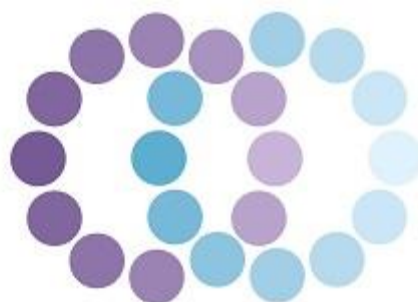


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Biofilm dormancy enhances antimicrobial tolerance in *S. epidermidis*

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Indwelling medical devices have been increasingly used in modern medicine and have saved millions of lives worldwide. However, they can also be an important source of infections, most commonly caused by coagulase negative-staphylococci, particularly by biofilm forming *Staphylococcus epidermidis*. A key feature of biofilms is its enhanced tolerance to antibiotics. Several mechanisms have been proposed to contribute to this phenomenon. We recently developed an in vitro model able to stimulate the induction or prevention of biofilm dormancy. Herein, we used that model to determine if biofilms with induced dormancy presented a distinct antimicrobial tolerance profile than biofilms with prevented dormancy. Both clinical or commensal isolates were included and a total of 43 unique isolates, from different parts of the world were tested. Biofilms were exposed to tetracycline, vancomycin and rifampicin and were analysed by flow cytometry, CFU counts and CLSM. Three unique observations were obtained. First, biofilm dormancy was found as a widespread condition in both clinical and commensal isolates, suggesting this is a fundamental process not only related to the infectious process. Second, while vancomycin did not present any significant effect on the tested biofilms, tetracycline and rifampicin significantly reduced the number of CFUs in biofilms with prevented dormancy tested (up to 4 log killing under 8 h), but were significantly less effective in biofilms with induced dormancy. The third and more curious observation was that the very high reduction in cultivable bacteria was not correlated with the reduction of total and viable cells. Overall, our data suggests in one hand that biofilms with induced dormancy are more tolerant to tetracycline and rifampicin and that those antibiotics further induce dormancy in biofilms, instead of effectively eliminating the biofilm bacteria.