Anti-microbial device-based approaches to implant-centered infection

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INTRODUCTION: Device-related infection remains an unresolved clinical problem with increasing numbers of patients across different device classes in different implant scenarios. Many types of materials designs and anti-microbial approaches continue to be levied against this problem, both in infection prophylaxis and in infection therapy. The increased use of implantable materials and increasing incidence of antibiotic resistant infection makes this problem compelling. This presentation reviews several recent approaches to impart medical implant devices with anti-microbial properties.

METHODS: Many different approaches have been historically used to counter device-related infection, including antibiotic lavages, locally tethered or released anti-microbials, device coatings, local electric fields and current applications, and newer approaches targeting bacterial adhesion mechanisms, communication pathways and virulence factors. These include:

- Immobilized antimicrobials
- Controlled release anti-microbials
- Non-adhesive device coatings
- Surgical antiseptic lavages
- Silver metallic and salt formulations
- Electroactive treatments
- Quorum sensing disruptors
- Nanotechnologies

Combination devices provide some new opportunities for innovation by allowing local antibiotic formulations to be released from established classes of implants.[1,2] Few strategies to date have shown much efficacy in vivo in humans despite promising in vitro anti-microbial efficacy and even some translation to animal implant models. New antimicrobial antibodies allow local and systemic delivery of anti-pathogen antibodies to neutralize infection at implant sites and exploit natural endogenous mechanisms of microbial clearance using immune system cascades.[3] Additionally, new tissue engineering strategies to out-compete bacterial colonization by pre-seeding biomaterials with cells do not appear to be effective.[4]

RESULTS: Selected results from orthopaedic prosthesis infection models in spine are reproduced below. The lapine spine implant model[5] is shown in Figure 1, with anti-microbial efficacy of locally delivered polyclonal human antibodies in these wound sites shown in Figure 2.[6]

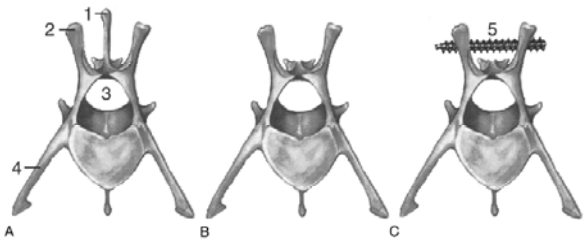

Fig. 1: Lumbar spine K-wire hardware infection model in rabbits for antimicrobial testing.[5]

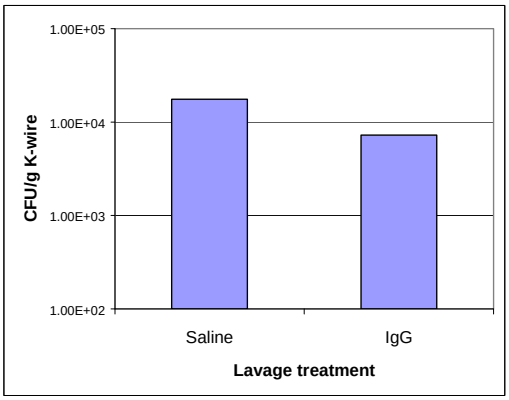

Fig. 2: Knock-down of MRSA in a spine K-wire hardware infection model in rabbits using human polycloncal antibodies.[6]

DISCUSSION & CONCLUSIONS: Antimicrobial strategies address important clinical challenges for increasing numbers of implanted devices and incidences of surgical infections. Unfortunately, most innovations fail to produce substantial improvements in clinical efficacy to date. Scientific issues involve inadequate evaluation methods, including problematic, non-predictive in vitro assays and also irrelevant animal models of infection with devices.

REFERENCES: [1]P. Wu, D.W. Grainger, *Biomaterials* 27, 2450 (2006);[2] I.A. Rojas, et al. *J. Control. Release* 63, 175 (2000); [3]D.W. Grainger, *Expert Opin. Biol. Therap.* 7, 1029 (2004); [4]R. Kuijer, et al. *Biomaterials 28* 5148 (2007). [5]K. Poelstra, et al., *Spine* 25, 406 (2000); [6]K. Poelstra, et al., *Tissue Eng.* 6, 401 (2000).

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