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Bacteriology and Biofilm (R663)

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Stuck in the glue – Biofilms, intracellular bacteria and neutrophil extracellular traps in otitis media

Presenting Author: **Ruth Thornton**

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Learning Objectives: Biofilms, intracellular infection and NET production all play a role in chronic and recurrent OM and need to be targeted if treatments are to be effective.

Introduction: Otitis media (OM) is a complex paediatric disease involving interactions between the child, their environment and the microbes that ultimately cause infection. While OM is mainly attributed to bacterial infections, antimicrobials have limited efficacy in treatment or prevention of chronic or recurrent disease. We have demonstrated that bacteria can evade antimicrobial treatments and the immune response both within biofilms and host cells. These bacteria appear to invade and proliferate within cells and may adopt a biofilm phenotype. Bacteria can also manipulate the immune response to release DNA from neutrophils in the form of neutrophil extracellular traps. This host DNA increases the viscosity of the middle ear effusion and assists in the formation of bacterial biofilms, permitting the persistence of infection. These persistence mechanisms represent targets for development of treatment or preventative strategies to combat chronic and recurrent OM.

Methods: Dornase alfa is a DNase used in treating cystic fibrosis and is able to digest the DNA in middle ear effusion *in vitro*. We have established a clinical trial to determine the safety and efficacy of Dornase alfa at the time of ventilation tube insertion (VTI) in children with OM to prevent complications following surgery and reduce the need for repeat surgery.

Results: The Dornase alfa trial is still blinded so efficacy has not yet been assessed, however direct installation into the middle ear at the time of VTI has been demonstrated to be safe.

Conclusions: Bacterial persistence mechanisms need to be fully characterised and understood if effective treatments and preventions are to be developed. Dornase alfa at the time of VTI represents a novel approach that may target the underlying persistence mechanisms.

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Bacteriology and Biofilm (R663)

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Bacteriology and Biofilm Panel (R663) 6–6 - Biofilms and Persister Cells in Infected Cholesteatomas

Presenting Author: **Richard Chole**

Richard Chole

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Learning Objectives: The objective of this presentation is to discuss the evidence for biofilms and persister cells in the pathophysiology of aggressive cholesteatomas.

Microbial biofilm formation has been observed in human and experimental cholesteatomas. These biofilms occur in the keratin matrix of the cholesteatoma. They are sometimes associated with inflammatory cells, but sometimes devoid of inflammatory cells. The most common organisms found in infected cholesteatomas are *Staphylococcus aureus* and *Pseudomonas aeruginosa.* These are well known biofilm forming organisms.

However, recent studies have shown that inoculation of *P. aeruginosa* mutants devoid of the ability to form biofilms (PA01ΔFleQ and others) are inoculated into experimental cholesteatomas, the persistence of infection and the tissue destruction observed are no different than when they are infected with the wild type bacterium (PA01). These studies raise questions about the role of biofilm formation, per se, in the chronicity of infections in aural cholesteatomas.

Recent evidence supports the concept that isolated bacterial cells, termed "persister cells" may be present in infected cholesteatoma in the presence or absence of a biofilm. Persister cells assume a very low metabolic rate and replicate only at minimal levels. These persister cells are highly tolerant to antibiotics, although viable and under the right conditions would begin replicating again and assume their planktonic phenotype.

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Bacteriology and Biofilm (R663)

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Past, present and future treatment of biofilms in otitis media

Presenting Author: **Mat Daniel**

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Learning Objectives: Understand how knowledge of biofilms in otitis media may improve future treatments of otitis media.

Introduction: Otitis media with effusion (OME) is common, and at least a quarter of children require grommets more than once, with attendant risks. Better treatments would be welcome, especially if they obviate the need for repeat surgery, or avoid the requirement for anaesthesia and surgery altogether. Recent advances in our understanding of the importance of biofilms in otitis media pathogenesis have opened up potential new treatment avenues that could improve patient care in the future.

Methods: Review of the treatment of biofilms in otitis media.

Results: Treatment of biofilms requires antibiotic levels that are typically 100 to 1000 times higher than concentrations that inhibit free planktonic bacteria. Systemically administered antibiotics do not reach levels in the middle ear