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A New Approach to Mitigate Biofilm Formation on Totally Implantable Venous Access Ports

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Keywords

central venous access port; biofilm; methylcellulose; polyethylene glycol

Use of intravascular catheters for patient care may be associated with increased risk of central line-associated bloodstream infections. It is estimated that up to 18 000 such infections occurred in intensive care units and up to 23 000 in inpatient wards of acute care hospitals in the United States in 2009 [1]. These device-associated infections result in significant morbidity, mortality, and costs of healthcare delivery in these patient populations. The infections result when microorganisms, introduced from the skin of the patient at the catheter insertion site, from a contaminated hub or needleless connector, or from hematogenous seeding, colonize the catheter and form a biofilm. The process of biofilm formation is initiated when microbial cells attach to the surfaces of the indwelling device. Microbial attachment is a complex process, affected by the chemical and physical characteristics of the substratum, host-produced conditioning films, hydrodynamics, characteristics of the aqueous medium, and properties of the microbial cell surface [2].

A distinguishing characteristic of biofilms is the presence of an extracellular polymeric substance matrix, also known as the *biofilm EPS (extracellular polymeric substance)*. The biofilm EPS matrix may be composed of polysaccharides, proteins, and extracellular DNA and may perform a number of important functions for the component organisms, including adhesion, aggregation, and protection from the host immune system and antimicrobial agents [3]. Inhibition of biofilm formation is preferred to eradication of an established biofilm because organisms rapidly develop tolerance to antimicrobial agents, a characteristic that worsens as the biofilm ages [4]. Biofilms on central venous catheters are difficult to eradicate, and for certain organisms (eg, *Staphylococcus aureus*), removal of the device may be the only option.

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In this issue of *The Journal*, Chauhan et al [5] provide a novel approach for significantly reducing bacterial adherence to silicone and titanium surfaces of a totally implantable central venous access port. Silicone septum and catheter surfaces were coated with a methylcellulose polymer nanofilm. Methylcellulose is a non-ionic water soluble polysaccharide that can reduce surface hydrophobicity when applied to the surface of silicone biomaterials [6]. Mussard et al [6] demonstrated that methylcellulose coating of silicone surfaces reduced nonspecific protein adsorption, and adhesion of mammalian cells and bacteria. Titanium ports of the device were coated with polyethylene glycol (PEG), which has been shown to reduce adhesion of bacteria and eukaryotic cells, including erythrocytes, by altering the physical and chemical characteristics of the surface [7–10]. Both methylcellulose and PEG coatings tend to render surfaces more hydrophilic and, therefore, less prone to bacterial attachment [2].

How relevant are these data? What is needed to translate these findings to the bedside? A myriad of experimental methods have been published for the evaluation of biofilm control strategies by clinically relevant microorganisms, ranging from simple microtiter-plate methods [11] to continuous flow biofilm reactors [12] to animal model systems [13]. Although in vitro methods tend to provide greater reproducibility, higher throughput, and lower costs, results may not predict the performance of the treated device in vivo owing to the absence of host-produced conditioning films and immune response and the physical or chemical characteristics of the bloodstream [14]. Chauhan et al [5] used a continuous flow in vitro model system to evaluate treatment efficacy against 2 important healthcare-associated pathogens, *S. aureus* and *Pseudomonas aeruginosa*. Their data suggest that coating of silicone and titanium surfaces of totally implantable venous access ports with methylcellulose and PEG, respectively, can significantly reduce bacterial attachment to these devices. Importantly, they were able to reproduce this effect under the more rigorous (and relevant) conditions of an animal model system.

However, there are questions outside the scope of this study that should enter into any discussion regarding this or other similar approaches designed to inhibit microbial biofilm formation on indwelling intravascular catheters. Foremost, it will be important to assess the potential of this treatment both to prevent bacterial colonization and to reduce bacteremia or blood-stream infections in the animal model. Second, what is the long-term sustainability of the treatment? Biofilms were significantly reduced but not prevented, suggesting the possibility of a rebound effect with prolonged usage. How might this affect the translational aspects of this approach? Finally, recent studies using culture-independent methods have revealed that the microbial communities on indwelling intravascular catheters and catheter access devices may be highly diverse [15, 16]. How effective might this treatment be in reducing colonization and biofilm formation by the potentially diverse communities that may develop on these devices?

Biofilm colonization of indwelling medical devices, such as totally implantable vascular access devices, continues to seriously affect healthcare delivery, and new technologies that can prevent or mitigate this process are crucial. Chauhan and colleagues [5] provide an interesting treatment strategy and a robust experimental approach that has the potential to

influence the science of biofilm prevention and the way potentially new technologies are evaluated.

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