From Bench to Bedside

From Bench to Bedside: It's Cold in There—Isn't It Time We Gave Our Implants a Coat?

Benjamin K. Potter MD

Impplant-related infections have existed, and proven problematic, for as long as orthopaedic surgeons have been placing hardware.

Many factors make these infections hard to treat and harder still to eradicate. Surgeons and patients prefer to retain implants when possible, and sometimes—such as in patients with

healing fractures or unstable vertebral columns—one needs to do so. Some bacteria form biofilms, which reduce the efficacy of antibiotic treatments. Other factors relating to the patient (such as immunosuppression, malnutrition, and diabetes) and the infecting organism (like antibiotic resistance) further complicate matters. Infection after limb-threatening, open lower-extremity fractures occur in as many as 25% of patients [10], but less infection-prone procedures, such as the fixation of closed fractures and primary total joint arthroplasty (TJA), represent the bulk of the national disease burden in this regard because those procedures are so much more common and because they can be more expensive to manage. Costs associated with the treatment of a patient with an infected TJA can exceed USD 90,000 [6]. There are also human costs in terms of morbidity—which can be staggering—and mortality, which, though rare, are always tragic.

The idea of preventing or mitigating implant-related infections via bioactive (generally antimicrobial) coatings or bonded materials is not at all new [11]. However, numerous techniques hold promise in this regard, as both in vitro culture and in vivo animal studies have demonstrated [4, 5].

A Note from the Editor-In-Chief:

I am pleased to present the next installment of “From Bench to Bedside,” a quarterly column by Benjamin K. Potter MD. Dr. Potter is a clinician-scientist in the Department of Orthopaedics at Walter Reed National Military Medical Center and in the Department of Surgery at the Uniformed Services University of Health Sciences, as well as the Deputy Editor for Translational Orthopaedic Research at CORR®. His column will investigate important developments that are making—or are about to make—the transition from the laboratory to clinical practice, as well as technologies and approaches that have recently made that jump.

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These include antibiotic, silver, iodine, and antiseptic coatings to name only a few. Actual coating and/or bonding techniques also vary, including covalent bonding, sol-gels, and plasma-sprays, with or without biocompatible or biodegradable carriers with variable antimicrobial-sulfate, hydroxyapatite, and chitosan [1–5, 7, 9, 12].

Although some promising work has been done in animal models, with the most prevalent, and perhaps most promising, approaches typically including vancomycin or silver [1, 2, 7, 9, 12], no relevant device or technique is, to my knowledge, currently being evaluated in humans for FDA approval. So it seems our devices must remain out in the biologic “cold” without a coat (or coating) for at least some time to come. Once approval is achieved by some implants, it is likely that the market will rapidly develop a veritable glut of available siblings in short order, due to the so-called 501(k) mechanism for “substantially equivalent” (but hopefully not patent-infringing) device approval.

When that happens, our work as practicing surgeons – and skeptical readers – will begin in earnest. There is little doubt that most of these coated implants will have been demonstrated effective for their primary purpose of preventing or mitigating established infections in animals and tightly constrained clinical protocols. Will they

be effective in more-general practice settings? Will they generate unintended consequences or new kinds of harm? We will need to read, and follow, the evolving research closely to find out before putting them into common practice. Despite the almost comical expense of many orthopaedic implants, the second-order bar of cost-effectiveness, either in reality or via mathematical sleight-of-hand, may also be achieved due to the overwhelming medical costs (not to mention human costs, lost income, etc...) associated with orthopaedic infections.

Once these two bars, or at least that of demonstrable effectiveness, are met, we must endeavor to continue to scrutinize our own clinical results, along with manufacturers’ claims, in other areas. Efficacy, even with the absence of overt complications from relatively small, efficacy-demonstrating studies, absolutely does not equate to safety, as recently highlighted in another *CORR*® editorial [8]. Likewise, will bio-effective concentrations of these coatings adversely affect fracture healing for fixation devices, limiting utility, or press-fit ingrowth of TJA implants, decreasing device longevity even as infection rates fall? What about coating(s) effect on the biologic ballet of TJA tribology and wear? And these issues say nothing of concerns

regarding antimicrobial resistance, allergic, foreign body or other host reactions, and so forth.

I, for one, will welcome the addition of effective implant coatings into our orthopaedic armamentarium. I believe that such techniques have greater potential to change the landscape of orthopaedic than any other technology currently on the horizon—there may be no better way to insulate our vulnerable devices against the “biologic cold.” When these devices do eventually arrive, however, we must individually and collectively endeavor to incorporate them into our practices with the appropriate scrutiny and due diligence that we owe both our patients and ourselves.

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