Review

Importance of biofilm formation in surgical infection

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Background: **Biofilms are ubiquitous, and have been observed in both acute and chronic wounds. Their role in wound healing and infection, however, remains controversial. The aim of this review was to provide an overview of the role and relevance of biofilms to surgical wounds.**

Methods: **A search of PubMed, Science Direct and Web of Science databases was performed to identify studies related to biofilms. Specifically, studies were sought in acute and chronic wounds, and the management and treatment of non-healing and infected skin and wounds.**

Results: **Biofilms may develop in all open wounds. In chronic wounds, biofilms may play a role in prolonging and preventing healing, causing chronic inflammation and increasing the risk of infection. Controversies exist regarding the methods presently employed for biofilm detection and management and few data exist to underpin these decisions.**

Conclusion: **Biofilms in acute surgical and chronic wounds appear to cause a delay in healing and potentially increase the risk of infection. Biofilms can be prevented and once developed can be controlled using wound desloughing and debridement.**

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Introduction

Acute wounds that do not heal in a timely manner, often within 6 weeks or more, are classified as chronic wounds[1]. These wounds may include surgical wounds as well as venous leg ulcers, diabetic foot ulcers and pressure ulcers. Owing to the patient's underlying pathophysiology and the polymicrobial nature of the wound environment, all chronic wounds are at high risk of developing an infection. As the wound environment is composed of microbes, micronutrients, surfaces and exudate, this provides an ideal support for the growth of three distinctive microbial phenotypic states. These are the free-floating state (planktonic), the attached state (sessile) and the quasi-sessile state (aggregates or flocs of microbes that first detach from a biofilm).

Sessile microbes on a surface actively undergo numerous divisions and aggregate together to form microcolonies, which in turn amalgamate to form a dynamic entity referred to as a biofilm[2]. Interestingly, the biofilm mode of growth contradicts Darwinism because growth of microbes within the biofilm follows a 'group selection' principle as opposed to 'individual selection'[3]. This has important implications for the management of infections that may be associated with biofilms, and modern medical microbiology.

Biofilms are defined as communities of micro-organisms attached to a surface, or one another, and encased within a matrix of extracellular polymeric substance (EPS)[4]. EPS makes up the largest component of the biofilm, and in the biological environment is generally composed of polysaccharides, proteins, glycolipids, blood products, cellular debris, extracellular enzymes, metal ions and extracellular DNA[4,5]. EPS accounts for over 80 per cent of the volume of the biofilm, and its physical and chemical configuration help to determine the inherent characteristics and properties of the biofilm.

Biofilms have been identified routinely in many animal[6,7] and human chronic conditions, including cystic fibrosis, prostatitis, dental caries, rhinosinusitis and otitis media. Biofilms are also responsible for the failure of many indwelling medical devices and increase the incidence of catheter-related bloodstream infections[8]. The National Institutes of Health has proposed that 80 per cent of all known human infections are associated with biofilms, and the Centers for Disease Control and Prevention (CDC) has reported that over 65 per cent of all hospital-acquired infections are attributable to biofilms.

In 2004, biofilms were conceptually reported to be an underlying reason for the non-healing and prolonged infections observed in most, if not all, chronic wounds[9]. However, it was not until 2008 that James and colleagues[10] confirmed this hypothesis and reported that 60 per cent of chronic wounds they sampled contained a biofilm. More recently, the role of biofilms in delayed healing and increasing infection risk in chronic wounds has been further supported by both *in vitro* and *in vivo* studies[11–20]. Römling and Balsalobre[21] in 2012 reported that at least 80 per cent of surgical-site infections (SSIs) are associated with biofilms. Despite this, guidelines[22] provided by the CDC advisory committee for the prevention of SSI make no reference to biofilms.

Biofilms in persistent infections are rarely overcome by the host's immune response[23], and induce an overproduction of polymorphonucleocytes and white blood cells, leading to chronic inflammation and therefore delayed wound healing[24]. This in turn leads to further complications in the tissue environment. A recent study by Akers and colleagues[25] has provided evidence that biofilms play a significant role in skin and wound infections, with the polymicrobial nature of the biofilm highlighted as a risk factor for relapsing skin and wound infections.

Studies have demonstrated that commercially available antimicrobials and wound dressings are often ineffective in managing infections, owing to biofilms[26]. Consequently, the development of smart and novel antibiofilm agents represents an area of growing importance in wound care, but also in medicine generally.

The aim of this review is to provide an overview of wound pathobiology with respect to chronic wounds and the relevance of biofilms to surgeons, including the controversies associated with the treatment of biofilms.

Basic pathobiology with respect to chronic wounds

Wounds that are closed during a surgical procedure heal by primary intention. However, wounds that are left open heal by secondary intention and take longer to heal[27]. The longer a wound remains open, the greater the risk of it becoming contaminated with microbes, which in turn increases the risk of biofilm formation and infection.

Although wound healing is complex at a cellular level, it can be divided into four phases, simplified into haemostasis, inflammation, proliferation and tissue remodelling[28]. As the skin represents the first line of defence that protects the tissues and organs of the body, it is imperative that its integrity is re-established very quickly to prevent loss of blood and invasion by micro-organisms. Inflammation functions to remove contaminants from the wound, enabling the formation of granulation tissue. During this phase phagocytosis of microbes occurs, growth factors are generated, vasodilating agents are released and matrix metalloproteinases upregulated. During the destructive phase, dead tissue is broken down and removed via proteases aided by macrophages and fibroblasts. Following the preparation of the wound, fibroblasts and epithelial cells begin to proliferate, which helps in the generation of granulation tissue. As granulation tissue is formed the wound quickly becomes re-epithelialized, resulting in wound closure. During the tissue remodelling phase of wound healing fibroblasts and proteases assist further to control mature granulation tissue, resulting in the formation of scar tissue. However, on occasions the 'normal' series of events involved in wound healing may be altered and the inflammatory stage is prolonged. In this situation, and if the acute wound has not healed in a timely manner, the wound is classified as chronic.

Table 1 Examples of factors affecting timely wound healing

Micro-organisms
Biofilms
Mechanical stress on the wound
Immunological status
Patient's underlying pathophysiology and medical state (diabetes)
Low albumin levels
Haematoma
Foreign bodies
Nutritional intake
Vascular supply

There are many factors that can affect timely wound healing. Some examples are listed in *Table 1*[28–30].

Microbiology of wounds

Research undertaken to determine the microbiology of a wound relies on the use of traditional culture techniques. However, these techniques have a number of limitations. The microbes isolated from a wound represent a gross underestimation of the true microbiology of the wound[31]. Historical studies and data generated based on culturable techniques alone have reported that the most common bacteria isolated from SSIs are endogenous Gram-positive cocci[32–34]. Other microbes also implicated in SSI include bacteria such as *Legionella pneumophila*, *Mycobacterium chelonae*[35], *Clostridium perfringens*, *Mycobacterium fortuitum*, *Staphylococcus aureus*[36], *Pseudomonas aeruginosa* and *Acinetobacter baumanii*, a common Gram-negative bacteria isolated from many skin and acute wound infections.

The utilization of molecular techniques, which are beneficial for detecting the viable but non-culturable bacteria, has confirmed that the majority of wounds, if not all, are polymicrobial in nature[37]. The specific molecular methods of PCR in conjunction with denaturing gradient gel electrophoresis (DGGE) have helped to highlight and overcome the limitation of culturable-based methods and demonstrate more conclusively that the microbial diversity of wounds is more complex than once thought[38,39]. Furthermore, historical studies undertaken on wound microbiology have reported that the majority of microbes present in the chronic wound are aerobic. However, it is now more evident that anaerobes represent a large proportion of the wound microbiota, particularly in chronic wounds[40,41].

What still remains overlooked in wound care and wound microbiology is the fact that three different microbial phenotypic states exist within the wound environment. These include the planktonic state, the sessile state (biofilm) and the quasi-sessile state (the microbial state following initial detachment from the biofilm; microbes continue to exhibit sessile phenotypic characteristics). These phenotypic states should not be considered to be mutually exclusive as they all have an influence and a role to play in the success or failure of wound management technologies and procedures, and general wound healing.

The basics of biofilm science

Engineers originally observed and defined biofilms as slime that affected water filtration and sanitization processes. Within medicine, biofilms were not cited until the early 1980s. Today, medicine is beginning to acknowledge and appreciate the significance of biofilms and their role in chronic diseases and infections.

A biofilm is an organized community of microbes attached to a surface and encased within a matrix of EPS. This extracellular material is derived from the adherent community of microbes and the body itself. The formation of a biofilm is divided into six stages (*Fig. 1*). Stage 1 involves the formation of a conditioning film. The conditioning film is evident on any existing or newly formed virgin surface, for example when a catheter is introduced into the human body. The conditioning film has an important role to play in the formation of a biofilm. In reference to medical devices, it is well documented that these surfaces become quickly conditioned, within milliseconds, with proteins, sugars and blood products when introduced into the body for the first time. Consequently, microbes that first attach to a new surface do not actually attach to the surface *per se*, but to the conditioning film that resides there. Interestingly, the modification of a surface, for example changing its hydrophilicity or hydrophobicity, has been shown to have little or no effect on microbial attachment and biofilm formation.

Following surface conditioning, microbial adhesion and co-adhesion occurs (stage 2). Depending on the length of time a microorganism remains on a conditioned surface, adhesion can be divided into either reversible or irreversible types. Reversible adhesion is the first stage of microbial attachment to a conditioned surface where the microbes, although attached, can undergo Brownian motion and easily be washed away from a surface and phagocytosed. However, within minutes following initial reversible adhesion, the microbes soon become attached irreversibly. At this stage the microbes are attached firmly on to the surface, aided by their secreted extracellular polymers, and cannot be washed off easily.

Sauer and Camper[42] found that within an hour after microbial attachment approximately 800 new proteins are expressed in sessile bacteria in comparison with their planktonic counterparts. Once attached irreversibly, microbes begin to multiply and start to form very distinctive microbial aggregates, called microcolonies (stage 3). Microcolonies represent the early-stage biomarkers signifying evidence of biofilms. Microcolonies can be visualized in biopsy samples taken from the wound or observed on abiotic surfaces (wound dressing) using simple Gram staining and visualization under light or confocal laser microscopy. As the biofilm matures, more EPS is produced, helping further to secure and cement the biofilm to the surface (stage 4). As the biofilm matures, its indigenous microbiology begins to climax and stabilize, resulting in microbial homeostasis (stage 5). Microbial detachment and reattachment continues on a regular basis throughout the whole biofilm life cycle (stage 6). The dissemination of microbes from the biofilm represents an important concern in infection control and cross-contamination.

The more mature biofilms are generally over 95 per cent fluid and are heterogeneous in nature, having characteristics similar to those of a multicellular organism. For example, water channels have been reported within *in vitro* biofilms, akin to a circulatory system, which aid the transportation of nutrients and oxygen to different niches within the biofilm, and also help to remove waste products within and out of the biofilm[43,44].

Wound–microbiology–biofilm continuum

The stages involved in the development of the wound's climaxing microbiology are shown in *Table 2*.

The pioneering microbes that first attach to the wound are often Gram-positive aerobic bacteria. However, the

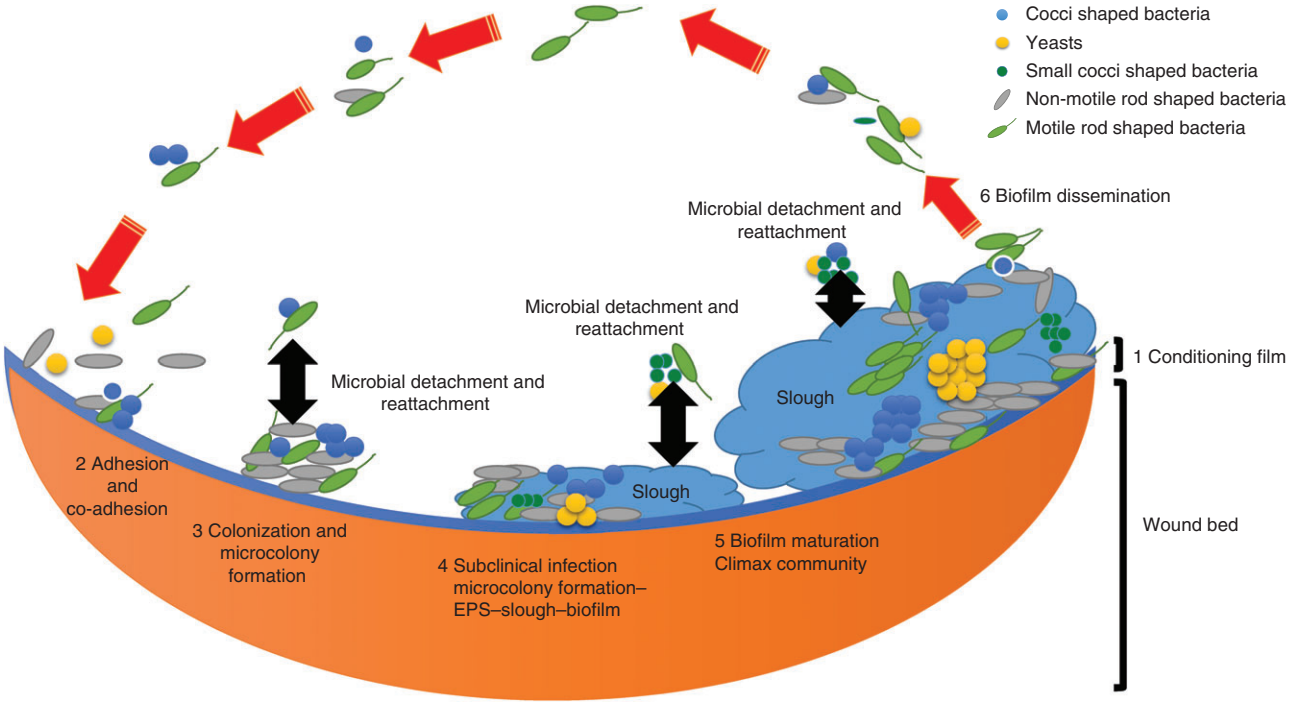

Fig. 1 Stages in the development of a mature biofilm in the wound bed. EPS, extracellular polymeric substance

Table 2 The wound–microbiology–biofilm continuum

Stage	Microbiological state	Clinical indicators
1	Contamination – microorganisms are present but are transient	No obvious clinical indicators. No damage to tissue
2	Adhesion and colonization – multiplication of microbes. Biofilm to planktonic ratio in favour of planktonic phenotypic state	No obvious clinical indicators, signs or symptoms. No damage to tissue
3	Subclinical or biofilm infected – often referred to as critically colonized. This stage involves multiplication of microorganisms. Biofilm to planktonic ratio in favour of biofilm phenotypic state	Wound healing delayed. No obvious clinical indicators and signs of infection or symptoms. 'Quiet' inflammation
4	Local infection – microbial growth, multiplication and invasion into host tissue causing a host immune response	Clinical indicators and signs of infection, such as inflammation, redness, swelling, warmth, pain, cellulitis, increased exudate. Damage to tissue
5	General infection/sepsis	Fever, increased heart rate, increased breathing, confusion

types of primary colonizer of a wound are dictated by both the location of the wound and its proximity to reservoirs of microorganisms. As the pioneering microbes multiply, they begin to alter the wound microenvironment and start to initiate a host immunological response leading to a 'quiet inflammatory' state but without obvious observable clinical symptoms or signs. At this stage in the wound–microbiology–biofilm continuum the wound is said to be colonized with microbes. Changing dynamics within the wound start to create an environment conducive to the manifestation and proliferation of further Gram-positive bacteria, Gram-negative bacteria, strict obligate anaerobic bacteria, yeasts and fungi. In routine microbiological analysis of wounds, anaerobes are frequently not investigated and therefore not reported. Therefore, the role of anaerobes in wound healing and wound infection is often overlooked. This is despite evidence that anaerobes are a significant concern in the wound, and play a role in prolonging non-healing and infection.

As the number of microbes in the wound increases, they will form many different collections of microcolonies that amalgamate and form biofilms. During this stage the microbes continue to multiply and elicit greater host

immunological responses, leading to inflammation. At this stage, the wound is traditionally referred to as being critically colonized or, more correctly, as biofilm infected or subclinically infected[45]. The biofilm has matured to a state of haemostasis and is now supporting a stabilized climaxed microbial population. During this stage of the wound–microbiology–biofilm continuum, the host continues its immunological onslaught on the recalcitrant biofilm. This may lead to ecological shifts in the microbiology and increase infection risk within the wound. Such a phenomenon has been observed in dentistry[46]. The longer a surgical and chronic wound remains open, the higher the risk of microbiological shifts, immunological upregulation, inflammation and, therefore, the increased risk of a local infection.

Critical colonization is a term cited routinely in wound care without any supporting clinical and microbiological evidence. Critical colonization should be regarded as a redundant term based on the lack of any microbiological or clinical merit. It implies that the risk of the wound becoming infected increases when microbes reach a critical level (10^5 colony-forming units per g tissue)[47]. It refers to a critical number of culturable bacteria and, if these numbers increase above a certain level, the likelihood of an infection increases. Unfortunately, this is an area that is difficult to determine microbiologically, owing to the evidence of viable and non-culturable microbes, anaerobic microorganisms, fungi and yeasts, which are all relevant to wounds and infection risk. Consequently, critical colonization does not address the entire microbiota. This is important as it is well recognized that many microbes that are viable but non-culturable have an important role to play in initiating and affecting infections[48].

Infection risk in a wound is related to the numbers of microbes (N) multiplied by their virulence (V) divided by the host's immunity (I) (infection risk = $V \times N/I$). Such an approach addresses both the microbiological and clinical aspects, as well as subclinical concerns, and is not just based on bacterial numbers alone, as defined by the term critical colonization. Other infection risks include the environment, the patient, the type of surgery and procedure, and the care provided.

Evidence for biofilms in wounds

As the wound represents a moist, highly nutritious environment it will support the development of biofilms. Biofilms were first identified on wound sutures in 1985[49], in a study that provided some initial evidence that the wound environment was conducive to biofilm formation. However, it was not until 2004 that biofilms were hypothesized to have a significant role in impeding wound healing[9]. Four years later James and colleagues[10] confirmed the clinical evidence of biofilm markers (microcolonies of bacteria observed using scanning electron microscopy) in both acute and chronic wounds.

Unfortunately, in all studies undertaken to date slough and necrotic tissue were not analysed for the presence of biofilms[50–54]. Slough and necrotic tissue represent biological surfaces for microbial attachment and therefore biofilm development, and, like a wound dressing, represent a reservoir of biofilms and microbes[55]. These biofilm supportive structures help to disseminate microbes, enabling them to recolonize other virgin surfaces.

Generalized signs of biofilm infection in surgery

A number of features provide an indication to a clinician that an acute or chronic wound is infected. Such features are based on both traditional and new criteria[56]. These include pain, abscess, cellulitis, a raised temperature, necrotic tissue, slough, a putrid smell, friable tissue that bleeds, a yellow discharge and slime, and excessive inflammation[57,58]. In contrast, the identification of biofilms in wounds represents a challenging task. Biofilms are microscopic and cannot be seen with the naked eye. They are patchy and non-confluent, and in their immature state induce only modest inflammation as opposed to a clinically visible chronic inflammation thought to be caused by more mature biofilms. Some possible indicators that could be used to indicate the presence of biofilms have been proposed[59].

To diagnose the presence of biofilms, biopsy samples are considered necessary and the standard for biofilm identification in wounds. These biopsy samples can be stained appropriately to visualize microbes, the EPS and immune cells. Microscopically, biofilms would be clinically identified as microcolonies of micro-organisms, surrounded by EPS including evidence of cellular changes (evidence of inflammatory cells). However, in the immunocompromised patient the development, maturation and sustainability of the biofilm increases, and many of the clinical markers may not be observable. In many clinical situations biopsies are not possible, and so the clinician has to rely on more generalized macroscopic criteria based on antimicrobial failures and recurring infections.

Routine swabbing of a wound does not provide evidence that a biofilm exists. Furthermore, in biofilm-related conditions swabs are also often found to be culture-negative[60]. Therefore, the microbes within a biofilm cannot be

Table 3 Criteria suggesting that biofilms may be responsible for surgical-site infections

Evidence of pathogenic micro-organisms
Direct examination of tissue that demonstrates evidence of aggregated (microcolonies) microbes in an extracellular polymeric subtance matrix
Confirmation of infection supported by clinical markers
Recalcitrance to antibiotic and antimicrobial treatment despite evidence of susceptibility of the isolated microbes in the planktonic state
Culture-negative samples irrespective of confirmation of microbes by culture-independent protocols
Ineffective host clearance and evidence of inflammatory cells
Recurring state of chronic inflammation
Recurring local infection
Infection returning after an antimicrobial intervention has been stopped

obtained by surface swabbing, leading to an underestimation of the true microbiology of a wound.

In the majority of patients, the diagnosis of wound biofilms should be based on a number of clinical, biological and therapeutic indicators (*Table 3*). These could include inflammation indicators, similar to those proposed to diagnose a wound infection, and effectiveness and efficacy of antimicrobials.

Relevance of biofilms to surgeons

Numerous scientific papers have demonstrated that biofilms in wounds have the ability to affect cellular proliferation and differentiation, the formation of granulation tissue, epithelialization and a reduction in the efficacy of the host's immune response[20,47,61–64]. Therefore, biofilms do not just represent an infection risk to a wound but may be responsible for delayed wound healing. Preventing the formation of a biofilm is an important consideration for all surgeons when undertaking any surgical procedure. Managing an already established biofilm represents a major, often unachievable, long-term and costly challenge. Established biofilms have an enhanced tolerance and resistance to antimicrobial interventions. Microbes growing within a biofilm have been reported to be up to 1000 times more tolerant to antimicrobials than their planktonic counterparts[65]. This phenotypic phenomenon has important implications in deciding the most appropriate and effective antimicrobial interventions for the control and management of infections associated with biofilms.

The main reasons for biofilm recalcitrance to antimicrobials are shown in *Table 4*[66,67].

Another important factor thought to increase tolerance to antimicrobials is the slow growth rate of the entrenched microbes within the biofilm[68]. This has important implications for effective therapeutic effects of antibiotics such as penicillin whose mode of action focuses on the bacterial cell wall.

Table 4 Examples of biofilm characteristics involved in antimicrobial ineffectiveness

	Description
Lack of antimicrobial penetration	Diffusion limitation owing to biofilm matrix
Phenotypic heterogeneity	Development of physiological gradients within the biofilm leads to distinct microenvironments and heterogeneity
Persister cells	Biofilm-specific phenotypes. A subset of cells that can tolerate prolonged antimicrobial treatment probably owing to metabolic dormancy

Microbes readily detach from the biofilm enabling them to colonize other sites within the human body, leading to remote infection. This is not uncommon in dental and catheter-related infections.

Controversies in treatment

To minimize biofilm development and reduce the risk of a wound infection a number of strategies can be employed. It is important to minimize the risk of cross-contamination from microbial reservoirs (such as open wounds), especially in immunocompromised patients. The use of antimicrobial prophylaxis is important if the surgical procedure is in an area where pathogenic microorganisms may reside. Appropriate aseptic techniques and antimicrobials should be employed. Skin preparation before a surgical procedure reduces biofilm formation because microbes such as *S. aureus* and *S. epidermidis* reside around hair follicles. These include alcohol, iodine or chlorhexidine-based skin preparations. Interestingly, the use of non-antimicrobial cyanoacrylates painted on to the skin before an incision may help to reduce microbial invasion into the wound.

It is important that the patient is discharged from hospital as quickly as possible following a surgical procedure to avoid microbial attachment and infection. Furthermore, appropriate choices of wound dressings have an important role to play in helping to manage the wound's microbial bioburden, cross-contamination, infection risk, and supporting the patient's ability to heal the wound. Wound dressings that are used for acute wounds must be able to absorb exudate, reduce pain and discomfort for the patient, allow visual inspection of the wound, protect and support the formation of newly formed tissue, support a moist wound environment, and immobilize/sequester microbes and prevent their dissemination into the wound bed.

Preventing the formation of a biofilm resides initially in the clinician complying with procedures that prevent microbial attachment and following appropriate protocols of care. These include the use of sterile gloves, procedures that prevent cross-contamination, use of disinfectants and antiseptics, and use of prophylactic antibiotics for high-risk patients. However, in certain situations, such as when implantable devices are involved, there are a large number of potential areas that could allow microbial contamination.

The first stage in an antibiofilm management strategy involves preventing microbes attaching on to a biological or non-biological surface that a patient may be exposed to. Preventing a biofilm forming helps to reduce long-terms issues for the patient and the associated healthcare costs. In chronic wounds, microbial colonization has already occurred. In this situation, wound bed preparation is very important for managing biofilms. The most effective procedure for the removal of a wound biofilm is sharp debridement[69]. However, this comes with significant risks and discomfort for the patient. Other antibiofilm methods include the use of topical antiseptics, lower-risk debridement methods and desloughing techniques[55].

As mentioned previously, wound dressings are employed routinely for the management of both acute and chronic wounds. However, the wound environment favours the formation of biofilms on wound dressings. The wound dressing itself represents a reservoir of microbes and biofilm, which lead to an increase in the wound microbial bioburden. Although the wound dressing remains an important entity for helping to manage the factors that can delay wound healing, it also acts as a bioreactor leading to dissemination of microbes into the wound bed. The wound dressing, therefore, leads to an enhanced upregulation of the biofilm phenotypic state. This increases the planktonic to biofilm ratio in favour of the biofilm within the wound environment; this represents a more challenging scenario than a wound without a wound dressing, which brings the planktonic to biofilm ratio to a more predominantly planktonic environment. Therefore, to reduce a more recalcitrant biofilm bias the choice of wound dressing is very important. Wound dressings that have the ability to sequester and immobilize microbes and so reduce microbial dissemination into the wound bed have a crucial role to play in both the prevention and treatment of biofilms. Wound dressings incorporating silver are used routinely to manage and prevent a wound infection. However, it has been well documented that a number of commercially available wound dressings are not effective on microbes isolated from a wound and biofilms.

Antibiotics are used routinely for the treatment of SSIs. Although effective in normal situations on planktonic microbes, they are found to be less effective in biofilm-related infections. Therefore, routinely used laboratory antimicrobial efficacy testing is unable to help guide clinical therapeutic levels of antibiotics. As discussed, there are many reasons for the lack of antimicrobial performance in biofilm-related infections[70–72].

Although they are observed in both acute and chronic wounds, significantly more research is needed to establish the role of biofilms in wound healing[73]. Differences in the cited definitions of biofilms in wounds within the literature continue to cause confusion to clinicians. Hopefully, this has been addressed in the present review. The lack of research into the composition (chemical and biological), architecture (physical) and clinical effects of biofilms within a wound environment is presently preventing consensus and therefore acceptance of the wound biofilm concept. Unfortunately, many scientific papers investigating the characteristics and composition of wound biofilms have based their research studies, and therefore findings and conclusions, on *in vitro* models, and data extrapolated from environmental and industrially based biofilm studies. It is clear that further clinical evidence, including the development of more robust and reproducible *in vivo* models investigating wound biofilms and the beneficial or detrimental effects they cause, is urgently required. Such an approach will ensure that more rigorous and reproducible evaluation of technologies being developed, and already available commercially in wound care claiming antibiofilm ability, are fit for purpose.

In situations where biofilms represent a significant infection risk, such as on implantable medical devices and in chronic wounds, preventing the formation of the biofilm is the first component of any antibiofilm strategy[12]. Appropriate prophylactic methods and procedures are needed to achieve this goal. In acute wounds this includes the use of topical antimicrobials before and after a surgical procedure[74,75]. Such an approach will help to reduce the wound's total microbial bioburden to enable clearance by the host's immune system. However, in immunocompromised patients, other interventions to support and enhance the immune response are also required.

Of greatest concern to the clinician is the fact that once a biofilm has become established its inherent recalcitrance to antimicrobials increases significantly. Consequently, in both SSIs and at-risk or infected chronic wounds, if topical antiseptics and systemic antibiotics are employed, lack of positive clinical outcomes is often reported. Such an outcome is a key indicator that a problematic pathogenic biofilm is present.

The major focus of published research is on the detrimental effects of biofilms. However, it seems probable that two forms of biofilm may exist in wounds, namely 'pathogenic' and 'benign' types. This concept is similar to the theory reported in many human infections where the commensal microbes (benign biofilm) can turn into problematic microbes (pathogenic biofilm) when the microenvironment changes or becomes more hostile and ecological shifts in the microbiology occur. The fundamental question is, what factors turn a relatively harmless and possibly beneficial biofilm that could be found in a wound, to a more pathogenic and, therefore, problematic biofilm? Unfortunately, no evidence exists to address this question. Many of the clinical studies undertaken to date have failed to establish whether the biofilms detected are in fact an issue, to identify and determine the composition of the EPS, and to establish what the biofilm is doing clinically.

By defaulting to the idea that all biofilms are problematic, many wound care companies are now focusing on developing antibiofilm wound dressings and technologies[76,77]. The use of higher concentrations and more cytotoxic antimicrobial compositions that are required to kill microbes in biofilms, compared with levels used for killing planktonic microbes, may in itself represent a significant risk to wound healing. Furthermore, the wound dressing itself is an important tool in the management of the wound environment. The choice of wound dressing is very important[78] and many can act as a biofilm bioreactor, resulting in dissemination of microbes into the wound bed leading to an increase in the wound's microbial bioburden[79].

Disclosure

The author declares no conflict of interest.

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