Use of Antiseptics in Managing Difficult Wounds

Joan Faoagali

Abstract

Wound care regimes have changed dramatically over the past 35 years. The principles of most types of wound healing have been investigated in detail and implemented with effect, as part of evidence-based wound healing practice compatible with the science of wound healing physiology. Occlusive dressings are important adjuncts to the armamentarium of the practitioner in charge of open wounds.

Topical antibioticis and antiseptics are of limited use and toxic to healing tissue. There is a wide range of literature on the use of antiseptics and other products on chronic wounds. Of the commonly used products (hypochlorites, phenol derivatives, povidone iodine, quaternary ammonium compounds, chlorhexidine, silver compounds), only in the case of cadexomer povidone iodine does a comprehensive literature base support its use in decreasing the tissue load of bacteria and increasing the healing rates of wounds.

Introduction

Topical antiseptics are toxic to healing tissue [1, 2] and should not be used on it [1], despite their *in vitro* efficacy [3].

Wound healing principles are the same in both humans and animals [4, 5]. Effective wound healing practices include wound irrigation, mechanical and chemical debridement and moist dressings.

In spite of the *in vitro* demonstration of inhibition of healing by some antiseptics, there is increasing data to indicate that healing of venous leg ulcers is inhibited by bacterial infection, and that a reduction in bacterial numbers can reduce inflammation and enhance healing [6].

Dr Joan Faoagali
MBChB FRCPA DHA FASM MPH

Director of Microbiology, Division of Microbiology and Deputy Managing Pathologist,
Department of Pathology
Queensland Health Pathology Services –
Royal Brisbane Hospitals Campus

Honorary Reader, Department of Microbiology
University of Queensland, St Lucia

Adjunct Professor, Faculty of Science and Technology
Griffiths University, Nathan, Queensland

Telephone: (07) 3253 8050
Facsimile: (07) 3252 1324

Definitions

- **Antisepsis** – antiseptic treatment (anti; against septikos; rotten) counteracts bacterial infection (putrefaction) by the use of chemical agents [7].
- **Disinfection** – any process that destroys the causes of infection [7].
- **Chemical debridement** – removal of dead tissue by the use of chemical agents (as compared to surgical debridement) [8].
- **Wound**:
  - any cut, bruise, hurt or injury caused by an external force [7];
  - any defect or break in the skin that results from physical, mechanical or thermal damage or that develops as the result of an underlying medical or physiological disorder [8].
- **Ulcer** – "a local defect or excavation of the surface of an organ or tissue produced by the sloughing of inflammatory necrotic tissue" [9].
- **Infection** – the presence of multiplying microorganisms and a concomitant tissue (inflammatory) response [9].
- **Slough** – visual yellow exudate [9].
- **Exudate** – a mixture of inflammatory cells (granulocytes and monocytes) and serum (protein). Bacteria may also be present if there is infection [9].
- **Pus** – purulent exudate that contains (mainly) polymorphonuclear leucocytes, cellular debris and bacteria [9].

- **Difficult wound** – one that is not 'easy' or is slow to heal [8].

Wound Healing

Uncomplicated wound healing or repair is exemplified by a clean, non-infected surgical incision (Figure 1). This is referred to as primary union or healing by first intention. It has been well studied and is described in basic pathology textbooks [9].

'Difficult' wounds can be described as those in which there has been more extensive loss of cells and tissue than described above. Infarction, inflammatory ulceration, abscess formation and large surface wound defects have a more complicated repair process than that which occurs in healing by first intention.

The common denominator in all such large wounds is the existence of a "tissue defect that must be filled" [8]. The healing occurs by secondary intention (Figure 2). Wound healing by secondary intention, also complex, is an orderly phenomenon that, again, is well described [9]. It requires viable cells, growth factors, adequate blood supply and regeneration of blood vessels, adequate nutrition, including proteins, and vitamin C and other chemicals, including zinc.

Growth factors known to be active in wound healing are shown in Table 1.

The orderly processes of wound healing can be modified by a large number of known and unknown factors [9], which are summarised in Table 2.

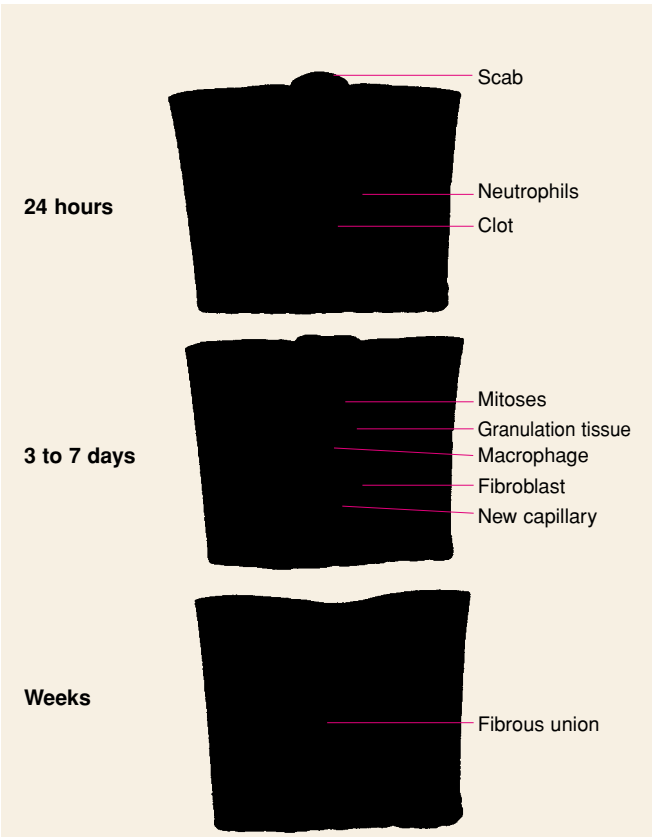
It is important to have an understanding of the 'normal' healing rate of wounds, in order to determine whether healing is unduly delayed. The healing rate of surgical wounds has been calculated by Marks *et al* [10, 11] and provides a useful 'rule of thumb' to monitor healing progress.

All wounds will be colonised by microorganisms, apart from 'thermal burns' immediately after their occurrence. The presence of microorganisms does not necessarily mean an infection is present.

Considering the complexity of wound healing, and the multitude of local, systemic and environmental factors that can inhibit or delay wound healing, it is important to maximise the factors known to promote or assist the process.

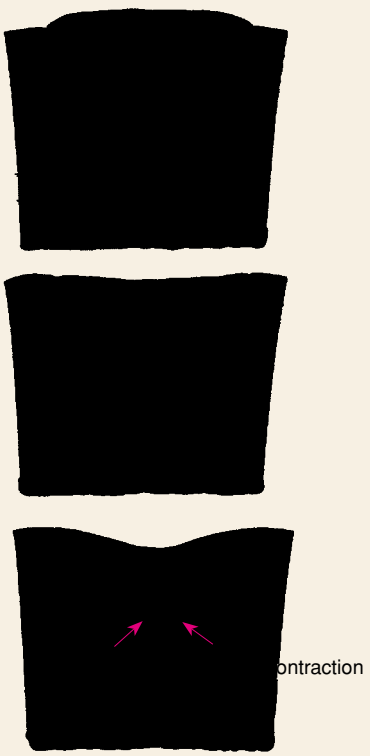
The bacteriology laboratory plays only a minor role in the treatment of chronic wounds. This is because the microbial flora of chronic wounds vary and reflect host mucosal and skin

Figure 1. Steps in wound healing by primary intention ***[adapted from reference 9].***



Steps in wound healing by first intention

Figure 2. Healing by secondary intention ***[adapted from reference 9].***



The resultant scar is much smaller than the original wound, owing to wound contraction.

Table 1. Growth factors active in wound healing.

Action	Chemical
Monocyte chemotaxis	PDGF, FGF, TGF-B
Fibroblast migration	PDGF, EGF, FGF, TGF-B, TNF
Fibroblast proliferation	PDGF, EGF, FGF, TN
Angiogenesis	VEGF, FGF
Collagen synthesis	TGF-B, PDGF, TNF
Collagenase secretion	PDGF, FGF, EGF, TNF, TGF-B inhibits

[Abbreviations: PDGF = platelet-derived growth factors; FGF = fibroblast growth factors; TGF-B = transforming growth factor beta; EGF = epidermal growth factors; TNF = tumour necrosis factor; VEGF = vascular endothelial growth factors.]

Table 2. Factors known to modify wound healing.

Factor	Effect	Result
Systemic and host factors	Nutrition • protein • vitamin C	Incubation of collagen synthesis, < Healing
Glucocorticoids	Anti-inflammatory	< Inflammatory response, < Fibroplasia
Local host factors	Infection	Delays healing
Mechanical factors	Increased abdominal pressure	Rupture of wounds, lower-limb lymphatic stasis
Inadequate blood supply	Atherosclerosis	Reduced blood supply delays healing
Foreign bodies (such as bone, metal, plant material)	Inflammation and infection	Retards healing

microbes as well as environmental bacteria (and fungi), which can originate either from an airborne source or direct contact/spread from epithelium adjacent to the wound [12].

If local or systemic signs of infection are present it is important to collect appropriate samples early (on presentation), so that pathogens such as MRSA, Group A beta haemolytic streptococci or *Pseudomonas aeruginosa* can be identified and targeted in the treatment protocols. These factors are particularly important in the successful treatment of leg ulcers [13].

Trengove *et al* [13] found that mixed microbes were present in samples cultured from leg ulcers and, although no particular bacterial group was associated with delayed healing, four or more different bacterial genera (indicating heavier colonisation) were associated with a slower rate of healing than when fewer than four bacterial genera were present.

Antiseptics and Other Agents Used in the Care of Difficult Wounds

Only in the 1960s was the concept of 'moist wound care' recognised [8] and it has taken almost 30 years for it to be accepted and widely utilised. Thomas [8] states that, prior to the '60s, wound care was similar to that "used by Florence Nightingale at the time of the Crimean War."

It is an accepted principle that wound cleansing is essential if optimum healing is to occur. All foreign material and devitalised tissue must be removed. Surgical debridement is the most rapid and effective technique, but there may be situations in which this is not possible and alternative methods of wound cleansing are requested.

Chemical debridement is the usual alternative and a wide variety of chemicals has been used for this purpose. Hypochlorite antiseptic solutions have been employed for more than 100 years, but they are rapidly inactivated by protein, dilution and physiological pH and are toxic to tissues, since they oxidise tissue enzymes. There are few studies comparing hypochlorite solutions and other desloughing agents.

One prospective study comparing hypochlorite and a hydrocolloid dressing on pressure sores showed that wounds treated with hypochlorite healed more slowly than those treated with the hydrocolloid [14].

Hydrogen peroxide (6 per cent) BP has limited *in vivo* antibacterial activity and is rapidly broken down into oxygen and water by tissue catalase. Oxygen can be toxic to granulating tissues but no recent comparative prospective published studies have re-examined this issue.

Cetrimide is a quaternary ammonium compound with excellent detergent action. Unfortunately, it is cytotoxic, even in low concentrations, and can damage granulating tissue. Chlorhexidine, alone or combined with cetrimide (as in Savlon), is an excellent detergent for cleaning wounds contaminated with oil or dirt. Use of low-dose chlorhexidine in burn baths has been shown to decrease the bacterial colonisation of burn wounds and improve their healing rates. Cetrimide is not appropriate for cleansing chronic wounds because of its cytotoxic effects.

Five per cent or 1 per cent acetic acid has been reported as reducing *Pseudomonas aeruginosa* colonisation of chronic wounds. However, Phillips *et al* [15] reported one study in which, when this product was used, there was an increase in *S.*

aureus and other Gram-negative wound isolates.

Povidone iodine products have been widely advocated for use on wounds, to decrease bacterial flora and promote healing. Studies have suggested that absorption of the iodine and hyper-sensitivity can occasionally occur, and even low concentrations of iodine are toxic *in vitro* to cells [8]. Recent reviews of phar-maceuticals containing iodine [16, 17, 18] highlight the differences between *in vitro* and *in vivo* use of such products. Recent human studies show enhanced healing of chronic venous ulcers after the use of slow-release (cadexomer) iodine products [16, 17].

Table 3 lists agents that enhance and delay wound healing and gives a brief summary of their mode of action (if known) and the reference source.

Discussion

The role of antiseptics in the care of chronic or difficult wounds has undergone many changes [39].

The belief that antiseptics assisted with wound healing existed from the mid-1800s – when Lister found that micro-organisms not only cause fermentation and putrefaction but also initiate suppuration in living tissues – until the mid-1980s, when Leaper and Simpson [40] (among others) reported that prolonged use of antiseptics and topical antibiotics delayed healing. In 1986 Leaper [40] listed six antiseptics currently used in wound care: chlorhexidine, povidone iodine, quaternary ammonium compounds (cetrimide), phenol derivatives (hexachlorophane, triclosan), silver compounds and hypochlorite. He noted in a later paper [41] that the wound toxicity of chlorhexidine and povidone iodine was (clinically) less than previously believed, probably due to increasing recognition of the role of bacteria in delaying wound healing and the importance of removing dead tissue, foreign material and slough and providing the new, clean granulation with optimum (moist wound) conditions in which to regenerate.

Cadexomer iodine preparations are new and well-researched slow-release povidone iodine products that have undergone extensive clinical trials and been shown useful in wound de-bridement and stimulation of granulation tissue. Fears of cytotoxicity and iodine absorption associated with the use of the previously available iodine products have resulted in infrequent use of these products to date, but the 1996 European Tissue Repair Society consensus conference concluded that they appeared both safe and effective in wound healing [16].

Natural products, including honey and sugar, also have their advocates [42], but recent papers from New Zealand and Australia confirm that the activity of honey is dependent on the

Table 3. Chemical agents used on wounds.

Chemical	Action	Reference
H_2O_2 (hydrogen peroxide)	Inhibits keratinocyte migration but does not affect tissue viability	O'Toole [19]
PVP-1 (polyvinyl pyrrolidine)	Absorption, metabolic acidosis, renal insufficiency, slows healing	Steen [20], Mertz & Ovington [21], Burks [22], Neidner [23]
Cigarette smoke (nicotine, carbon monoxide, hydrogen cyanide)	Decreases collagen production, vasoconstriction decreases platelet adhesiveness and proliferation of fibroblasts, decreases O_2 transport metabolism and oxidative metabolism	Jorgensen *et al* [24], Silverstein [25], Haverstock [26]
PVI additives (amonium honoxynol-4-sulfate and lauramide DEA)	Tissue damage, delayed healing	Goldenheim [27]
Eusol (Edinburgh University, solution of lysol)	Tissue damage	Ryan [28]
Three per cent boric acid	Toxic to handle	Borrelly [29]
Silver sulphadiazine	Faster healing in rat wound healing experiments	Lansdown [30]
Chlorhexidine gluconate 0.2 per cent, Irgasan 0.2 per cent, Eusol half-strength	Decrease in granulation and epithelialisation	Archer *et al* [31], Doughty [32]
Nitric oxide, platelet and other activating factors	Enhance tissue granulation	Higgins & Ashry [33], Heggers *et al* [34]
Maggots	Desloughing agents	Church [35]
Eupatorium odoratum (eupolin)	Proliferation of fibroblasts and epithelial cells	Phan *et al* [36]
GMCSF (granulocyte cell stimulating factor)	Stimulates cell division	El Sagher [37]
Prolidase	Desloughing agent	Oono [38]
Aloe vera	Effects inconclusive	Heggers *et al* [34]

pollen source [43].

The use of larvae (maggots) has also seen a resurgence, due to recognition of the active desloughing that results from their activities [35].

Conclusions

There is increasing evidence both for and against the use of antiseptics for the treatment of chronic and/or difficult wounds.

The principles of chronic wound care include the following essential components: assessment of the presence or absence of infection; removal of slough, which prevents epithelialisation, and investigation and control of underlying disease.

Antiseptics may be useful in decreasing bacterial load (in association with antibiotics if there are overt signs of infection) in sloughy wounds. The antiseptic chosen should be non-toxic, effective and not delay healing. Current published data suggest that the new preparations of slow-release cadexomer iodines appear to be effective antibacterial agents and to depress excessive inflammatory responses. Over 30 published papers have reviewed almost 10,000 treated, assessable patients. Leaper [41] states: " … antiseptics alone are unlikely to cure chronic wounds and a multidisciplinary approach has the most chance of success."

Routine bacterial cultures of non-inflamed chronic ulcers are not indicated, but cultures must be collected if there are signs of infection. Published evidence for the efficacy of many of the other proposed treatments of chronic wounds is not available. Clinicians should aim to use validated treatments or set up studies to provide the comparative data needed to support their choices.

References

1. Cho CY & Lo JS. Dressing the part. Dermatol Chin 1998; **16**(1):25-47.
2. Brown CD & Zittelli JA. Choice of wound dressings and ointments. Otolaryngol Clin N Amer 1995; **28**(5):1081-91.
3. Michel D & Zach GA. Antiseptic efficacy of disinfecting solutions in suspension test *in vitro* against MRSA, *P. aeruginosa* and *E. coli* in pressure sore wounds after spinal cord injury. Dermatol 1997; **195**(S2):36-41.
4. Liptak JM. An overview of the topical management of wounds. Aus Vet J 1997; **75**(6):408-13.
5. Johnston DE. Care of accidental wounds. Vet Clin N Amer – Small Animal Practice 1990; **20**(1):27-46.
6. Pierard-Franchimont C, Paquet P, Arrese JE & Pierard GZ. Healing rate and bacterial necrotizing vasculitis in venous leg ulcers. Dermatol 1997; **194**(4): 383-87.
7. Chambers Family Dictionary. United Kingdom:W & R Chambers Ltd CLB, 1990.
8. Thomas S. Wound Management and Dressings. London: The Pharmaceutical Press, 1990.
9. Cotran RS, Kumar V, Robbins SL & Schoen FJ. Pathologic Basis of Disease (5th ed). Philadelphia, Sydney: WB Saunders, 1994.
10. Marks J. Prediction of healing time. World J Surg 1983; 7:641-45.
11. Marks J. Pilonidal sinus. Br J Surg 1985; **72**:637-40.
12. Lawrence JC, Harding KG & Moore DJ. The use of antiseptics in wound care. J Wound Care 1996; **5**(1):44-47.
13. Trengove NS, Stacey MC, McGechie DF & Mata S. Qualitative bacteriology and leg ulcer healing. J Wound Care 1996; **5**(6):277-80.
14. Johnson A. Towards rapid tissue healing. Nurs Times 1984; **80**:39-43.
15. Phillips I. Acetic acid in the treatment of superficial wounds infected by *Pseudomonas aeruginosa*. Lancet 1968; **1**:11-14.
16. Falanga V. Iodine-containing pharmaceuticals: a reappraisal. In: Meller R. Proc 6th Conf Adv Wound Management. London: McMillan Magazines Ltd, 1997.
17. Sundberg J & Meller R. A retrospective review of the use of cadexomer iodine in the treatment of chronic wounds. Wounds: A Compendium of Clinical Research and Practice 1997; **9**(3):68-85.
18. Lawrence JC. The use of iodine as an antiseptic agent. J Wound Care 1998; **7**(8):421-27.
19. O'Toole EA, Goel M & Woodley DT. Hydrogen peroxide inhibits human keratinocyte migration. Dermatolog Surg 1996; **22**(6):525-29.
20. Steen M. Review of the use of povidone iodine (PVP-I) in the treatment of burns. Postgrad Med J 1993; 69(53):584-92.
21. Mertz PM & Ovington LG. Wound healing microbiology. Dermatol Clin 1993; **11**(4):739-47.
22. Burks RI. Povidone-iodine solution in wound treatment. Phys Ther 1998; **78**(2):212-28.
23. Neidner R. Cytotoxicity and sensitisation of povidone-iodine and other frequently used anti-infective agents. Dermatol 1997.
24. Jorgensen LN, Kallehave F, Chris Fensen E, Siana JE & Gottrup F. Less collagen production in smokers. Surg 1998; **123**(4):450-55.
25. Silverstein P. Smoking and wound healing. Am J Med 1992; **93**(IA):225-45.
26. Haverstock BD & Mandracchia VJ. Cigarette smoking and bone healing. J Foot & Ankle Surg 1998; **37**(1):69-74.
27. Goldenheim PD. An appraisal of povidone iodine and wound healing. Postgrad Med J 1993; **69**(53):S97-S105.
28. Ryan TJ. Antibacterial agents for wounds and burns in developing worlds: report on a workshop. J Trop Med & Hyg 1992; **95**(6):397-403.
29. Borrelly J, Blech MF, Grosdidier G, Martin-Thomas C & Hartmann P. Contribution of a 3% solution of boric acid in the treatment of deep wounds with loss of substance. Ann de Chirurgie Plas et Esthet 1991; **36**(1):65-69.
30. Lansdown AB. Zinc in the healing wound. Lancet 1996; **347**(9003):706-07.
31. Archer HG, Barnett S, Irving S, Middleton KR & Seal DV. A controlled model of moist wound healing: comparison between semipermeable film, antiseptics and sugar paste. J Experim Pathol 1990; **71**(2):155-70.
32. Doughty D. A natural approach to the use of topical antiseptics. J WOCN 1994; **21**(6):224-31.
33. Higgins KR & Ashry HR. Wound dressings and topical agents. Clin Pod Med & Surg 1995; **12**(1):31-40.
34. Heggers JP, Elzaim H, Garfield R, Goodheart R, Listengarten D, Zhao J & Phillips LG. Effect of combination of aloe vera, nitroglycerin and L-NAME on wound healing in rat excisional model. J Alter & Compl Med 1997; **3**(2):149-53.
35. Church JC. The traditional use of maggots in wound healing and the development of larva therapy (biosurgery) in modern medicine. J Alter & Compl Med 1996; **2**(4):525-27.
36. Phan TT, Hughes MA & Cherry GW. Enhanced proliferation of fibrobasts and epithelial cells treated with an extract of the leaves of *Chromolaena odorata* (Eupolin), a herbal remedy for treating wounds. Plas & Recon Surg 1998; **107**(3):756-65.
37. El Saghir NS, Bizri AR, Shabb NS, Husami TW, Salem Z & Shamseddine AI. Pressure ulcer accelerated healing with local injections of macrophage-colony stimulating factor. J Dermatol 1997; **35**(2):179-82.
38. Oono T, Fujiwara Y, Yoshioka T & Arata J. Prolidase activity in chronic wound and blister fluids. J Dermatol 1997; **24**(10):826-29.
39. Williams C. Wound measuring methods. Comm Nurse 1997; **3**(8):46-48.
40. Leaper DJ & Simpson RA. The effect of antiseptics and topical antimicrobials on wound healing. J Antimicrob Chemother 1986; **2**:135-37.
41. Leaper DJ. Antiseptics in wound healing. Nurs Times 1996; **92**(19):63-69.
42. Efem S. Clinical observations on the wound healing properties of honey. Br J Surg 1988; **75**:679-81.
43. Davis, Cox W-A, Poole S & George N. Australian Honey – An Emerging Medical Opportunity. AIFST Annual Meeting, October 1999.