

Use of oxidised regenerated cellulose (ORC) and collagen dressings (PROMOGRAN™ Protease Modulating Matrix and PROMOGRAN PRISMA™ Wound Balancing Matrix) to kick-start the treatment of chronic wounds

KEY WORDS

- ▶▶ Chronic wounds
- ▶▶ Infection
- ▶▶ Inflammation
- ▶▶ Oxidised regenerated cellulose (ORC)
- ▶▶ Self-care
- ▶▶ Silver

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The treatment of chronic, non-healing wounds is one of the biggest challenges faced by healthcare providers (Irving, 2019), costing the NHS £5.3 billion per annum (Guest et al, 2015). PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix have been shown to help stimulate healing and reduce the risk of a wound becoming hard-to-heal. A working group of key opinion leaders met in June 2019 to discuss the use of PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix to kick-start the treatment of chronic wounds, and to develop a decision pathway for clinical practice to support clinicians. The group's recommendations on appropriate use are presented here.

Chronic wounds are a burden to patients and the NHS and are predicted to increase at a rate of 12% per year as a result of delayed healing (Guest et al, 2017a). Chronic wounds can have a profound impact on quality of life for patients, resulting in pain, feelings of isolation, reduced mobility, lack of personal hygiene and financial concerns, which in turn can affect adherence to treatment. Patients with chronic wounds have increased rates of hospitalisation and antibiotic usage compared to people without wounds and a small number have been shown to consume a disproportionate amount of resources (Guest et al, 2015), creating further significant challenges to the health system.

The aims and objectives of the meeting were to:

- ▶▶ Identify the challenges of managing chronic wounds in practice
- ▶▶ Draw on clinical experience and evidence base for using PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix
- ▶▶ Suggest a framework to develop a pathway for

PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix aligned with the National Wound Care Strategy for venous leg ulcers (VLUs) and diabetic foot ulcers (DFUs), which is currently under development.

CURRENT CHALLENGES FACED IN WOUND CARE

A working group of key opinion leaders initially discussed the extent of the problem caused by chronic wounds, focusing on the importance of the patient's perspective. Patient empowerment and self-care in wound management has continued to gain momentum, with patients now playing a central role in their own healthcare if they are able and willing, which has proven to be beneficial for both patient and clinician (Wounds International, 2016). In addition, the amount of involvement patients have in their care can impact the overall reduction in wound management costs (Kapp et al, 2012).

Table 1 includes common challenges that can be frustrating for both the clinician and patient,

Table 1. Common challenges	
Problem	Supporting evidence and group comments (<i>pink</i>)
Delayed referral	<p>Prevalence of chronic wounds will increase at a rate of 12% per year due to delayed healing (Guest et al, 2017a).</p> <p><i>“Delayed referral can put patients’ limbs and lives at risk.”</i></p> <p>Delayed healing increases the risk of complications, such as infection and results in reduced quality of life (Gouin and Kiecolt-Glaser, 2011).</p> <p><i>“It is a concern when patients are seen by the same clinician week on week when the wound is not progressing, or worse, is deteriorating, and the patient is not referred to a specialist.”</i></p>
Increased risk/Fear of amputation	<p>Previous research suggests that cost-saving preventative actions for amputations should be instigated early and incorporate a comprehensive wound management strategy. Appropriate interventions and management for wounds can lower the risk of amputation by 47–72% depending on strategy (e.g. education, multidisciplinary approaches, wound monitoring, vascular surgery interventions, and the use of therapeutic foot wear; Yazdanpanah et al, 2015).</p> <p><i>“The personal cost of an amputation for the patient is huge – it can be challenging adjusting to life after losing a limb and there may be a need for home environments to be adapted to make it more accessible.”</i></p>
Infected wounds	<p>Chronic wound infections are responsible for considerable morbidity and significantly contribute to the escalation in the cost of health care (Siddiqui and Bernstein, 2010). Frequent use of antibiotics increases risk of resistance (Llor and Bjerrum, 2014).</p> <p><i>“Patients with infected wounds can experience pain, swelling, increased exudate and odour. It is important for patients to receive appropriate care to stop the infection becoming systemic and leading to more severe complications, such as sepsis.”</i></p>
Inflammation	<p>Wound inflammation is an essential, non-specific, innate immune response, which involves the breakdown of tissue and clean-up of cellular, extra-cellular and pathogen debris (Zhao et al, 2016).</p> <p><i>“Prolonged inflammation can cause wounds to become stalled, and may result in increased scarring or chronic wounds. It is important for clinicians to identify and manage local and systemic factors.”</i></p>
Quality of life	<p>Patients with chronic wounds are often unemployed, marginalised and isolated. In a study of 21 patients with DFUs, 79% of patients reported an inability to maintain employment secondary to decreased mobility and fear of someone inadvertently stepping on their affected foot (Kinmond et al, 2003).</p> <p><i>“Chronic wounds can ultimately have a devastating effect on the lives of patients and their close family. Staff caring for patients with non-healing wounds can become demoralised and may inappropriately label patients as non-concordant.”</i></p>

which can contribute to wound healing rates. Other challenges include the lack of a cohesive multidisciplinary team (MDT), delays in care provision, variations in practice and establishing shared care plans. It is understood by healthcare professionals that there are challenges to service delivery due to external factors (e.g. budgets, geography) that may cause gold standard treatment to remain unachievable.

The group agreed that in order to anticipate these challenges and to optimise treatment early, good patient triage criteria and referral systems for gold standard treatment should be in place. For the care of patients with diabetic foot ulceration and venous leg ulceration, there are national guidelines that

clinicians can follow; however, there is a need to work towards establishing and standardising care pathways in other chronic wound types.

It is important to acknowledge these challenges in practice, to prioritise patient experience, and to work as part of a MDT in order to optimise assessment and care. The MDT approach has been shown to be effective in promoting continuity of care (Kjaer et al, 2005; Harding, 2006). Patients who are encouraged to actively participate in their plan of care can be supported through education to allow them to self-manage (Wounds UK, 2015). Partnered with a structured treatment pathway, this approach has the potential to improve patient outcomes and reduce variation in practice.

Box 1. First principles of care

- Assessment and referral
- Good patient–clinician relationship
- Dressing selection/suitability
- Framework for practice

FIRST PRINCIPLES OF CARE

The basic first principles of care therefore need to be implemented routinely (*Box 1*) and it is important for healthcare professionals to understand the importance of an accurate holistic assessment and know when a referral needs to be made to a specialist.

Assessment and referral

Current blockages in care restrict capability – these may include product availability, or skill gaps. For example, Guest et al (2017b) identified that the ankle brachial pressure index (ABPI) is often not performed on patients with lower limb ulceration. This may occur for many reasons including, lack of appropriate equipment, skill or confidence in carrying out the procedure, along with a perceived lack of time (hand-held doppler assessment can be perceived as time-consuming). Blockages can also occur due to patient refusal and non-adherence to treatment. Good leadership is required to address these challenges. The aim should be to help simplify the decision-making process, so that it is not always deferred to the senior nurse to make decisions or carry out certain diagnostic procedures. This can ultimately save time in the long-term, as correct diagnosis and management should improve overall healing rates. Appropriate onward referral should be seen as a sign of strength, not a sign of weakness. Many clinicians are anxious that they will be perceived as not knowing what they are doing or always seeking help if they make a referral – but an appropriate referral indicates good clinical knowledge and self-awareness. Nevertheless, before a referral is made, the basic first principles of wound care, including a thorough assessment, should be completed.

Good patient–clinician relationship

Healthcare systems can do more to create more effective patient-centred models of wound care. Ultimately, a good patient–clinician relationship enables provision of consistent delivery of care as the patient moves through services (Wounds UK, 2019). Maintaining clear communication with patients is important in order to maintain their confidence in their main care provider, it should be explained to them why they are being referred onwards and how this decision has been reached based on the gold standard care delivered so far. It is also helpful to discuss with the patient what the potential outcomes of the referral will be.

Dressing selection/suitability

Dressing selection for the management of exudate remains one of the primary clinical challenges in wound management (Acton and Moyna, 2018). Selecting the most appropriate dressing to manage the symptom requires a good understanding of the disease aetiology and the dressing mode of action. Once an appropriate product has been selected it is important for regular reassessment to be carried out. A step-up and step-down approach should be followed, whereby the dressing is matched to the wound and the levels of exudate being produced. The timing of re-assessment is important as it allows management plans to be followed and for products to have an effect, while also being responsive to the patient experience. Selection of the most appropriate product can both reduce frequency of dressing change and reduce the wound-associated symptoms which challenge the patient (Bajjada, 2017).

Knowledge of the wound-healing process, previous clinical experience and an accurate wound diagnosis can aid healthcare professionals in selecting the most appropriate dressings for use, based on a sound rationale, which will provide an optimum wound-healing environment.

Framework for practice

Pathways have been shown to provide a framework to structure assessment and management (Greatrex-White and Moxey, 2013). They are an effective tool in standardising care, establishing safe practice and assisting healthcare professionals with decision-making. These pathways can prompt the clinician to consider if the wound is progressing as expected, the basic principles of wound care have been adhered to and if onward referral is required. When using a pathway it is essential to establish the patient's objectives and to jointly set realistic expectations.

A PATHWAY FOR USE IN PRACTICE

The group devised a pathway to aid appropriate use of PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix in practice (*Figure 1*).

PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix are designed to provide an optimum wound-healing environment and to modify wound biochemistry by reducing excess protease activity and offer a kick-start to healing (Cullen and Ivins, 2010). PROMOGRAN™ Matrix may be used on chronic wounds without infection and stuck in inflammation

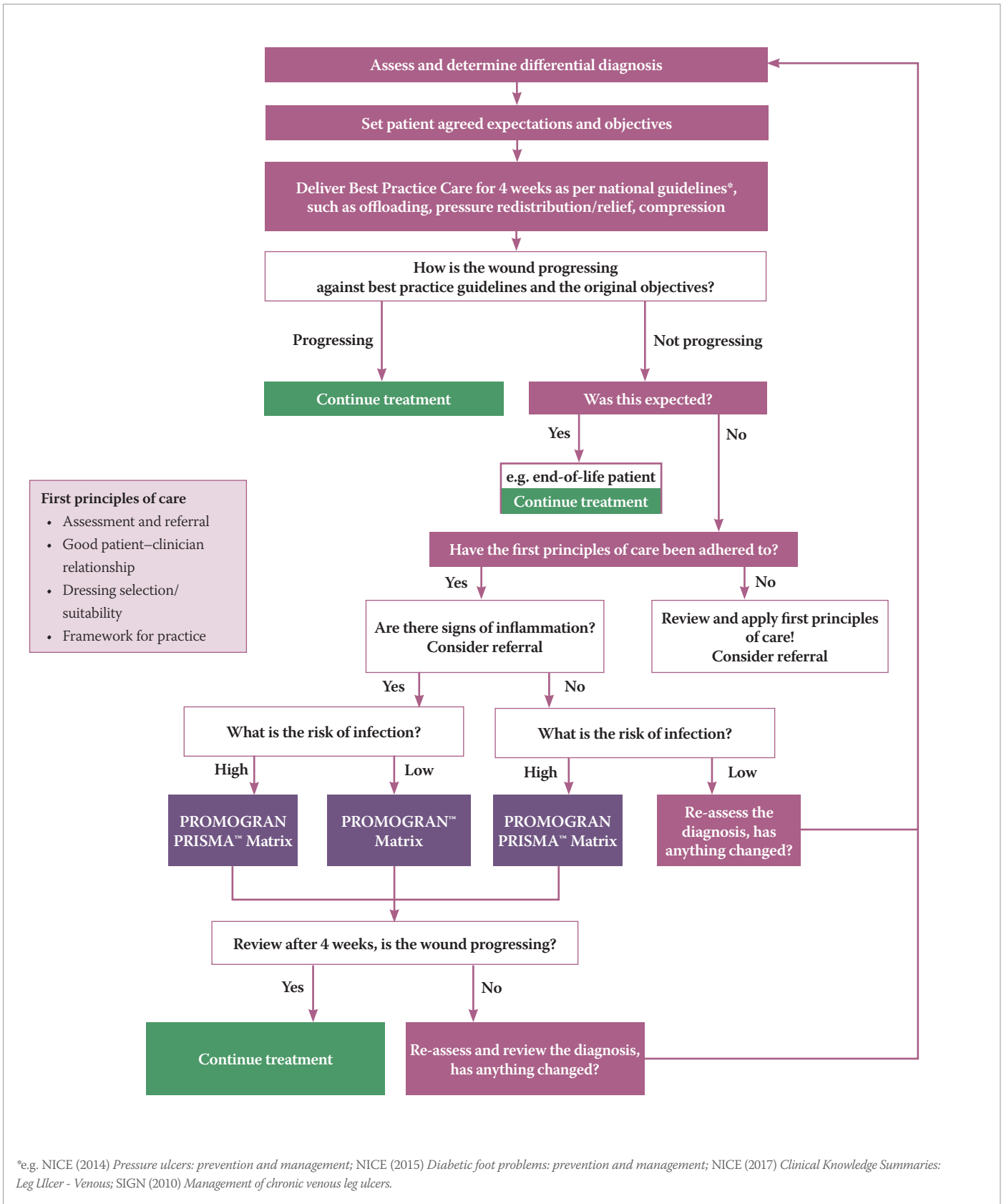


Figure 1. Pathway for use of PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix in practice

Table 2. Properties of PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix

	PROMOGRAN™ Matrix	PROMOGRAN PRISMA™ Matrix
Composition	A sterile, freeze-dried composite of 55% collagen and 45% oxidised regenerated cellulose (ORC), which transforms into a soft and conformable biodegradable gel on contact with fluid	A sterile, freeze-dried composite of 55% collagen, 44% oxidised regenerated cellulose (ORC) and 1% silver-ORC. It contains silver - a broad spectrum antimicrobial, shown to be effective against wound pathogens
Indications	<ul style="list-style-type: none"> • Non-infected wounds • Healing by secondary intent which are clear of necrotic tissue, including diabetic ulcers, venous ulcers, pressure ulcers, ulcers caused by mixed vascular aetiologies and traumatic and surgical wounds 	<ul style="list-style-type: none"> • All wounds • Healing by secondary intent which are clear of necrotic tissue, including diabetic ulcers, venous ulcers, pressure ulcers, ulcers caused by mixed vascular aetiologies and traumatic and surgical wounds. Systemic antimicrobial therapy should be considered when wound infection is evident

phase, and that are at low risk of infection. PROMOGRAN PRISMA™ Matrix may be used on chronic wounds that are stuck in inflammation phase and may also be used when wound infection is evident and in conjunction with antimicrobial therapies to impede bacterial growth. PROMOGRAN PRISMA™ Matrix has been optimised so that it is not detrimental to fibroblasts, *in-vitro*, and has been shown to protect against infection in clinical studies (Gottrup et al, 2013). Table 2 shows the dressing composition and the indications for use.

One way to ensure good practice is to follow a standard framework for assessment, for example TIME: Tissue, Infection/Inflammation, Moisture balance, Edge advancement (Schultz et al, 2003). Within the TIME acronym, 'I' stands for infection or inflammation (Schultz et al, 2003). However, in most instances, the focus is on infection and the management of bacterial bioburden rather than inflammation, as this is less well understood or

recognised. It is important to consider inflammation and its causes, and to differentiate this from infection, as signs can often overlap (Figure 2).

HOW PROMOGRAN™ MATRIX AND PROMOGRAN PRISMA™ MATRIX WORK

Chronic wounds have been shown to contain elevated levels of inflammatory cytokines, free radicals and proteases; all of which can be damaging to wound healing. PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix have the ability to reduce harmful proteases, free radicals and remove excess metal ions, whilst simultaneously protecting matrix proteins and growth factors, which increases the formation of tissue, as the wound progresses towards healing.

Haemostasis is the first phase of wound healing – the body’s natural response to trauma, which occurs when the blood vessels constrict, and the platelets create substances that form a clot and subsequently pause bleeding. This is followed by inflammation, the second

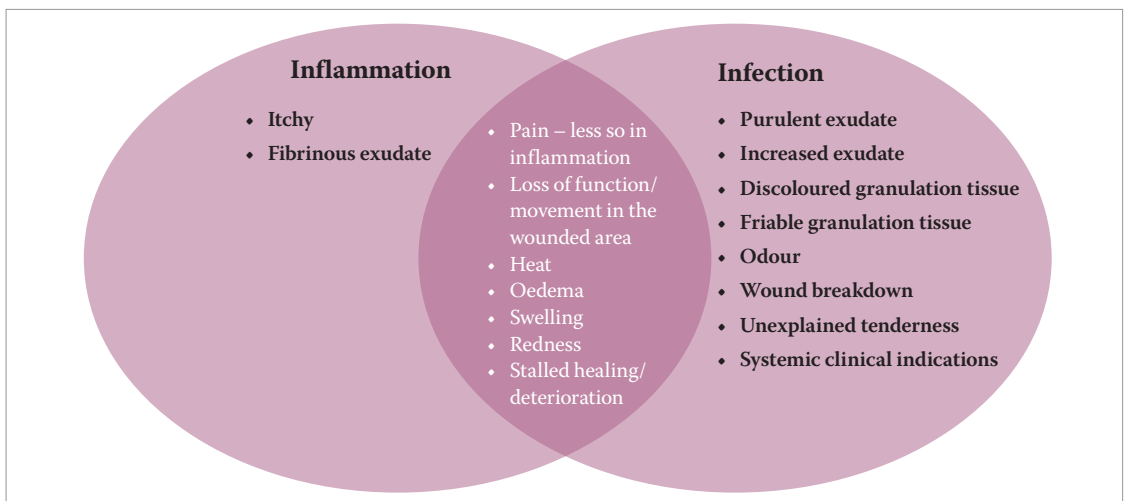


Figure 2. Signs of inflammation and infection (Cutting and Harding, 1994; Dowsett and Newton, 2005; Wound Source, 2016; World Union of Wound Healing Societies, 2019)

phase, which begins once the injured blood vessels have leaked transudate (fluid pushed through the capillary as a result of high pressure). It can be recognised from the presence of heat, redness, pain and swelling. During this phase, pathogens, bacteria and damaged cells are removed from the wound. During the inflammatory phase matrix metalloproteinases (MMPs) assist in the breakdown and clearance of damaged tissues and microbes. Their activity is well regulated by tissue inhibitors of matrix metalloproteases (TIMPs) and ceases as the wound moves into maturation. Chronic wounds that have become stuck in the inflammatory stage of wound healing may present clearly in some patients. For others, where the inflammatory response is inhibited or dampened, the usual signs or symptoms may be less apparent or indeed absent.

Wounds that do not progress beyond the inflammatory phase often demonstrate an increased activity of proteases such as MMPs and elastase, as well as the persistence of inflammatory cells (Leaper et al, 2012). There is also a down regulation of TIMP activity. It is important to note that inflammation may be caused by a number of non-infective, autoimmune diseases, such as systemic lupus erythematosus or arthritis. All chronic wounds have elevated levels of proteases and these include MMPs and elastase, which are affected by a number of factors, including patient and wound characteristics. MMPs are part of the larger family of metalloproteinase enzymes that play an important part in wound healing (Parks, 1999; Page-McCaw et al, 2007), along with the activity of elastase. It is well established that healing can only be achieved when the right amount of proteases are in the right place and for the right duration, in order to promote granulation tissue formation and stimulate wound healing. Once holistic assessment and best practice have been carried out and infection has been excluded, it is important for clinicians to consider why the wound is still failing to progress to healing and whether excess host proteases, such as MMPs and elastase, are the underlying cause.

Use of PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix is beneficial in managing the underlying biochemistry of chronic wounds. Along with this, these dressings are able to encourage the increase of new tissue formation by protecting positive factors such as matrix proteins and growth factors (Cullen and Ivins, 2010) and are supported by a body of high level clinical evidence, including randomised controlled trials. Guest et al (2018) showed that the treatment of DFUs using a collagen-containing

dressings plus standard care, instead of standard care alone, has the potential to improve outcomes, but for less cost. Educational support should be provided to healthcare professionals before the introduction of PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix. The use of these dressings should be monitored in practice and outcomes of care measured. An evaluation of PROMOGRAN PRISMA™ Matrix in hard-to-heal chronic wounds is presented in case studies 1 and 2.

PROMOGRAN™ Matrix Family of wound matrix dressings provide an interactive wound therapy that transform into a soft, conformable, biodegradable gel in the presence of exudate, maximising contact with the wound bed and optimising moisture levels. The application of these dressings, along with accurate holistic assessment and the use of this new pathway, could help to decrease wound inflammation, restart healing in wounds that have stalled and dramatically improve outcomes in hard-to-heal wounds.

CONCLUSION

PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix should be considered when no progression is seen after 4 weeks of delivering best practice care, in order to kick-start healing in chronic wounds. The new proposed pathway for use in practice will help clinicians to identify a clear stop point of when these dressings should no longer be used, when to consider referral and when to re-assess and review the diagnosis, patient objectives and expectations. PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix have the potential to stimulate healing and reduce the risk of a wound becoming hard-to-heal, which could lead to improved healing rates for both the patients and the NHS. WUK

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Case studies: Evaluation of PROMOGRAN PRISMA™ Matrix in hard-to-heal chronic wounds

Luxmi Dhoonmoon, Hana Hassan and Colette Spoard, Central and North West London NHS Foundation Trust, November 2019

CASE STUDY 1

This was a 78-year-old female patient living alone with chronic mixed aetiology leg ulcers for more than 10 years. Other medical history included essential hypertension and macular degeneration. She had previously been able to carry out activities of daily living independently; however, due to pain, mobility had declined, and she had become housebound. Previous treatment had been carried out by a district nurse. The patient was referred to a tissue viability nurse as the wound was non-healing, despite standard practice for leg ulcer management being followed.

Initial assessment: The wound was static and showed no signs of progress for more than 4 weeks, although appropriate wound care had been implemented. Exudate levels and malodour were high, which was problematic to the patient as she could not sleep or eat. After full holistic assessment and Doppler,

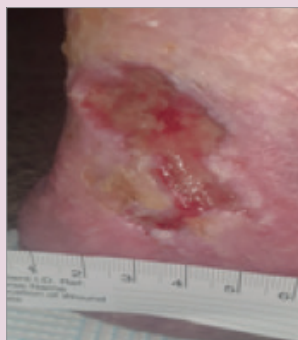


Figure 3a: Initial assessment

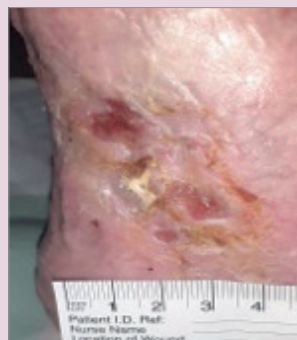


Figure 3b: +55 days

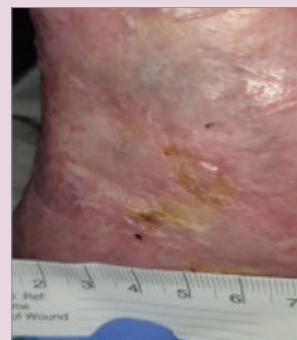


Figure 3c: +5 months

compression bandaging (after vascular review) was applied, despite mixed aetiology, as the patient had declined vascular intervention. PROMOGRAN PRISMA™ Matrix was used to dress the wound to stimulate healing, following discussion with the patient (*Figure 3a*).

Results: After 55 days of treatment that included PROMOGRAN PRISMA™ Matrix for 5 weeks, the wound had reduced

in size and comprised 100% healthy granulation tissue. Pain had reduced and malodour was no longer present. Mobility had also improved, with no concerns reported by the patient (*Figure 3b*).

After 5 months, the wound had healed (*Figure 3c*). The use of PROMOGRAN PRISMA™ Matrix encouraged wound healing, and the patient was able to return to her daily activities.

CASE STUDY 2

This was a 94-year-old female with a venous leg ulcer, which had rapidly deteriorated after the death of her husband. The patient had been emotionally, psychologically and physically low and despite the wound previously healing, she had not managed hosiery well and the leg had deteriorated.

Initial assessment: After being re-assessed by the tissue viability nurse, tendon could be seen in the wound bed. The wound management regimen had previously included antimicrobials and hydrogel dressings to manage the wound bed. The district nursing team worked very closely with the tissue viability nurse to ensure adequate wound bed preparation and skin care. Despite the planned intervention, no improvement was observed and it was agreed, as a team, to start PROMOGRAN



Figure 4a: Initial assessment



Figure 4b: +4 weeks



Figure 4c: +5 months

PRISMA™ Matrix immediately, following sharp debridement (*Figure 4a*). Treatment also included a multi-layer compression bandage, as oedema was not well controlled with her hosiery. Pain, odour and exudate were the most inconvenient factors for the patient at this time.

Results: PROMOGRAN PRISMA™ Matrix contributed positively in speeding the wound

healing process (*Figure 4b*), despite tendon being visible. Pain, exudate and odour were now also under better control (*Figure 4c*).

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