Treating Biofilm and Bioburden

New tools and products signal a revolution in wound care.

BY WINDY COLE, DPM

Introduction

Acute wounds heal by a progression through a complex, but orderly, series of physiologic and molecular processes (Figure 1). In contrast, chronic wounds, those that fail to heal within 30 days, are characterized as having stalled in this healing progression due to a variety of systemic and local factors. Such factors include high microbial burden and excessive devitalized tissue. Within 48 hours of developing an open wound, bacteria from the environment or the patient’s skin flora can infiltrate the wound. Wound healing becomes potentially compromised once bacteria have invaded. Chronic wounds account for 70% to 90% of total ulcers reported. Optimal wound-bed preparation consists of regular debridement to remove devitalized tissues, control infection, and establish a balanced healing environment.

A crucial component of wound management is regular debridement. The goal of debridement is the removal of all necrotic, fibrous, and devitalized tissue. Within 48 hours of developing an open wound, bacteria from the environment or the patient’s skin flora can infiltrate the wound.

Continuing Medical Education / Wound Management

Objectives

1) Explain the current clinical information available with regard to our knowledge on bioburden and biofilm in the wound care arena.

2) Examine the role bioburden and biofilm has on delayed healing in complicated wounds.

3) Introduce the wound care provider to new and innovative wound care technologies used to treat biofilm and bioburden.

4) Understand evidence-based evaluation of emerging technologies to achieve better patient outcomes.

5) Review the latest trends in advanced wound care and ways to implement them into current practice.

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Following this article, an answer sheet and full set of instructions are provided (pg. 118). — Editor

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Biofilm bacteria form attachments with one another. At this juncture, the bacterial community has formed more permanent attachments to the wound surface and have created a more cohesive symbiotic community. They then are able to share information and gene-expression through a cell-cell communication mechanism called quorum sensing. Finally, biofilm colonies will begin to secrete a protective glycocalyx that also adheres to the wound surface. This entire process typically occurs in two to four days, unless disrupted. This extra polymeric substance is difficult to penetrate with systemically administered antibiotics and topical therapies. Mature biofilms house mostly senescent bacteria that function at a lower energy state than active planktonic bacteria. As biofilms continue to evolve, they continue to change their phenotype and they share their resistance to antibiotics with the community. These factors make effective biofilm management, however, a more complicated problem.

Identifying and managing biofilm have recently become two of the most important aspects of wound care.
film elimination a complicated matter. Even with thorough debridement, biofilms may still persist. These bacterial colonies have a significant impact on wound healing by causing prolonged inflammatory responses in the patient as well as contributing to acute bacte-

Even after an aggressive debridement, biofilm can reform in as little as 24 hours.

rial infections. Common wound care interventions include management of systemic conditions, proper off-loading in plantar surface wounds, compression therapy in venous wounds, and interventions to optimize arterial flow. Once all of these factors are addressed, biofilms may be the most important single cause of persistent wounds and delayed wound healing. Over 90% of chronic wounds contain bacteria living within the biofilm construct.

Wound care professionals must understand the best practices in biofilm management in order to be successful. Debridement is still thought to be the most effective way to remove biofilm. Even after an aggressive debridement, biofilm can reform in as little as 24 hours. It is unlikely that complete removal of biofilm is able to be achieved with debridement alone. Debridement only temporarily eliminates biofilms. A newer thought process in wound care treatment is that adjunctive therapy in addition to regular debridement is necessary. Mature biofilm bacteria tend to spread peri-vascually below the surface of the wound enabling them to reform very rapidly. Studies have shown that the best window of opportunity for biofilm prevention exists directly following debridement up to 24 hours. Biofilm is at its most susceptible and data illustrates that topical therapies are most effective during this period. Optimizing the effects of regular debridements utilizing a multi-tiered treatment approach is the most promising way to effectively address biofilm in chronic wounds.

Emerging Technologies in Biofilm Management and Treatment to Watch

Revolutionary research in the management and treatment of biofilms is ongoing. As treatment and diagnostic technology evolve, more advanced therapies are entering into the market to help manage chronic wounds and address biofilm formation. It is important to continually monitor the most recent literature to ensure patients are receiving the most updated care available. In this segment, we will highlight some new therapies and innovations available to combat biofilm.

Auto-fluorescence Imaging

It is unlikely that biofilm can be seen with the naked eye since they are often less than 100 micron and have no macroscopically distinguishable features. A novel advancement in wound imaging called the MolecuLight i:X may be able to detect the presence of biofilm bacteria. This hand-held device is an easy-to-use, non-invasive, portable point-of-care fluorescence imaging device (Figure 3). The MolecuLight i:X instantly visualizes potentially harmful bacteria on the wound surface and surrounding tissues not otherwise visible with the naked eye. The device emits a violet light (405 nm) that illuminates the wound and surrounding area, exciting the wound tissues and bacteria and resulting in endogenous production of fluorescence signals, without the need for additional contrast agents. Optical filters built into the device remove non-informative colors, without any digital processing, and the resulting image is viewed on the display touch screen in real-time.

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Biofilm (from page 113)

in combination with antibiotic treat-
ments to treat biological biofilms.30

Pulsed Acoustic Cellular Expression (PACE™) is a new modality based
on extracorporeal shockwave technol-
ogy (ESWT), which was introduced
over 30 years ago for use in lithotripsy.

PACE employs high-pressure acoustic
waves in the shock wave spectrum
created through an electrohydraulic
method (Figure 5). New research has
shown that the extremely rapid in-
creases in energy created by acous-
tics.19,20 The MolecuLight i:X has been extensively validat-
ed in pre-clinical21 and clinical stud-
ies involving patients with chronic
wounds.22-25 Clinical trials have shown
that endogenous, red fluorescent por-
phyrins emitted from bacteria allow
the visualization and location of bac-
teria present at loads ≥ 10^4 CFU/g.23

The device has been noted to de-
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ucts on and beneath the surface of
wounds, up to ~1.5mm depth.23 It
should be noted that numerous por-
phyrin-producing bacterial species can
colonize on chronic wounds and cause
a red fluoresce, but Staphylococcus au-
reus is the most commonly found bac-
terial species.22-27 Pyoverdine is unique
to Pseudomonas aeruginosa; thus, it
is the only bacteria to fluoresce cyan14
(Figure 4). The information captured
in the images can aid in improved de-
cision-making throughout the dynam-
ic wound treatment pathway (e.g.,
pre-debridement, post-debridement),
and in determining the need for anti-
microbial therapy.24

Shockwave Energy Transfer

Shockwaves are high-ener-
gy waves travelling at a superson-
in combination with antibiotic treat-
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(Figure 4). The information captured
in the images can aid in improved de-
ic speed. Unlike pressure waves, a
shockwave is a single event of ener-
gy dissipation and therefore no fre-
quency is associated with it. Energy
transfer methods such as shockwave
therapy have been shown to aid in
physically disrupting biofilm.28 These
therapies can selectively target biofilm
while sparing the host cells.28 Studies
have shown that shock waves can
disrupt the polysaccharide matrix sur-
rounding the biofilm, thus freeing the
encased bacteria. It is hypothesized
that this would allow for increased
access to antibiotic and/or topical
therapies.29 Gnanadhas, et al. showed
that shockwave therapy can be used
in combination with antibiotic treat-
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Continued on page 115
Biofilm (from page 114)

tic pressure-focused shockwaves produce membrane ruptures for micro-organisms (bacteria, viruses, giardia, cryptosporidium, fungi, etc.) that generate their death/lysis. Malfunction of bacterial membrane mechanotransduction (translation of mechanical forces in biochemical signals that activate ion channels for exchange of fluids through bacterial membrane) produced by shockwaves can also generate biofilm disruption (Figure 5).

PACE technology works by using the phenomenon of transient cavitation. The bubbles created by the device undergo rapid expansion followed by collapse producing micro-jets with speeds upwards of 100 m/s that can generate ruptures in the membranes of micro-organism membrane producing lysis, and bacterial membrane malfunctions producing bacterial death. The use of this technology has widespread applications in treating recalcitrant biofilm infections in both the hospital and out-patient setting. More studies are being conducted and will have a profound impact on the therapeutic use of shock wave therapy in wound care in the near future.

A new class of wound management tools consisting of antimicrobial collagen matrices has entered into the wound care market. One such product is PuraPly AM™.

Electrifying Wound Care

An innovative class of dressings called electroceuticals have recently hit the wound care market. These bandages employ electrical impulses to accelerate wound healing. Procellera™, one such wound dressing, consists of elemental silver and zinc embedded in the surface (Figure 6). In the presence of moisture, the dressing generates a microcurrent that minimizes or prevents the growth of biofilm producing micro-organisms. This current is able to break through the extra polymeric substance surrounding the bacteria, thus destroying the biofilm. The potent bactericidal activity of the silver-zinc coupled electroceutical wound dressing has been shown effective against antibiotic-sensitive strains and multiple antibiotic-resistant strains of wound pathogens commonly contributing to biofilm and infection formation in chronic wounds. These dressings have also been shown to increase healing rates by increasing epithelialization. Some silver containing dressings on the market have also made claims to decrease bacterial contamination in this class of wounds. It has been documented that when used in high level concentrations, silver in certain forms contained in a variety of these dressings can, in fact, impede wound healing. More studies and trials are needed to examine the mechanism and effects of electroceutical dressings.

Antimicrobial Matrices

Collagen matrices have long been used to treat chronic wounds. Collagen serves as a sacrificial substrate for matrix metalloproteinases and elastase that are found in chronic wounds in increased levels. Clinical data has illustrated that collagen matrices are supportive of the extracellular matrix and are helpful in protecting tissue collagen deposition. A new class of wound management tools consisting of antimicrobial collagen matrices has entered into the wound care market. One such product is PuraPly AM™. This purified collagen matrix predominantly consists of cross-linked type 1 collagen that has been processed to remove cells and cellular debris and inactivate viruses. PuraPly AM collagen is then coated with
the antimicrobial polyhexamethylene biguanide (PHMB) (Figure 7). PuraPly AM has a cross-linked matrix allowing it to resist proteolytic degradation and retain a continuous antimicrobial effect. PHMB is an extensively studied cationic topical antimicrobial that is effective in binding to bacterial walls and causing disruption in biosynthesis and catabolic function of biofilm bacteria. The ability for PHMB to also bind to biofilm extra polymeric substance degrading and retaining a continuous matrix allowing it to resist proteolytic degradation and retain a continuous matrix is increasingly found to be a causative factor in these infections and has been identified as a major barrier in wound healing. An ever-expanding amount of clinical evidence suggests that healing outcomes are improved with aggressive biofilm identification and control. Early data demonstrates that this is not a ‘one-size-fits-all’ concern.

A targeted disruptive strategy consisting of several concomitant therapies including: visualization, debridement, energy transfer therapy, antimicrobials, and other similar adjunctive therapies has proven to be the most effective cohesive strategy against biofilm.

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Biofilm (from page 116)

Biofilm is a diverse and dynamic ecosystem that consists of bacterial cells enveloped in a self-produced matrix of extracellular polymeric substances (EPS). These biofilms are typically found in various environments, including the human body, where they can contribute to infections and chronic wounds. Biofilms are known to be resistant to antibiotics and other treatments, making them difficult to eliminate. The presence of biofilms in chronic wounds can delay healing and increase the risk of infection.

1) Which is a true statement in regard to chronic wounds?
A) Chronic wounds heal quickly by a progression through a complex, but orderly, series of physiologic processes.
B) Chronic wounds heal within 30 days.
C) Chronic wounds are characterized as having stalled in healing progression due to a variety of systemic and local factors.
D) Chronic wounds do not typically have high microbial burden and excessive devitalized tissue.

2) Why is debridement important for chronic wound management?
A) Devitalized tissue in wounds produces a physical barrier to formation of new tissue and therefore decreases healing rates.
B) Devitalized tissue in the wound bed bacterial colonization is more likely.
C) The presence of devitalized tissue increases concealed dead spaces and decreases visualization.
D) All of the above.

3) All of the following statements about biofilms are true except:
A) The U.S. Centers for Disease Control and Prevention and the National Institutes of Health have estimated that between 15-20% of infections are caused by biofilms.
B) Generally, it is believed that biofilms develop in stages.
C) The first biofilm stage is composed of small communities of bacteria that begin to attach to the wound surface.
D) Biofilms are polymicrobial colonies commonly composed of bacteria, fungi, as well as other microorganisms.

4) Biofilm bacteria and planktonic bacteria differ in what way?
A) Biofilm bacteria form attachments with one another.
B) Planktonic bacteria are able to share information and gene-expression through a cell-cell communication mechanism called quorum sensing.
C) Biofilm colonies secrete a protective glycocalyx that also adheres to the wound surface.
D) Both a and c.

5) What characteristics of biofilm bacteria do not contribute to the difficulty in treatment?
A) Mature biofilms are composed of senescent bacteria that are very responsive to systemic antibiotic therapy.
B) As biofilms evolve, they continue to change their phenotype.
C) Biofilms share their resistance to antibiotics with the community.
D) Even with thorough debridement biofilms may still persist.

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