

## Resistance of Coagulase-negative Staphylococci biofilms to antibiotics

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*Staphylococcus epidermidis* and similar coagulase-negative staphylococci (CoNS) are now well established as major nosocomial pathogens associated with infections of indwelling medical devices. The major virulence factor of these organisms is their ability to adhere to medical devices and form biofilms. When in biofilms, CoNS are more resistant to antibiotics. The mechanisms that protect microorganisms in biofilms to antimicrobial agents are still being elucidated. While many authors argue that biofilms present a diffusion barrier to antibiotics, it seems that this mechanism can only partially explain the resistance phenotype generally present in clinical biofilms. In this study, we evaluated the susceptibility of several CoNS biofilms to antibiotics with different mechanisms of action: inhibitors of cell wall synthesis (cefazolin, vancomycin and dicloxacillin), inhibitors of proteins synthesis (tetracycline) and inhibitors of RNA synthesis (rifampicin), and compared susceptibility with that of planktonic cells. A kinetic study was performed on cells both in suspension and in biofilms cells during 6 hours. The antibiotic concentration used was the peak serum (PS) value for each different antibiotic. In planktonic cells, all three inhibitors of cell wall synthesis were highly effective over a 3-hour period. Tetracycline was the least effective antibiotic against planktonic cells, and rifampicin presented an intermediate efficiency. As expected, biofilms were much less susceptible than planktonic cultures to the tested antibiotics, particularly to inhibitors of cell wall synthesis, though, the susceptibility to tetracycline and rifampicin was less affected by the biofilm phenotype. These results demonstrated that antibiotics that target cell wall synthesis have a reduced activity in biofilms, but antibiotics that target RNA and protein synthesis have similar activities in planktonic cells as they do in biofilms, suggesting that increased resistance to cell-wall active antibiotics by biofilm organisms may be due to their being in a quiescent state with minimal requirements for ongoing cell wall synthesis.

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