

M.O.I.S.T. Concept for the Local Therapy of Chronic Wounds: An International Update

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MaryAnn Liebert
A Part of Sage

Abstract

Chronic wounds remain a significant clinical challenge both for those affected and for healthcare systems. The treatment is often comprised and complex. All patients should receive wound care that is integrated into a holistic approach involving local management that addresses the underlying etiology and provides for gold standard therapy to support healing, avoid complications and be more cost effective. There have been significant advances in medicine over the last few decades. The development of new technologies and therapeutics for the local treatment of wounds is also constantly increasing. To help standardize clinical practice with regard to the multitude of wound products, the M.O.I.S.T. concept was developed by a multidisciplinary expert group. The M stands for moisture balance, O for oxygen balance, I for infection control, S for supporting strategies, and T for tissue management. Since the M.O.I.S.T. concept, which originated in the German-speaking countries, is now intended to provide healthcare professionals with an adapted instrument to be used in clinical practice, and a recent update to the concept has been undertaken by a group of interdisciplinary experts to align it with international standards. The M.O.I.S.T. concept can now be used internationally both as an educational tool and for the practical implementation of modern local treatment concepts for patients with chronic wounds and can also be used in routine clinical practice.

Keywords

M.O.I.S.T. concept, wound healing, wound treatment, chronic wounds, local therapy

Introduction

Chronic wounds substantially influence the quality of life of affected people and have a huge economic impact on health system budgets.¹ Worldwide, about 1% of the adult population suffers from a chronic wound, which can have very aetiologies with estimates of significant increase due to an aging population.² Most chronic wounds can be categorized as diabetic foot ulcers, venous leg ulcers, ischemic wounds due to peripheral arterial disease, or pressure injuries. Alongside the categorization of these wounds an understanding and appreciation of all other factors and rare wounds that can impair wound healing capability both intrinsic and extrinsic is important.^{3,4}

The key to successful therapy of patients with chronic wounds is a combined approach of identifying and managing the cause of the wound, optimizing systemic disease processes and pathophysiology.⁵ The importance of correct diagnostics has been recently highlighted, as it is the basis of successful wound management.⁶ Additionally local wound therapy should always be provided to support wound healing and

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avoid complications.⁷ There are many products, therapies, and techniques for local wound treatment available, so the individual choice can often be difficult. Meanwhile, it has also been scientifically proven that the use of advanced moist wound therapy supports the healing rates of chronic wounds.⁸

The choice of therapy and products is often based on the experience of the healthcare professionals (HCP), local guidelines and recommendations, and guidance from the evidence presented in scientific research. When scientific evidence is present this should be included in the decision-making process.⁹

Local Wound Therapy From TIME to M.O.I.S.T

The diversity of options and changing landscape in wound care can be challenging for HCP to maintain oversight while maintaining a clinical role. Various concepts have been introduced to help structure the local therapy of chronic wounds. Internationally, the TIME concept has been the most widely adopted of these concepts.¹⁰ TIME was developed in 2003 by international experts and originally focused on the wound bed preparation. The acronym stands for Tissue, Inflammation or Infection, Moisture balance and Edges of wound or Epithelial advancement.¹¹ Since this concept was introduced, there have been many advancements in therapies and emerging aspects of wound healing that cannot be represented directly in this concept.

The aim of the WundDACH, the umbrella organization of the German-speaking professional society in the field of wound treatment, was to evolve the proven TIME concept by including new therapy options for the local management of chronic wounds. In 2017, they published in German the first article of the M.O.I.S.T. concept,¹² with a further update in 2022.¹³ In the development of M.O.I.S.T., the letters of the TIME concept described with T, I, and M were still considered to be contemporary and important and were therefore adopted in a slightly modified form for the M.O.I.S.T. concept. The letter E was originally used to describe factors about Epidermis¹⁰ and later Edge,¹⁴ that is, the advancement of the wound margin. In the M.O.I.S.T. concept, the letter E was not included because the group felt that these aspects, although important, were not directly part of local wound care. The nonulcerated skin of the wound edge and surrounding area must

nevertheless be treated; however, no wound dressings are usually optimized for this. Instead of E, the WundDACH felt there was a greater importance of including the letters O for Oxygen balance and S for Supporting strategies to include new treatment options for targeted therapy in a much more differentiated way (Table 1).

Since the M.O.I.S.T. concept originally came from the German-speaking countries and this took into account many national recommendations, it was now the plan of an interdisciplinary group of experts to revise and adapt this concept from an international point of view.

Letters of the M.O.I.S.T. Concept

M—Moisture Balance

The scientific work of George D. Winter in 1962 showed for the first time in a mouse model that a moist wound environment promoted wound healing.¹⁵ Until then, treating wounds with a dry approach was often the standard of care. Winter's findings led to a new paradigm shift in therapeutic concepts. However, at that time, appropriate products were still lacking to enable the therapy to be implemented well in practice. Primarily moist cotton compresses were used, which had to be moistened several times a day. In the following decades, the advantage of moist wound treatment was also confirmed in numerous clinical studies, so today this concept represents the gold standard of wound care for most chronic wounds.¹⁶

Providing local wound therapy is based on many different factors and should consider, among other things, the wound healing phases, exudate volumes and viscosities (Table 2). In moist wound therapy concepts, wounds should be neither too moist nor too dry.¹⁷ For example, dry wounds can be moistened with hydrogels. More often, however, there is an excess of exudate especially in venous leg ulcers and ulcers due to other causes of oedema. Therefore, wound products such as alginates, gelling fibers, or foams can be used. For larger amounts of exudate, superabsorbents or negative pressure wound therapies (NPWT) may be better suited. In addition to the selection of the primary wound dressing, it is often the secondary wound dressings that should absorb appropriate amounts of exudate.¹⁸

O—Oxygen Balance

The cells in the human body need a continuous supply of oxygen for almost all metabolic processes necessary to

Table 1. The Acronym M.O.I.S.T. Is Used to Describe a Modern Concept for the Local Therapy of Chronic Wounds.

- **M** = Moisture balance
- **O** = Oxyge balance
- **I** = Infection control
- **S** = Supporting strategies
- **T** = Tissue management

Table 2. Examples of Types of Wound Dressings Depending on the Amount of Exudate.

- Low: hydrogels, hydrocolloids, semipermeable films
- Moderate: foams, alginates, fibers
- High: foams, fibers, superabsorbents

support function and life. Since wound healing is accompanied by increased energy metabolism, the oxygen requirement here is even significantly higher compared to intact skin; in the case of infected wounds, this increases even further considerably.¹⁹ When oxygen is absent from tissue, it is termed hypoxic. Hypoxia occurs not only due to reduced blood flow in arterial disease patterns but also in almost all types of chronic wounds due to increased cellular activity/demands.²⁰ If hypoxia persists, wound healing stagnates, and progressive tissue loss may occur in more severe cases. Normally, the partial pressure of oxygen (pO₂) in healthy tissue should be about 100 mmHg. In contrast, values below 30 mmHg are often found in chronic wounds with stagnant wound healing. Transient hypoxia after tissue injury is initially physiological and promotes among other things angiogenesis and thus wound healing. However, prolonged hypoxia leads to stagnation of wound healing.²¹

With the development of new technologies including near-infrared spectroscopy, tissue oxygen tension, transcutaneous oxygen tension, or remission spectroscopy oxygen content in tissue can now be measured, therefore confirming if hypoxia is present.²² The current guidelines also recommend the measurement of skin perfusion pressure as a proven method for determining microcirculation. First the need for revascularization and accompanying aspects such as edema reduction through compression therapy should be clarified. However, these centrally important measures are not a direct component of the M.O.I.S.T. concept. This also applies to hyperbaric oxygen therapy (HBOT), in which the proportion of physically dissolved oxygen in the plasma when a patient breathes 100% oxygen while inside a treatment chamber at a pressure that is higher than sea-level pressure.²²

To provide additional oxygen to chronic wounds, various therapeutic approaches for local therapy have also been developed in recent years (Table 3).²³ All methods have in common that the oxygen is applied directly or indirectly to the wound surface, whereby different forms of application are used.

Small portable, battery-powered oxygen generators have been developed for the continuous delivery of nonpressurized oxygen, delivering a continuous stream of pure oxygen into occlusive dressings on wounds for 24 h a day.²⁴ Low-pressure, constant-pressure devices consist of

a simple plastic chamber or cuff that is placed around the wound. A constant pressure of up to 35 mmHg is then maintained in the chamber.²⁵ Higher pressure oxygen devices combined with humidification apply oxygen locally at a pressure between 5 and 50 mmHg in a cyclic pressure waveform.²⁶ When oxygen is delivered through a dressing or gel, it releases pure oxygen that is either embedded in a dressing or releases oxygen that is produced by a biochemical reaction in a hydrogel.²⁷ For oxygen transfer, hemoglobin is used as an oxygen carrier in a wound spray. The mode of action is based on the physical effect of facilitated delivery in hypoxic areas.²⁸

There is now increasing well-documented scientific evidence that local therapies with oxygen sustain healing, particularly in otherwise refractory chronic wounds.²⁹ It is therefore not surprising that local oxygen therapy is one of the treatment methods recommended in the IWGDF guidelines for the treatment of people with DFU.³⁰ Although the best data quality is available for patients with diabetic foot ulcers, it is now discussed that, in principle, almost all patients with chronic wounds can benefit from supplemental oxygen therapy.²³

Infection Control

The presence of microorganisms in wounds is physiological and does not always interfere with wound healing or contribute to causing infection. However, the clinical detection of wound infections can be challenging in patients with chronic wounds. A failure to diagnose and properly manage wound infections can lead to serious consequences that may range from delayed wound healing, to spreading infection and sepsis.³¹ Diagnosis and interpretation of microbiological results are often difficult.³² For example, the validated Therapeutic Index for Local Infections (TILI) score is suitable for clinical diagnosis of local wound infections³³ or the diabetic foot infection wound score.³⁴ If systemic infection is suspected, serologic testing should be performed in addition to clinical signs and symptoms. To aid clinicians in the diagnosis and management of wound infections, several expert groups have provided guidelines and recommendations as to best practices.^{35,36}

Infection control describes all antimicrobial strategies in the context of wound treatment. Topical antimicrobial wound therapy should be applied individually and specifically.³⁵ Providing local delivery of topical antiseptics may yield several advantages over systemic approaches with the use of antibiotics. The latter remains the subject of much debate with current recommendations of the avoidance of using antibiotics as opposed to antiseptics topically for treating wound infections.³⁷ As to clarify herein, the use of systemic antibiotics is not part of the "I" in M.O.I.S.T., as this covers the systematic approach for providing local wound therapy. As part of local wound infection control,

Table 3. Therapeutic Approaches With Oxygen for the Local Therapy of Chronic Wounds (Modified According to Gottrup et al.)²²

-
- Continuous delivery of nonpressurized oxygen
 - Low constant pressure oxygen in a contained chamber
 - Higher cyclical pressure oxygen
 - Oxygen release through dressing or gel
 - Oxygen transfer
-

clinicians need to understand the potential infectious wound microenvironment,³⁸ which includes the types of bacteria responsible for causing the infection process, the type of infection (acute or chronic, local, or spreading) in addition to host factors such as immunocompromised.

One example to consider is wounds lacking clinical signs of infection but failing to respond to standard of care, which should raise suspicion of potential biofilm as a cause of chronic infection. Whether biofilm actually delays wound healing remains controversial.³⁹ Nevertheless, targeted antibiofilm strategies with proven efficacy in laboratory models, animal models and in human wounds could be employed. Additionally, there are various other topical antimicrobial (including antiseptics) substances available to clinicians for use against a wide variety of wound pathogens or microbial phenotypes (ie, planktonic, biofilm) that are recommended for use by expert opinion for the management of chronic wound infection/bioburden. Despite the heterogeneity in proven efficacy of topical antimicrobials for biofilm good scientific evidence is available for traditional antiseptics against planktonic bacteria such as octenidine (with phenoxyethanol), polihexanide, hypochlorous acid, and silver.^{40,41} The choice of type and mode of a topical antiseptic approach is also wide and usually includes antimicrobials that manage bacteria in the dressing and act as a barrier to microbial contamination. Delivery materials for such dressings include gelling fibers, ointments, pastes, gels, and novel systems such as chitosan, nanoparticle, and collagen matrices.³²

Which specific format is best for the patient ultimately depends upon the wound microenvironment with factors such as high or low exudate levels, anatomical location, and space to be filled, all being examples of factors which may lead clinicians to choose a specific topical antiseptic agent over another. More recently, nonmedicated dressings and devices have grown in popularity on the back of antimicrobial resistance fears. These dressings claim alternate mechanisms of antimicrobial action. Some examples include materials, which rely on physiochemical properties such as hydrophobic interactions with irreversible binding of bacteria to the dressing.⁴² Others report a hydroresponsive action causing passive wound exudate which contains bacteria from the wound to be drawn into the dressing with collateral bacterial trapping. An example for an

innovative physical treatment approach is cold atmospheric plasma therapy.⁴³

Regardless of the infection control strategy used, a critical review of the therapy should be performed on a regular basis. A suggested schedule is a review every 10 to 14 days. It should then be determined whether the treatment regimen should be continued or changed.⁴⁴

S—Supporting Strategies

There is an increasingly large heterogeneous group of wound products that are intended to actively intervene in the dysfunctional processes of wound healing (Table 4). The primary goal is then the targeted active influence of the wound environment. To be able to intervene specifically here, it is important to understand the various pathophysiological processes of wound healing with the corresponding biomarkers.^{45,46} However, much of this knowledge is currently based on basic science findings or studies from animal models. Although there are also some studies on this of humans with chronic wounds, reliable findings that also lead to targeted therapy based on individual diagnostics are largely lacking.^{47,48}

Currently, the most widely used approach in this wound therapy sector is the therapeutic interaction with matrix metalloproteinases (MMPs) because of their imbalance in the microenvironment of chronic wound.⁴⁹ Matrix metalloproteinases are a group of zinc-dependent endopeptidases that catalyze the cleavage of peptide bonds. The physiological counterparts are the tissue inhibitors of metalloproteinases (TIMPs). The centrally important role of MMPs in physiological wound healing has been described primarily in the context of the degradation of extracellular matrix proteins.⁵⁰ Matrix metalloproteinases also have numerous other functions in the regulation of physiological and pathological processes. They are important for angiogenesis, tumor growth, and as signaling molecules, among others. It has been shown that in most chronic wounds there is an impaired ratio of MMPs and TIMPs. This excess of MMPs is the attack point of various wound products that include, for example, collagen and cellulose, polyhydrated ionogens-5, or sucrose octasulfate.^{51,52} Good evidence with multiple RCTs exists for the potassium salt of sucrose octasulfate.^{53,54}

In other therapeutic approaches, growth factors are used to support wound healing in chronic wounds. They regulate a wide variety of intracellular processes and play a particularly important role in tissue development. In the context of wound healing, the effects of growth factors in angiogenesis have been studied extensively. Growth factors currently used for wound treatment are for example platelet-derived growth factor,⁵⁵ granulocyte-macrophage colony-stimulating factor,⁵⁶ and epidermal growth factor.⁵⁷ In addition, there are several procedures in which fractions with growth factors are obtained from

Table 4. Examples of Therapeutic Points of Action that Are Already Used to Actively Support Wound Healing.

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- Cytokines
 - Growth factors
 - Macrophages
 - Matrix metalloproteinases
 - pH values
 - Reactive oxygen species
 - Stem cells
-

the patient's blood for wound treatment.⁵⁸ Other biological products such as amniotic membrane, adipose-derived,⁵⁹ or mesenchymal stem cells⁶⁰ also be used. In this context, other skin substitute products for wound treatment can be mentioned.⁶¹

It has been known for a long time that the pH value influences all processes in the human body. In this respect, it is obvious to actively influence the pH value in wound healing. The current findings on the pH values in wounds are very much dependent on the measurement methods used and many other factors are and can be influenced.⁶² Every wound product has a pH value and can therefore potentially actively influence the wound milieu. Only a few wound products have the pH value specified by the manufacturers. In addition, today there is also a lack of precise knowledge about when which wounds benefit from which pH values, so currently this targeted wound treatment cannot be used.⁶³ Other very interesting therapeutic approaches to actively support the healing process include local therapies with negatively charged microspheres,⁶⁴ chitosan,⁶⁵ coagulation factors,⁶⁶ or extracellular matrix proteins.⁶⁷

Even if some measurement instruments for the wound environment have already been developed,⁶⁸ it is currently still not possible to reliably measure the multitude of potentially influential aspects of the wound environment in clinical practice. In addition, there is a lack of meaningful studies demonstrating when values should be actively changed and what constitutes an optimal wound environment. In this respect, the use of these certainly very interesting wound healing products is mostly carried out in otherwise therapy-refractory wounds according to the trial-and-error principle. This will certainly change in the future as soon as appropriate measurement methods are available. Here, it is wearables or smart dressings that measure individual factors in real time and then, if necessary, treat them specifically.⁶⁹

T—Tissue Management

Tissue management describes all measures of local wound therapy that contribute to wound bed preparation. The first step usually involves measures of wound cleansing and debridement.⁷⁰ Wound cleansing or wound irrigation

means the removal of nonadherent components with solutions. Although the scientific evidence of this wound cleansing has not yet been conclusively demonstrated,⁷¹ it is part of the gold standard of modern wound treatment concepts in patients with chronic wounds.³¹ In addition to residual dressings, it is often dried wound exudates that are removed as atraumatically as possible. Sterile or preserved solutions should be used and adapted to the respective national or local specifications.¹⁸

In chronic wounds, debridement describes the removal of adherent, dead tissue, crusts, or foreign bodies (Table 5). The main goals are to prevent and combat wound infections, biofilm formation, improve the assessability of the wound, and promote wound healing.⁷² Surgical debridement refers to the complete removal of devitalized tissue down to intact tissue structures. This usually involves tissue and vascular injury with bleeding.⁷³ Various forms of therapy are summarized as mechanical debridement, in which loosely adherent wound components are removed from the wounds as far as possible atraumatically, for example with cotton compresses or monofilament-fiber pads. Biosurgery is the treatment of wounds with sterile cultured fly maggots. During autolytic debridement, the body's own proteolytic enzymes are released, and phagocytes are activated among other things. Autolytic debridement is facilitated by the creation of a moist wound healing environment. For proteolytic debridement, products containing bromelain, collagenase, or streptokinase and streptodornase, which hydrolyze peptide bonds, are most commonly used. The group of technical debridements includes, for example, hydrosurgery, lasers, or ultrasound devices.⁷²

For further wound treatment, neutral wound dressings, or physical devices such as NPWT can subsequently be used. Negative pressure wound therapy is an active wound management system that utilizes controlled negative (subatmospheric) pressure, which is applied uniformly to the wound through an open cell foam or other interface dressing in a continuous or intermittent fashion. There is now good evidence available for this wound treatment method in improving wound healing in various types of chronic wounds.⁷⁴

Other physical treatment options that can currently be used for wound treatment include for example electrostimulation, extracorporeal shock waves, concurrent optical and magnetic stimulation, low-intensity laser therapy, or water-filtered infrared A-light.⁷⁵

Table 5. Options for Debridement in Chronic Wounds (Modified According to Strohal et al.)⁷²

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- Autolytic debridement
 - Biosurgical debridement
 - Mechanical debridement
 - Osmotic debridement
 - Proteolytic/enzymatic debridement
 - Surgical/sharp debridement
 - Technical debridement
-

Discussion

The basis of successful wound management relies in accurate diagnostics and after that comes the decision of local therapy (Figure 1). When using the M.O.I.S.T. concept, it is important to keep in mind that not all letters need to be considered for all patients. Rather, it is a matter of at least considering each of the aspects and then considering the applicability based on a through wound assessment.

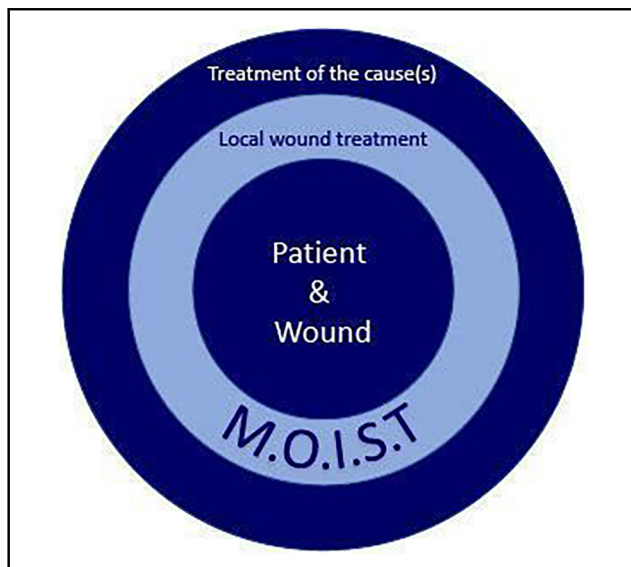


Figure 1. The patient is always at the center of holistic wound treatment. The M.O.I.S.T. concept then describes the local treatment of wounds. In addition, however, it is essential to treat the underlying cause(s). Successful wound treatment can only be achieved through the coordinated interaction of these different components.

For example, treating all chronic wounds with antimicrobials is unnecessary. However, an appropriate assessment of the presumed bioburden should always be made. Furthermore, it should be noted that the implementation of therapy according to the letters of the M.O.I.S.T. concept does not have to be done successively. Therefore, it should be understood as an overall concept. For example, in many patients, it may make sense to start wound treatment with T, that is, debridement. It is also clear that the effects of the individual treatment methods are not always clearly attributable to one letter. As an example, NPWT, which is usually used primarily for T, can also support M and be used in combination with an antimicrobial instillation for I. However, this should generally be seen as advantageous, as treatment concepts then need to be planned in a less complex manner.

When making the final decision on which wound care products to use for which patients individual and economic factors should always be considered. It is very important to consider the individual needs and capabilities of patients in a shared decision-making process.⁷⁶ In addition, products must also be available and fit the patient's particular form of care. This is particularly important when self-management is planned and supported with education.

Conclusion

Treatment concepts for patients with chronic wounds should always include adequate local wound therapy based on

accurate diagnostics. Local wound therapy cannot replace causative treatment strategies, but it will support wound healing and prevent complications if integrated into a comprehensive overall management plan. To better structure the multitude of wound products, the M.O.I.S.T. concept was developed. This concept offers HCP support for systematic planning and education with regard to the local therapy of patients with chronic wounds.


Declaratio of Conflicting Interests


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References

1. Graves N, Phillips CJ, Harding K. A narrative review of the epidemiology and economics of chronic wounds. *Br J Dermatol.* 2022;187(2):141-148.
2. Falanga V, Isseroff RR, Soulika AM, et al. Chronic wounds. *Nat Rev Dis Primers.* 2022;8(1):50.
3. Beyene RT, Derryberry SL, Barbul A. The effect of comorbidities on wound healing. *Surg Clin North Am.* 2020;100(4):695-705.
4. Isoherranen K, Ó'Brien JJ, Barker J, et al. Atypical wounds. Best clinical practice and challenges. *J Wound Care.* 2019;28(Suppl. 6):1-92. doi:10.12968/jowc.2019.28.Sup6.S1
5. Bosanquet DC, Harding KG. Wound healing: potential therapeutic options. *Br J Dermatol.* 2022;187(2):149-158.

6. Isoherranen K, Montero EC, Atkin L, et al. Lower leg ulcer diagnosis and principles of treatment. *J Wound Manage.* 2023;24(2 Suppl. 1):1-76.
7. Dissemond J, Augustin M, Eming S, et al. Modern wound care—practical aspects of non-interventional topical treatment of patients with chronic wounds. *J Dtsch Dermatol Ges.* 2014; 12(7):541-554.
8. Heyer K, Augustin M, Protz K, et al. Effectiveness of advanced versus conventional wound dressings on healing of chronic wounds: systematic review and meta-analysis. *Dermatology.* 2013;226(2):172-184.
9. Chaby G, Senet P, Vaneau M, et al. Dressings for acute and chronic wounds: a systematic review. *Arch Dermatol.* 2007;143(10):1297-1304. doi:10.1001/archderm.143.10.1297
10. Schultz GS, Sibbald RG, Falanga V, et al. Wound bed preparation: a systematic approach to wound management. *Wound Repair Regen.* 2003;11(Suppl 1):1-28. doi:10.1046/j.1524-475X.11.s2.1.x
11. Leaper DJ, Schultz G, Carville K, Fletcher J, Swanson T, Drake R. Extending the TIME concept: what have we learned in the past 10 years? *Int Wound J.* 2012;9(Suppl 2):1-19.
12. Dissemond J, Assenheimer B, Gerber V, et al. M.O.I.S.T.—a concept for the topical treatment of chronic wounds. *J Dtsch Dermatol Ges.* 2017;15(4):443-445.
13. Dissemond J, Assenheimer B, Gerber V, et al. M.O.I.S.T. Concept for the local therapy of chronic wounds. *Dtsch Med Wochenschr.* 2023;148(7):400-405.
14. Schultz GS, Barillo DJ, Mozingo DW, et al. Wound bed preparation and a brief history of TIME. *Int Wound J.* 2004; 1(1):19-32.
15. Winter GD. Formation of the scab and the rate of epithelization of superficial wounds in the skin of the young domestic pig. *Nature.* 1962;193:293-294.
16. Nuutila K, Eriksson E. Moist wound healing with commonly available dressings. *Adv Wound Care.* 2021;10(12): 685-698.
17. Parnham A. Moist wound healing: does the theory apply to chronic wounds? *J Wound Care.* 2002;11(4):143-146.
18. Eriksson E, Liu PY, Schultz GS, et al. Chronic wounds: treatment consensus. *Wound Repair Regen.* 2022;30(2):156-171.
19. Gupta S, Mujawdiya P, Maheshwari G, Sagar S. Dynamic role of oxygen in wound healing: a microbial, immunological, and biochemical perspective. *Arch Razi Inst.* 2022;77(2): 513-523.
20. Dissemond J, Kröger K, Storck M, Risse A, Engels P. Topical oxygen wound therapies for chronic wounds: a review. *J Wound Care.* 2015;24(2):53-63.
21. Sen CK. Wound healing essentials: let there be oxygen. *Wound Repair Regen.* 2009;17(1):1-18.
22. Gottrup F, Dissemond J, Baines C, et al. Use of oxygen therapies in wound healing. *J Wound Care.* 2017;26(Suppl. 5):1-43. doi:10.12968/jowc.2017.26.Sup5.S1
23. Frykberg R, Andersen C, Chadwick P, et al. Use of topical oxygen therapy in wound healing. *J Wound Care.* 2023; 32(Suppl. 8b):1-32. doi:10.12968/jowc.2023.32.Sup8b.S1
24. Serena TE, Bullock NM, Cole W, et al. Topical oxygen therapy in the treatment of diabetic foot ulcers: a multicentre, open, randomised controlled clinical trial. *J Wound Care.* 2021;30(Sup5):7-14. doi:10.12968/jowc.2021.30.Sup5.S7
25. Gordillo GM, Roy S, Khanna S, et al. Topical oxygen therapy induces vascular endothelial growth factor expression and improves closure of clinically presented chronic wounds. *Clin Exp Pharmacol Physiol.* 2008;35(8):957-964.
26. Tawfick W, Sultan S. Does topical wound oxygen (TWO2) offer an improved outcome over conventional compression dressings (CCD) in the management of refractory venous ulcers (RVU)? A parallel observational comparative study. *Eur J Vasc Endovasc Surg.* 2009;38(1):125-132.
27. Davis P, Wood L, Wood Z, Eaton A, Wilkins J. Clinical experience with a glucose oxidase-containing dressing on recalcitrant wounds. *J Wound Care.* 2009;18(3):116-121. doi:10.12968/jowc.2009.18.3.39812
28. Hu J, Guo S, Hu H, Sun J. Systematic review of the efficacy of topical haemoglobin therapy for wound healing. *Int Wound J.* 2020;17(5):1323-1330.
29. Carter MJ, Frykberg RG, Oropallo A, et al. Efficacy of topical wound oxygen therapy in healing chronic diabetic foot ulcers: systematic review and meta-analysis. *Adv Wound Care.* 2023;12(4):177-186.
30. Chen P, Vilorio NC, Dhatariya K, et al. Guidelines on interventions to enhance healing of foot ulcers in people with diabetes (IWGDF 2023 update). *Diabetes Metab Res Rev.* 2024;40(3):3644. doi: 10.1002/dmrr.3644
31. Murphy C, Atkin L, Swanson T, et al. Defying hard-to-heal wounds with an early antibiofilm intervention strategy: wound hygiene. *J Wound Care.* 2020;29(Suppl. 3b):1-26. doi:10.12968/jowc.2020.29.Sup3b.S1
32. Malone M, Schultz G. Challenges in the diagnosis and management of wound infection. *Br J Dermatol.* 2022; 187(2):159-166.
33. Dissemond J, Strohal R, Mastronicola D, et al. Therapeutic Index for Local Infections score validity: a retrospective European analysis. *J Wound Care.* 2020;29(12):726-734.
34. Lipsky BA, Polis AB, Lantz KC, et al. The value of a wound score for diabetic foot infections in predicting treatment outcome: a prospective analysis from the SIDESTEP trial. *Wound Repair Regen.* 2009;17(5):671-677.
35. Swanson T, Ousey K, Haesler E, et al. IWII Wound Infection in Clinical Practice consensus document. *J Wound Care.* 2022;31(Suppl. 12):10-21.
36. Senneville É, Albalawi Z, van Asten SA, et al. IWGDF/IDSA guidelines on the diagnosis and treatment of diabetes-related foot infections (IWGDF/IDSA 2023). *Clin Infect Dis.* In press. doi: 10.1093/cid/ciad527
37. Lipsky BA, Dryden M, Gottrup F, Nathwani D, Seaton RA, Stryja J. Antimicrobial stewardship in wound care: a position paper from the British Society for Antimicrobial Chemotherapy and European Wound Management Association. *J Antimicrob Chemother.* 2016;71(11):3026-3035.
38. Bjarnsholt T, Whiteley M, Rumbaugh KP, et al. The importance of understanding the infectious microenvironment. *Lancet Infect Dis.* 2022;22(3):e88-e92. doi:10.1016/S1473-3099(21)00122-5
39. Swanson T, Ousey K, Haesler E, et al. IWII wound infection in clinical practice consensus document: 2022 update. *J Wound Care.* 2022;31(Suppl. 12):10-21. doi:10.12968/jowc.2022.31.Sup12.S10
40. Cwajda-Białasik J, Mościcka P, Szewczyk MT. Antiseptics and antimicrobials for the treatment and management of

- chronic wounds: a systematic review of clinical trials. *Postepy Dermatol Alergol.* 2022;39(1):141-151.
41. Kramer A, Dissemond J, Kim S, et al. Consensus on wound antisepsis: update 2018. *Skin Pharmacol Physiol.* 2018;31(1):28-58.
 42. Seckam AM, Twardowska-Sauchka K, Heggemann J, Süß-Burghart A, Augustin M. Clinical performance and quality of life impact of an absorbent bacteria-binding foam dressing. *Br J Nurs.* 2021;30(5):21-30. doi:10.12968/bjon.2021.30.5.S21
 43. Assadian O, Ousey KJ, Daeschlein G, et al. Effects and safety of atmospheric low-temperature plasma on bacterial reduction in chronic wounds and wound size reduction: a systematic review and meta-analysis. *Int Wound J.* 2019;16(1):103-111.
 44. Dissemond J. Diagnostics and treatment of local wound infections. *Z Gerontol Geriatr.* 2023;56(1):48-52.
 45. Patel S, Maheshwari A, Chandra A. Biomarkers for wound healing and their evaluation. *J Wound Care.* 2016;25(1):46-55.
 46. Pastar I, Balukoff NC, Marjanovic J, et al. Molecular pathophysiology of chronic wounds: current state and future directions. *Cold Spring Harb Perspect Biol.* 2023;15(4):041243. doi:10.1101/cshperspect.a041243
 47. Gohel MS, Windhaber RA, Tarlton JF, Whyman MR, Poskitt KR. The relationship between cytokine concentrations and wound healing in chronic venous ulceration. *J Vasc Surg.* 2008;48(5):1272-1277.
 48. Stacey MC, Phillips SA, Farrokhyar F, Swaine JM. Evaluation of wound fluid biomarkers to determine healing in adults with venous leg ulcers: a prospective study. *Wound Repair Regen.* 2019;27(5):509-518.
 49. Kandhwal M, Behl T, Singh S, et al. Role of matrix metalloproteinase in wound healing. *Am J Transl Res.* 2022;14(7):4391-4405.
 50. Tardáguila-García A, García-Morales E, García-Alamino JM, et al. Metalloproteinases in chronic and acute wounds: a systematic review and meta-analysis. *Wound Repair Regen.* 2019;27(4):415-420.
 51. Chen J, Qin S, Liu S, et al. Targeting matrix metalloproteases in diabetic wound healing. *Front Immunol.* 2023;14:1089001.
 52. Lazaro JL, Izzo V, Meaume S, Davies AH, Lobmann R, Uccioli L. Elevated levels of matrix metalloproteinases and chronic wound healing: an updated review of clinical evidence. *J Wound Care.* 2016;25(5):277-287.
 53. Dissemond J, Augustin M, Dietlein M, et al. Efficacy of MMP-inhibiting wound dressings in the treatment of chronic wounds: a systematic review. *J Wound Care.* 2020;29(2):102-118.
 54. Edmonds M, Lázaro-Martínez JL, Alfayate-García JM, et al. Sucrose octasulfate dressing versus control dressing in patients with neuroischaemic diabetic foot ulcers (explorer): an international, multicentre, double-blind, randomised, controlled trial. *Lancet Diabetes Endocrinol.* 2018;6(3):186-196.
 55. Jian K, Yang C, Li T, et al. PDGF-BB-derived supramolecular hydrogel for promoting skin wound healing. *J Nanobiotechnology.* 2022;20(1):201.
 56. Ead JK, Armstrong DG. Granulocyte-macrophage colony-stimulating factor: conductor of the wound healing orchestra? *Int Wound J.* 2023;20(4):1229-1234.
 57. Shakhakarmi K, Seo JE, Lamichhane S, Thapa C, Lee S. EGF, a veteran of wound healing: highlights on its mode of action, clinical applications with focus on wound treatment, and recent drug delivery strategies. *Arch Pharm Res.* 2023;46(4):299-322.
 58. Game F, Jeffcoate W, Tarnow L, et al. Leucopatch system for the management of hard-to-heal diabetic foot ulcers in the UK, Denmark, and Sweden: an observer-masked, randomised controlled trial. *Lancet Diabetes Endocrinol.* 2018;6(11):870-878.
 59. Nasiry D, Khalatbary AR, Noori A, Abouhamzeh B, Jamalpoor Z. Accelerated wound healing using three-dimensional amniotic membrane scaffold in combination with adipose-derived stem cells in a diabetic rat model. *Tissue Cell.* 2023;82:102098.
 60. Kerstan A, Dieter K, Niebergall-Roth E, et al. Allogeneic ABCB5 + mesenchymal stem cells for treatment-refractory chronic venous ulcers: a phase I/IIa clinical trial. *JID Innov.* 2022;2(1):100067.
 61. Vecin NM, Kirsner RS. Skin substitutes as treatment for chronic wounds: current and future directions. *Front Med.* 2023;10:1154567.
 62. Schneider LA, Körber A, Grabbe S, Dissemond J. Influence of pH on wound-healing: a new perspective for wound-therapy? *Arch Dermatol Res.* 2007;298(9):413-420.
 63. Derwin R, Patton D, Avsar P, Strapp H, Moore Z. The impact of topical agents and dressing on pH and temperature on wound healing: a systematic, narrative review. *Int Wound J.* 2022;19(6):1397-1408.
 64. Lázaro-Martínez JL, García-Madrid M, López-Moral M, et al. Clinical and histological outcomes of negatively charged polystyrene microspheres applied daily versus three times per week in hard-to-heal diabetic foot ulcers: a randomized blinded controlled trial. *Int J Low Extrem Wounds.* 2022;15347346221104946.
 65. Maita KC, Avila FR, Torres-Guzman RA, et al. Local anti-inflammatory effect and immunomodulatory activity of chitosan-based dressing in skin wound healing: a systematic review. *J Clin Transl Res.* 2022;8(6):488-498.
 66. Kleber C, Sablotzki A, Casu S, et al. The impact of acquired coagulation factor XIII deficiency in traumatic bleeding and wound healing. *Crit Care.* 2022;26(1):69.
 67. Diller RB, Tabor AJ. The role of the extracellular matrix (ECM) in wound healing: a review. *Biomimetics.* 2022;7(3):87.
 68. Serena TE, Cullen BM, Bayliff SW, et al. Defining a new diagnostic assessment parameter for wound care: elevated protease activity, an indicator of nonhealing, for targeted protease-modulating treatment. *Wound Repair Regen.* 2016;24(3):589-595.
 69. Jiang Y, Trotsyuk AA, Niu S, et al. Wireless, closed-loop, smart bandage with integrated sensors and stimulators for advanced wound care and accelerated healing. *Nat Biotechnol.* 2023;41(5):652-662.
 70. Tran DL, Huang RW, Chiu ES, et al. Debridement: technical considerations and treatment options for the interprofessional team. *Adv Skin Wound Care.* 2023;36(4):180-187.
 71. Fernandez R, Green HL, Griffiths R, Atkinson RA, Ellwood LJ. Water for wound cleansing. *Cochrane Database Syst Rev.* 2022;9(9):CD003861.

72. Strohal R, Dissemond J, Jordan O'Brien J, et al. An updated overview and clarification of the principle role of debridement. *J Wound Care*. 2013;22(Suppl.):1-52.
73. Darji D, Perse J, Arnold Y. Stepwise surgical technique used to treat recalcitrant pretibial ulcerations: a case series. *Wounds*. 2023;35(1):47-52. doi:10.25270/wnds/21080
74. Shehata MS, Bahbah E, El-Ayman Y, et al. Effectiveness of negative pressure wound therapy in patients with challenging wounds: a systematic review and meta-analysis. *Wounds*. 2022;334(12):126-134. doi:10.25270/wnds/21061
75. Hess CL, Howard MA, Attinger CE. A review of mechanical adjuncts in wound healing: hydrotherapy, ultrasound, negative pressure therapy, hyperbaric oxygen, and electrostimulation. *Ann Plast Surg*. 2003;51(2):210-218.
76. Heerschap C, Nicholas A, Whitehead M. Wound management: Investigating the interprofessional decision-making process. *Int Wound J*. 2019;16(1):233-242.