Research & Innovation

Bursting the Bubble on Spine Infection

By Noreen Hickok, PhD

When it comes to infection, the rates and stakes for spinal implant surgery are among the highest of any orthopaedic procedure. These infections are life-altering, causing prolonged disability and even death.

The surgeries are often long, leaving the patient open to the environment. Surgeons can treat joint infections by removing the implants and even amputating in the worst cases, but that flexibility just isn't on the table with the spine. Because spinal stability must be maintained, an implant is generally required, complicating treatment, while the implant itself diminishes immune response in its vicinity and is an ideal surface for bacterial growth.

In the current clinical algorithm, surgeons commonly preempt infection by sprinkling in antibiotics before closing an incision, a practice that seems to help. The surgical drains, which we believe rapidly deplete antibiotic levels, are removed after 2-3 days just before the patient is sent home.

Is this treatment sufficient? The answer is not straightforward because the infecting bacteria form mucous-like clusters of bacteria that can be visible to the naked eye (biofilms) on the spinal instrumentation. These biofilms are like bacterial homesteads comprised of a latticework of proteins from the blood and organic polymers secreted by the microorganisms.

In this state, bacterial metabolism decreases, making the organisms less sensitive to antibiotics, while the biofilm itself acts as a physical barrier to antibiotics. Taken together, this

means systemic antibiotic levels must be very high to be effective—so high as to lead to kidney toxicity.

The good news? We're well on our way to changing this reality through a collaboration led by me, Chris Kepler, MD, a Rothman spine surgeon, and John Eisenbrey and Flemming Forsberg, two PhD ultrasound experts from Jefferson's Department of Radiology.

Our team is doing the unintuitive and using ultrasound, not as a diagnostic modality, but as a therapeutic tool by attacking the problem of orthopaedic infection from two directions: prevention and early-stage intervention.

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For the first, we envision not so much a reinvention, but a remix of how things are currently done in the OR. We've created an antibiotic reservoir sealed by a biodegradable coating that clips onto the standard spinal stabilization rods surgeons use. After the usual post-operative care, a physician could use noninvasive, high-intensity ultrasound to excite gas pockets in the clip's cover to burst the shell and expel an antibiotic cocktail into the wound—a 10-minute procedure that will eradicate any remaining pathogens.

Our second solution, applicable in the spine and joint, uses ultrasound contrast microbubbles, a specialty of Drs. Eisenbrey and Forsberg, in order to chip away at biofilm before it has had a chance to fully form. The bubbles—about the size of red blood cells—are typically used just before an ultrasound exam to help highlight blood vessels. While tissue is relatively rigid, microbubbles, composed of only a shell and gas, are flexible enough to make irregular motions and double-beats, which stand out under ultrasound and make them an effective contrast agent.

In our hands, the microbubbles are injected into the infected area and then burst with a high-intensity ultrasound beam. The force from millions of popping microbubbles is relatively small, but in the confined space of the joint environment, it's enough to break up the biofilm. Our trials in cadaver joints have shown that any remaining clusters are softened by the sound waves, reactivating bacterial metabolism and making antibiotics 1000 times more effective.

Though we are still years away from human trials, our experiments have yielded the essential proofs of concept. In the meantime, as our projects are funded and the data pile up, we will continue to improve the tools and techniques we're using to change the tune of ultrasound and orthopaedic research.

Dr. Noreen Hickok, PhD, is an Associate Professor in the research division of the Department of Orthopaedic Surgery. She is an expert on cell and microbiology, and publishes widely on prophylaxes and treatment of orthopaedic infection. Her current research centers on preventing bacterial colonies from forming on orthopaedic implants. Contact: Noreen.Hickok@jefferson.edu