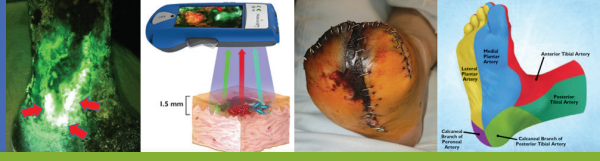

Treating Biofilm and Bioburden

New tools and products signal a revolution in wound care.

BY WINDY COLE, DPM

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***

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.[1] Within 48 hours of developing an open wound, bacteria from the environment or the patient's skin flora can infiltrate the wound.[2,3] Wound healing becomes potentially compromised once bacteria have invaded. Chronic wounds account for 70% to 90% of total ulcers reported.[4-5] Optimal wound-bed preparation consists of regular debridement to remove devitalized tissues, control infection, and establish a balanced healing environment.[6]

Within 48 hours of developing an open wound, bacteria from the environment or the patient's skin flora can infiltrate the wound.

A crucial component of wound management is regular debridement.[6] The goal of debridement is the removal of all necrotic, fibrous, and devitalized

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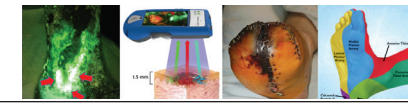

Biofilm (from page 111)

tissue from the wound bed.[7] Devitalized tissue in wounds produces a physical barrier to formation of new tissue, and therefore decreases healing rates. If devitalized tissue remains in the wound bed, bacterial colonization is more likely. The presence of devitalized tissue increases concealed dead spaces, increasing the potential bacterial content in and around the wound. Standard of care remains that unhealthy tissue be sharply debrided to bleeding tissue to: 1) allow for visualization of the extent of the ulcer, 2) to detect underlying exposed structures, deep bacterial contamination or abscesses, and 3) to assess the quality of the peri-wound tissue. Frequent and thorough debridement reduces bacterial bioburden.[7] In some cases, although the debridement adequately removes devitalized tissue, the remaining wound bacteria may become problematic.

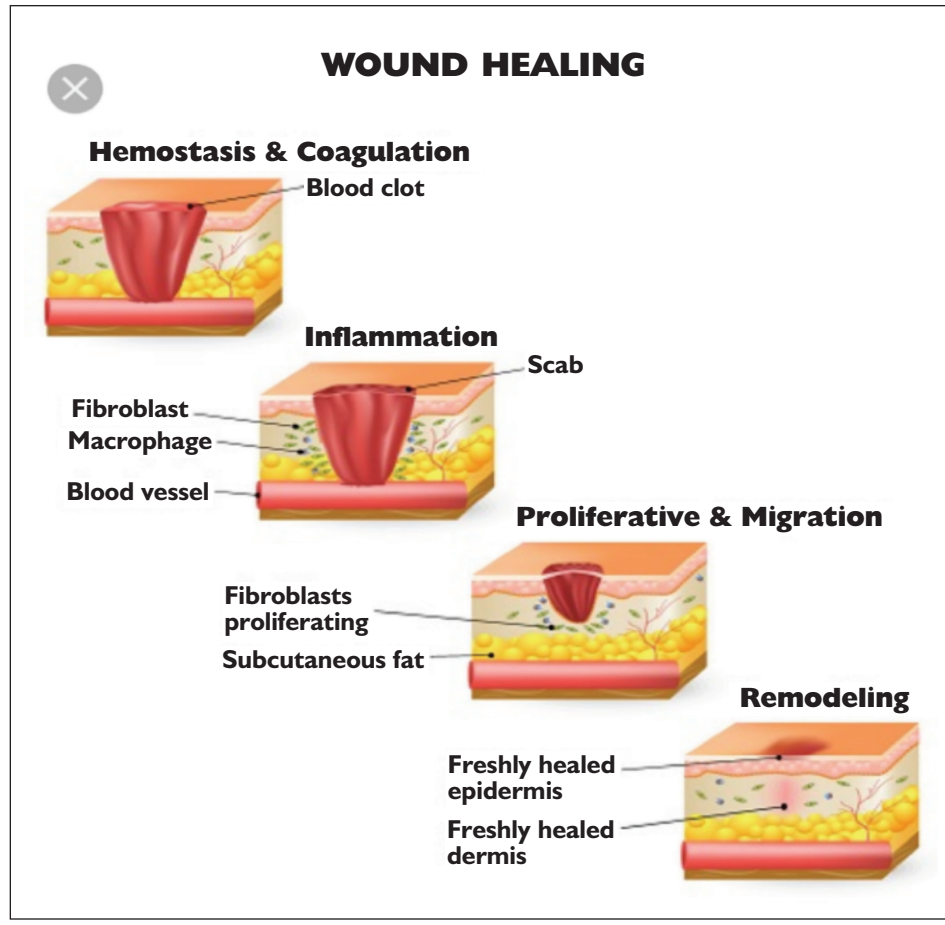

Figure 1: Phases of wound healing

Bioburden is an all-encompassing term that includes necrotic material, non-viable tissue, wound exudate, and bacteria and other microbes (e.g., fungi). Bioburden tends to continually accumulate in chronic wounds as a result of the underlying pathogenic abnormality caused by systemic conditions such as diabetes or venous disease. The inability to fully resolve these fundamental physiologic issues makes chronic wound bed management with aggressive and complete debridement even more crucial.

Identifying and managing biofilm have recently become two of the most important aspects of wound care.

Biofilm management, however, is a more complicated problem. Biofilm is an assemblage of surface-associated microbes enclosed in a self-produced matrix. Identifying and managing biofilm have recently become two of the most important aspects of wound care. The U.S. Centers for Disease Control and Prevention and the National Institutes of Health have estimated that between 65-80% of infections are caused by biofilms.[8] Generally, it is believed that biofilms develop in stages (Figure 2). The initial stage is composed of small communities of bacteria that begin to attach to the wound surface. These polymicrobial colonies are commonly composed of bacteria, fungi, as well as other micro-organisms.

Biofilm is most susceptible to debridement and topical therapies at this stage. Unlike planktonic bacteria, 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.[9] Finally, biofilm colonies will begin to secrete a protective glycocalyx that also adheres to the wound surface.[10] 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.[11]

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 bio-

Continued on page 113

Biofilm (from page 112)

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 bacterial infections.[12] 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.[12,13] Over 90% of chronic wounds contain bacteria living within the biofilm construct.[14]

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-vascularly below the surface of the wound enabling them to reform very rapidly.[15] 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.[16] Optimizing the effects of regular debridements utilizing a multi-tiered treatment approach is the most promising way to effectively address biofilm in chronic wounds.

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

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.

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.

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.[17] 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.[18]

The fluorescence signals (i.e., colors) produced are tissue-specific,[17] endogenous tissue components; collagen will fluoresce green, while clinically relevant bacteria producing metabolic by-products like porphyrins fluo-

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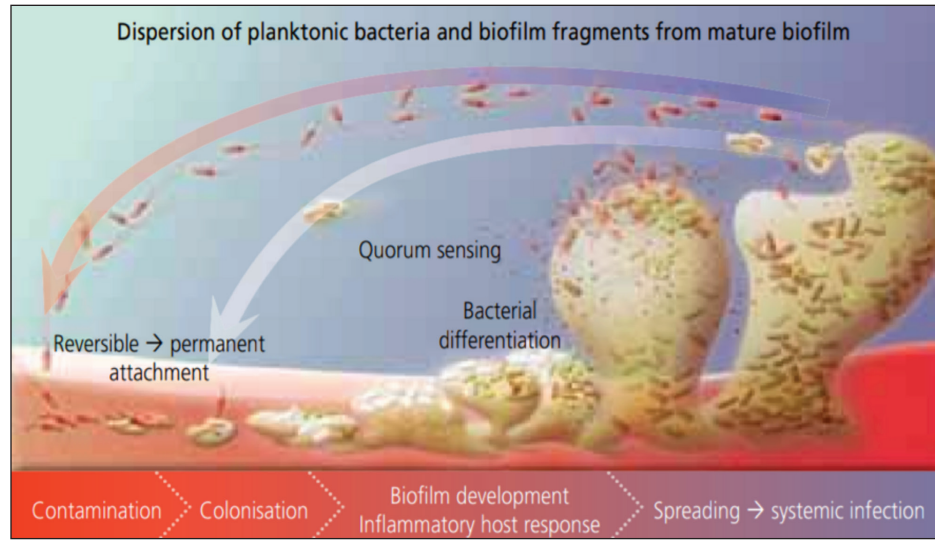
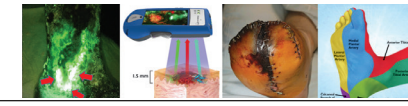


Figure 2: Biofilm development



Biofilm *(from page 113)*

resce red, and pyoverdine fluoresce cyan (blue-green).[19,20] The MolecuLight i:X has been extensively validated in pre-clinical[21] and clinical studies involving patients with chronic wounds.[22-25] Clinical trials have shown that endogenous, red fluorescent porphyrins emitted from bacteria allow the visualization and location of bacteria present at loads ≥ 10^4 CFU/g.[23]

The device has been noted to detect these fluorescent bacterial by-products on and beneath the surface of wounds, up to ~1.5mm depth.[23] It should be noted that numerous porphyrin-producing bacterial species can colonize on chronic wounds and cause a red fluoresce, but Staphylococcus aureus is the most commonly found bacterial species.[22,27] Pyoverdine is unique to Pseudomonas aeruginosa; thus, it is the only bacteria to fluoresce cyan[14] (Figure 4). The information captured in the images can aid in improved decision-making throughout the dynamic wound treatment pathway (e.g., pre-debridement, post-debridement), and in determining the need for antimicrobial therapy.[24]

The MolecuLight i:X instantly visualizes potentially harmful bacteria on the wound surface and surrounding tissues not otherwise visible with the naked eye.

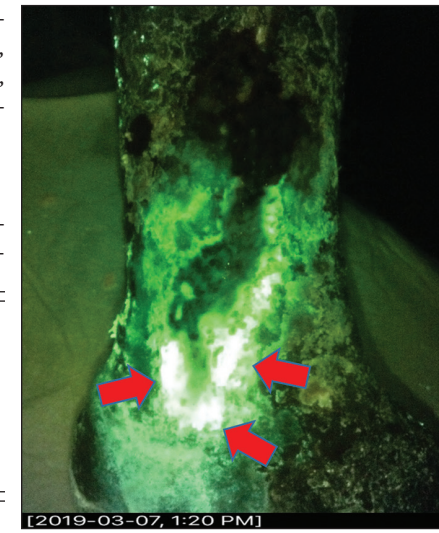


Figure 4: Pyoverdine is unique to Pseudomonas aeruginosa; thus, it is the only bacteria to fluoresce cyan

Shockwave Energy Transfer

Shockwaves are high-energy waves travelling at a supersonic speed. Unlike pressure waves, a shockwave is a single event of energy dissipation and therefore no frequency 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 surrounding 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 treatments to treat biological biofilms.[30]

Pulsed Acoustic Cellular Expression (PACE™) is a new modality based on extracorporeal shockwave technology (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 increases in energy created by acous-

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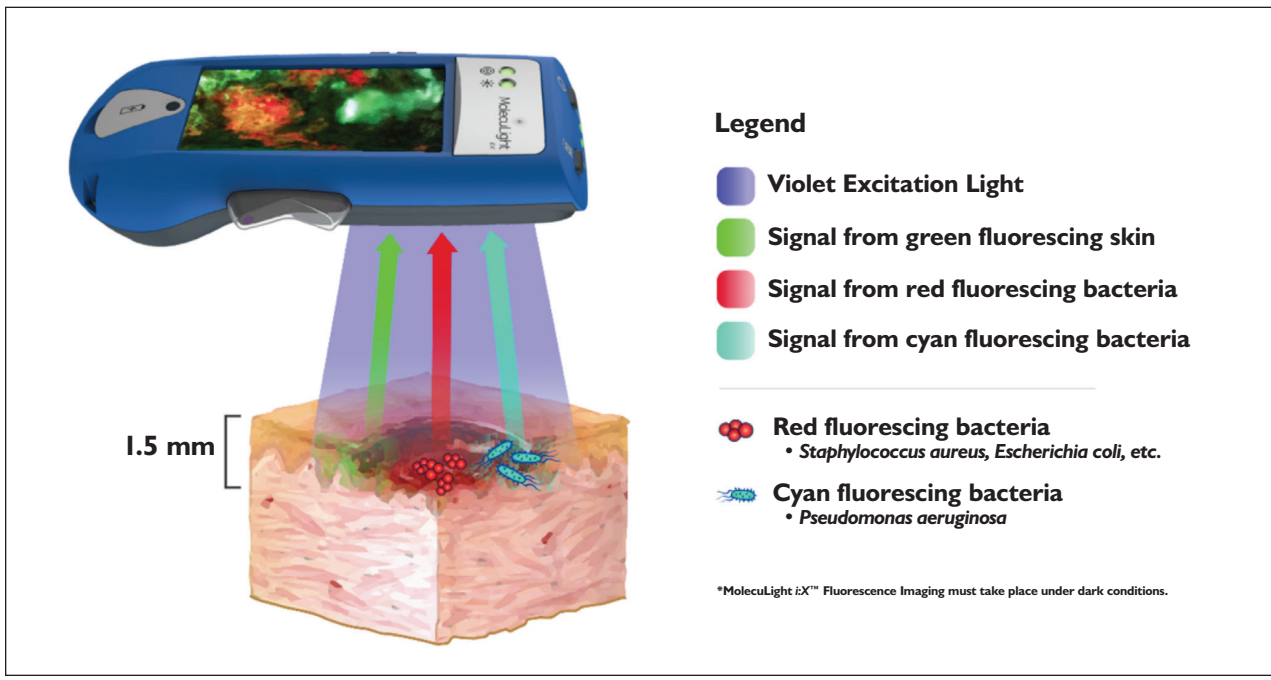

Figure 3: MolecuLight i:X Device

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.[31] 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).

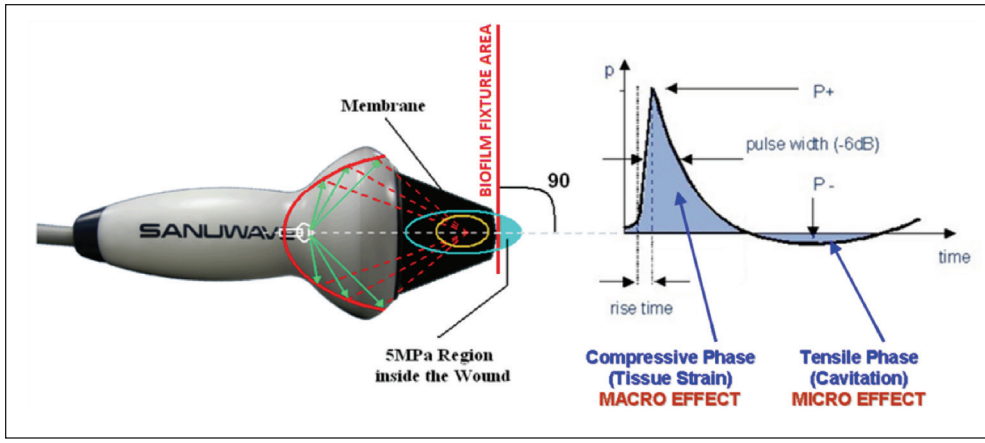

Figure 5: PACE high pressure acoustic waves in the shock wave spectrum

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.[32]

Figure 6: Procellera wound dressing: elemental silver and zinc embedded in the surface

Figure 7: PuraPly AM collagen coated with the antimicrobial polyhexamethylene biguanide

These dressings have also been shown to increase healing rates by increasing epithelialization.[33] 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.[34] PuraPly AM collagen is then coated with

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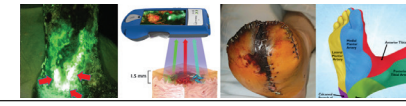

Biofilm (from page 115)

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.[35] 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.[36] The ability for PHMB to also bind to biofilm extra polymeric substance concentrating with application thus creating a toxic environment for the biofilm bacteria.[36]

The antimicrobial activity of PHMB is broad including both gram positive and gram negative bacteria. Conversely, PHMB has been regarded as non-toxic to human cells and very biocompatible when used in wounds, showing little to no cytotoxicity. There are no reported cases of antimicrobial resistance to PHMB. The use of PuraPly in chronic wounds of patients with biofilm and bioburden present, along with good wound care, can positively impact heal rates in recalcitrant wounds.

Conclusion

A key component to successfully treating chronic wounds is bioburden control. One of the most costly issues of modern medicine is management of chronic wound infections. Thus, it is not surprising that wound biofilm 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. The current consensus guidelines suggest that chronic wounds may benefit from a biofilm strategy of using multiple treating agents simultaneously with frequent adjustments to this regimen as the biofilm changes. We are at the beginning of a new revolution in the management of chronic wounds. **PM**

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.

References

[1] Edwards, R. & Harding, K.G. Bacteria and wound healing. Curr Opin Infect Dis 17, 91-96 (2004).

[2] Barret JP, Herndon DN: Effects of burn wound excision on bacterial colonization and invasion. Plast Reconstr Surg 2002:111(2):744-50.

[3] Blumenthal E, Jeffery SLA: The use of MolecuLight i:X in managing burns. J Burn Care Res 2017;39(1):154-61.

[4] Valencia IC, Falabella A, Kirsner RS, Eaglestein WH. Chronic venous insufficiency and venous leg ulceration. J. Am. Acad. Dermatol. [Internet]. 44(3), 401-21: quiz 422-4 (2001).

[5] Sen CK, Gordillo GM, Roy S, et al. Human skin wounds: a major and snowballing threat to public health and the economy. Wound Repair Regen. [Internet]. 17(6), 763-71 (2009).

[6] Leaper, D.J., et al. Extending the TIME concept: what have we learned in the past 10 years?(*). Int Wound J 9 Suppl 2, 1-19 (2012).

[7] Schultz GS, Sibbald RG, Falanga V, et al: Wound bed preparation: a systemic approach to wound management. Wound Repair Regen 2003; 11(2): S1-28.

[8] Coenye, T. & Nelis H. In vitro and in vivo model systems to study microbial biofilm formation. Journal of Microbiological Methods 83,89-105 (2010).

[9] Parsek M, Greenberg EP. Sociomicrobiology: the connections between quorum sensing and biofilms. TRENDS in Microbiology Vol. 13 No.1 January 2005.

[10] Neu T, Lawrence J. Extracellular polymeric substances in microbial biofilms. Microbial glycobiology, 733-758, 2010.

[11] Wolcott R, Sanford N, Gabrilska R, Oates JL et al. Microbiota is a primary cause of pathogenesis of chronic wounds. J Wound Care 2016; 25 (Suppl. 10): S33-43.

[12] Schultz GS, Bjarnsholt T, James G, et al: Consensus guidelines for the indentification and treatment of biofilms in chronic nonhealing wounds. Wound Repair Regen 2017; 25 744-757.

[13] Bjarnsholt T. The role of bacterial biofilms in chronic infections. APMIS Suppl 2013; 136: 1-51.

[14] Phillips PL, et al. Wounds International. 2010; 1(3):1-6.

[15] Davis SC, Ricotti C, Cazzaniga A, et al.; Microscopic and physiologic evidence for biofilm associated wound colonization in vivo. Wound Regen 2008; 16: 23.

[16] Wolcott RD, Rumbaugh KP, James G, Schultz G, Phillips P, Yang Q, et al. Biofilm maturity studies indicate sharp debridement opens a time-dependent therapeutic window. J Wound Care 2010; 19:320-8. Wu CY, Smith M, Chu A, Lindvere-Teene L, et al: Handheld fluorescence imaging device detects subclinical wound infection in an asymptomatic patient with chronic diabetic foot ulcer: a case report. Int Wound J 2015; doi: 10.111/iwj.12451.

[17] Rennie MY, Dunham D, Lindvere-Teene L, Raizman R, Hill R, Linden R. Understanding Real-Time Fluorescence Signals from Bacteria and Wound Tissues Observed with the MolecuLight i:X™. Diagnostics. 2019; 9(1):22

[18] DaCosta RS, Anderson H, Cirocco M, Marcon NE, WilsonBC: Auto-fluorescence characterization of isolate whole crypts and primary cultured human epithelial cells from normal, hyperplastic, and andenomatous colonic mucosa. J Clin Path 2005; 58(7):766-74.

[19] DaCosta RS, Anderson H, WilsonBC: Molecular fluorescence excitation-emission matrices relevant to tissue spectroscopy. Photchem Photobiol 2003; 78(4): 384-92.

[20] Wu YC, Kulbatski I, Medeiros PJ, et al: Autofluorescence imaging device for real-time detection and tracking of pathogenic bacteria in a mouse skin wound model: preclinical feasibility studies. J Biome Opt 2-14; 19(8): 1-9.

[21] Rennie, M.Y.; Lindvere-Teene, L.; Tapang, K.;Linden,R. Point-of-care fluorescence imaging predicts the presence of pathogenic bacteria in wounds: A clinical study. J Wound Care 2017, 26,452-460.

[22] DaCosta RS, Kulbatski I, Lindvere-Teene L, et al: Point-of-care auto-fluo-

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rescence imaging for real-time sampling and treatment guidance of bioburden in chronic wounds: first-in-human results. PLoS One 2015; 10(3): e0116623.

[23] Hill, R.; Rennie, M.Y.; Douglas, J. Using Bacterial Fluorescence Imaging and Antimicrobial Stewardship to Guide Wound Management Practices: A Case Series. Ostomy Wound Manag. 2018, 64, 18–28.

[24] Blackshaw, Ellen L; Jeffrey, Steven L.A.: Efficacy of an imaging device at identifying the presence of bacteria in wounds at a plastic surgery outpatients clinic. J Wound Care. 2018, 27, 20-26.

[25] Ottolino-Perry K, Chamma E, Blackmore KM, et. al: Improved detection of wound bacteria using fluorescence image guided wound sampling in diabetic foot ulcers. Int Wound J. 2017, 5,833-841.

[26] Blumenthal E, Jeffery S: Autofluorescence imaging for evaluating debridement in military and trauma wounds. Military Medicine, Vol 183, March-April Supplement 2018.

[27] Schalk, I.J.; Guillon, L. Pyoverdine biosynthesis and secretion in Pseudomonas aeruginosa: Implications for metal homeostasis. Environ. Microbiol. 2013, 15, 1661–1673.

[28] Attinger C, Wolcott R. Clinically Addressing Biofilm in Chronic Wounds. Advances in Wound Care, Volume 1, NUMBER 3. 2012.

[29] Wanner, S. et al. Low-energy shock waves enhance the susceptibility of staphylococcal biofilms to antimicrobial agents in vitro. Journal of Bone & Joint Surgery, British Volume 93B, 824-827 (2011).

[30] Gnanadhas, DP, et al. Successful treatment of biofilm infections using shock waves combined with antibiotic therapy. Sci Rep. 5, 17440;doi: 10.1038/srep17440 (2015).

[31] Cioanta L, James G. Acoustic Pressure Shockwave Application. Poster. Centers for Biofilm Engineering. Montana State University.

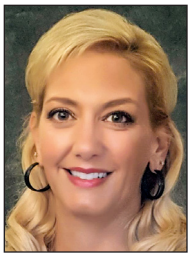
[32] Dusane DH, Lorchab V, Stoodley P, et al. Electroceutical Treatment of Pseudomonas aeruginosa Biofims. Scientific Reports 9, Article number: 2008 (2019).

[33] Wirsing PG, Habrom A, Zehnder TM, Friedli S, Blatti M. Wireless micro current stimulation—an innovative electrical stimulation method for the treatment of patients with leg and diabetic foot ulcers. Int Wound J. 2013; Dec 30.

[34] Hardin-Young J, Carr RM,Downing GJ, Condon KD, Termin PL. Modification of native collagen reduces antigenicity but preserves cellcompatibility. Biotechnol Bioeng. 1996(6):675-682.

[35] Hubner NO, Kramer A. A review on the efficacy, safety and clinical applications of polihexanide, a modern wound antiseptic. Skin Pharmacol Physiol. 2010;23(suppl):17-27.

[36] Gillover S.PHMB: a well-tolerated antiseptic with no reported toxic effects. J Wound Care. 2009;Suppl:9-14.



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CME EXAMINATION

SEE ANSWER SHEET ON PAGE 119.

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 difficultly 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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6) Common chronic wound care interventions include all except:
- A) Proper off-loading in plantar surface wounds.
- B) Compression therapy in venous wounds.
- C) Optimization of arterial flow to the wound.
- D) Complete surgical excision of all wounds.

7) Auto-fluorescence imaging may be useful in the treatment of biofilms because:
- A) The device can instantly visualize potentially harmful bacteria on the wound surface not otherwise visible with the naked eye.
- B) It is a handheld device that is easy to use, non-invasive, and portable.
- C) The information captured in the images can aid treatment decision-making and in determining the need for antimicrobial therapy.
- D) All of the above.

8) How does shockwave therapy disrupt biofilm?
- A) Shockwave therapy works by causing radio-frequency increases.
- B) Shockwaves cause multiple events of energy dissipation over time.
- C) Extremely rapid increases in energy created by acoustic pressure focused shockwaves can produce membrane ruptures for micro-organisms.
- D) Shockwaves cannot disrupt the polysaccharide matrix surrounding the biofilm-encased bacteria.

9) Which statement is correct regarding electroceutical bandages?
- A) These dressings cause pain when applied to open wounds.
- B) Elemental silver and zinc embedded in the surface of the dressing generates a micro-current that prevents biofilm.
- C) This current is not able to break through the extra polymeric substance surrounding the bacteria.
- D) No change in heal rates have been noted with use of these bandages.

10) PHMB-treated collagen matrices can help treat chronic wounds by doing which of the following?
- A) Effectively binding to bacterial walls and causing disruption in biosynthesis and catabolic function of biofilm bacteria.
- B) Increasing in concentration within the wound, thus preventing the reformation of biofilm bacteria.
- C) Providing a non-toxic supportive environment for the extracellular matrix. thus increasing tissue collagen deposition.
- D) All of the above.

SEE ANSWER SHEET ON PAGE 119.

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Over, please

ENROLLMENT FORM & ANSWER SHEET *(continued)*

EXAM #6/19
Treating Biofilm and Bioburden
(Cole)

Circle:

1.	A	B	C	D	6.	A	B	C	D
2.	A	B	C	D	7.	A	B	C	D
3.	A	B	C	D	8.	A	B	C	D
4.	A	B	C	D	9.	A	B	C	D
5.	A	B	C	D	10.	A	B	C	D

Medical Education Lesson Evaluation

Strongly agree [5]	Agree [4]	Neutral [3]	Disagree [2]	Strongly disagree [1]

1) This CME lesson was helpful to my practice ____

2) The educational objectives were accomplished ____

3) I will apply the knowledge I learned from this lesson ____

4) I will makes changes in my practice behavior based on this lesson ____

5) This lesson presented quality information with adequate current references ____

6) What overall grade would you assign this lesson?

A B C D

7) This activity was balanced and free of commercial bias.

Yes _____ No _____

8) What overall grade would you assign to the overall management of this activity?

A B C D

How long did it take you to complete this lesson?

_____hour _____minutes

What topics would you like to see in future CME lessons ? Please list :

_____

_____

_____

_____

_____