

IMPLANT-ASSOCIATED INFECTION

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Orthopedic procedures, including fracture fixation and arthroplasty, have a low but significant infection rate. In humans, the overall rate of implant-associated infection is estimated to be approximately 5% in clean surgical procedures. In veterinary medicine, it is estimated that the infection rate is somewhat higher due to the propensity for animals to self-traumatize incisions by licking or scratching. A recent retrospective study involving 902 dogs undergoing surgery for cranial cruciate rupture reported the infection rate following TPLO to be 8.4% (Frey et al. JAVMA 2010). Infections associated with orthopedic implants are characterized by bacterial colonization and biofilm formation on the implanted device and infection of the adjacent tissues. Bacteria within biofilms are far more resistant to antibiotics and result in persistent infection despite aggressive antibiotic therapy.

Risk factors that may add to the possibility of implant-associated infection include extensive soft tissue trauma, anatomic location of the implant (e.g. oral cavity versus extremity), whether the wound is open or closed, and patient co-morbidities such as obesity, diabetes or the use of immune-suppressing medications such as chemotherapy or corticosteroids. In addition to patient-related factors, it must also be recognized that the material and surface of any fracture fixation device plays a role in the potential development of implant-associated infection. Implant-associated factors found to influence the susceptibility of a particular device to infection include: material, biocompatibility, topography, surface area available for colonization of bacterial, presence of dead space, and tissue or bone compression adjacent to the implant causing necrosis. Of the commonly available orthopedic implant materials, stainless steel and titanium, stainless steel is associated with an increased infection rate in comparison with titanium in animal models. This observation has been attributed to two factors: the improved biocompatibility of titanium over stainless steel and the increased observation of fibrous capsule formation around stainless steel implants. Steel is usually electropolished to a smooth surface whereas titanium in its standard form has a micro-rough surface. Improved adhesion of tissue to titanium over stainless steel has been proposed to be the reason for the reduced prevalence of capsule formation around titanium implants (Moriarty et al. J Mater Sci Med 2009). The fluid filled fibrous capsule that is often observed to form around stainless steel is not vascularized and is poorly accessible to local immune defenses.

Staphylococcus aureus, a common infectious agent associated with implant-related infections, as well as other bacteria, can persist in the surgical site despite aggressive and specific antibiotic therapy. The prevalence of methicillin-resistant *Staphylococcus aureus* has been growing for more than a decade and is particularly prominent in orthopedic trauma and joint replacement patients. These infections are associated with a high morbidity. Treatment often involves multiple debridement procedures, surgical revisions and long term antibiotic therapy. Even with aggressive treatment, many of these infections are never fully eradicated and often lead to implant loosening, failure, soft tissue loss and even limb loss. This resistance to treatment is primarily due to the development of a bacterial biofilm on the implant material. A biofilm is a microbially-derived, highly organized community of bacteria irreversibly attached to a surface or substrate and embedded in a matrix, that have developed more aggressive growth rates and resistance to antimicrobial therapy. The matrix provides a physical barrier to the penetration of antimicrobial agents. In addition, bacteria living within a biofilm acquire biofilm-specific genes

that code for efflux pumps to remove antimicrobials from the microenvironment. It is estimated that biofilms are involved in greater than 65% of all infections. The prevalence of methicillin-resistant *Staphylococcus aureus* has been growing for more than a decade and is particularly prominent in orthopedic trauma and joint replacement patients.

The most-effective strategy for managing implant-related infections is, obviously, prevention. Appropriate sterile technique, responsible antimicrobial use and strict attention to minimizing tissue trauma, debridement and minimizing dead space are paramount. The treatment of established implant-related infections involves surgery (debridement with or without implant removal) and long-term antibiotic therapy. The choice of therapy depends upon duration of infection, stability of the implant, antimicrobial susceptibility of the pathogen and condition of the surrounding soft tissue. Local and systemic antibiotic therapy is often utilized in conjunction with implant removal where possible. This approach seems to have the best clinical outcome; however, implant removal is not always possible. These cases remain a clinical challenge.

Developing strategies to prevent or treat implant-associated infections involve novel implants with surface characteristics resistant to biofilm formation, gene therapy to confer antibiotic sensitivity to biofilm-established organisms, targeted agents designed to dispersing the biofilm matrix molecules, and early biofilm detection techniques. These strategies will become more and more important as emerging antibiotic-resistance becomes more challenging.