NEW DIRECTIONS TO COMBAT ORTHOPEDIC INFECTIONS
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Key Points:
- Infection is a major problem in equine orthopedics
- The move to local antibiotics has improved the prognosis but newer techniques are required
- Understanding the behavior of bacteria and biofilm formation is crucial to developing new methods to combat infection
- Current research is focused on preventing biofilm formation

The Problem
Orthopedic surgery in horses is a challenging undertaking as they are particularly unforgiving patients. Complications are common and varied, often with severe and potentially fatal consequences. Of these complications postoperative infection is the most common and devastating. Reported infection rates associated with equine orthopedic procedures range from 8-52%. It is extremely important to have an understanding of surgical site infections (SSI) and available methods to combat its development to improve surgical success and patient survival.

Antibiotics – Systemic to local but not enough
The development and use of antimicrobials has been arguably the most significant medical discovery of the past century. Over the last decade, the use of antimicrobials in humans and horses has shifted from systemic to concentrated local administration as this has been shown to be more effective. Despite improvements in our understanding and application of antimicrobial agents, infection still too commonly occurs.

Microbiology Ecology – biofilm formation
Engineers in the 1980’s first coined the term biofilm. Since then an understanding of biofilm (glycocalyx – extracellular polysaccharide) formation and its importance has increasingly taken a central role in the fight against SSI’s.

Microorganisms exist in the environment in one of two forms – suspended/free floating (planktonic) or attached (sessile). These two forms are not mutually exclusive but exist simultaneously. A vast majority of microorganisms (99.9%) prefer to be attached rather than be suspended and often reside in biofilms. Current routine culture methods were developed for identifying bacteria in acute infections caused by bacteria in their planktonic form. A majority (~99%) of bacteria in the environment are viable yet not culturable as they are in their sessile state. However, these same microorganisms can be clearly demonstrated using advanced techniques. (Fig. 1) Not only is their detection difficult but treatment of infection that has an established biofilm often fails without removal of the infected implant. In human medicine it has been reported that all device related infections and 65% of all bacterial infections in general are caused by slime enclosed communities or biofilm protected microorganisms. Furthermore, bacteria encased in biofilms can be 50-500 times more resistant to antimicrobials than unprotected bacteria. Another benefit for the microorganisms in biofilms is that it has recently been demonstrated that many bacteria use cell-to-cell communication systems (quorum sensing) to regulate diverse physiological processes some of which may be responsible for development of antimicrobial resistance.

Overall, with the preponderance of sessile bacteria, their increased antimicrobial resistance with biofilm formation, and their potential to communicate antimicrobial resistance, it is easy to see why often our current methods to combat SSI’s fail.
Current Focus to Combat SSI’s

The basic principle: Colonization of an implant is the prelude to infection. Hence a device that prevents or reduces bacterial colonization can potentially protect against infection.

Cutting edge research currently focuses on means to find effective treatments against established biofilms and perhaps more excitingly on methods to prevent its formation. The development of a clinically applicable technique that prevents biofilm formation on orthopedic devices will be of enormous benefit to our equine patients. Ideas have ranged from identifying biofilm dispersing proteins within maggot excretions, finding effective combinations or antimicrobial therapy, enzymatic degradation of biofilm matrix, electrical currents to disrupt biofilms, to developing biofilm resistant coatings for implants. Efforts have focused on developing biologically active surfaces or “smart implants” that are able to prevent biofilm formation.

The Comparative Orthopedic Research Laboratory (CORL) at the University of Pennsylvania’s New Bolton Center has been involved in developing and evaluating novel techniques to combat orthopedic infection mostly for human application. A large animal model has been developed of an infected ovine tibial osteotomy to investigate these techniques in vivo. Currently select techniques have been applied in a limited number of equine patients but it is envisioned that the application of some of these technologies will be increasingly used to combat orthopedic infection in the future.

The concept of smart implants focuses on prevention of biofilm formation via surface modification of hardware components. This may involve a coating, degradable sleeve or covalent tethering of a drug to the surface of the implant (Figure 2). The drug may then elute over time or in some cases be permanently tethered to the surface. These techniques have been extensively researched and shown to have beneficial effects in preventing SSI (Figure 3). A major concern with the application of these technologies is the potential development of bacterial resistance to the drug used to protect the implant surface.

The development of practical and cost-effective methods to prevent biofilm formation on trauma hardware and hence avoid SSI will be a significant benefit for the equine orthopedic surgeon. Preventing or at least reducing the incidence of infection should allow for more successful treatment of these challenging cases.
**Figure 1**: Scanning electron microscopy (SEM) of Staph aureus biofilm formation on an orthopedic implant after implantation in vivo at the UPENN CORL.

**Figure 2**: Anti-Vancomycin fluorescence demonstrating Vancomycin covalently tethered to a Titanium orthopedic implants prior to implantation in vivo at the UPENN CORL.

**Figure 3**: In vivo study results from a large animal infection model performed at UPENN CORL. Treatment - Vancomycin tethered implant, Control - no treatment. (A. Gross pathology, B. Micro-CT, C. Histology, D. SEM examinations)