three months later, a significant improvement of the post-amputation wound was observed: the inflammation and exudate volume steadily decreased and his pain levels improved markedly (VAS fell to 2–4) (Fig 7c–d). The wound margins were calm and there was significantly less dehiscence. The oedema had reduced and the medial flap appeared viable.

At 6 months, the wound continued to heal uneventfully (Fig 7e–f). The medial rotation flap had been almost entirely incorporated. At 8 months, when the signs of local infection had disappeared, the PMM with 1% SSD was replaced with the pure PMM gel. At his last visit, 14 months' postamputation, the wound had fully healed, the rotation flap was stable and the oedema had disappeared (Fig 7g–h). There was still a tendency for hyperkeratosis to occur, which was sharp debrided every 2–3 weeks.

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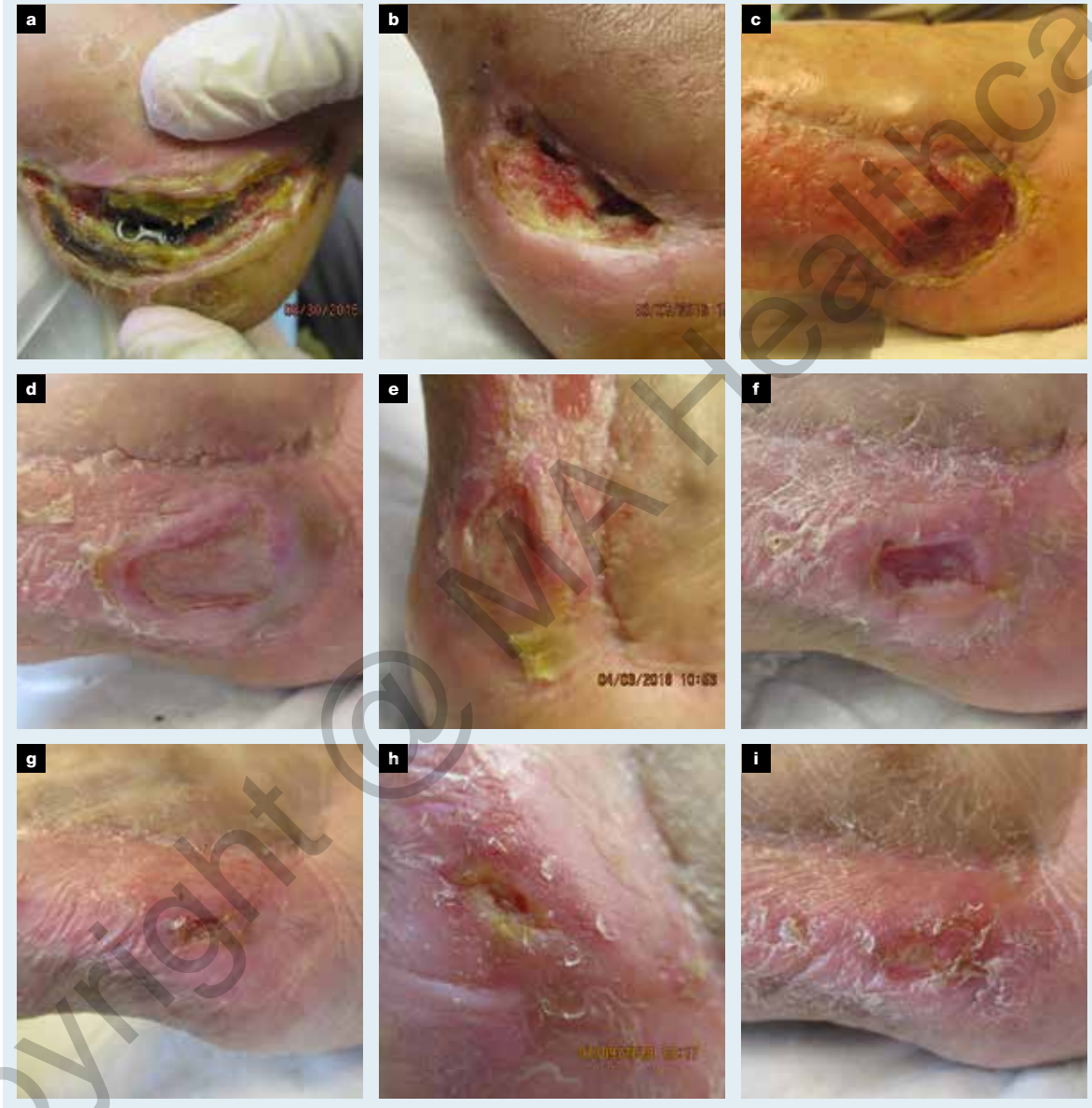
Fig 8. Case 7. August 2016: initial presentation of open surgical wound with exposed hardware (**a**). October 2016: return visit; open wound with exposed bone (**b**). July 2017: treatment is resumed after multiple surgeries and, ultimately, a full-thickness skin graft (**c**). March 2018: wound measures 2.4cm^2. Initiation of treatment with PMM (**d**). April 2018: wound measures 1.4cm^2 (**e**). May 2018: wound is 0.55cm^2 (**f**). June 2018: wound is 0.15cm^2 (**g**). July 2018: wound is 0.09cm^2 (**h**). August 2018: wound is closed (the wound is fully covered with epithelial tissue; the surrounding pink is fresh epithelial tissue left when the dried skin was removed from the edge) (**i**)



The patient's joint mobility was unrestricted and he was able to move around independently in his nursing home. His HRQoL had improved significantly as he no longer experienced wound-related pain, he felt more independent and was able to participate in his nursing home's social activities again.

In summary, treatment with the PMM gel, in combination with offloading and debridement, led to rapid reduction in inflammation, exudate and pain, avoiding the need for a below-the-knee amputation.

Case 7

This concerns a 53-year-old man with an open surgical wound. He had a significant medical history of hypertension and smoked one pack of cigarettes a day.

The patient fell from a roof, sustaining a calcaneal fracture. He underwent open reduction and fixation with hardware. As he is a landscaper, he was unable to work because of the ensuing disability. His orthopaedic surgeon referred him to the wound healing centre with an open surgical wound with exposed hardware on his

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right lateral heel (Fig 8a). He was referred back to orthopaedics for further surgery, during which the hardware was removed. He returned to the clinic 5 weeks later with exposed bone (Fig 8b) and underwent further surgical debridement of the bone. In the ensuring months, he had multiple surgeries due to infections and healing challenges and, ultimately, had a full-thickness skin graft.

Almost a year after the original visit, he returned to the clinic with a continued open wound at the base of his skin graft, with non-granular tissue (Fig 8c) Over the next 8 months, the wound was treated primarily with sharp debridement, an enzymatic ointment and moist gauze or antimicrobial foam, with little change in its status. The patient continued receiving disability benefits; the ensuing loss of income, as well as his ongoing pain, caused him and his wife much frustration. In March his wound surface area was 2.4cm^2, having reduced by only 4.5cm in the previous 8 months (Fig 4). Treatment was initiated with the PMM gel and a saline-moistened gauze secondary dressing, which, at his own request, the patient changed at home daily after showering. At each subsequent monthly return visit, there was a significant percentage reduction in area. He and his wife were excited to share the progress at each visit, and were relieved that the wound finally appeared to be healing. Full closure was achieved in August (Figs 8d–i).

Discussion

Chronic wounds are associated with an increased bioburden, and thus potentially both planktonic and biofilm infection. Chronic and some acute wounds also have cellular damage, either from trauma or, particularly in chronic wounds, from the damage to cellular membranes from ROS type agents that are associated with chronic inflammation. Both of these phenomena (microbiome issues, as well as cellular damage) lead to the ensuing clinical signs of prolonged inflammation and local infection, such as increased pain, high levels of exudate, malodour and non-healing. These sequelae can significantly impair patients' HRQoL and wellbeing. Pain can reduce mobility, restricting the individual's ability to undertake activities of daily living, while leakage and strikethrough of exudate and malodour can increase self-consciousness and embarrassment, resulting in self-imposed social isolation. For younger patients, chronic wounds can have unfortunate implications at work. The psychological consequences of this for individual patients can be imagined.

Holistic assessment and care, which determines the underlying aetiology and considers the whole patient, is needed to address this. Treatments that assist wound bed preparation by cleansing the wound and targeting the wound microbiome, particularly biofilms, have a role to play within this. This article, which is based on a recent closed panel discussion, describes the participants' experiences with a surfactant wound gel, which is designed to cleanse the wound bed as part of wound bed preparation. Published evidence indicates the ability of this biomaterial to change biofilm status as well as to salvage damaged or dying cells. The cases support published *in vitro* and *in vivo* evidence that the PMM gel manages devitalised tissues. The ensuing reduction in inflammation can help relieve some of the symptoms of chronic wounds, including pain, thus increasing patient comfort and improving HRQoL. In many of the cases described here, the PMM gel was used as a long-term adjunct to standard care and was observed to help promote healing.

A limitation of this article is that the clinical evidence presented here consists of randomly selected case studies from a committed group of PMM gel users. It could therefore be said to constitute expert opinion. Well-designed clinical evaluations, with larger sample sizes and, ideally, a comparator, are needed to determine if these findings can be replicated on a wider scale.

Conclusion

This article demonstrates that the clinical signs associated with prolonged inflammation in chronic wounds can significantly impair patients' HRQoL and wellbeing. Treatments are therefore required that can help reduce the causes of the inflammation. This article describes case studies showing that use of the PMM gel, used in combination with standard care, helped reduce inflammation and bioburden, thereby alleviating symptoms that had previously impaired the patients' health-related quality of life and wellbeing. JWC

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