

doi:10.1017/S0022215116002231

**Bacteriology and Biofilm (R663)****ID: 663.1****Stuck in the glue – Biofilms, intracellular bacteria and neutrophil extracellular traps in otitis media**Presenting Author: **Ruth Thornton**Ruth Thornton<sup>1</sup>, Stephanie Jeffares<sup>2</sup>, Shyan Vijayasekaran<sup>1</sup>, Lea-Ann Kirkham<sup>1</sup>, Selma Wiertsema<sup>1</sup>, Peter Richmond<sup>1</sup>, Harvey Coates<sup>1</sup><sup>1</sup>University of Western Australia, <sup>2</sup>Telethon Kids Institute**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.

doi:10.1017/S0022215116002243

**Bacteriology and Biofilm (R663)****ID: 663.2****Bacteriology and Biofilm Panel (R663) 6–6 - Biofilms and Persister Cells in Infected Cholesteatomas**Presenting Author: **Richard Chole**

Richard Chole

Washington University in St. Louis School of Medicine

**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 (PA01  $\Delta$ FleQ 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.

doi:10.1017/S0022215116002255

**Bacteriology and Biofilm (R663)****ID: 663.3****Past, present and future treatment of biofilms in otitis media**Presenting Author: **Mat Daniel**

Mat Daniel

Nottingham University Hospitals

**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

sufficiently high to eradicate biofilms (at least not without causing systemic toxicity). Ventilation tube insertion dries the middle ear and thus could suppress biofilms, but it may not eradicate them, possibly accounting for the high rate of OME recurrence after VT extrusion. Biofilms in the middle ear could be eradicated by administering antibiotics directly to the middle ear, to reach an antibiotic level that is locally high enough to eradicate biofilms; drug delivery methods could include slow-release formulations placed surgically, or trans-tympanic delivery. Oral treatment strategies could also be useful, but rely on appropriate selection of antibiotics that work well against biofilms, perhaps potentiated by agents to disrupt biofilm matrix and middle ear mucus.

*Conclusion:* Better understanding of biofilms in otitis media has the potential to lead to development of better treatments in the future.

doi:10.1017/S0022215116002267

## Bacteriology and Biofilm (R663)

**ID: 663.4**

### Biofilms in Otitis Media

Presenting Author: **Romain Kania**

Romain Kania

Lariboisiere University Hospital, Paris  
Sorbonne Cite

*Learning Objectives:* To describe: 1. the existence of biofilms in otitis 2. the role of biofilms in the pathogenesis of otitis media 3. the potential targets of treatment.

Biofilms are multicellular network of bacteria encased in a matrix and are noticeably resistant to both antibiotics and host defenses. Biofilms exist in otitis media, cholesteatoma, chronic otitis media, onto prostheses and in adenoids. Demonstration of biofilms in otitis media has shown different mechanisms of persistence of bacteria into the middle ear. Substantial effort in understanding the biologic nature of biofilms has resulted in evidence supporting their importance in otitis media and adenoids. The predominant role played by in biofilms is important, both from the perspective how pathogens develop viable communities in the middle ear as well as how this structure impedes successful antibiotic therapy. Understanding the nature of the biofilm component in the pathogenesis of chronic otitis media will likely have a meaningful influence on the development of novel strategies of treatment.

doi:10.1017/S0022215116002279

## Free Papers (F664)

**ID: 664.1**

### A study of the otological outcomes of otitis media with effusion in children with primary ciliary dyskinesia

Presenting Author: **Reshma Ghedia**

Reshma Ghedia<sup>1</sup>, Jonny Harcourt<sup>2</sup>, Annakan Navaratnam<sup>2</sup>, Jahangir Ahmed<sup>2</sup>

<sup>1</sup>Imperial College Healthcare Trust, <sup>2</sup>Imperial College NHS Trust

*Learning Objectives:*

*Introduction:* Primary Ciliary Dyskinesia (PCD) describes a group of inherited disorders that result in abnormal ciliary motion leading to mucous stasis. Clinical features almost always include otitis media with effusion (OME). PCD patients provided us with a cohort of patients with OME that is not treated with ventilatory tube insertion as these have been shown to result in chronic otorrhoea, early extrusion and persistent perforation without significant improvement to hearing in the long term. The most popular theory of cholesteatoma formation is invagination of the tympanic membrane due to a negative middle ear pressure, as found in OME. We used this cohort to investigate whether children with PCD and OME were predisposed to Cholesteatoma formation.

*Methods:* We performed a retrospective observational review of all the children attending a multi-disciplinary PCD clinic at a national quaternary referral centre. With thorough review of the documentation from their clinic appointments and audiology assessments we collected data regarding the management of the OME.

*Results:* We found that out of 144 patients on their database, almost all of them had a diagnosis of otitis media with effusion at some point. Of these, the only children who had insertion of a ventilatory tube were those who had the procedure before the diagnosis of PCD was made. The majority of children had none or mild hearing loss and therefore did not require any intervention. Those with moderate to severe hearing loss were referred for fitting of hearing aids. None of the children with OME were diagnosed with a Cholesteatoma in the time they had been followed up in the PCD clinic.

*Conclusions:* Cholesteatoma has not been found to occur in children with PCD despite having OME which is conservatively managed. This contradicts the traditional invagination theory of cholesteatoma formation and in these patients, the mucosal stasis may in fact provide a protective factor against cholesteatoma formation.

doi:10.1017/S0022215116002280

## Free Papers (F664)

**ID: 664.2**

### Cholesteatoma: The effects of poverty and ethnicity in New Zealand's North Central Region

Presenting Author: **Stephen Toynton**

Stephen Toynton<sup>1</sup>, David Schreiber<sup>2</sup>

<sup>1</sup>Hawke's Bay Hospital, <sup>2</sup>Central-Technical Advisory Service, Analysis

*Learning Objectives:* Appreciation of social factors is important as delivering health care within ethnic groups is generally more effective.