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CORR Insights

CORR Insights®: Antibiotic-tolerant *Staphylococcus aureus* Biofilm Persists on Arthroplasty Materials

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Where Are We Now?

Periprosthetic joint infection (PJI) is a devastating complication of total joint arthroplasty. The retained hardware can develop a glycocalyx film, making antibiotic treatment of these infections difficult. Perhaps for this reason, treatment of infected TJA by irrigation and débridement with antibiotics generally does not work [2, 4, 6]. The authors of the current study focused their NIH-supported study on a laboratory investigation applying methicillin sensitive *Staphylococcus aureus* to several orthopaedic materials. Increasing doses of antibiotics resulted in no further reduction of biofilm. Antibiotic resistance showed phenotypic behavior due to increasing cefazolin exposure. Biofilm antibiotic tolerance was not a function of the depth of the biofilm. There was no statistically meaningful difference between the viability at the surface versus base of the biofilm. The authors also found that the toxin-antitoxin system used in this study was associated with antibiotic stress.

Where Do We Need To Go?

Although the current study furthers our knowledge, there are several questions that remain unanswered. How do antibiotic resistance and biofilm thickness work together to make treatment more difficult, and what strategies would help us to defeat glycocalyx-forming bacteria in this setting? What role does the effect of toxin-antitoxin systems have on the role of antibiotic stress? Understanding the underlying biochemical and immunologic barriers to successful treatment of these catastrophic and costly infections is important because treatment with antibiotics, irrigation, and débridement is generally unsuccessful. For this reason, studies should be performed at the cellular and molecular levels, similar to cancer studies that can turn on and off gene expression or inhibit proteins that can cause antibiotic resistance in the face of prosthetic implants.

The results of the current study may not be entirely clinically applicable in that biofilms and bacterial behavior within them can differ in vivo versus in vitro [1]. While we must begin in vivo and in animal models, our goals are to develop strategies that work in patients, and we simply are not

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there yet. Strategies that penetrate the glycocalyx in the lab do not always survive the leap from bench to bedside.

We need to determine how to better treat patients with PJI, and many question remain unanswered. Would more rapid diagnosis or earlier detection of PJI improve outcomes [5]? What other mechanisms might we explore that would prevent biofilm adherence?

How Do We Get There?

Future research should further evaluate antibiotic-coated implants and protein inhibitors directed to bacterial persisters [3]. The authors of this study recognized only one toxin-antitoxin, but future research should test other toxin-antitoxins in the laboratory trials and in vivo. Collaboration with microbiologists, immunotherapy experts, and other basic scientists involved in drug designs of cancer therapies and bacterial resistance should be involved in future study designs that potentially treat PJI. Surgeons may be equipped with antibiotic-coated implants capable of combating antibiotic persisters or have other technologies capable of preventing the formation of biofilm in other ways besides antibiotic therapy. As the burden of PJI increases, it is paramount that research efforts be directed to this difficult problem so the medical community can effectively treat this prevalent disease.

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