Biofilms: A Clinical Conundrum

Recognition and management of wounds affected by biofilms

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Attendees of this session learned about the following:

- the sequential phases of normal wound healing and the beneficial effects of controlled inflammation and protease activities;
- the detrimental effects on healing of chronic inflammation caused by planktonic and biofilm bacteria, which lead to elevated protease and reactive oxygen species (ROS) in wounds;
- the unique properties of bacteria in biofilm communities that provide increased tolerance; and
- the concepts of biofilm-based wound care, including effective debridement, prevention of planktonic bacteria from reforming biofilms and treatments that reduce biofilms (e.g. dressings, negative-pressure wound therapy).

Biofilm formation

There are 4 stages of wound healing, said Gregory Schultz: 1) hemostasis; 2) inflammation; 3) repair; and 4) remodelling. He noted that "chronic wounds often get 'stuck' in the inflammatory phase of wound healing," which can result in the development of biofilms. Indeed, a study published in 2008 identified biofilms in 60% of biopsies of chronic wounds and only 6% of acute wounds.[1]

Schultz indicated that bacteria in biofilms are difficult to kill due to the following factors.

- Biofilms have an exopolymeric composition (i.e. they are composed of a dense matrix that impairs diffusion of large antibodies).
- Bacteria synergistically secrete antibiotic resistance proteins and enzymes (e.g. catalase).
- Oxygen diffusion is limited, which promotes the growth of anaerobic bacteria.
- "Persister" bacteria have low metabolic activity, and all antibiotics require metabolic activity to kill bacteria.

Thus, if bacteria in biofilms are extremely hard to kill with topical or systemic antibiotics, antimicrobials or antiseptics, how can we treat biofilms? The answer, said Schultz, is to locate and remove biofilms with effective debridement techniques, and then prevent their reformation by applying effective dressings, antibiotics, antimicrobials or antiseptics.[2]

In summary, Schultz noted the following:

- Chronic wounds frequently have bacterial biofilms that are very tolerant to inflammatory cells and antibodies, as well as to antibiotics, antiseptics and disinfectants.
- Biofilms cause elevated levels of proinflammatory cytokines, leading to chronic inflammation and elevated levels of proteases and ROS.
- Proteases and ROS destroy proteins that are essential for healing.
- The 2 principles of optimal biofilm-based wound care are: 1) debride; and 2) prevent planktonic bacteria from reforming biofilm colonies by using bacterial barrier dressings.

Dr. Gregory Rose noted that biofilms are a familiar problem in the wound care milieu: 60–80% of clinical infections are complicated by biofilms, particularly in the presence of artificial materials and devitalized tissues. The common approach to infection is to: 1) establish diagnosis; 2) attempt to identify the etiologic pathogen; 3) initiate appropriate antimicrobial coverage; and 4) arrange for source control.

Rose asked, when establishing a diagnosis, do biofilms always signal an infection? In acute infections, he said, there is a rapidly evolving process of tissue invasion and host response, which is caused by motile, planktonic, bacteria that deploy endotoxins, enzymes and response-evading virulence factors. The host tissue then undergoes cell lysis and digestion, resulting in classic inflammation (i.e. redness, swelling, heat, pain and loss of function).

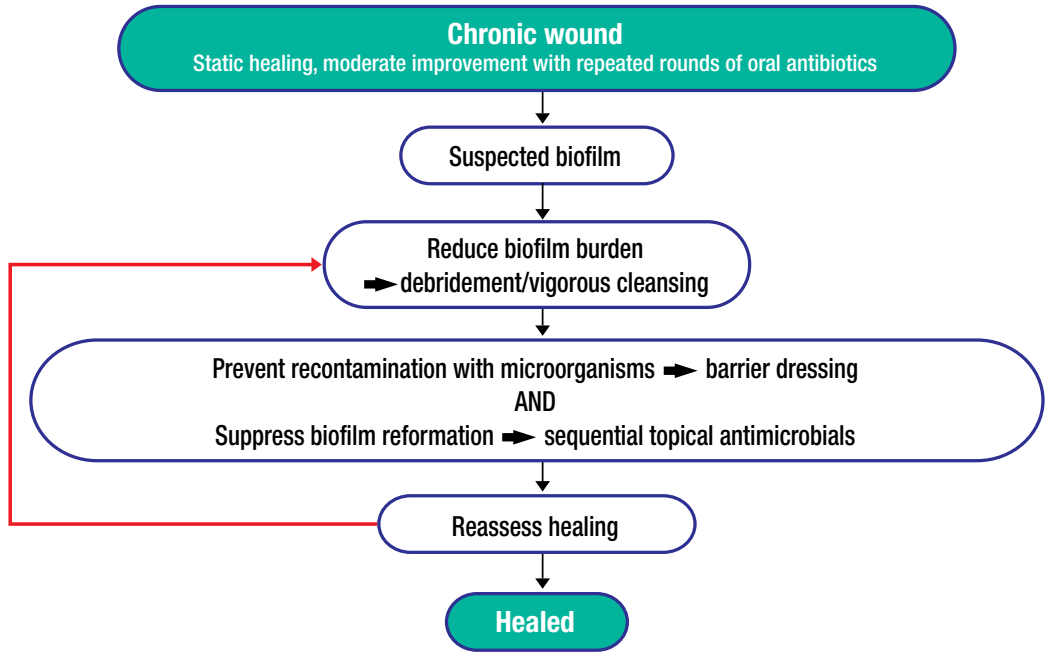
However, biofilms can form in a wound during colonization. Bacterial extracellular polymeric substance functions as an extracellular digestive organ, and its chief nutrient source is host exudate (e.g. plasma). It delays wound epithelialisation and prolongs the nutrient source.

Resistance vs. persistence in biofilms

Resistance is related to genetic characteristics, leading to antimicrobial failure. The presence of biofilm can promote this, due to the hypermutability of embedded

FIGURE 1

Principles of wound biofilm management[3]



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bacteria and increased horizontal gene transmission. Persistence is the failure of antimicrobial therapy despite lack of genetic resistance mechanisms.

Treatment

Physical removal remains the mainstay of biofilm therapy, and this includes removal of prosthetic material and debridement of wounds. The first principle of the application of antimicrobials is to limit their use and duration. "Biofilm-active" agents that are currently used include: rifampicin and colistin, to penetrate the biofilm; and azithromycin and daptomycin, to reduce the biofilm. Combination therapy is sometimes used. Debridement should be performed concurrently (Figure 1).[3]

Novel approaches to source control include inhibition (chelating agents [lactoferrin, EDTA], xylitol) and dispersal (enzymes [cellulose, alginates, DNase, proteases], species-specific QS analogues, inhibitors).

Conclusions

Shultz and Rose offered the following key conclusions:

- Biofilms are highly associated with chronic wounds: they are polymicrobial collections of monomicrobial islands, and culturing may be insufficient for diagnosis.
- Biofilms decrease antimicrobial efficacy through resistance and persistence mechanisms, and current susceptibility testing does not address this issue.
- Physical disruption is key to biofilm removal.

References

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