Undisturbed wound healing: a narrative review of the literature and clinical considerations

This review explores the etymology of the phrase undisturbed wound healing (UWH)

to determine how this concept may educate healthcare providers and promote evidence-based moist wound healing. Keyword searches identified 117 articles from three databases, with 60 articles included for review. Thematic analysis identified 10 common themes considered relevant to clinical practice in four key categories: the patient, the provider, the wound and cost of care. There is considerable need to raise

the standard of care to reflect these distinct priorities to improve outcomes.



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A cute wound complications and chronic wounds impose substantial health and economic burdens globally. In a study of Medicare patients in the USA, over 15% of Medicare beneficiaries had at least one type of wound or wound infection, with total Medicare spending for all wound types ranging between \$28.1bn to \$96.8bn (Nussbaum et al, 2018). Moreover, chronic wounds, such as diabetic foot ulcers, cost the Medicare system between \$6.2bn and \$18.7bn per year alone, with outpatient locations having the highest cost. Recently, it was reported that pressure ulcers cost the USA healthcare system over \$26.8bn annually (Padula and Delarmente, 2019).

Meanwhile, the UK has up to 190,000 individuals with venous leg ulcer (VLU) and over 400,000 patients develop a new pressure ulcer (PU) annually (Cheng et al, 2018). In geriatric populations, data from the UK suggest VLU incidence is up to four times higher than PU incidence, with VLU rates even higher in patients over 80 years old compared to younger comparators (Gould et al, 2015).

Wound care clinicians are faced with the difficult challenge of managing acute and chronic wounds and selecting appropriate treatments to improve clinical outcomes and control costs. The basic principles of wound bed preparation and moist wound healing are needed to maximise wound healing capacity by preparing the wound to heal and not delay the healing process (Sood et al, 2014), which underpins the concept of undisturbed wound healing (UWH).

The goal of this review paper is to explore the etymology of the phrase 'UWH' and determine how this reflects goals of clinical practice. A thematic analysis of the literature relating to UWH was performed and a discussion of wound bed preparation and dressing features to achieve these goals are presented.

Methods

A narrative review of the literature was conducted utilising PubMed, CINAHL and Google Scholar. Article inclusion was based on the phrase 'UWH', used in MeSH major topic and title and abstract searches, or by description of wound healing specifically, including the concept of being undisturbed, optimal or uninterrupted in the progression of healing or the process of rendering care. Full texts were reviewed in all cases to determine the context used.

Results

A total of 117 articles were identified. Following removal of duplicates and exclusion of papers 60 articles were included for review. Thematic analysis of these manuscripts identified 10 common themes, which are presented in *Table 1*.

UWH was commonly associated with the natural, timely, spontaneous/untreated (Vignoletti et al, 2012) and autolytic process of healing through the principles of moist wound

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Table 1. Common themes of undisturbed wound healing (UWH).				
Theme	Context Descriptor	References		
Tissue trauma during dressing change	Undisturbed wounds would not have dressings adhering to wounds resulting in wound bed or periwound injury.	Loos et al (2007); Pillen et al (2009); Barrett (2012); Upton and Solowiej (2012); Upton et al (2012); Davis et al (2013); Meuleneire (2014)		
Frequency of dressing changes/cost of care	The more undisturbed the wound, the less frequent the dressing changes and associated costs.	Pillen et al (2009); Barrett (2012); Lo et al (2012); Upton et al (2012); Tang, et al (2015)		
Healing by timely, uninterrupted wound healing phases	The capability of the wound to proceed seamlessly and without delay through the phases of healing, based on properties of a dressing or surgical technique.	Wokalek and Ruh (1991); Ger (1996); Menovsky et al (2003); Covani et al (2004); Ovington (2007); Aigner and Conrad (2008); Rippon et al (2012); Fassbender et al (2014); Karadsheh et al (2017)		
Biochemistry	Particularly in relation to chronic inflammation. Products or conditions which limited/managed/reduced/ controlled inflammation had more undisturbed healing.	Henningsen and Holtz (1974); Schramm et al (1977); Staindl et al (1981); Engelhardt et al (1998); Thamm et al (2015); Papathanasiou et al (2017)		
Structural integrity/remodeling potential of ECM/	Undisturbed healing was directly connected to ECM structure, deposition, remodeling potential and tissue regeneration in multiple studies.	Staindl (1979); Augthun et al (1995); Alves-Rezende et al (1997); Seifert and Mrowietz (2009); Wolbank et al (2015); MacEwan et al (2017)		
	Wounds with suboptimal conditions resulted in ECM degradation or lack of fibrinolysis of denatured ECM structures, causing disturbed and, thus, delayed healing.			
Quality of life; psychological factors associated with healing	UWH was directly related to frequency of dressing changes and capacity of the dressing to manage physical symptoms, resulting in high anticipatory stress/anxiety and lower quality of life.	Lo et al (2012); Upton and Solowiej (2012); Upton et al (2012); Tang et al (2015)		
	UWH was stated to be closest to a 'normal' life for the patient while in the process of wound healing.			
	Many articles assessing quality of life in chronic wounds reported pain, anxiety and stress. A dressing that could be left undisturbed during changes, left the wound/skin/ hair undisturbed and the providers care plan undisturbed may be the optimal answer to these needs.			
Pain	Undisturbed wounds have less pain (during wear and during changes).	Coulling (2007); Barrett (2012); Rippon (2012); Upton and Solowiej (2012)		
Stability of wound, stable performance resistant to outside influences which decrease describe performance.	Stability in the wound bed, periwound and resistance to outside forces.	Karlbauer and Gasperschitz (1987); Schulz et al (2000); Haslik et al (2007); Haslik et al (2010); Lee and Park (2012); Lo et al (2012)		
uecrease dressing performance	Optimal dressing characteristics were: water-proof, conformable and preventing infection.			
Absence of infection/biofilm	UWH occurs with levels of bacteria that are managed by the body and do not delay healing through prophylaxis, maintenance or direct intervention to remove bacteria.	Rennekampff et al (2006); Matalon et al (2013); Odekerken et al (2014); Yu and Zheng (2018)		
Natural, untouched, autolytic wounds	Principles of moist wound healing. Undisturbed wounds are those left to the physiologic closure of the body's typical acute wound response, leading to healing without complication.	Schmelzeisen et al (1992); Jansen et al (1994); Hom et al (1999); Buser et al (2000); Nitsch et al (2005); Schwarz et al (2007); Retsky et al (2009); Burkhardt and Lang (2010); Zimmermann et al (2010); Lee and Park (2012); Rippon et al (2012); Vignoletti et al (2012); Wolbank et al (2015); Rieder et al (2016)		

management (Wokalek and Ruh, 1991). It was reported in treatment protocols following surgical implant (Jansen et al, 1994; Rieder et al, 2016), pre-surgical capacity to heal (Buser et al, 2000; Schulz et al, 2000; Zimmermann et al, 2010), the avoidance of complications to healing surgical sites postoperatively (Schmelzeisen et al, 1992; Ger, 1996; Covani et al, 2004; Aigner et al, 2008; Burkhardt et al, 2010) and avoiding frequent manipulation of new surgical wounds with percutaneous catheters (Lee and Park, 2012). Undisturbed healing was associated with the ability to achieve timely wound closure (Fassbender et al, 2014), often linked to appropriate surgical technique to achieve minimal scarring (Menovsky et al, 2003; Seifert and Mrowietz, 2009).

A common theme in many recent manuscripts involved the assumption that UWH referred to dressing characteristics that would not adhere



to or traumatise the wound during dressing changes. Charlesworth et al (2014) sought to identity clinical sequelae and resource use associated with dressing-related trauma in the UK.

Major concepts identified included skin reactions, adherence of the product to the wound bed, medical adhesive-related skin injury, maceration, desiccation of the wound and wound plugging. The authors indicated that these findings underpinned the development of complications, such as wound size and exudate increase, infection, pain, itching, bleeding and patient anxiety, among others. Various dressings addressed clinician and patient concerns, such as prevention of disturbance of the wound healing phases via prevention of repetitive trauma, as demonstrated in clinical performance studies. For example, an in vivo porcine model comparing silicone interface dressings with Safetac® Technology (Mepitel®, Mepitel® One; Molnlycke Health Care, Gothenburg, Sweden) with polyester and cellulose mesh dressings, with and without silicone, showed that the Mepitel dressings remained attached to noninjured periwound skin, while having the lowest overall adhesion to the wound bed at day three and total non-adhesion at day six (Davis et al, 2015). These principles were similarly supported by a review of Mepitel One (Barrett, 2012).

Another important consideration with UWH is the relationship to frequency of dressing changes and associated cost of care. In a study comparing silver sulfadiazine dressings with a silver impregnated soft silicone foam dressing (Mepilex[®] Ag, Mölnlycke Health Care, Gothenburg, Sweden), Tang et al (2015) did not find significant differences in healing times between the two dressings, however, there was a significant reduction in number of dressing changes, and a return toward 'normal life'. Undisturbed healing was demonstrated by limiting dressing changes and, thus, not interfering with the patient's quality of life. Lower quality of life scores were demonstrated in individuals with malignant fungating wounds as dressing change frequency and reduced wound dressing comfort added to the symptom burden (Lo et al, 2012; Loos et al, 2007). Dressings with the ability to stay in situ for 5–7 days were also more cost effective (Pillen et al, 2009).

Interestingly, UWH was directly related to healing via provision of a viable extracellular matrix (ECM) to achieve wound proliferation. MacEwan et al (2017) implied that supporting the (undisturbed) development of a functional ECM without degradation to be optimal for wound healing. Studies investigating fibrin degradation described the process of monitoring ECM degradation in real time, indicating that without controlled autolytic wound bed preparation undisturbed healing was not possible, leading to wound chronicity (Wolbank et al, 2015).

Central to this concept was the role of uncontrolled or inappropriate inflammation in the chronic wound. The disruption of normal healing due to pro-inflammatory mediators was highlighted in dental research as therapies that control or prevent high levels of inflammation may return the wound to a state of uninterrupted tissue remodeling (Papathanassiou et al, 2017). Specific tissue enzymes and biomarkers, such as Factor XIII, were noted as indicators of the course or potential of healing in both human and animal studies (Henningsen and Holtz, 1974; Schraam et al, 1977; Engelhardt et al, 1998; Kalkhof et al, 2014). These studies looking at specific matrix metalloproteases highlighted the need for irrigation and managing wound exudate so that circulating inflammatory mediators were removed and spread away from the wound bed to limit their destructive impact on the developing ECM.

From a holistic perspective, UWH is connected to the psychological impact of providing wound care, including the management of procedural pain and the importance of selecting dressing materials and techniques, which alleviate pain on removal and decrease change frequency (Coulling, 2007; Barrett, 2012). In a prospective study, patients receiving atraumatic dressings reported lower numerical pain and stress ratings, as well as lower mean heart rate, blood pressure and salivary cortisol levels during dressing changes, compared with conventional dressings (Upton and Solowiej, 2013). However, overall anxiety and perceived stress scores were similar between groups, indicating a high psychosocial burden of chronic wound healing over time.

Frequency of dressing change is dependent upon multiple factors, including wound type, exudate volume and consistency, risk of infection and patient comfort (Ovington, 2007; Rippon 2012). However, frequent changes are also dependent on the ability of a dressing to remain in place, absorb exudate of various viscosities and volumes, manage bioburden and allow for movement of a patient during rehabilitative care or activities



of daily living (Sharma et al, 2017). UWH was described as limiting the influence of external forces which may directly impact healing or dressing security, including techniques such as postoperative splinting (Karlbauer et al, 1987; Schulz et al, 2000; Haslik et al, 2007).

Dressing selection to meet the needs of acute and chronic wound healing relies on the dressing performance to manage a variety of wound presentations and complex locations. For example, in acute wounds following hip and knee arthroplasty, the ideal dressing can manage exudate, provide a bacterial barrier, protect against periwound complications and provide flexibility allowing normal movement (Sharma et al, 2017).

Progressive understanding of bioburden and biofilm in wound healing has led to UWH being used as a gauge of bacterial contamination levels. Specifically, Yu and Zheng (2018) stated that prevention of re-infection allowed for undisturbed healing while in vivo studies indicated UWH as a research endpoint compared with deep infection after orthopedic implant placement (Odekerken, et al, 2014). Additionally, the potential for infection and prolonged inflammation caused by various types of suture material were described as preventing UWH based on in vitro investigation (Matalon et al, 2013). In high risk wounds, such as burns, bacterial load and bioburden management were a key feature in achieving undisturbed healing and supported the successful application and viability of skin grafts (Rennekampff et al, 2006).

Finally, authors indicated that optimal dressings achieved the goals of moist wound healing (Hom, et al, 1999; Ovington, 2007) and contributed to the achievement of undisturbed healing through supporting the acute phases of healing. A comprehensive review of dressings for UWH suggested the following necessary qualities may lead to improved quality of life, decreased injury from frequent changes and decreased risk of infection (Rippon et al, 2012):

- Absence of toxic components
- No foreign bodies, or incidental deposition of fragments into the wound
- Provide a barrier to bacteria
- Have water resistant adhesives, easily removed from skin without trauma
- Provide minimal tissue movement during dressing changes
- Protect the periwound tissues from moisture and maceration
- Prevent pain and trauma during changes.

Discussion

This review does not suggest that all wounds should simply be covered with a dressing and left to its own devices, but that wound bed preparation should be combined with UWH to achieve the best outcomes. Schultz et al (2003) stated the principle components of managing non-healing wounds included: ongoing debridement, management of exudate and resolution of bacterial imbalance. A critical understanding of wound healing involves an appreciation that there are certain clinical time periods where a wound may need to purposefully be disturbed more than others. Debridement is an example of when wound disturbance is critical to wound outcome. Following appropriate wound bed preparation, selection of an appropriate secondary dressing that incorporates UWH characteristics is important to manage elements such as heavy or thick wound exudate or support the action and incorporation of more advanced wound management products.

Treatment recommendations should consider wound etiology and UWH principles, based on themes identified in the literature review [*Table 2*]. However, when a patient's wound is clinically infected, or is at high risk of clinical infection, more frequent assessment of the wound may warrant an increased frequency of dressing change. The goals of care dictate the principles of management, where assessment, frequent irrigation and application of topical antimicrobials may be necessary.

For example, Category I and II skin tears may benefit from UWH through maintenance of moist wound healing, approximation of skin flaps and prevention of wound adherence. This is best accomplished through a dressing that can remain in place during the period of epithelialisation, while protecting against periwound skin damage and re-injury through the avoidance of aggressive adhesive dressings and tapes. These principles are part of a multidisciplinary approach, as indicated in expert consensus statements and guidelines for care (Leblanc et al, 2011; Leblanc, 2015).

Implications for practice

The 10 identified themes of UWH identified in this review can be consolidated into four primary categories for adopting UWH:

- The patient: select dressings that provide patient comfort, reduce frequency of wound interruption, decrease pain, stress and anxiety associated with wound trauma
- The wound: select dressings that do not



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Products & technology

Table 2. Wound treatment with undisturbed wound healing (UWH) principles.				
Wound diagnosis	Etiology	UWH theme	Treatment considerations	
Skin Tear	Shear, friction or blunt trauma resulting in partial-thickness separation, partial loss or full loss of the skin flap. Wounds typically occur in patients with altered epidermal-dermal anatomy caused by advanced age, chronic steroid use, profound oedema, etc.	 Tissue trauma at dressing change Frequency of changes; cost of care Uninterrupted healing Quality of life Pain Stability of dressing performance; resistance to outside influences 	 Type 1 and 2 tears, re-approximate skin flap over wound Note skin flap approximation and direction for dressing removal to prevent trauma Decrease frequency of changes to every 5–7 days. Select dressing capable of remaining attached at body location 	
Venous leg ulcer	Multifactorial: venous hypertension and high sustained ambulatory venous pressures, typically with inefficient calf- muscle pump.	 Biochemistry Structural integrity of extracellular matrix (ECM) Quality of life Pain Decreased frequency of changes Stability of performance (under compression) Infection/biofilm 	 Dressings designed for viscous, high exudate absorption and retention. Dressings that mobilise exudate away from wound bed, maintain low profile under compression. Decrease frequency of changes for patient comfort/satisfaction 	
Diabetic foot ulcer	Multifactorial: neuropathic versus neuropathic ischaemic. Autonomic, sensory and motor neuropathic changes result in enhanced risk of ulceration due to ambulatory impact pressure and tangential shear. Ischaemia complicates infection risk and capacity to heal.	 Biochemistry Structural integrity of ECM Quality of life Decreased frequency of changes Stability of performance (under offloading/mobile areas) Infection/biofilm 	 Debridement (callus and necrosis) Dressing designed to impact inflammatory proteases. Antimicrobials with broad spectrum/ anti-biofilm modalities Dressings manufactured for increased flexibility and mobility Dressings designed for advanced exudate management and retention. Cellular tissue products. 	
Pressure ulcer	Pressure, shear, microclimate and friction resulting in ischaemia and/or deformation injury, usually over a bony prominence or under medical device.	 Tissue trauma at dressing change Frequency of changes; cost of care Uninterrupted healing Biochemistry Structural integrity of ECM Quality of life Pain Stability of dressing performance; resistance to outside influences 	 Debridement Dressing designed to impact inflammatory proteases. Antimicrobials with broad spectrum/ anti-biofilm modalities Dressings manufactured for increased flexibility and mobility Dressings designed for advanced exudate management and retention. Cellular tissue products. 	

damage, adhere to, or directly insult the wound bed or the developing ECM, with the capability of wicking away or mitigating proinflammatory mediators and removing, killing or trapping bacteria

- The caregiver: select dressings that provide confidence of dressing performance so that frequency of change is based on clinical assessment and not on potential for dressing failure. Utilising a dressing management plan that reduces patient interruption builds trust and rapport during the patient-provider interaction
- Time/money: select dressings that decrease overall cost of care. Cheaper

dressings that have poor performance are ultimately more expensive due to repetitive changes, waste and poor clinical outcomes.

Obstacles to UWH

While providers may understand the benefit of selecting appropriate wound care products to deliver UWH it may be the care setting, the organisation formulary, or a national tender, which ultimately guides product use and wound outcome. Additionally, in the community setting, dressing change frequency may result from habitual practices.

Acute care settings may be impacted by poor dressing performance capabilities, which



result in poor exudate management, inability to conform to anatomical locations, or detach from the skin prior to the scheduled change date. Additionally, staff may be influenced to change dressings repeatedly to avoid the stigma that a dressing looks dirty or uncared for, based upon exudate or blood staining on the outer surface. In these cases, it is necessary for education on the benefit of advanced wound dressings designed for longer wear time, which can wick away and prevent the stagnant collection of exudate on the wound or surrounding skin, to demonstrate performance to the patient or family.

The acute care (hospital) setting is also challenged by shorter lengths of stay, complexity of acute wounds in the intensive care unit and a lack of appreciation of how wound outcomes impact cost of care after hospital discharge. For example, a national UK study assessing the 12-month costs and outcomes of patients with unhealed surgical wounds from initial presentation in the community found that the management of infected wounds was considerably more costly than non-infected wounds (£5,000-£12,000 versus £2,000; Guest et al, 2018). These results either indicate a lack of understanding or acknowledgement that acute wounds still require appropriate wound management after discharge.

Non-acute settings, including nursing home facilities, long-term care and home health services are often adept at selecting products supporting the principles of undisturbed healing, as reimbursement and payment structures are often reserved for providing therapies no more than three times weekly. Therefore, products are often selected that have the capability for being left on for longer periods of time, due to restrictions on reimbursement alone, allowing the wound to benefit from a stable wound microenvironment.

An increasing trend in all settings is that dressing choice may often be decided based on unit cost alone, with procurement and value analysis workers believing they will save money by bringing in low-cost products. However, ultimately, it is the total cost of care that needs to be considered. If a low unitcost dressing provides less wear time due to poor performance (stay-on-ability, exudate management, comfort and conformability), then overall costs, provider visits and risks of complications, such as infection, will all increase. These decisions not only remove the provider from the decision-making process, but additionally, research suggests that focusing only on up-front wound care costs is not a valid method for reducing the cost of care. A study looking at chronic wound management in Wales calculated the total cost of wound care was £328,839,408 (£1,728.53 per patient; Phillips et al, 2016). The cost of wound dressings represented only 2.9% of total costs (£9,669,602), whereas the number of district nurse visits (703,479) represented 18.3% of the cost (£60,053,085), while outpatient attendances, additional general practitioner visits and inpatient episodes represented 76.2% (£250,545,866) of the remaining costs. This indicates that attempting to reduce costs by focusing solely on cost of dressings alone may be a futile exercise. Instead, care considerations that decrease nursing visits, hospital readmissions, GP appointments and outpatient visits would be more cost effective. Therefore, wound dressing selection based on contribution to improved healing and decreased resource utilisation would result in increased cost savings.

To validate these UWH themes and provide a better understanding of current care practices and how they relate to the challenges in a variety of care settings, a survey of over 1,500 wound-healing providers across the globe is presently under way and the results will be presented in a subsequent publication.

Conclusions and recommendations

Clinicians should challenge their current dressing selections and change dressing frequency to mirror the recommendations of proper wound bed preparation and UWH. Frequent dressing changes may impair wound healing, decrease patient satisfaction, cause pain or frequent exposure of the wound to cross contamination or infection. Therefore, identifying key wound care needs associated with establishing a healing microenvironment may allow for selecting optimal dressing change frequency. When making dressing selection recommendations for wound management, the provider should reflect how the products will impact the wound, the patient's response to care, the provider's time, resource allocation and the total cost of care. Focusing only on the wound, or the cost of a dressing, undermines the importance of holistic healing, patient satisfaction, achieving clinical outcomes and WINT overall costs.

References

Aigner F, Conrad F (2008) Fissurectomy for treatment of chronic anal fissures. *Dis Colon Rectum* 51(7): 1163;



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author reply 1164

- Alves-Rezende MC, Okamoto T (1997) Effects of fibrin adhesive material (Tissucol) on alveolar healing in rats under stress. *Braz Dent J* 8(1): 13–9
- Augthun M, Yildirim M, Spiekermann H, Biesterfeld S (1995) Healing of bone defects in combination with immediate implants using the membrane technique. *Int J Oral Maxillofac Implants* 10(4): 421–8
- Charlesworth B, Pilling C, Chadwick P, Butcher M (2014) Dressing-related trauma: Clinical sequelae and resource utilization in a UK setting. *Clinicoecon Outcomes Res* 6: 227–39
- Barrett S (2012) Mepitel One: a wound contact layer with Safetac technology. *Br J Nurs* 21(21): 1271–2, 1274–7
- Bonham PA, Flemister BG, Droste LR et al (2016) 2014 Guideline for Management of Wounds in Patients With Lower-Extremity Arterial Disease (LEAD): an executive summary. *J Wound Ostomy Continence Nurs* 43(1): 23–31
- Braun LR, Fisk WA, Lev-Tov H et al (2014) Diabetic foot ulcer: an evidence-based treatment update. *Am J Clin Dermatol* 15(3): 267–81
- Burkhardt R, Lang NP (2010) Role of flap tension in primary wound closure of mucoperiosteal flaps: a prospective cohort study. *Clin Oral Implants Res* 21(1): 50–4
- Buser D, von Arx T, ten Bruggenkate C, Weingart D (2000) Basic surgical principles with ITI implants. *Clin Oral Implants Res* 11 Suppl 1: 59–68
- Cheng Q, Graves, Pacella RE (2018a) Economic evaluations of guideline-based care for chronic wounds: a systematic review. *Appl Health Econ Health Policy* 16(5): 633–51
- Coulling S (2007) Fundamentals of pain management in wound care. Br J Nurs 16(11): S4–6, S8, S10 passim
- Covani U, Bortolaia C, Barone A, Sbordone L (2004) Bucco-lingual crestal bone changes after immediate and delayed implant placement. *J Periodontol* 75(12): 1605–12
- Crawford PE, Fields-Varnado M, WOCN Society (2013) Guideline for the management of wounds in patients with lower-extremity neuropathic disease: an executive summary. *J Wound Ostomy Continence Nurs* 40(1): 34–45
- Davis SC, Li J, Gil J et al (2015) A closer examination of atraumatic dressings for optimal healing. *Int Wound J* 12(5): 510–6
- Engelhardt E, Toksoy A, Goebeler M et al (1998) Chemokines IL-8, GROalpha, MCP-1, IP-10, and Mig are sequentially and differentially expressed during phase-specific infiltration of leukocyte subsets in human wound healing. *Am J Pathol* 153(6): 1849–60
- Enoch S, Grey JE, Harding KG (2006) Recent advances and emerging treatments. *BMJ* 332(7547): 962–5
- Fassbender M, Minkwitz S, Thiele M, Wildemann B (2014) Efficacy of two different demineralised bone matrix grafts to promote bone healing in a critical-size-defect: a radiological, histological and histomorphometric study in rat femurs. *Int Orthop* 38(9): 1963–9
- Frank CB, Adams M, Kroeber M et al (2011) Intraoperative subcutaneous wound closing culture sample: a predicting factor for periprosthetic infection after hip- and knee-replacement? *Arch Orthop Trauma Surg* 131(10): 1389–96
- Ger R (1996) Wound management by constant tension approximation. Ostomy Wound Manage 42(9): 40–6

- Gould L, Abadir P, Brem H et al (2015) Chronic wound repair and healing in older adults: current status and future research. *J Am Geriatr Soc* 63(3): 427–38
- Guest JF, Fuller GW, Vowden P (2018) Costs and outcomes in evaluating management of unhealed surgical wounds in the community in clinical practice in the UK: a cohort study. *BMJ Open* 8(12): e022591
- Gupta S, Andersen C, Black J et al (2017) Management of chronic wounds: diagnosis, preparation, treatment, and follow-up. *Wounds* 29(9): S19–S36
- Haslik W, Kamolz L-P, Nathschläger G et al (2007) First experiences with the collagen-elastin matrix Matriderm as a dermal substitute in severe burn injuries of the hand. *Burns* 33(3): 364–8
- Haslik W, Kamolz L-P, Manna F et al (2010) Management of full-thickness skin defects in the hand and wrist region: first long-term experiences with the dermal matrix Matriderm. *J Plastic Reconstr Aesthet Surg* 63(2): 360–4
- Henningsen B, Holtz W (1974) [Histochemical study on succinate dehydrogenase activity in the course of undisturbed wound healing on fascia tissue in the rabbit]. *Langenbecks Arch Chir* Suppl: 241–3
- Hom DB, Adams G, Koreis M, Maisel R (1999) Choosing the optimal wound dressing for irradiated soft tissue wounds. *Otolaryngology Head Neck Surg* 121(5): 591–8
- Jansen JA, PA quay YG, van der Waerden JP (1994) Tissue reaction to soft-tissue anchored percutaneous implants in rabbits. *J Biomed Mater Res* 28(9): 1047–54
- Jørgensen SF, Nygaard R, Posnett J (2013) Meeting the challenges of wound care in Danish home care. J Wound Care 22(10): 540–2, 544–5
- Kalkhof S, Förster Y, Schmidt J et al (2014) Proteomics and metabolomics for in situ monitoring of wound healing. *BioMed Res Int* 2014: 934848
- Karadsheh M, Nelson J, Rechner B, Wilcox R (2017) Application of a Skin Adhesive to Maintain Seal in Negative Pressure Wound Therapy: Demonstration of a New Technique. *Wounds* 29(11): E106–E110
- Karlbauer A, Gasperschitz F (1987) High-pressure injection injury: a hand-threatening emergency. J Emerg Med 5(5): 375–9
- Kelechi TJ, Johnson JJ, WOCN Society (2012) Guideline for the management of wounds in patients with lowerextremity venous disease: an executive summary. J Wound Ostomy Continence Nurs 39(6): 598–606
- Krzyszczyk P, Schloss R, Palmer A, Berthiaume F (2018) The role of macrophages in acute and chronic wound healing and interventions to promote pro-wound healing phenotypes. *Front Physiol* 9: 419
- Leblanc K, Campbell K, Beeckman D et al (2018) *ISTAP Best Practice Recommendations for the Prevention and Management of Skin Tears in Aged Skin*. Wounds International, London. Available at: https://bit. ly/2WcMBpM (accessed 12.04.2019).
- LeBlanc K, Baranoski S, International Skin Tear Advisory Panel, 2013 (2014) Skin tears: the forgotten wound. *Nurs Manage* 45(12): 36–46; quiz 46–47.
- LeBlanc K, Baranoski S, Skin Tear Consensus Panel Members (2011) Skin tears: state of the science: consensus statements for the prevention, prediction, assessment, and treatment of skin tears©. Adv Skin Wound Care 24(9 Suppl): 2–15
- Lee A, Park Y (2012) Reducing peritoneal dialysis catheter exit site infections by implementing a standardised postoperative dressing protocol. *Renal Society of Australasia Journal* 8(1): 18–22



- Lo S-F, Hayter M, Hu W-Y et al (2012) Symptom burden and quality of life in patients with malignant fungating wounds. J Adv Nurs 68(6): 1312–21
- Loos B, Kopp J, Hohenberger W, Horch RE (2007) Postmalignancy irradiation ulcers with exposed alloplastic materials can be salvaged with topical negative pressure therapy (TNP). *Eur J Surg Oncol* 33(7): 920–5

MacEwan MR, MacEwan S, Kovacs TR, Batts J (2017) What makes the optimal wound healing material? A review of current science and introduction of a synthetic nanofabricated wound care scaffold. *Cureus* 9(10): e1736

Martin P, Nunan R (2015) Cellular and molecular mechanisms of repair in acute and chronic wound healing. *Br J Dermatol* 173(2): 370–8

Matalon S, Kozlovsky A, Kfir A et al (2013) The effect of commonly used sutures on inflammation inducing pathogens - an in vitro study. *J Craniomaxillofac Surg* 41(7): 593–7

- Menovsky T, Beek JF (2003) Carbon dioxide laser-assisted nerve repair: effect of solder and suture material on nerve regeneration in rat sciatic nerve. *Microsurgery* 23(2): 109–16
- Meuleneire F (2014) A vapour-permeable film dressing used on superficial wounds. *Br J Nurs* 23(15): S36, S38–43
- Molnlycke Healthcare ((n.d.)) Mepilex Border Flex-- Fluid Handling capacity. Report no. PD-527642_01. Data on file.
- Molnlycke Healthcare ((n.d.)) Mepilex Border Flex--Waterproofness. Report no. PD-532095_01. Data on File.
- Molnlycke Healthcare ((n.d.)) Mepilex Border Flex-Conformability. Report no. PD-528870_01. Data on File.
- Nelson D (2018) Better Outcomes for Skin Tears with New 5 Layer Bordered Foam Dressings. Paper presented at the Wound Ostomy Continence Nurses Society National Conference. Scientific Poster. Philadelphia, PA; June 3–6, 2018
- Nitsch A, Pabyk A, Honig JF (2005) Cellular, histomorphologic, and clinical characteristics of a new octyl-2-cyanoacrylate skin adhesive. *Aesthetic Plast Surg* 29(1): 53–8

Nussbaum SR, Carter MJ, Fife CE et al (2018a) An economic evaluation of the Impact, cost, and Medicare policy implications of chronic nonhealing wounds. *Value Health* 21(1): 27–32

- Odekerken JCE, Brans BT, Welting TJM, Walenkamp GHIM (2014) (18)F-FDG microPET imaging differentiates between septic and aseptic wound healing after orthopedic implant placement: a longitudinal study of an implant osteomyelitis in the rabbit tibia. *Acta Orthop* 85(3): 305–13
- O'Donnell TF, Passman MA, Marston WA et al (2014) Management of venous leg ulcers: clinical practice guidelines of the Society for Vascular Surgery [®] and the American Venous Forum. *J Vasc Surg* 60(2 Suppl): 35–59S
- Ovington LG (2007) Advances in wound dressings. *Clin* Dermatol 25(1): 33–8
- Papathanasiou E, Trotman CA, Scott AR, Van Dyke TE (2017) Current and emerging treatments for postsurgical cleft lip scarring: effectiveness and mechanisms. *J Dent Res* 96(12): 1370–7
- Phillips CJ, Humphreys I, Fletcher J et al (2016) Estimating the costs associated with the

management of patients with chronic wounds using linked routine data. Int Wound J 13(6): 1193–7

- Pillen H, Miller M, Thomas J et al (2009) Assessment of wound healing: validity, reliability and sensitivity of available instruments. *Wound Pract Res* 17(4): 208–17
- Rennekampff H-O, Schaller H-E, Wisser D, Tenenhaus M (2006) Debridement of burn wounds with a water jet surgical tool. *Burns* 32(1): 64–9
- Retsky MW, Hrushesky WJM, Gukas ID (2009) Hypothesis: primary antiangiogenic method proposed to treat early stage breast cancer. *BMC Cancer* 9: 7
- Richardson R, Slanchev K, Kraus C et al (2013) Adult zebrafish as a model system for cutaneous woundhealing research. *J Invest Dermatol* 133(6): 1655–65
- Rieder D, Eggert J, Krafft T et al (2016) Impact of placement and restoration timing on single-implant esthetic outcome — a randomized clinical trial. *Clin Oral Implants Res* 27(2): e80–6
- Rippon M, Davies P, White R (2012) Taking the trauma out of wound care: the importance of undisturbed healing. J Wound Care 21(8): 359–60, 362, 364–8
- Schmelzeisen R, McIff T, Rahn B (1992) Further development of titanium miniplate fixation for mandibular fractures. Experience gained and questions raised from a prospective clinical pilot study with 2.0 mm fixation plates. *J Craniomaxillofac* 20(6): 251–6
- Schramm W, Schaarschmidt K, Schmidtler F, Schildberg FW (1977) [The pathogenesis of postoperative abdominal wound dehiscence. Part II: Hemostasiological checks during the course in selected patient groups (author's transl)]. *MMW Munch Med Wochenschr* 119(20): 690–4
- Schultz GS, Sibbald RG, Falanga V et al (2003) Wound bed preparation: a systematic approach to wound management. *Wound Repair Regen* 11 Suppl 1: S1–28
- Schulz A, Hilgers RD, Niedermeier W (2000) The effect of splinting of teeth in combination with reconstructive periodontal surgery in humans. *Clin Oral Investig* 4(2): 98–105
- Schwarz F, Herten M, Ferrari D et al (2007) Guided bone regeneration at dehiscence-type defects using biphasic hydroxyapatite + beta tricalcium phosphate (Bone Ceramic) or a collagen-coated natural bone mineral (BioOss Collagen): an immunohistochemical study in dogs. *Int J Oral Maxillofac Surg* 36(12): 1198–206
- Schwarz F, Sahm N, Becker J (2014) Combined surgical therapy of advanced peri-implantitis lesions with concomitant soft tissue volume augmentation. A case series. *Clin Oral Implants Res* 25(1): 132–6
- Seifert O and Mrowietz U (2009) Keloid scarring: bench and bedside. Arch Dermatol Res 301(4): 259–72
- Sharma G, Lee SW, Atanacio O et al (2017) In search of the optimal wound dressing material following total hip and knee arthroplasty: a systematic review and meta-analysis. *Int Orthop* 41(7): 1295–305
- Sood A, Granick MS, Tomaselli NL (2014) Wound Dressings and Comparative Effectiveness Data. *Adv Wound Care* 3(8): 511
- Staindl O (1979) The healing of wounds and scar formation under the influence of a tissue adhesion system with fibrinogen, thrombin, and coagulation factor XIII. Arch Otorhinolaryngol 222(4): 241–5
- Staindl O, Galvan G, Macher M (1981) The influence of fibrin stabilization and fibrinolysis on the fibrinadhesive system. A clinical study using radioactively



marked fibrinogen as a tracer. Arch Otorhinolaryngol 233(1): 105–16

- Tang H, Lv G, Fu J et al (2015) An open, parallel, randomized, comparative, multicenter investigation evaluating the efficacy and tolerability of Mepilex Ag versus silver sulfadiazine in the treatment of deep partial-thickness burn injuries. *J Trauma Acute Care Surg* 78(5): 1000–7
- Thamm OC, Koenen P, Bader N et al (2015) Acute and chronic wound fluids influence keratinocyte function differently. *Int Wound J* 12(2): 143–9
- Upton D, Solowiej K (2012) The impact of atraumatic vs conventional dressings on pain and stress. *J Wound Care* 21(5): 209–15
- Upton D, Solowiej K, Hender C, Woodyatt KY (2012) Stress and pain associated with dressing change in patients with chronic wounds. *J Wound Care* 21(2): 53–4, 56, 58 passim
- Vercelli S, Ferriero G, Bravini E et al (2017) Cross-cultural adaptation, reproducibility and validation of the Italian version of the Patient and Observer Scar Assessment Scale (POSAS). Int Wound J 14(6): 1262–8
- Vignoletti F, Discepoli N, Müller A, de Sanctis M, Muñoz F and Sanz M (2012) Bone modelling at fresh extraction sockets: immediate implant placement versus spontaneous healing: an experimental study in the beagle dog. J Clin Periodontol 39(1): 91–7
- Weissman O, Hundeshagen G, Harats M et al (2013) Custom-fit polymeric membrane dressing masks in the treatment of second degree facial burns. *Burns* 39(6): 1316–20

- Winter GD (1962) Formation of the scab and the rate of epithelization of superficial wounds in the skin of the young domestic pig. *Nature* 193: 293–4
- Winter GD (1995) Formation of the scab and the rate of epithelisation of superficial wounds in the skin of the young domestic pig. 1962. *J Wound Care* 4(8): 366–7; discussion 368–71
- Wokalek H and Ruh H (1991) Time course of wound healing. *J Biomat Appl* 5(4): 337–62
- Wolbank S, Pichler V, Ferguson JC et al (2015) Noninvasive in vivo tracking of fibrin degradation by fluorescence imaging. *J Tissue Eng Regen Med* 9(8): 973–6
- Wolcott R (2015a) Economic aspects of biofilm-based wound care in diabetic foot ulcers. *J Wound Care* 24(5): 189–90, 192–4
- Wus L, Manning M, Entwistle JWC (2015) Left ventricular assist device driveline infection and the frequency of dressing change in hospitalized patients. *Heart Lung* 44(3): 225–9
- Yu X, Zheng H (2018) Infections after photodynamic therapy in Condyloma acuminatum patients: incidence and management. *Environ Sci Pollut Res Int* 25(14): 14000–5
- Zimmermann A, Roenneberg C, Wendorff H et al (2010) Early postoperative detection of tissue necrosis in amputation stumps with indocyanine green fluorescence angiography. *Vas Endovascular Surg* 44(4): 269–73

