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Current surgical approach to CSOM (R816)**ID: 816.1****Evidence based approach and quality control in management of otitis media with effusion and recurrent acute otitis media**Presenting Author: **Anna Granath**

Anna Granath

*Karolinska University Hospital**Learning Objectives:*

In Sweden approximately 10 000 children per year have surgery with tube insertion. The Swedish National Register for Tube Treatment includes children with otitis media with effusion (OME) or recurrent acute otitis media (rAOM). Clinics participate on a voluntary basis. The first version (1997–2008) of the register collected about 40000 cases. Data showed that a majority (75%) of the registered cases had tubes inserted due to OME. More boys (52%) than girls (42%) were included, supposedly mirroring the clinical situation. In 2008 the Swedish Council on Health Technology Assessment (SBU) initiated a systematic review on tube treatment in rAOM and OME. Based on this report national guidelines for tube treatment were drawn up, and the register was revised and later rebooted in 2013. The treatment guidelines include recommendations for hearing tests before and after tube insertion in cases of OME. Pre- per- and postoperative questionnaires are submitted by the participating clinics and there is also a postoperative questionnaire answered by the parents (6 months postoperatively). Data extracted from the new registry on hearing results and patients satisfaction are now being reviewed. At present the new register contains about 7000 cases. Resent analysis indicate that the rate of pre-operative hearing tests is to low according to treatment guidelines. The gender difference with a majority of cases being male remains. The group of children with rAOM is younger than the OME-group. There is room for improvement concerning pre- and post-operative hearing tests, improved collections rates for the parent's questionnaires and the total rate of clinics participating in the register. A consultant group works on solutions for improvement, together with Centre of Registers Västra Götaland, which is the national hub for all the ENT-registers. Methods for using the register in clinical research are being developed, in order to answer relevant clinical questions.

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Current surgical approach to CSOM (R816)**ID: 816.2****Systematic approach to the surgical management of chronic suppurative otitis media and cholesteatoma**Presenting Author: **Joe Kutz**

Joe Kutz

University of Texas Southwestern Medical Center

Learning Objectives: 1. Describe a systematic approach for the surgical management of CSOM and cholesteatoma 2. Explain management options for challenging intraoperative findings 3. Discuss the decision making process on staging surgery.

Chronic suppurative otitis media (CSOM) and cholesteatoma are perhaps the most common surgical conditions encountered by the otologist. Surgical management is challenging because of the variability in the extent of the disease and the potential for recurrence. In this presentation, I will present a systematic approach to the surgical management of CSOM and cholesteatoma. In addition, the management of particularly challenging intraoperative findings and potential solutions will be discussed. Finally, the decision process for staging surgery will be discussed.

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Current surgical approach to CSOM (R816)**ID: 816.3****One-stage transcanal atticotomy for epitympanic and mesotympanic cholesteatoma in adults: surgical techniques, anatomical and functional results**Presenting Author: **Daniele Bernardeschi**

Daniele Bernardeschi, Olivier Sterkers

*Pitié-Salpêtrière Hospital**Learning Objectives:*

Objectives/Hypothesis: Surgical management of cholesteatoma limited to the attic and/or mesotympanum remains controversial. The aim of this study was to evaluate the anatomical and the functional results of transcanal atticotomy (TA) in this pathological situation.

Study design: Retrospective medical record review.

Methods: Records of 27 adult patients treated from 2008 to 2014 who underwent TA for primary cholesteatoma surgery were reviewed. Preoperatively, physical examination, audiometry, and CT-scan have been analyzed. Intraoperative findings have been described as well as the surgical technique. Anatomical and functional results have been evaluated with a mean follow up (FU) of 24 ± 12.2 months and the results of CT-scan imaging performed 1 year after surgery to evaluate the presence of residual disease.

Results: Surgeries were uneventful. During the FU, 1 patient (4%) experienced retraction of the attical reconstruction, all the other patients had a well-healed tympanic drum with stable attical reconstruction. The mean air-bonap was 19 ± 12.2 dB and 10 ± 7.3 dB pre-operatively and post-operatively, respectively (mean \pm SD, $p = 0.001$, paired t-test). Twenty-two patients (81%) had no opacity suggesting residual cholesteatoma in CT-scan. Four patients (15%) presenting opacity at CT-scan underwent MRI study that was negative for residual

cholesteatoma. One patient (4%) had displacement of the ossicular prosthesis.

Conclusion: Cholesteatomas restricted to the attic and/or mesotympanum can be removed in a one-stage technique with no residual visible at 1 year and closure of ABG by 50%.

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Inflammation in the middle ear: initiation, regulation and pathophysiology (K823)

ID: 823.1

Inflammation in the middle ear: Initiation, regulation and pathophysiology

Presenting Author: **Allen F. Ryan**

Allen F. Ryan

University of California, San Diego

Learning Objectives: Inflammatory reactions in the middle ear (ME) are significant contributors to otologic disease, including cholesteatoma and otitis media. A major source of ME inflammation is the activation of pattern recognition receptors (PRRs), either by bacteria, viruses or damage-associated molecules patterns (DAMPs) released from dying cells. Ligand binding to PRRs, including Toll-like (TLR), NOD-like (NLR) and C-type lectin receptors, in turn activates pro-inflammatory signaling pathways including the NFκB and JNK cascades. This leads to the production of pro-inflammatory cytokines, chemokine leukocyte chemoattractants, and growth factors that enhance tissue hyperplasia. Studies in mice with deletion of genes encoding PRRs, downstream signaling molecules and their major transcriptional targets clarify the relative roles of PRRs in mediating ME inflammation. These studies implicate TLR signaling via MyD88 and NOD receptor signaling via RIPK2 as major mediators of ME inflammation. They further indicate that the cytokines TNF alpha and IL-1 beta, and the chemokine CCL3, are critical effector molecules downstream from PRRs. Transcriptome analysis of the ME following activation of PRRs further clarifies the nature and timing of ME inflammatory events, with a large number of PRRs and pro-inflammatory mediators rapidly up-regulated. Expression profiles also highlight the role of anti-inflammatory genes, which are activated in response to PRR activation with similar kinetics to that observed for pro-inflammatory mediators. These serve to blunt inflammation and prevent bystander injury to ME tissues. Inflammation also down-regulates tissue growth suppression genes in the ME, including the transmembrane oncogene *ecrg4*. ECRG4 protein is also enzymatically cleaved in response to inflammation, further eliminating growth suppression and releasing an extracellular fragment with growth-promoting activity. In addition, the fragment complexes with the TLR4/CD14/MD2 endotoxin receptor, forming another link between tissue growth and inflammation. The inflammatory pathways activated in cholesteatoma include up-regulation of TLRs, NLRs and their downstream signaling molecules. This includes TLR4, which has been linked to cholesteatoma pathogenesis. TLR4 functions not only as a receptor for bacteria that may disperse from

cholesteatoma biofilms but also for DAMPs released from necrotic cells, such as S100A and HMGB1 both of which are up-regulated in cholesteatoma. Understanding the complex intracellular web that regulates ME inflammation provides potential targets for manipulation as pharmacological interventions. Supported by grants DC000129 and DC012595 from the US NIH/NIDCD.

Inflammation in the middle ear (ME) contributes to disease including cholesteatoma and otitis media. Activation of pattern recognition receptors (PRRs) by bacteria, viruses or damage-associated molecules patterns (DAMPs) activate PRRs, including Toll-like (TLR), NOD-like (NLR) and C-type lectin receptors. These in turn activate pro-inflammatory signaling including the NFκB and JNK cascades, inducing pro-inflammatory cytokines, chemokines, and growth factors that contribute to pathogenesis.

Studies in gene deletion mice clarify the roles of various PRR signaling molecules in ME inflammation, while transcriptome analysis following PRR activation further reveals the nature and timing of ME inflammatory events, with a large number of PRRs and pro-inflammatory mediators rapidly up-regulated. Anti-inflammatory genes are activated with similar kinetics, to blunt inflammation and prevent bystander injury to ME tissues. Inflammation also down-regulates tissue growth suppression genes in the ME, including the transmembrane oncogene *ecrg4*. The ECRG4 protein is also enzymatically cleaved in response to inflammation, further eliminating growth suppression and releasing an extracellular fragment with growth-promoting activity. In addition, the fragment complexes with the TLR4/CD14/MD2 endotoxin receptor, forming another link between tissue growth and inflammation.

Inflammatory pathways in cholesteatoma include TLRs, including TLR4 which has been linked to cholesteatoma pathogenesis, NLRs and their downstream signaling molecules. TLR4 functions not only as a receptor for bacteria but also for DAMPs released from necrotic cells, such as S100A and HMGB1 both of which are up-regulated in cholesteatoma.

Understanding the complex intracellular web that regulates ME inflammation provides potential targets for manipulation as pharmacological interventions.

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Genetics in Otology (R831)

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Genetics of Cholesteatoma Project

Presenting Author: **Peter Prinsley**

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Learning Objectives: The support of BSO to identify affected families is sought.