

Advancement of Wound Healing: A Review

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ABSTRACT

There are many antimicrobial dressings available for the prevention and management of wound infection. An awareness of their different properties, as well as their clinical and cost-effectiveness is crucial. In addition, the clinician should have an understanding of the varying states of wound bioburden and use this information as a guide to starting and stopping antimicrobial therapy. Finally, antimicrobials should only be used as part of an overall package of care that considers and addresses all the factors that may be contributing to wound infection. Antimicrobials should not be used indiscriminately, but in a timely and appropriate manner to reduce time to healing for the patient, and to minimise the impact of wound infection on patients, healthcare systems and society.

Keywords: Antimicrobial Dressings, Healthcare, Bioburden, Tissues And Wounds.

I. INTRODUCTION:

A wound may be defined as a disruption to the physiological arrangement of the skin cells and a disturbance to its function in connecting and protecting underlying tissues and organs. It may be primary caused by accidental cut, tear, scratch, pressure, extreme temperatures, chemicals, and electrical current, or secondary to surgical intervention or disease (i.e., diabetes, ulcers, or carcinomas) [1]. It ranges from superficial (affecting the epidermis) to partial-thickness (affecting both epidermis and parts of the dermis) and full-thickness (including subcutaneous fat and bones) wounds [2]. Wound healing is a physiological process, by which the living body repairs tissue damages, restores its anatomical integrity, and regains the functionality of the injured parts. A wound can be closed by primary intention or left to heal by secondary intention, and in both ways the healing process occurs through a series of overlapping events and is influenced by a number of intrinsic and extrinsic factors [3].

Antimicrobials

Antimicrobials are agents that kill micro-organisms. Antimicrobial is an 'umbrella' term that includes: disinfectants, antiseptics and antibiotics. Disinfectants refer to chemical agents or biocides that are used to inhibit or kill microbes on inanimate objects such as dressing trolleys and instruments, for example, alcohol, sodium hyperchlorite and glutaraldehyde. Antiseptics, on the other hand, are biocides used to inhibit or kill micro-organisms present within a wound (the bioburden) or on intact skin [4]. The antimicrobial activity of disinfectants and antiseptics varies considerably and these agents are referred to as bactericidal, fungicidal, virucidal or sporicidal when they kill microbes, and bacteriostatic, fungistatic, sporistatic or virustatic if they inhibit the growth of microbes. Some of the more traditional biocides such as sodium hyperchlorite and iodine have been used as disinfectants and antiseptics for over a century and their cytotoxic effect in wounds has been recognised for many years [5]. Many disinfectants and antiseptics have broad-spectrum antimicrobial activity and microbial resistance is uncommon. Antibiotics are naturally occurring or synthetically produced chemical substances that can act selectively and can be administered both topically (normally not recommended in wound care) or systemically. Microbial resistance to antibiotics is common and an increasing international concern.

Antimicrobial dressing

For the purpose of this document, antimicrobial dressings refer to wound dressings which have an antiseptic agent incorporated and does not include products/dressings which incorporate antibiotics. As described above, traditionally the term antiseptic has been used to refer to solutions that damage healthy tissue. Such solutions have a broad action and can be highly effective in killing microorganisms but may compromise healthy tissue. Thus, their use in ongoing wound management has been questioned

and limited to reducing the load of pathogens on intact skin [6].

Recent advances in antiseptic technology have led to the development of a number of products that are less harmful to healthy tissue, while being highly effective in destroying pathogens. These include antiseptics such as silver, cadexomer iodine, polyhexamethyl biguanide (PHMB) and honey. Dressings incorporating these antiseptics can successfully be used in topical management to reduce the load of a variety of pathogens, not just bacteria. Partly due to the rising prevalence of drug-resistant antibiotics (thought to be in part a result of their indiscriminate and over-use), these antimicrobial dressings incorporating antiseptic agents are increasingly being used in wound management [7, 8]. Antimicrobial dressings offer many benefits. They are:

- Relatively easy to use n Widely available
- Frequently cost less than antibiotics
- Available without prescription
- Have less risk of resistance.

Antiseptic role

The commonly encountered antiseptic agents are listed in Box 1. Antimicrobial dressings are applied topically to the wound where they exert a broad spectrum of non-selective antibacterial action. They act at multiple sites within microbial cells, thus reducing the likelihood of bacteria developing resistance. This helps to explain their relatively low levels of bacterial resistance. This is unlike antibiotics which act selectively against bacteria and can be administered topically (not usually recommended) or systemically.

Table 1: Antiseptic agents and their formulation.

Antiseptic	Formulation/notes
Potassium permanganate	Solution, tablets for dissolution
Acetic acid	Solution
Honey	Amorphous honey or impregnated dressings
Polyhexamethylbiguanide (PHMB)	Solution, impregnated dressings
Chlorhexidine	Solution, powder, impregnated dressings. Chlorhexidine may be used as an alternative for patients allergic to iodine
Iodine	Povidone iodine: solution, cream, ointment, sprays, impregnated dressings
Silver	Silver sulfadiazine: cream, impregnated dressings

Wound bioburden and antimicrobial dressings

All wounds contain micro-organisms, yet the majority are not infected and go on to heal successfully. In these cases, the bioburden of the wound and the host’s immune system are in balance. However, if this balance shifts in favour of the microbes, or if wound healing is impaired, the micro-organisms (usually bacteria) multiply and

invade tissues resulting in a prolonged and inappropriate inflammatory response, tissue damage and delayed healing and, if left unchecked, systemic illness [9]. When this shift in balance occurs, immediate intervention is needed. From a clinical management perspective, it is this recognition of the state of the wound with respect to bacterial load that is a challenge [10].

Table 2: Wound bioburden and the need for antimicrobial intervention [11, 12].

Term	Definition
Infection	Bacteria multiply, healing is disrupted and wound tissues are damaged (local infection). The wound may extend into previously healthy tissue. Topical agents may control bacterial growth and improve the wound healing environment. Patients with poor host defence may need systemic antibiotic therapy. Bacteria may produce problems nearby (spreading infection), or cause infection throughout the body (systemic infection), for which both systemic antibiotics and topical antimicrobial dressings are indicated
Critical colonisation/ covert infection	Micro-organisms multiply to an extent that wound healing is impaired. While classical clinical signs and symptoms of infection may be absent (pain, heat, erythema, oedema and purulence), more subtle local signs

	and symptoms may be present especially in chronic wounds ^{1, 7, 13} . Topical antimicrobial dressings are indicated
Colonisation	Micro-organisms multiply, but wound tissues are not damaged. Wound healing should occur successfully without topical antimicrobial dressing intervention UNLESS there are concerns about the patient's overall health or immune system function
Contamination	Micro-organisms do not increase in number or cause clinical problems. Wound healing should occur successfully without topical antimicrobial dressing intervention

Table 2 outlines the relationship between wound bioburden and the need to intervene with antimicrobial dressing. It is important to consider if the wound is not healing because of a rising bacterial load (in which case antimicrobial dressings may assist wound healing), or if the bacterial load is increasing because the wound is not healing (antimicrobial dressings are unlikely to assist wound healing but may help prevent spreading infection).

Identifying wound infection

Identification of wound infection is a clinical skill and clinicians should be aware of the signs and symptoms, e.g. erythema, pain, swelling, localised heat and purulence, particularly those that occur in the wound type they encounter most frequently (since infection may produce different signs and symptoms in wounds of different types and aetiologies [13]).

acute or surgical wounds in otherwise healthy patients, infection is usually obvious. However, in chronic wounds and debilitated patients, diagnosis may rely on recognition of subtle local signs or nonspecific general signs (such as malaise and loss of appetite). Other criteria include [13]:

- Increased discharge
- Delayed healing
- Wound breakdown
- Pocketing at the base of the wound
- Epithelial bridging n Unexpected pain or tenderness
- Friable granulation tissue
- Discolouration of the wound bed
- Abscess formation
- Malodour.

A thorough patient history and good clinical assessment skills should enable the clinician to establish if the wound is infected and if antimicrobial intervention is necessary [14]. It is important to recognise and differentiate the signs

and symptoms of localised, spreading and systemic infection.

How do I recognise when a wound is at risk of infection?

Clinicians need to be extra vigilant of patients with an increased risk of wound infection. These include those who are taking medication which dampens down the immune system, such as corticosteroids, cytotoxic agents and immunosuppressants. Also, those with comorbidities such as diabetes mellitus, an immunocompromised status, hypoxia and poor tissue perfusion due to anaemia or arterial/cardiac/respiratory disease, renal impairment, malignancy, rheumatoid arthritis, obesity and malnutrition are at an increased risk [15].

Clinicians should remain clinically suspicious of wound infection, particularly in patients at increased risk, and be ready to act quickly to initiate antimicrobial dressings or refer to relevant diagnostic or clinical services.

What factors should be considered when selecting an antimicrobial dressing?

Once the need for topical antimicrobial dressings has been identified, it is important to select a product that provides optimum conditions to support healing [16]. All of the antimicrobial products available have different physical properties, such as the level of antimicrobial they release, the duration of effective action, the carrier dressing's ability to handle different volumes of exudate, or manage odour or pain. Therefore, specific products should be chosen to reflect the overall treatment requirements of the wound following thorough wound assessment. Clinical condition, comorbidities, personal circumstances, preferences and expectations of the patient should also influence choice [17]. An understanding of how the product works and its efficacy and safety is important, as well as knowledge of the costs involved and the dressing's availability. The

clinical problem gives an example of the use of an antimicrobial dressing in clinical practice.

Properties of the ideal antimicrobial dressing:

- Broad spectrum of activity against micro-organisms, including resistant strains of bacteria.
- Bacteriocidal not just bacteriostatic
- Rapid but sustained activity
- Suitable for use on broken skin/mucus membrane
- Non-irritant and non-toxic to tissue/environment
- Easily soluble in a non-toxic carrier
- Not inhibited by body fluids, wound exudate or biofilms
- Stable, easy to use and store
- Assists in wound bed preparation, e.g. debridement/ moisture management
- Cost-effective
- Reduces malodour
- Conforms to site and shape of the wound
- Satisfies patient and clinician expectations

When should antimicrobial therapy be started and stopped?

The use of antimicrobial dressings in wound management is recommended for:

- Prevention of infection in patients at increased risk of wound infection
- Treatment of localised wound infection
- Local treatment of wound infection in cases of spreading or systemic wound infection in conjunction with systemic antibiotics.

Once started, the effect of antimicrobial dressings on the wound must be closely monitored. A failure to respond or a further deterioration of the wound will indicate the need for a full reassessment to exclude contributing causes other than infection and may indicate the need for an alternative approach or the addition of systemic therapy. For wounds that improve, antimicrobial dressings should be continued for 14–21 days [18], at which time the need for further antimicrobial therapy should be re-assessed. For most wounds antimicrobial dressings can be stopped at this stage, but careful observation of the wound should continue in case signs of an increasing bacterial load recur. Not all wounds will respond to topical antimicrobial dressings. In such cases bacterial culture results will assist in the selection of appropriate treatment. Bacterial culture results will also allow identification of patients with resistant strains of bacteria within the wound which will inform their subsequent management [19]. In

locally infected wounds antimicrobial dressings should be considered. When there are no longer signs of local infection or spreading infection, the antimicrobial dressing should be discontinued. If the wound continues to show signs of infection, a systemic antibiotic should be considered [20].

In patients with conditions that put them at high risk of infection, such as poor vascularity, or in which the immune system is compromised, experienced clinicians may consider the use of systemic antibiotics since these conditions may mask the signs of infection [21]. Blood cultures should be taken of wounds which are assessed as having spreading and/or systemic infection to identify the offending organism and to assess for differential diagnosis [22]. The patient should be treated with broadspectrum antibiotics which may be given intravenously. Topical antimicrobial dressings should also be used to help reduce wound bioburden locally.

In addition to the use of antimicrobial dressings, it is important to ensure that all other factors that can contribute to wound infection are addressed as far as possible as part of the patient's overall package of care [23].

Optimise the patient's immune response:

Measures which will optimise the patient's ability to fight infection will enhance their healing potential, e.g. improved nutritional intake and hydration. Systemic factors that may have contributed to the development of the wound and/or infection, should also be addressed. For example, glycaemic control in patients with diabetes should be optimized [24].

Clinical problem

A patient with a known venous ulcer that initially responded to compression bandaging with simple non-adherent dressings developed increasing exudate, wound pain and wound odour. The removed dressing was stained green indicating possible pseudomonas colonisation. The dependent periwound skin shows signs of maceration and the granulation tissue, which had been healthy, developed a coating of slough and appeared dark and friable. There was no evidence of systemic infection or cellulitis [25].

Action plan
n Take wound swab. Swab confirmed pseudomonas and mixed flora
n Clean wound and periwound skin, removing as much necrotic tissue and wound debris/slough as possible
n Select appropriate barrier product to protect the

periwound skin. Consider if antimicrobial dressing is appropriate at this stage — Yes. Consider wound requirement and area to be treated — select product with high absorbency and high levels of available antimicrobial agent such as a silver/foam or silver/alginate combination. Dressing should be known to function under compression. In this case, ACTICOAT® Absorbent (Smith & Nephew) was chosen because of its absorbency and its ability to maintain sufficient levels of silver. Continue compression therapy, but increase dressing change frequency until exudate leakage is controlled. Continue ‘maintenance’ debridement and wound cleansing at each dressing change. Monitor closely for signs of spreading infection and cellulitis and review bacterial swab results. If wound continues to deteriorate add systemic therapy based on sensitivity results. Set treatment goals and review date, planning to discontinue antimicrobial dressing after 14–21 days. In this case, antimicrobial dressings were continued for 21 days (six dressing changes), at which stage the patient returned to a simple foam dressing under compression and weekly dressing changes [25].

Reduce the wound’s bioburden

Removal of necrotic tissue, pus and slough, all of which can act as a growth media for micro-organisms, will promote healing. The bacterial load of the wound should also be reduced through effective and personal hygiene and preventative measures to maximise the effects of the antimicrobial dressing. This can be done through the use of appropriate infection control procedures and protecting the wound with an appropriate dressing. Other than cases of peripheral ischaemia where a positive decision has been taken to ‘mummify’ a digit or wound, it is not helpful to place an antimicrobial dressing onto a wound that is covered in dry eschar — such tissue would need to be debrided before the antimicrobial dressing could have a therapeutic effect [26]. Wound cleansing at each dressing change by irrigation should effectively remove debris and micro-organisms without damaging the wound or driving micro-organisms into the tissues. The importance of these factors should not be overlooked. Indeed, in some circumstances, particularly surgical wounds, infection control measures in addition to cleansing, debridement and drainage may be sufficient to reduce bacterial load to a level where healing can take place [27].

Current issues surrounding the use of antimicrobial dressings

The publication of a study comparing silver-containing dressings with non-medicated dressings in venous ulcers, and subsequent reviews [28], has resulted in some people mistakenly presuming that antimicrobial dressings are not suitable for treatment of critical colonisation/local infection [29], and has had repercussions on their availability and use in some areas of clinical practice. The lack of evidence from randomised controlled trials (RCTs) concerning antimicrobial dressings in general might also restrict their use. Antimicrobial wound dressings, which are classed as medical devices, should not be judged as pharmaceuticals and other levels of evidence should be considered to guide their use in practice [30]. The use of antimicrobial dressings such as silver is a key component of the management of patients with signs of wound infection and without the use of these products, patients may be put at risk [31]. A lack of knowledge regarding the use of this product group could put patients at risk of delayed healing and untreated local infection which could progress to systemic sepsis [32].

By using antimicrobial dressings to stop local infection spreading, unnecessary complications and costs are prevented. The most obvious example being a reduction in hospitalisation. It is important not to use these products when infection is not present, or where there is no significant clinical risk of infection, since some antimicrobial dressings can result in damage to healthy tissue [33].

Cost-effectiveness:

In vulnerable and critically ill patients, infection is obviously associated with increased risk of morbidity and mortality. It is possible to show that the costs of infections such as surgical site infections (SSIs) and cellulitis have a heavy financial and social burden and impact greatly on nurses’ time, costs of long-term treatment and hospital stays [27, 28, 29]. Although published studies on cost-effectiveness are currently lacking, clinicians are increasingly aware of the potential of antimicrobial dressings to reduce costs of care.

Future of antimicrobial dressings. The current controversy surrounding the use of antimicrobial dressings such as silver has demonstrated the need for a framework for antimicrobial dressing usage. Work is ongoing aimed at developing and integrating better strategies to facilitate appropriate and judicious use

of topical antimicrobial dressings [1, 14]. Improvement in diagnosing infection and recognising patients at risk will have important implications in knowing when intervention is needed and is an important part of future developments. Laboratory and clinical studies are ongoing and required to better understand which agent to use when and with what delivery system to maximise the benefits of the antiseptic agent used. For now, clinicians must draw on available literature and be vigilant in adhering to local protocols to avoid unnecessary and prolonged treatment [34].

II. CONCLUSION

Antimicrobials should only be administered as a part of a comprehensive plan of care that takes into account and treats all potential risk factors for wound infection. To speed up the patient's healing and lessen the effects of wound infection on patients, healthcare systems, and society, antibiotics should not be used carelessly but rather promptly and appropriately.

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