The Hidden Danger of Biofilms

Bacterial infections represent a major threat to patients in the acute and post-acute setting, particularly in patients who are immunocompromised, suffering from multiple comorbidities, or recovering from surgery. This tenuous time requires vigilance in preventing infections—and this is why the hidden specter of biofilms can be so dangerous and even life-threatening. Biofilms, which are complex communities of microorganisms that can attach to both biotic and abiotic surfaces, represent one of the greatest challenges in controlling hospital-acquired infections (HAIs).[1-3] This is due to their ability to act as a safe haven for those microorganisms that are of public health significance (e.g., MRSA and CRE)—protecting them from a broad range of antimicrobials—as well as their ability to spread bacteria into the bloodstream or surrounding tissues when present on an indwelling medical device.[1-2,4]

A "New" yet Centuries-Old Problem

The concept of biofilms dates back to 1684 when the Dutch scientist Antonie van Leeuwenhoek made the discovery that bacteria could attach to a surface. However, it was not until 1978 that scientists coined the term "biofilm" and proposed a theory for biofilm formation.[5] It took another four years before evidence was discovered that definitively implicated biofilms in medical device-related infections.[7] Since then, an appreciation for the significance of biofilms within the infectious disease and infection prevention community has grown exponentially.[5] Today, a staggering 80% of all microbial infections are attributed to biofilms.[5,8]

Biofilms: Tough Design & Tough to Kill

In order to understand the infection control challenges posed by biofilms, it is critical to understand their physiology. Bacteria exist in one of two states: 1. A planktonic state, in which they are free-floating, and 2. A sessile state, in which they adhere to a surface. The behavior of bacteria is vastly different between the two states.[5] In fact, as soon as bacteria attach to a surface and become sessile, a dramatic transformation begins. Genes encoding for an exopolysaccharide (EPS) matrix are activated, resulting in the rapid encasement of the bacteria within this "slimy" shield.[5-6] Once protected from the external involvement in this EPS, bacteria release chemical signals, called auto-inducers, that literally "auto-induce" a number of physical changes within the bacteria themselves, including increased motility, sporulation, and release of virulence factors—all of which enhance bacterial survival.[2] It is quite simply a spectacular fortress that allows the shielded bacteria to proliferate and thrive on skin, medical devices, surgical instruments, and hospital surfaces, largely unaffected by external environmental factors….*and* antibiotics.[2,5,7]

The Problem With Antibiotics

Biofilms have presented a formidable challenge for antibiotics for as long as they've been known to exist. This challenge stems from what scientists have theorized are a number of different resistance mechanisms, including:

- **The EPS "Shield"**: Before any antibiotic can target a bacteria, it must first penetrate the EPS matrix; however, many antibiotics are unable to completely infiltrate this tenacious barrier.[2,5-7] Additionally, the EPS itself has been shown to neutralize some antimicrobial agents, rendering them ineffective. Studies have demonstrated that mature biofilms may require 500 to 5,000 times the concentration of antibiotics required to effectively kill planktonic cells of the same bacteria species.[2,5,7]
- **A Slow Growth Rate:** Many antibiotics achieve their bactericidal effect by targeting phases of cellular growth in a bacteria; however, within certain areas of a biofilm, the growth rate is thought to be significantly slower, limiting the efficacy of those antibiotics that are able to penetrate the EPS.[2,5-7]
- **Genetic Resistance:** Exchange of genetic material conferring antibiotic resistance is thought to occur at a higher rate between bacterial cells within biofilms, enhancing both natural and antibiotic-induced resistance.[2,5-7] This includes genes encoding for the nemesis efflux pumps that literally pump antibiotics out of the bacterial cell before they can achieve their bactericidal effect.[2,5,7]
- **A Harsh Environment:** Nutrient and oxygen levels are lower within the biofilm matrix than they are outside of it, and some research suggests this reduces the efficacy of antibiotics' ability to infiltrate the EPS.[2,5-7]
- **Persister Cells:** Even when an antibiotic is able to overcome all of the other resistance mechanisms employed by the biofilm, there is a small population (<1%) of bacteria that appear to enter a dormant phase and "tolerate" the antibiotic—without possessing any resistance genes. Persister cells are thought to be responsible for the relatively high rate of infection "relapse" that occurs when antibiotics are withdrawn. These cells essentially hide in the biofilm, surviving both the antibiotic course and innate host immunity, and then begin to repopulate the biofilm after antibiotics.[2,5,7]

This resistance to antibiotics is a huge concern for healthcare facilities as they combat infections that occur in hospitals and other healthcare facilities. Even more concerning is when multidrug-resistant bacteria—or "superbugs"—are associated with biofilms. These bacteria constitute what the Centers for Disease Control and Prevention calls "one of the biggest health challenges of our time" and represent the most serious threat to patients with an in-dwelling medical device such as a catheter or ventilator.[9]

Understanding Biofilms

Peter Elias, M.D., discusses the hidden dangers of biofilms and the importance of finding biofilm-penetrating therapies.

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The Medical Device Connection

As previously mentioned, biofilms can form on living and non-living surfaces.[2] In the healthcare setting, this translates into biofilms that develop on human tissue, such as chronic venous leg ulcers or the lungs of patients with cystic fibrosis, and those that develop on inanimate objects such as reusable

medical/surgical instruments, environmental surfaces, and indwelling medical devices.[2] While they are all formidable treatment challenges, the biofilms that develop on indwelling medical devices arguably represent the biggest threat because they account for the vast majority of healthcare-associated infections (HAIs).[1] In fact, as many as 50%-70% of all HAIs are attributed to medical device-related infections.[1]

It makes logical sense that when you insert a medical device into a human orifice or blood vessel, there is a risk of simultaneously introducing microogranisms.[2-3,7] And while these microorganisms can come from a number of sources including the ambient environment and healthcare workers' hands,[2] they most often come from bacteria residing on a patient's skin in and around the insertion site.[2,10-13]

Time is an important element in both biofilm development and biofilm-associated, device-related infections. The longer a device remains inserted in a patient, the greater the chance that bacteria will begin to colonize that device.[2-3,7] Similarly, the longer bacteria have to adhere to the surface of a device, the more irreversibly attached they become, triggering the series of events that results in biofilm formation.[2-3] Finally, the longer a device remains in place, the more extensive the biofilm generally becomes and the greater the opportunity for detachment of bacterial cells from the biofilm into the bloodstream or surrounding tissues .[2-3] It is this latter phenomenon that causes the many device-related infections including central line-associated bloodstream infections (CLABSIs), ventilator-associated pneumonias (VAPs), surgical site infections (SSIs), and catheter-associated urinary tract infections (CAUTIs).[3]

The CAUTI Example

CAUTIs are the most common HAIs reported to the National Healthcare and Safety Network and a prime example for the pathophysiology of a biofilm-associated, device-related infection. When a urinary catheter is inserted into a patient's bladder, bacteria residing on the patient's perineal skin or a healthcare worker's hands (if proper hand hygiene or aseptic technique is not performed) can be introduced into the urinary tract both on the internal and external surface of the catheter.[14]

As the catheter remains in place, manipulation of the catheter system can also result in migration of bacteria within the internal lumen of the catheter into the bladder. However, the most common means of bacterial entry occurs via ascension from the urethral meatus along the external catheter surface. These bacteria are either skin residents in the perineal area or fecal contaminants that migrate up the catheter-urethral interface where they can attach to the catheter surface and/or exposed sites on the urethral lining that may have been damaged during catheter insertion. Once attached, the cascade of events leading to biofilm formation is triggered. Subsequent shedding of bacterial cells from the mature biofilm or shearing effects from manipulation of the catheter can then spread bacteria throughout the urinary tract system, leading to symptomatic infection.[14]

Numerous strategies designed to prevent biofilm formation related to CAUTIs have been investigated. Three of these strategies—antimicrobial-coated catheters, antibiotic/antiseptic irrigation of catheter systems, and prophylactic antibiotics—are not recommended by the Infectious Disease Society of America (IDSA) or the Society for Healthcare Epidemiology (SHEA).[15-16] Instead, practice recommendations from these organizations, also endorsed by the CDC, focus on appropriate indications

for use of catheters, aseptic technique for insertion, proper maintenance of catheter systems, and early removal.[15]

Key to these strategies is maintaining proper perineal hygiene both before catheter insertion and throughout the duration of catheter use to minimize the potential for bacterial introduction from the perineum into the urinary tract system. This is especially important for bedridden patients who may have bowel incontinence, leading to the spreading of fecal pathogens into the perineal area. IDSA/SHEA CAUTI prevention guidelines do not recommend the use of antiseptics for cleaning the meatal area[15] and, in fact, one of the most commonly used antiseptics used for generalized patient bathing, chlorhexidine gluconate, is contraindicated for use in the perineum.[17] Instead, proper perineal cleaning technique along with use of an agent that cleans skin while enhancing the skin's innate immunity and promoting a healthy microbiome are critical to avoiding the ascension of bacteria along the catheter system.

Tackling the Problem

CAUTI is only one of a number of medical device-related HAIs associated with biofilm formation, but the fundamental pathophysiology *and* prevention principles are the same for all indwelling medical device-related biofilm infections. Since antibiotics are not a reliable solution to this problem, the scientific community has looked to novel technologies designed to treat biofilms. These range from strategies targeting persister cells, inhibitors of the auto-inducer chemical signals, and mechanical debridement of the biofilm.[1]

However, as with most things in healthcare, the most effective means of addressing the biofilm threat is prevention—eliminating the free-floating bacteria before they can attach to surfaces and initiate the cascade of events that lead to biofilm formation. And, while this includes investigating the efficacy of manipulating both the geometric and physiochemical design of medical devices, the most basic components of prevention involve clean and healthy patient skin, strict protocols for device utilization, high compliance with medical staff hand hygiene, sterilization of instruments, and aseptic technique when inserting medical devices into the body. With, for example, one case of CLABSI estimated to cost $45,814 and the total burden of HAIs in the US estimated to be $9.8 billion in 2012—not to mention the physical and psychosocial impact on patients, there is much to be gained in re-evaluating how these prevention components are implemented.[18]

Need More Information About Biofilms?

If you have questions about biofilms and ways to help safeguard against them in your facility, contact us at Theraworx Protect. Our experts can help you identify potential gaps in biofilm prevention efforts, particularly those that affect the biggest source of microbial contaminants in biofilms: the skin.[2-3]

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