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Letter to the Editor

Letter to the Editor: *CORR* Insights®: Does Extracellular DNA Production Vary in Staphylococcal Biofilms Isolated From Infected Implants Versus Controls?

Beata Zatorska MSc, Elisabeth Presterl MD, MBA

To the Editor,

Examining microbial biofilms in orthopaedic infections can be difficult because biofilms require robust laboratory methods that allow for accurate diagnoses and appropriate treatment options [1, 5, 8].

Biofilms are complex biological structures dependent on environmental conditions. For those reasons, effective study of biofilms—defined as research that will emulate in vivo conditions—necessarily will involve the evaluation of many different pathogenic bacteria under a variety of experimental conditions. Standardized biofilm methods require all strains of pathogenic bacteria that work in differential local environments [9]. Is this possible?

As bacteria grows in biofilm, it utilizes genes stored within extracellular DNA (eDNA) that are freely available in the biofilm matrix. Additionally, every environmental change influences which bacterial genes are activated or deactivated [4]; this process, called epigenetics, allows the same bacterial genome to be environmentally adaptable [3].

When exposed to antimicrobial substances, bacteria in biofilms are less vulnerable than planktonic bacterial cells. Many in vitro studies use monospecies biofilms produced by staphylococci and *Pseudomonas spp,* but other bacteria should be considered including *Propionibacterium acnes,* an emergent pathogen of prosthetic joint infection [6, 7]. Additionally, there is a possibility that multiple bacteria are involved in an in-vivo biofilm infection. Thus, we need a common trait to diagnose and combat bacteria in a biofilm community. As in our study, eDNA is present in all experimental bacterial biofilms [10, 11].

eDNA in clinical settings is less-well understood [6]. Vorkapic and colleagues [10] presented the multifaceted roles of extracellular DNA, as mentioned in your *CORR* Insights®, in bacterial physiology. For example, eDNA is a nutrition source, which means the degradation of eDNA destabilizes the biofilm and also serves

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B. Zatorska MSc (✉),
E. Presterl MD, MBA
Department of Infection Control and Hospital Epidemiology, Medical University of Vienna, Vienna, Austria
e-mail: beata.zatorska@meduniwien.ac.at

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as deprivation of nutrients in important life cycles of bacteria [2, 10]. Therefore, eDNA could be used to combat biofilm-associated infections.

In clinical research, different models reflecting clinical biofilm conditions can provide insight into the complexities of biofilm biology. Models can feature the different characteristics and stages of the in vivo biofilms and the environmental factors, such as architecture of the surroundings, nutrition, temperature, and perhaps others.

However, for clinical diagnosis, robust and well-defined tests with well-known test properties (such as sensitivity, specificity, positive-predictive value, and negative-predictive value) are needed to give comparable results for clinical strategies. Therefore, future in vitro and clinical studies should include reproducible methods, clearly defined case definitions, and end-points that can contribute to the understanding, diagnosis, and improved clinical outcomes of orthopaedic implant infections.

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