Part1: Integrating infection prevention practice with chronic wound and burn management

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Introduction

The prophylactic and unnecessary use of topical antiseptics, antimicrobial dressings and antibiotics on uncomplicated, colonised, normally progressing wounds is a cause for concern, evidenced by an increasing number of community-associated strains of methicillin-resistant *Staphylococcus aureus* which are also resistant to mupirocin, and multidrug-resistant Gram-negative isolates. This is the first in a two-part series. The role of the medical microbiologist in superficial wound sampling will be highlighted in this article, and key principles in the appropriate selection and use of topical antimicrobial agents summarised.

The successful management of chronic and complicated wounds requires the seamless integration of sound infection control principles with an understanding of the wound bed microbiome. Not only is it in the best interests of individual patient safety and healing outcomes, it also has an impact at community and environmental level by supporting the principles of antimicrobial stewardship and reducing long-term "selective pressure" with regard to the development of resistant microorganisms.

The objectives of biofilm-based wound management include:

- Appreciating the value of polymicrobial colonisation and its positive influence on healing.
- Performing a risk assessment of the most likely microbial strains at wound bed level, which are usually representative of local flora and the patient's physical environment.
- Understanding that superficial sampling is of limited diagnostic value, i.e. the growth of bacteria from swabs is not synonymous with infection, and treatment based on culture results alone is not warranted.
- Using currently accepted wound assessment criteria in conjunction with other infection markers (e.g. a full blood count, procalcitonin and C-reactive protein) and patient co-morbid risk factors to select appropriate topical antimicrobial products and/or justify the use of systemic antibiotics.
- Using a rational approach for the selection and use of topical antimicrobial products for "maintenance" wounds (e.g. malignant, fungating or critically ischaemic), where the long-term control of bioburden, exudate and odour, or the prevention of drug-resistant opportunistic infection, are the primary goals.

What is a biofilm?

Biofilm is everywhere. Biofilm comprises a complex matrix of microbial secreted polymer compounds called extracellular polymeric substance. This matrix facilitates the adherence of bacteria and fungi to the wound bed, and also provides a medium for chemical signalling (quorum sensing), and sophisticated protection from the action of antibodies, neutrophils and antimicrobial agents.

Biofilm formation commences within hours of the initial wound contamination and subsequent colonisation, and the social structure (i.e. cooperation, mutual protection versus competition) within a biofilm depends largely on the types of microbial species present.

As the number of cells and chemical signals within clusters increases and the critical level or quorum is exceeded, gene expression within the cells changes, and biofilm development is initiated or accelerated. The final stage of biofilm formation and maturation is known as dispersion, in which the biofilm spreads and colonises new surfaces.

Bacteria within biofilm are up to 1 000 times more resistant to antimicrobial agents than the same bacteria in suspension. The three-dimensional structure of bacterial biofilm is depicted in Figure 1.

Whether or not to collect a swab

Swabs should only be collected when the clinical criteria point to a wound infection and before any antimicrobial interventions have been initiated. However, superficial sampling is considered to be of little clinical value and is generally unreliable in identifying the pathogens responsible for deeper infection.

In order to remove superficial debris and surface contaminants, and also to provide more specific results, thorough cleansing of the wound bed with sterile saline or water should be undertaken prior to microbiological sampling.

Preferred clinical specimens include aspirate from a sinus or abscess, while a tissue biopsy or curettage from the deep wound bed compartment is regarded as the reference standard when diagnosing infection. It is important to ensure that the specimen reaches the laboratory within three hours, or is refrigerated it if a delay is expected.

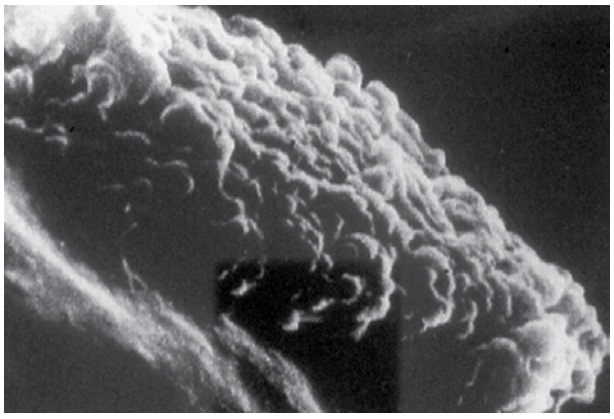


Figure 1: The three-dimensional structure of biofilm

The following species are invariably cultured from long-standing wounds:

- *Staphylococcus aureus* and/or methicillin-resistant *S. aureus* (MRSA).
- Enterococci, including Vancomysin resistant strains (VRE).
- Enterobacter species.
- *Klebsiella, Acinetobacter* and *Pseudomonas* species.
- Anaerobes eg. Clostridium difficile (underneath slough and necrotic eschar).

The presence of >15 leucocytes/mm^3 on direct microscopy may be suggestive of an inflammatory process or infection. Semi-quantitative laboratory analysis, reported as a colony count > 10^5 colony-forming units (CFUs)/g tissue, i.e. 100 000 CFUs, may be a predictor of critical colonisation or local wound infection.

Liaison with the medical microbiologist is advisable when there is a history of or suspected drug resistance, especially Enterobacteriaceae, which are extended-spectrum beta lactamase and carbapenemase producers. If resources are available, PCR methods are able to detect most species of pathogens in a wound in a matter of hours, including antimicrobial resistance.

It is possible to summarise the pathogens which are known to be associated with certain environments or patients with chronic underlying conditions, and it would be wise to observe careful infection prevention precautions in these instances (Table I).

Antimicrobial stewardship: clinical guidelines for the use of topical antimicrobial agents

The increasing prevalence of antibiotic-resistant microbial strains and the persistent nature of biofilm presents an ongoing challenge when treating complicated infected and colonised wounds.

Table I: Pathogens and at-risk patient populations

Microrganisms	Sites commonly found	Patient risk profile
• *Staphylococcus aureus and/or MRSA* • *Enterococci and/or VRE* • *Pseudomonas aerugonisa* • *Eschericha coli* • *Klebsiella spp.* • *Acinetobacter spp.*	• *Skin, hands and nares* • *Clothing and linen* • *Sputum* • *Urine* • *Chronic wounds, e.g. pressure ulcers, lower limb and diabetic foot ulcers*	• *Regular hospitalisation* • *Gyms, boarding schools and prisons* • *Frail care* • *Wound clinics* • *HIV* • *Renal dialysis and ICUs* • *Diabetes mellitus* • *COPD* • *Corticosteroid treatment* • *Malignancy* • *Stroma, urostomy and catheter*
Candida spp. (spores)	• *Skin and oropharynx* • *Gastrointestinal tract* • *Urine* • *Chronic wounds*	• *COPD* • *Corticosteroid treatment* • *Malignancy* • *HIV* • *Wound clinics*
Clostridium difficile (spores)	• *Deep wounds* • *Skin* • *Patient surfaces after faecal soiling*	• *Frail care and the elderly* • *ICUs* • *Broad-spectrum antibiotic treatment*

HIV: human immunodeficiency virus, ICU: intensive care unit, COPD: chronic obstructive pulmonary disease, MRSA: methicillin-resistant *Staphylococcus aureus,* VRE: vancomycin-resistany enterococci

Because bacteria need to be metabolically active in order for antibiotics to act, sessile (hibernating) bacteria in biofilm are unaffected by antibiotics that would normally kill active bacteria. Research has shown that the lowest concentration of antimicrobial agents required to kill bacteria in biofilm actually exceeds the maximum prescription levels for the antibiotics. In other words, the standard dose that would be normally bacteriocidal to susceptible bacteria when grown in suspension in a clinical laboratory may have little or no antimicrobial effect on the same type of bacteria in biofilm form in the patient.

The most widely used broad-spectrum topical microbicidal agents are iodine, honey, polyhexamethylene biguanide (PHMB) and silver – available in a range of formulations and carrier mediums. Although currently there is a lack of consensus on which antimicrobial agent is preferable as a first-line treatment, practical and economic considerations should be based upon patient or caregiver ability, the frequency of dressing changes required (e.g. heavily exuding wounds), and importantly, on a considered holistic assessment as to whether or not a topical antimicrobial agent is indeed necessary.

Biofilm penetrative and reducing agents

Flavonix™ cytoflam gel

Flavonix™ cytoflam gel is a combination of agents which targets inflammation and bacterial biofilm formation by reducing inflammatory cytokines and increasing the growth factors.

Prontosan™ solution and wound gel

Prontosan™ solution and wound gel is a combination of a PHMB and Betaine, a surfactant cleanser. It disrupts lipoproteins in biofilm, thus lowering the surface tension; interferes with chemical signalling (quorum sensing) and promotes effective debridement.

Topical antiseptics

The principle site of action of topical antiseptics is the bacterial cell membrane, ideally in concentrations that are not cytotoxic, exhibit sustained release and are chemically stable in the presence of organic matter, e.g. blood and pus. Examples include:

- PHMB solution.
- Chlorhexidine gluconate, povidone and cadexomer iodine products.
- Medical-grade Manuka Honey® products, which are astringent (oedema reduction), and have anti-inflammatory, high osmolarity and broad-spectrum microbicidal properties, including MRSA. These agents also promote the production of hydrogen peroxide by macrophages, and optimal moisture levels at the wound bed to facilitate autolytic debridement.

Topical microbicidal dressings

Hydrophobic dressings

Hydrophobic dressings, e.g. Cutimed® Sorbact®, sequestrate bacteria and fungi, binding them irreversibly to the dressing material through hydrophobic interaction with the dialkylcarbamoylchloride fatty acid coating on the dressing surface. An added advantage of this technology is that the microorganisms remain intact after death (potentially harmful endotoxins and intracellular contents are not released back to the wound interface), and are then disposed of at the dressing change. The risk of bacterial resistance or sensitisation is avoided as antibiotic agents are not involved.

Miscellaneous silver products

Miscellaneous silver products include alginate, activated charcoal, carboxymethylcellulose, chitosan film, collagen, hydrocolloids, hydrofibre, hydrogel, nanocrystalline or nanoparticles and polyurethane foams. Silver-containing products, whether in elemental or ionic form, achieve their antimicrobial effect via the release and action of silver cations. Although the exact mechanism of action is not yet fully understood, silver cations (Ag+) are thought to target and bind with multiple negatively charged sites on the bacterial cell, thereby:

- Affecting critical functional and structural proteins in the bacterial cell membrane and cytoplasm.
- Binding with essential enzymes, inhibiting respiration and preventing nutrient absorption.
- Interacting with the nucleotide bases in the bacterial DNA and preventing cell division and multiplication.

Safety considerations when using silver-based products

Safety considerations when using silver-based products include the following:

- Silver should be used with caution on epithelialising wounds or wounds with a low bioburden.
- The amount of silver cations released into the wound environment is affected by the production and viscosity of the wound exudate, extracellular matrix components and the frequency of dressing changes.
- Currently, there is no standard method with which to evaluate the silver release from dressings.
- They should not be used in conjunction with hydrogen peroxide or eusol.
- Silversulphadiazine and ionic Ag+ dressings are contraindicated in pregnancy, neonates, severe renal or hepatic impairment and wounds with a large surface area, e.g. in Stevens-Johnson syndrome.
- Silver products should not be used during magnetic resonance imaging scans, radiation therapy or diathermy.

In practice, the selection of one antimicrobial wound care product over another should be based upon holistic patient risk assessment, the appearance of the wound and supporting clinical evidence of critical colonisation or infection. Treatment objectives also vary, depending on whether the wound is healable or "non-healable" (i.e. "maintenance" wounds) (Figure 2).

"Pearls" for nursing practice

It is important to recognise that there is a fluctuating continuum in the wound microbiology lifecycle. Bacterial populations in chronic wounds are polymicrobial, and will represent regional skin flora and the care environment.

All wounds are colonised. The presence of microorganisms in a wound does not in itself define an infection, and treatment based on culture results alone is not warranted.

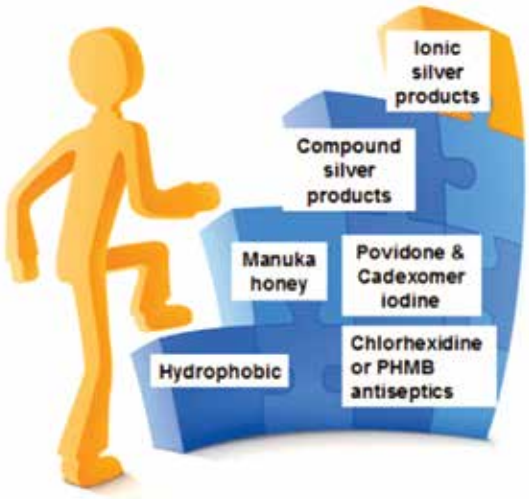
Stalling of the healing process, an unexplained increase in exudate production, or failure to heal within the expected time frame, may be suggestive of critical colonisation or local infection.

The cornerstones of wound management include debridement, the management of inflammation and/or infection, and exudate management.

A "step ladder" approach should be used to control the bacterial bioburden prior to the use of ionic silver products because the latter should be conserved in the event that they are needed to manage a drug-resistant infection.

A trial period of at least 10-14 days should be permitted before a decision is made to change the type of topical antimicrobial agent in use.

If a wound is not 30% smaller by week 4, it is unlikely to heal by week 12. It is important to reassess the treatment plan, and consider interdisciplinary involvement to manage the co-morbidities.



PHMB: polyhexamethylene biguanide

Figure 2: The author's approach to the rational use of topical antimicrobial products

The care and toilet of the peri-wound skin e.g. the use of chlorhexidine gluconate antibacterial liquid soap, is as important as the care of the wound itself.

"Dipstick" urinalysis should be undertaken to exclude asymptomatic bacteriuria in patients with poorly progressing wounds.

The "whole patient" should be treated – not just "the hole" in the patient!

Useful (free) website resources

Useful and open website resources include the following:

- *Wound Healing Association of South Africa:* www.whasa.org
- *Wound Healing Southern Africa:* www.woundhealingsa.co.za
- *Wounds International:* www.woundsinternational.com
- *Ostomy Wound Management:* www.o-wm.com
- *European Pressure Ulcer Advisory Panel:* www.epuap.org

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