The role of the biofilm lifecycle in paediatric otorhinolaryngology

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Introduction
New technologies have identified biofilm involvement in many paediatric otorhinolaryngology conditions from Glue ear, recurrent adenotonsillitis to cochlear implant arrays. Greater appreciation of the biofilm lifecycle has demonstrated a complex set of defence mechanisms including; Production of extracellular matrix (Glycolax) which traps nutrients, excludes antibiotic molecules and hinders activation of compliment/opsonisation. Dense cell concentration within the biofilm causes changes in metabolite, oxygen and carbon dioxide concentration throughout the film producing sessile low metabolic rate bacteria with greater mutation rates. Intercellular Signaling alters cells metabolism initiating a change in the biofilm state, production of antimicrobial compounds and biofilm dispersion. Over the past 10 years many laboratories have been attempting to curtail and interfere with these processes to compliment the bactericidal effects of antibiotics to prevent antimicrobial resistance.

Methods

Results
Current management of biofilms in routine practice includes long duration antibiotic therapies, surgical debridement and removal of prosthesis. Long duration antibiotic therapy is often not effective and can lead to increased resistance within the biofilm. Surgical debridement and prosthesis removal is not often feasible and can involve significant complications. Recent appreciation of the biofilm lifecycle has lead to many technologies under development to destroy biofilms and potentiate the effects of antibiotics 1.

Antimicrobial compounds such as silver have long been used in production of catheters, dressings, tracheostomy tubes and disinfectants. More recently studies have tested their efficacy in both vitro and vivo models against biofilms. Silver particles 40 nanometers in diameter were effective in killing S. aureus biofilms in vitro and a C. elegans in vivo model while causing minimal cytotoxicity on human relevant cell lines such as bronchial epithelial and macrophage cell lines 2.

Bacteriophage treatment utilises viruses that infect bacteria to replicate and cause lysis and have been used as an antibacterial agent for over 100 years. Bacteriophage K710 and P68 were combined and demonstrated to lyse 85% of bacterial isolates from chronic rhinosinusitis patients. Furthermore testing of the combination as a sinus rinse showed its safety profile in sheep demonstrating no side effects, no presence of phages in the bloodstream of the sheep 3. Bacteriophages have been demonstrated to significantly reduce biofilm, biomass in P. aeruginosa biofilms even in the most developed biofilms and in mice models of cystic fibrosis infected lungs 4.

Modulation of biofilm metabolic pathways is currently under investigation and has shown promise in dispersal and potentiation of antibiotic effects in P. aeruginosa, S. pneumoniae and S. aureus biofilms. Increased levels of nitric oxide have been demonstrated to stimulate phosphodiesterases which degrade the intracellular messenger c-di-GMP, initiate dispersal and potentiate the bactericidal effects of tobramycin and H2O2 in P. aeruginosa biofilms 5. Nitric oxide has been shown to have direct bactericidal effects on in vitro S. pneumoniae biofilms in a dispersion independent manner. It also greatly potentiates the bactericidal effects of clavulanic acid and amoxicillin on ex-vivo paediatric adenoids with S. pneumoniae biofilms present and appears to change the transcriptional profile to that which closely resembles that of planktonic bacteria 6. A number of nitric oxide donor prodrugs have shown potentiation of the bactericidal effects of amoxicillin in profile when treating S. pneumoniae biofilms 7,8. Similarly P. aeruginosa biofilms were susceptible to nitric oxide or arginine treatment in anaerobic conditions that increases metabolism of organisms and susceptibility to ciprofloxacin and tobramycin 9.

Conclusions
Antimicrobial compounds, bacteria specific viruses, quorum sensing inhibitors, metabolic pathway modulators and light therapy are promising new adjuncts to treat biofilms. In the future we will rely on new novel antibiofilm compounds to combat antimicrobial resistance and treat paediatric otorhinolaryngological conditions.

References

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