JUNE 7-11, 2015
GAYLORD NATIONAL RESORT
& CONVENTION CENTER
NATIONAL HARBOR, MD

18TH INTERNATIONAL SYMPOSIUM ON RECENT ADVANCES IN OTITIS MEDIA

INTERNATIONAL SOCIETY FOR OTITIS MEDIA

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SCHEDULE AT A GLANCE

SUNDAY, JUNE 7		
03:45 PM	**05:00 PM**	Newcomer's gathering and orientation session
06:00 PM	**08:00 PM**	Welcome Reception
MONDAY, JUNE 8		
8:00 AM	**8:30 AM**	Welcome & Special Remarks
8:30 AM	**9:45 AM**	Plenary 1: CSOM
9:45 AM	**10:15 AM**	Coffee Break
10:15 AM	**11:15 AM**	Parallel Sessions: Minsymposium 1 & 2
11:15 AM	**12:00 PM**	Parallel Sessions: Podium 1 & 2
12:00 PM	**01:30 PM**	Lunch
01:30 PM	**02:30 PM**	Parallel Sessions: Panel 1 & NIH Workshop
02:30 PM	**03:15 PM**	Parallel Sessions: Podium 3 & 4
03:15 PM	**03:45 PM**	Coffee Break
03:45 PM	**05:00 PM**	Parallel Sessions: Panel 2 & Workshop 1
05:00 PM	**05:30 PM**	Parallel Sessions: Podium 5 & Workshop 1 (continued)
05:30 PM	**08:00 PM**	Poster Reception
TUESDAY, JUNE 9		
8:00 AM	**9:45 AM**	Plenary 2: Current clinical practice guidelines for OM
9:45 AM	**10:15 AM**	Coffee Break
10:15 AM	**11:15 AM**	Parallel Sessions: Minsymposium 3 & 4
11:15 AM	**12:00 PM**	Parallel Sessions: Podium 6 & 7
12:00 PM	**01:30 PM**	Lunch
01:30 PM	**02:30 PM**	Parallel Sessions: Panel 3 & 4
02:30 PM	**03:15 PM**	Parallel Sessions: Podium 8 & 9
03:15 PM	**03:45 PM**	Coffee Break
03:45 PM	**04:45 PM**	Parallel Sessions: Workshop 2 & Panel 5
04:45 PM	**05:30 PM**	Parallel Sessions: Panel 6 & 7
05:30 PM	**06:30 PM**	ISOM General Assembly (members only)
WEDNESDAY, JUNE 10		
8:00 AM	**9:45 AM**	Plenary 3: Vaccine
9:45 AM	**10:15 AM**	Coffee Break
10:15 AM	**11:15 AM**	Parallel Sessions: Minsymposium 5 & 6
11:15 AM	**12:00 PM**	Parallel Sessions: Podium 10 & Minisymposium 6 (continued)
12:00 PM	**01:30 PM**	Lunch
01:30 PM	**02:30 PM**	Parallel Sessions: Panel 8 & 9
02:30 PM	**03:15 PM**	Parallel Sessions: Podium 11 &12
03:15 PM	**03:45 PM**	Coffee Break
03:45 PM	**04:45 PM**	Parallel Sessions: Podium 13 & 14
04:45 PM	**05:30 PM**	Parallel Sessions: Podium 15 & 16
07:00 PM	**10:00 PM**	ISOM Banquet
THURSDAY, JUNE 11		
8:00 AM	**9:45 AM**	Parallel Sessions: Minisymposium 7 & 8
9:45 AM	**10:15 AM**	Coffee Break
10:15 AM	**12:00 PM**	Plenary 4: OMICS
12:00 PM		Closing Remarks and Symposium Adjournment

ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the American College of Surgeons and the International Society of Otitis Media. The American College of Surgeons is accredited by the ACCME to provide continuing medical education for physicians.

AMA PRA Category 1 Credits™

The American College of Surgeons designates this live activity for a maximum of 24.0 *AMA PRA Category 1 Credits™.* Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Disclosure Information

In compliance with ACCME Accreditation Criteria, the American College of Surgeons, as the accredited provider of this activity, must ensure that anyone in a position to control the content of the educational activity has disclosed all relevant financial relationships with any commercial interest. All reported conflicts are managed by a designated official to ensure a bias-free presentation. Please see the insert to this program for the complete disclosure list.

AMERICAN COLLEGE OF SURGEONS
DIVISION OF EDUCATION
Accredited with Commendation by the
Accreditation Council for Continuing Medical Education

AMERICAN COLLEGE OF SURGEONS
Inspiring Quality:
Highest Standards, Better Outcomes

100+*years*

SYMPOSIUM DIRECTOR'S WELCOME LETTER

Welcome to the 18th International Symposium on Recent Advances in Otitis Media (OM2015), a recurring premier event on otitis media and its associated complications including medical and surgical management of hearing loss. This important, multidisciplinary meeting is attended by over 400 clinicians, students, researchers, health professionals, and policy makers.

OM2015 celebrates 40 years of symposia and is the first sponsored by the new International Society for Otitis Media (ISOM). The ISOM adds transparency, accountability, and opportunity to a long tradition of otitis media symposia and research meetings. The most obvious change is that we no longer distinguish "ordinary" (US-based) vs. "extraordinary" (outside the US) symposia; every symposium will have the same structure and nomenclature as stated in our bylaws, with an organizing committee, vendor relations committee, and a program committee of up to 12 members.

The program committee for 2015, chaired by Jian-Dong Li, has diverse, international representation from the United States, Europe, Asia, Scandinavia, and South America. In contrast to prior symposia, where the program committee had a strong regional focus, this new structure encourages transparency and promotes opportunity for all. Moreover, all program committee members are first vetted and approved by the ISOM Board of Directors.

OM2015 provides a unique blend of education, inspiration, and networking, in a venue that is fun, affordable, and family-friendly. The Gaylord National Resort is moments from Washington, DC, in National Harbor Maryland, the region's newest waterfront dining and entertainment district. The 42-acre hotel and conference facility is just 5 miles from Old Town Alexandria, 7 miles from Reagan National Airport, 9 miles from the National Mall, and 35 miles from Dulles International Airport. Transportation options include taxi, limousine, shuttle bus, water taxi, and DC Metro Rail (via continuous shuttle service and MetroBus).

OM2015 is the premier global event for otitis media knowledge and networking, but this does not preclude having fun – and lots of it. Options for fun and family abound in National Harbor, including shops, dining, watersports, fitness trails, nightly shows, and a carousel, Ferris wheel, a children's museum, and Tanger Factory Outlets with 90 premium shops and retailers in walking distance. Who could ask for a better venue to see old friends, make some new ones, and engage in the most stimulating and cutting-edge otitis media discussions on the planet, not to mention the "formal" launch of the ISOM?

Sincerely,

Richard Rosenfeld, MD, MPH
OM2015 Symposium Director and ISOM President

TABLE OF CONTENTS

ISOM MISSION STATEMENT

The International Society for Otitis Media is a non-profit organization that provides an international forum to advance the frontiers of research, education, and patient care as they relate to otitis media. The Society will achieve this mission by (a) disseminating information about otitis media, (b) supporting, coordinating, and enhancing efforts to improve communication and collaboration among Society Members, related disciplines, and related societies, (c) facilitating otitis media research by creating and exchanging knowledge, and (d) sponsoring meetings at which those interested in otitis media can present new research, identify research needs, and work collaboratively to promote optimal clinical management.

ISOM BOARD OF DIRECTORS

Officers

President

Richard Rosenfeld, MD, MPH, Brooklyn, NY, US

Secretary

Joseph Kerschner, MD, Milwaukee, WI, US

Treasurer

Margaretha Casselbrant, MD, PhD, Pittsburgh, PA, US

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Allan Cripps, PhD, Southport, Australia
Sten Hellström MD, PhD, Stockholm, Sweden
Keeyhun Park, MD, PhD, Suwon, Republic of Korea
Tania Sih, MD, Sao Paulo, Brazil

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Paola Marchisio, MD, Milan, Italy
Stephen Pelton, MD, Boston, MA, US
Andrés Sibbald, MD, Buenos Aires, Argentina
Noboru Yamanaka, MD, Wakayama-shi, Japan
Rupa Vedantam, MS (ENT), DLO, Velore, India

OM2015 COMMITTEES

Organizing Committee

Richard Rosenfeld, Symposium Director
Lauren Bakaletz, Symposium Co-Director
Joseph Kerschner, Symposium Co-Director
Margaretha Casselbrant, Symposium Co-Director
Jian-Dong Li, Program Committee Chair
Kenny Chan, Vendor Relations Committee Chair

Program Committee

Jian-Dong Li, Chair (United States)
Mahmood Bhutta (United Kingdom)
Garth Ehrlich (United States)
Anne Hermansson (Sweden)
Kevin Mason (United States)
Shi-Nae Park (South Korea)
Janak Patel (United States)
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Tania Sih (Brazil)
Noboru Yamanaka (Japan)
Richard Rosenfeld, ex officio (United States)
Joseph Kerschner, ex officio (United States)
Sten Hellström, ex officio (Sweden)

Vendor Relations Committee

Kenny Chan, Chair
Eric Simoes
Audie Wolley
Margaretha Casselbrant (ex officio)

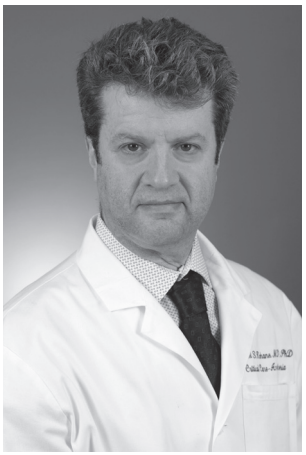
INVITED KEYNOTE SPEAKERS

Noam A Cohen, M.D., Ph.D.

University Of Pennsylvania, Otorhinolaryngology - Head And Neck Surgery, Philadelphia, PA, USA

Cecil Czerkinsky, Ph.D.

International Vaccine Institute



Daniel S Kohane, M.D., Ph.D.

Children's Hospital Boston, Anesthesia, Boston, MA, USA

Axel Visel, Ph.D.

Lawrence Berkeley National Laboratory, Genomics Division, Berkeley, CA, USA

GENERAL SYMPOSIUM INFORMATION

Registration Location and Hours

The attendee registration desk is located on the 2nd Floor of the Gaylord National Resort & Convention Center in the Cherry Blossom Foyer. The registration desk will be open for advance and onsite registration as well as any attendee issues during the following hours:

Sunday, June 7: 7:00 am – 6:30 pm

Monday, June 8: 7:00 am – 5:30 pm

Tuesday, June 9: 7:00 am – 5:30 pm

Wednesday, June 10: 7:00 am – 6:30 pm

Thursday, June 11: 7:00 am – 4:00 pm

Friday, June 12: 7:00 am – 11:00 am

Educational Sessions

The following meeting rooms will be used:

Prince George's Exhibit Hall A

Technical Exhibits, Scientific Posters, Breakfast and Lunch

Cherry Blossom Ballroom and Foyer

General Session, Parallel Sessions, Welcome Reception

Baltimore 3-5

Parallel Sessions, Research Joint Session

Mezzanine 1-6

Research Breakouts

Camelia 2-3

Research Breakouts

Please refer to the hotel map on p. 21 for room locations.

Industry Support Displays

A commercial display of scientific interest will be available during the meeting, providing attendees with an opportunity to view products and services from various corporations. We invite you to visit our exhibitors in Prince George's Exhibit Hall A of the Gaylord National Resort & Convention Center during the hours of:

Monday, June 8, 2015: 7:00 AM – 3:45 PM

Tuesday, June 9, 2015: 7:00 AM – 3:45 PM

Wednesday, June 10, 2015: 7:00 AM – 3:45 PM

*Breakfast, coffee breaks and lunches will be served in the exhibit hall.

Poster Presentations

Poster presentations will be held in Prince George's Exhibit Hall A. Please see page 289 for the complete poster listing. The Poster Reception will take place Monday, June 8 from 5:30 – 8:00 pm.

Speaker Ready Room

Presentations are loaded at the tech station in the general session room. Please give presentations to the AV Tech at least 2 hours before your presentation.

You should plan to review your presentation(s) in the Speaker Ready Room to ensure the integrity of your presentation (fonts, bullets, outlines, animations, video, etc.). If you have any changes to your presentation, we ask that you submit these changes to the AV Tech no less than 2 hours prior to the start of your presentation.

Location: The Speaker Ready Room will be located in **Magnolia 1.**

Hours of operation:

Sunday, June 7	12:00 pm – 7:00 pm
Monday, June 8	7:00 am – 6:15 pm
Tuesday, June 9	7:00 am – 6:15 pm
Wednesday, June 10	7:00 am – 6:15 pm
Thursday, June 11	7:00 am – 12:00 pm

Your final presentation needs to be brought to the back of your session room (either the Cherry Blossom Ballroom or Baltimore 3-5) so it can be loaded onto the presentation computer; this needs to be done no later than two hours prior to your presentation.

It is the presenter's responsibility to collect portable media (i.e. USB drives) at the conclusion of the session.

Meals

Breakfast: A continental breakfast will be provided in the Exhibit Hall Monday through Wednesday mornings from 7:00 - 8:00 am. Thursday breakfast will be served in the Cherry Blossom Foyer from 7:00 - 8:00 am.

Lunch: Boxed lunches will be provided in the Exhibit Hall Monday through Wednesday from 12:00 - 1:00 pm.

Dinner: On your own. A list of local restaurants is available at the Registration Desk. The hotel concierge will also be able to recommend dining options. Two receptions have been planned—a Welcome Reception in the Cherry Blossom Ballroom on Sunday from 6:00 - 8:00 pm, and a Poster Reception in the Exhibit Hall on Monday from 5:30 - 8:00 pm.

Offsite Event:

Wednesday, June 10 from 7:00-10:00pm; Tickets are $110 per person; availability is limited.

Join your colleagues for a night of nostalgia at Virtue Feed & Grain, an American style tavern, housed in an historic building from the 1880's used then as a feed warehouse. You will travel from the Gaylord via ferry boat to the Alexandria waterfront, enjoy dinner featuring traditional American tavern fare, and then head back to the Gaylord via the ferry.

The ferry will leave the Gaylord dock at 7:00 pm for your 7:30 pm dinner; the return ferry will leave Alexandria at 9:30 pm. Ticket price includes round-trip ferry transportation, dinner and two drinks.

Identification

Please wear your conference identification at all times during the meeting as it will be required for admittance into conference functions. Please note that the following events are ticketed functions:

Welcome Reception	Sunday, June 7	6:00 – 8:00 pm
ISOM Banquet	Wednesday, June 10	7:00 – 10:00 pm

Cell Phones and Taping

As a courtesy to your colleagues, please silence cell phones while in the scientific sessions.

No audio or videotaping is permitted in the scientific sessions, workshops, or exhibit areas.

Announcements

We are pleased to offer attendees the opportunity to post announcements on the designated poster board located in the registration area.

Lost and Found

Lost and found is located at the Registration Desk. After the meeting, any unclaimed items will be turned in to hotel security.

Emergency Information

All Gaylord National Safety Services Officers are CPR, AED and first aid certified. All emergencies or suspicious activities should be reported immediately to Safety Services. Safety Services can be contacted by any house phone or dialing 333 from your guest room phone.

FedEx Office Printing and Shipping Center

The Business Center is located on the hotel's second floor.

All shipments received and shipped by the hotel will incur a standard per-piece handling charge based on weight. The business package room is open from 6:00 am to 9:00 pm Sunday through Saturday. They can be contacted at 301-567-0457. Twenty-four hour self-service printing, copying and internet access is available.

Conference Management

Association Management Services

c/o American College of Surgeons

633 N. Saint Clair St.

Chicago, IL 60611-3211

Representatives from ACS will be present at the conference and will be wearing recognizable identification. Please feel free to approach them at any time with questions, comments, concerns, or if you require additional assistance of any kind.

Disclaimer

Attendees voluntarily assume all risks involved in travel to and from OM2015 and in attendance of and participation in the program. ISOM and ACS Association Management Services shall not be liable for any loss, injury, or damage to person or property resulting directly or indirectly from any acts of God, acts of government or other authorities, civil disturbances, acts of terrorism, riots, thefts, or from any other similar causes.

CONTINUING EDUCATION

CME Credits and Certificates of Attendance may be claimed online on the conference website (http://isom2015.com/). Should you have any questions or concerns, please visit the Registration Desk or contact ACS Conference Management via email at isom@facs.org. Certificates of Attendance may also be requested at the Registration Desk during registration hours.

Symposium Learning Objectives

Following the program, participants should be able to:

- Identify the advances in the pathogenesis and diagnosis of otitis media
- List the recent changes in the etiologies of otitis media
- Numerate the complications of otitis media and their impacts
- Understand the medical treatments of otitis media including the advances in the role of vaccines and the role they play to prevent otitis media
- Discuss the surgical treatment of the various forms of otitis media and particularly the complications of otitis media in terms of both conductive and sensorineural hearing loss
- Describe the advances in the care of otitis media from a global standpoint and the differences seen in developed and underdeveloped countries

Course Description

The 18th International Symposium on Recent Advances in Otitis Media will bring together investigators whose research and clinical interests were focused on diseases of the middle ear; these include otolaryngologists, pediatricians, infectious disease experts, immunologists, pharmacologists, epidemiologists, statisticians, public health officials, and experts from government and industry from all continents interested in relieving the burden of otitis media and its sequelae from our patients and their families. Over the years, the symposia have served as a magnet for presentations of new information and meeting of young and senior investigators to stimulate new and productive research, to review current investigations, and consider the most productive avenues for future research.

RECOGNITION OF SYMPOSIUM SPONSORS

The 18th International Symposium on Recent Advances in Otitis Media wishes to gratefully acknowledge the following exhibitors:

Diamond Level

Alcon http://www.alcon.com/

As a global leader in eye care, Alcon's mission is to provide innovative products that enhance quality of life by helping people see better.

Otonomy http://www.otonomy.com/

Otonomy is a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapeutics for diseases and disorders of the ear.

Platinum Level

Olympus America, Inc. http://medical.olympusamerica.com/

Olympus offers a complete line of vent tubes, middle ear implants, hand instruments and many other ENT products for both the office and OR.

Silver Level

Elsevier http://www.elsevier.com/

ELSEVIER is a leading publisher of health science publications, providing superior reference information, decision support tools to doctors, nurses, health practitioners and students. Our media spectrum — print, online and handheld, provides information in the most convenient format.

Kurz Medical http://www.kurzmed.com/

KURZ is one of the world's leading manufacturers of middle ear prostheses in Titanium and Nitinol. The company provides prostheses and specialized precision instruments for middle ear surgery.

Grace Medical http://www.gracemedical.com/

Grace Medical provides innovative product solutions for the ENT surgeon, including Titanium and HA adjustable implants, Nitinol Stapes and Malleus Pistons, Ventilation Tubes and Instrumentation.

University of Illinois at Urbana – Champaign

The University of Illinois at Urbana-Champaign and PhotoniCare, Inc. have pioneered a technique that provides a non-invasive view through the eardrum to observe and measure effusions, biofilms, and other disease indicators in real-time.

HOUSING & TRAVEL INFORMATION

Venue and Housing Information

Gaylord National Resort & Convention Center, 201 Waterfront Street, National Harbor, MD 20745; 301-965-4000, Fax 301-965-4098; http://www.marriott.com/hotels/travel/wasgn-gaylord-national-resort-and-convention-center.

The Gaylord National Resort & Convention Center, a Washington, D.C. resort, anchors the 300 acre National Harbor waterfront entertainment district, located eight miles south of D.C. The Gaylord National Resort & Convention Center offers visitors everything they are looking for in a convention destination, vacation getaway or business trip. This first-class destination offers fun for everyone including fine dining and casual restaurants, unique shopping experiences, an indoor pool and 20,000 square foot spa and fitness center. The Gaylord offers a spectacular 19-story glass atrium welcoming you with sweeping views of the Potomac River, Washington D.C. and Old Town Alexandria in the distance. Guestrooms offer mini-fridges, coffee makers and 2 bottled waters per day, 32" flat-screen TVs and pay-per-view movie services, in-room high-speed internet access and in-room safes fitted with AC outlets, designed to accommodate and recharge laptop computers.

Hotel reservations must be cancelled by 72 hours in advance of day of arrival in order to avoid penalty; check-in is 4:00pm and check-out is 11:00am.

Taxi Service

Gaylord National offers Express Car services that can either be scheduled in advance or picked up on our front drive at your service. Express Car Service offers flat rate fees and accepts credit cards. Local taxis are also available; requests can be made through the doorman.

Transportation to and from Reagan National Airport (DCA): Super Shuttle's shared one way fare is $18.00 (reservation required); approximate taxi cab fare is $25.00.

Personal Vehicle

Follow signs to George Washing Parkway South to Alexandra. Veer right at the sign to Slaters Lane, make a right at traffic light. Follow signs to US Route 1 and merge onto US-1. Follow signs to I-95 North (Maryland). Veer right at signs toward I-95. Veer left toward I-95 and merge onto I-95 North / I-495 East (Capital Beltway). Cross Woodrow Wilson Bridge toward Maryland. Take exit 2A toward National Harbor. Turn right on Waterfront Street. The resort is on the right.

Airport address: Reagan National Airport, 2401 Smith Boulevard, Arlington VA 22202

PARKING

Self Parking:

$6 – up to 1 hour

$12 – 1-2 hours

$16 – 2-3 hours

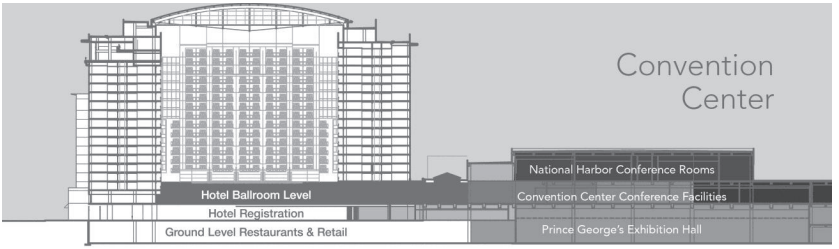
$24 – 3-24 hours

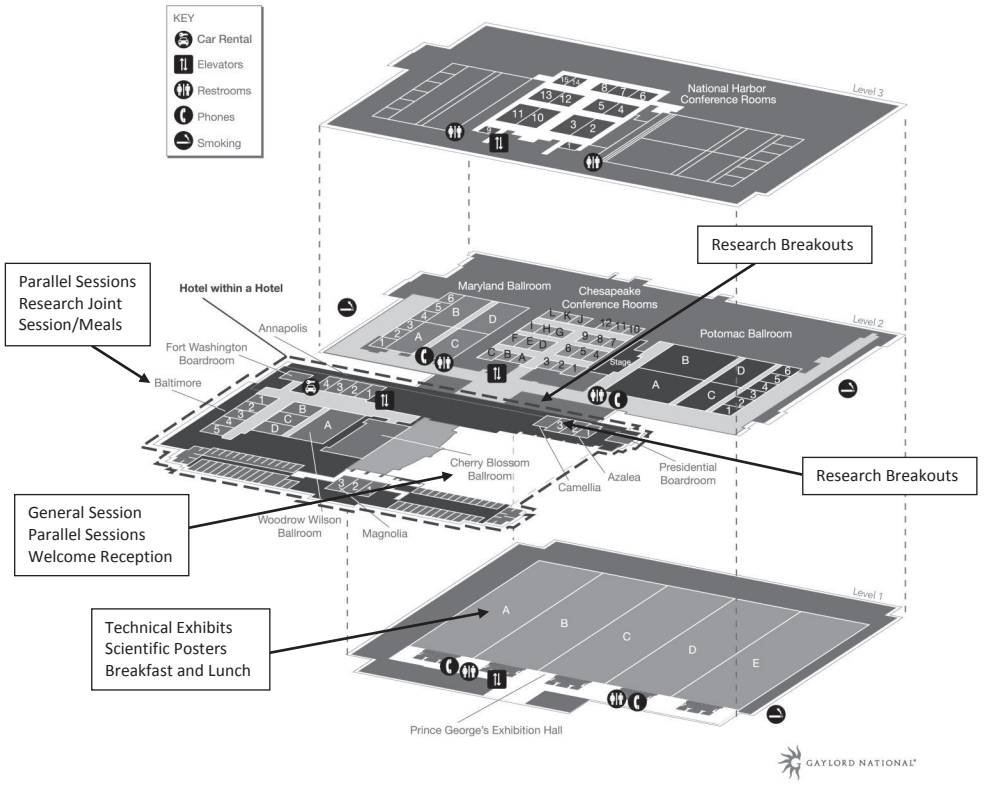
$24 – overnight rate (in/out access included)

Valet Parking:

- $20 – up to 3 hours
- $35 – 3-24 hours
- $35 – overnight rate (in/out access included)

HOTEL MAP


Convention Center
National Harbor Conference Rooms
Convention Center Conference Facilities
Prince George's Exhibition Hall
Hotel Ballroom Level
Hotel Registration
Ground Level Restaurants & Retail


KEY
Car Rental
Elevators
Restrooms
Phones
Smoking
National Harbor Conference Rooms
Level 3
Research Breakouts
Parallel Sessions
Research Joint
Session/Meals
Hotel within a Hotel
Maryland Ballroom
Chesapeake Conference Rooms
Potomac Ballroom
Level 2
Annapolis
Fort Washington Boardroom
Baltimore
Cherry Blossom Ballroom
Camellia
Azalea
Presidential Boardroom
Research Breakouts
General Session
Parallel Sessions
Welcome Reception
Woodrow Wilson Ballroom
Magnolia
Technical Exhibits
Scientific Posters
Breakfast and Lunch
Level 1
Prince George's Exhibition Hall
GAYLORD NATIONAL

SYMPOSIUM SCHEDULE

SYMPOSIUM SCHEDULE

MONDAY, JUNE 8 – 8:00 AM – 9:45 AM

CHERRY BLOSSOM BALLROOM
ALL ATTENDEES

8:00 AM **Welcome & Special Remarks**

8:00 - 8:10 AM
Welcome, Richard Rosenfeld, M.D., MPH, President, ISOM (US)

8:10 - 8:15 AM
Special Remarks, Bracie Watson, Ph.D., Program Director, NIH/ NIDCD (US)

8:15 - 8:20 AM
Announcement of OM2017, Allan Cripps, Ph.D. (Australia)

8:20 - 8:30 AM
Program Overview, Jian-Dong Li, M.D., Ph.D., Chair, Program Committee (US)

8:30 AM **Plenary Session 1 (C): CSOM**

Moderators: Tania Sih (Brazil), Stephen Pelton (US)

Speakers:

8:30 - 8:45 AM
IS CHRONIC SECRETORY OTITIS MEDIA A SOCIAL DISEASE?
Tania Sih (Brazil)

8:45 - 9:00 AM
EPIDEMIOLOGY AND PATHOGENESIS OF CHRONIC SUPPURATIVE OTITIS MEDIA: IMPLICATIONS FOR PREVENTION AND TREATMENT REVISITED
Stephen Pelton (US)

9:00 - 9:15 AM
RECURRENT OTORRHEA IN CHRONIC SUPPURATIVE OTITIS MEDIA – IS BIOFILM THE MISSING LINK?
Ramon Jensen (Denmark)

9:15 - 9:30 AM
COMMUNITY-LEVEL SOCIAL AND ENVIRONMENTAL RISK FACTORS ASSOCIATED WITH CHRONIC SUPPURATIVE OTITIS MEDIA IN 26 REMOTE ABORIGINAL COMMUNITIES IN NORTHERN AUSTRALIA
Anna Stephen (Australia)

9:30 - 9:45 AM **Q&A**

9:45 AM **Coffee Break in Exhibit/Poster Hall**

MONDAY, JUNE 8 – 10:15 AM – 5:30 PM

CHERRY BLOSSOM BALLROOM
CLINICAL SCIENCE

10:15 AM **Minisymposium 1 (C): Global differences in OM**

Moderators: Margaretha Casselbrant (US), Vedantam Rupa (India)

Speakers:

10:15 - 10:31 AM
OTITIS MEDIA FROM A GLOBAL PERSPECTIVE
Margaretha Casselbrant (US)

10:31 - 10:47 AM
EPIDEMIOLOGY OF ACUTE SUPPURATIVE OTITIS MEDIA IN THE FIRST 2 YEARS OF LIFE IN INDIAN INFANTS
Vedantam Rupa (India)

10:47 - 11:03 AM
EVOLUTIONARY FORCES IN OTITIS MEDIA: AN OVERVIEW AND AN EXPLANATION FOR THE HIGH PREVALENCE IN INDIGENOUS POPULATIONS
Mahmood Bhutta (UK)

11:03 - 11:15 AM Q&A

11:15 AM **Podium 1: Treatment 1**

Moderator: Anna Granath (Sweden)

Speakers:

11:15 - 11:22 AM
EVIDENCE BASED TUBE TREATMENT-ARE WE WORKING ACCORDING TO PLAN? SWEDISH NATIONAL GUIDELINES AND NATIONAL REGISTRY FOR TUBE TREATMENT.
Anna Granath (Sweden)

11:22 - 11:29 AM
OTITIS MEDIA OUTCOMES DATABASE
Mallory O'Niel (US)

11:29 - 11:36 AM
EFFICACY OF SOLITHROMYCIN (CEM-101), FOR EXPERIMENTAL OTITIS MEDIA (EOM) DUE TO EITHER NONTYPEABLE HAEMOPHILUS INFLUENZAE (NTHI) AND STREPTOCOCCUS PNEUMONIAE (SP)
Marisol Figueira (US)

11:36 - 11:43 AM
RANDOMISED TRIAL SHOWS SUPER-ADDED RAOM IN OME CASES BENEFITS SUBSTANTIALLY FROM VENTILATION TUBES
Misha Verkerk (UK)

11:43 - 11:50 AM
COST-EFFECTIVENESS OF TREATMENT FOR ACUTE OTORRHEA IN CHILDREN WITH TYMPANOSTOMY TUBES: A PRAGMATIC RANDOMIZED CONTROLLED TRIAL
Thijs Van Dongen (Netherlands)

11:50 AM - 12:00 PM Q&A

12:00 PM **Lunch in Exhibit/Poster Hall**

1:30 PM **Panel 1 (C): Complications to AOM**

Moderator: Ann Hermannson (Sweden)

Panelists:
Ann Hermannson (Sweden)
Michal Luntz (Israel)
Anne Schilder (The Netherlands)

2:30 PM **Podium 3: Treatment 2**

Moderator: Harvey Coates (Australia)

Speakers:

2:30 - 2:37 PM
INITIAL RESULTS OF A PILOT TRIAL OF TISSUE ENGINEERED MYRINGOPLASTIES IN WESTERN AUSTRALIA
Harvey Coates (Australia)

2:37 - 2:44 PM
BALLOON DILATION IN REFRACTORY EUSTACHIAN TUBE DYSFUNCTION
Cuneyt Alper (US)

2:44 - 2:51 PM
INTRANASAL RAGWEED CHALLENGE IN SENSITIZED ADULTS DOWNGRADES EUSTACHIAN TUBE FUNCTION
Juliane Banks (US)

2:51 - 2:58 PM
EFFICACY DEMONSTRATED IN TWO PHASE 3 CLINICAL TRIALS OF INTRATYMPANIC EXTENDED-RELEASE CIPROFLOXACIN GEL IN CHILDREN WITH MIDDLE EAR EFFUSION UNDERGOING TYMPANOSTOMY TUBE PLACEMENT
Albert Park (US)

2:58 - 3:05 PM
COMPARATIVE EFFICACY AND SAFETY OF ANTIBIOTICS FOR PEDIATRIC ACUTE OTITIS MEDIA: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS
Huaili Jiang (China)

3:05 - 3:15 PM Q&A

3:15 PM **Coffee Break in Exhibit/Poster Hall**

3:45 PM **Panel 2 (C): Conductive hearing loss in newborns**

Moderator: Lisa Hunter (US)

Panelists:
Richard Rosenfeld (US)
Amanda Hall (UK)
Lisa Hunter (US)
Susan Nittrouer (US)
Albert Park (US)

5:00 PM **Podium 5: Epidemiology**

Moderator: Marie Gisselsson-Solen (Sweden)

Speakers:

5:00 - 5:07 PM
INFORMATION ON COMORBIDITIES COLLECTED BY HISTORY IS POTENTIALLY USEFUL IN PREDICTING OTITIS MEDIA RISK IN CHILDREN
Margaretha Casselbrant (US)

5:07 - 5:14 PM
EFFECTS OF EARLY ONSET ACUTE OTITIS MEDIA ON THE RISK OF ACUTE OTITIS MEDIA RECURRENCE AND HEALTHCARE RESOURCE USE: THE WHISTLER STUDY
Marieke De Hoog (Netherlands)

5:14 - 5:21 PM
RARE VARIANTS WITHIN A2ML1 CONFER SUSCEPTIBILITY TO OTITIS MEDIA
Regie Lyn Santos-Cortez (US)

5:21 - 5:30 PM Q&A

5:30 PM **Poster Reception**

8:00 PM **Poster Reception Adjourns**

MONDAY, JUNE 8 – 10:15 AM – 5:30 PM

BALTIMORE 3-5
BASIC SCIENCE

10:15 AM **Minisymposium 2 (B): Biofilm management**

Moderators: W. Edward Swords (US), Noboru Yamanaka (Japan)

Speakers:

10:15 - 10:27 AM
POLYMICROBIAL BIOFILMS IN OTITIS MEDIA
W. Edward Swords (US)

10:27 - 10:39 AM
PATHOGENESIS OF BIOFILM OTITIS AND TREATMENT STRATEGIES
Noboru Yamanaka (Japan)

10:39 - 10:51 AM
NUTRITIONAL INFLUENCE ON BIOFILM ARCHITECTURE AND INTRACELLULAR BACTERIAL COMMUNITY DEVELOPMENT OF NONTYPEABLE HAEMOPHILUS INFLUENZAE: A LINK TO PERSISTENCE?
Kevin Mason (US)

10:51 - 11:03 AM
PATHOGENESIS OF NONENCAPSULATED STREPTOCOCCUS PNEUMONIAE IN EXPERIMENTAL OTITIS MEDIA
Larry McDaniel (US)

11:03 - 11:15 AM Q&A

11:15 AM Podium 2: Animal & Cell Model/Genetics

Moderator: Qing Zheng (US)

Speakers:

11:15 - 11:22 AM
THE JUNBO MUTANT MOUSE; A TRANSLATIONAL MODEL FOR NTHI MIDDLE EAR INFECTION
Derek Hood (UK)

11:22 - 11:29 AM
PATHOLOGICAL FEATURES IN A NEW MOUSE MODEL OF HUMAN OTITIS MEDIA AND EXPRESSION OF TOLL-LIKE RECEPTOR 2 AND 4 IN HUMAN CHRONIC OTITIS MEDIA
Yan Zhang (China)

11:29 - 11:36 AM
A TRANSCRIPTOME-WIDE VIEW OF ACUTE OTITIS MEDIA HOST RESPONSE IN THE CHINCHILLA ANIMAL MODEL
Shirng-Wern Tsaih (US)

11:36 - 11:43 AM
ROLE OF NEUTROPHIL EXTRACELLULAR TRAPS IN THE PATHOGENESIS OF PSEUDOMONAS AERUGINOSA INDUCED OTITIS MEDIA
Rahul Mittal (US)

11:43 - 11:50 AM
THE FIRST LARGE-SCALE ASSOCIATION STUDY FOR CHRONIC OTITIS MEDIA IDENTIFIES ASSOCIATION WITH THE LOCI TGIF1 AND FBXO11
Mahmood Bhutta (UK)

11:50 AM - 12:00 PM Q&A

12:00 PM **Lunch in Exhibit/Poster Hall**

1:30 PM **Special NIH Workshop: NIH Funding Opportunities & Grant Review**

Speakers:
Bracie Watson (US), NIH/NIDCD
Alberto Rivera-Rentas (US), NIH/NIDCD
Alexander Politis (US), NIH/CSR

2:30 PM **Podium 4: Pathogenesis 1**

Moderator: Wenzhou Hong (US)

Speakers:

2:30 - 2:37 PM
ROLES OF LUXS/AI-2 QUORUM SENSING REGULATION IN PNEUMOCOCCAL BIOFILM FORMATION, GENE EXPRESSION AND PATHOGENICITY IN OTITIS MEDIA
Wenzhou Hong (US)

2:37 - 2:44 PM
IMPACT OF EXPERIMENTAL OTITIS MEDIA TREATMENT ON CHINCHILLA MUCIN GENES
Joseph Kerschner (US)

2:44 - 2:51 PM
INTEGRATION HOST FACTOR AND EXTRACELLULAR DNA ARE RELEASED BY NON-TYPEABLE HAEMOPHILUS INFLUENZAE DURING GROWTH AND BIOFILM FORMATION
Joseph Jurcisek (US)

2:51 - 2:58 PM
ISOLATION AND CHARACTERIZATION OF MIDDLE EAR AND NASAL EPITHELIAL CELLS FOR DEVELOPMENT OF AN IN VITRO OTOPATHOGENIC INFECTION MODEL
Apoorva Mulay (UK)

2:58 - 3:05 PM
COMPUTATIONAL ANALYSIS OF SONOTUBOMETRY AND EUSTACHIAN TUBE FUNCTION
Justo Torres-Rodriguez (US)

3:05 - 3:15 PM Q&A

3:15 PM **Coffee Break in Exhibit/Poster Hall**

3:45 PM **Workshop 1 (B): Chinchilla Genomics**

Speakers:
Joseph Kerschner (US)
Mary Shimoyama (US)

5:30 PM **Poster Reception**

8:00 PM **Poster Reception Adjourns**

TUESDAY, JUNE 9 – 8:00 AM – 9:45 AM

CHERRY BLOSSOM BALLROOM
ALL ATTENDEES

8:00 AM **Plenary 2 (C): Current clinical practice guidelines for OM: opportunities, controversies and challenges**

Moderator: Richard Rosenfeld (US)

Speakers:

8:00 - 8:18 AM
SWEDISH NATIONAL GUIDELINES FOR MANAGEMENT OF AOM
Sten Hellström (Sweden)

8:18 - 8:36 AM
CURRENT GUIDELINES FOR OTITIS MEDIA
Richard Rosenfeld (US)

8:36 - 8:54 AM
THE DUTCH AOM GUIDELINE IN A HISTORIC PERSPECTIVE
Roger Damoiseaux (Netherlands)

8:54 - 9:12 AM
THE ITALIAN GUIDELINE ON ACUTE OTITIS MEDIA
Paola Marchisio (Italy)

9:12 - 9:30 AM
A BRIEF INTRODUCTION TO THE AAOHNS TYMPANOSTOMY TUBE CLINICAL PRACTICE GUIDELINE
David Tunkel (US)

9:30 - 9:45 AM Q&A

9:45 AM **Coffee Break in Exhibit/Poster Hall**

TUESDAY, JUNE 9 – 10:15 AM – 5:30 PM

CHERRY BLOSSOM BALLROOM
CLINICAL SCIENCE

10:15 AM **Minisymposium 3 (C): Complementary and alternative therapy for OM**

Moderators: Sujana Chandrasekhar (US), Tulio Valdez (US)

Speakers:

10:15 - 10:27 AM
INTRANASAL SURFACTANT FOR OTITIS MEDIA
Sujana Chandrasekhar (US)

10:27 - 10:39 AM
EFFECT OF ANTI-CD25 MONOCLONAL ANTIBODY ON CHRONIC OTITIS MEDIA IN MICE MODEL
Takashi Hirano (Japan)

10:39 - 10:51 AM
BREAKING DOWN THE NETS – NO EVIDENCE OF OTOTOXICITY WHEN DORNASE ALFA IS ADMINISTED AT THE TIME OF VENTILATION TUBE INSERTION
Ruth Thronton (Australia)

10:51 - 11:03 AM
CARTILAGE MYRINGOPLASTY COMBINED WITH TYPE TYMPANOPLASTY III IN THE TREATMENT OF ADHESIVE OTITIS MEDIA
Zhigang Zhang (China)

11:03 - 11:15 AM Q&A

11:15 AM Podium 6: Treatment 3

Moderator: Shi-Nae Park (South Korea)

Speakers:

11:15 - 11:22 AM
OFFICE INSERTION OF TYMPANOSTOMY TUBES WITHOUT ANESTHESIA IN YOUNG CHILDREN: SAFETY, TECHNIQUE, AND EXPERIENCE MANAGEMENT
Richard Rosenfeld (US)

11:22 - 11:29 AM
EFFECTS OF OXYMETAZOLINE ON THE BLOOD TO MIDDLE-EAR GAS EXCHANGE-RATE
Miriam Teixeira (US)

11:29 - 11:36 AM
EFFICACY OF TRANSTYMPANIC CIPROFLOXACIN GEL FORMULATION AGAINST EXPERIMENTAL OTITIS MEDIA IN A CHINCHILLA MODEL DUE TO NON TYPABLE HEMOPHILUS INFLUENZA
Vishakha Sabharwal (US)

11:36 - 11:43 AM
ANTIBIOTICS FOR ASYMPTOMATIC ACUTE OTITIS MEDAI (AAAOM): WILL THIS PREVENT POOR OUTCOMES IN AUSTRALIAN ABORIGINAL CHILDREN?
Amanda Leach (Australia)

11:43 - 11:50 AM
EFFICACY OF EUSTACHIAN BALLOON DILATION ON REFRACTORY CHRONIC OTITIS MEDIA WITH EFFUSION
Maojin Liang (China)

11:50 AM - 12:00 PM Q&A

12:00 PM **Lunch in Exhibit/Poster Hall**

1:30 PM **Panel 3 (C): Diagnosis**

Moderator: Mark Haggard (UK)

Panelists
Mark Haggard (UK)
Yasuaki Harabuchi (Japan)
Sun Jianjun (China)
Snezana Andric Filipovic (Serbia)

2:30 PM **Podium 8: Treatment 4**

Moderator: Sten Hellström (Sweden)

Speakers:

2:30 - 2:37 PM
A DELAYED HEALING OF TYMPANIC MEMBRANE PERFORATIONS IN DIABETIC MICE CAN BE CURED BY PLASMINOGEN
Sten Hellström (Sweden)

2:37 - 2:44 PM
INTACT EXTERNAL CANAL SLEEVE FLAP TECHNIQUE - A NEW MODIFIED TECHNIQUE OF OUTER SURFACE GRAFTING FOR TYMPANIC MEMBRANE RECONSTRUCTION BY POSTAURICULAR APPROACH
Sun Jianjun (China)

2:44 - 2:51 PM
COMPUTATIONAL MODELING OF SURFACTANT THERAPY ON EUSTACHIAN TUBE FUNCTION
Samir Ghadiali (US)

2:51 - 2:58 PM
COMPARISON BETWEEN THE ADULT AND CHILD MASTOIDITIS PATIENT – IS THERE A DIFFERENCE IN CLINICAL APPEARANCE?
Karin Stenfeldt (Sweden)

2:58 - 3:05 PM
CAREGIVER QUALITY OF LIFE AND DAILY FUNCTIONING IN RELATION TO VENTILATING TUBE TREATMENT
Christian Heidemann (Denmark)

3:05 - 3:15 PM Q&A

3:15 PM **Coffee Break in Exhibit/Poster Hall**

3:45 PM **Workshop 2 (C): OM Guidelines**

Speakers:
Richard Rosenfeld (US)
Stephanie Jones (AAO-HNS)

4:45 PM **Panel 6 (C): Family Medicine**

Moderator: Jørgen Lous (Denmark)

Panelists:
Jørgen Lous (Denmark)
Johanna Uitti (Finland)
Snezana Andric Filipovic (Serbia)

5:30 PM **Adjournment**

TUESDAY, JUNE 9 – 10:15 AM – 5:30 PM

BALTIMORE 3-5
BASIC SCIENCE

10:15 AM **Minisymposium 4 (B): Pathogenesis/Genetics**

Moderators: Mahmood Bhutta (UK), Anna Granath (Sweden)

Speakers:

10:15 - 10:27 AM
THE PHENOTYPE LANDSCAPE OF OTITIS MEDIA
Mahmood Bhutta (UK)

10:27 - 10:39 AM
NITRIC OXIDE IN THE HUMAN MIDDLE EAR MILIEU
Anna Granath (Sweden)

10:39 - 10:51 AM
UNRAVELING THE GENETICS/GENOMICS OF OTITIS MEDIA
Xuezhong Liu (US)

10:51 - 11:03 AM
ADAPTIVE IMMUNITY IN THE MIDDLE EAR MUCOSA OF THE MUTANT MICE WITH KNOCKOUT OF Id1 AND/OR Id3
Jizhen Lin (US)

11:03 - 11:15 AM Q&A

11:15 AM **Podium 7: Pathogenesis 2**

Moderator: Mahmood Bhutta (UK)

Speakers:

11:15 - 11:22 AM
EFFECT OF SUB-AMBIENT MIDDLE EAR PRESSURE AND HYPOXIC CONDTIONS ON PRO-INFLAMMATORY SIGNALING AND MUCIN GENE EXPRESSION
Natalia Higuita-Castro (US)

11:22 - 11:29 AM
REDUCTION CAPSULAR PRODUCTION OF S.PNEUMONIAE BY SUB-MIC LEVELS OF CLARITHROMYCIN.
Saori Takeda (Japan)

11:29 - 11:36 AM
THE EXPRESSION OF TREM-2 AND ITS BONE DESTRUCTION IN MIDDLE EAR CHOLESTEATOMA
Huaili Jiang (China)

11:36 - 11:43 AM
STABLE ISOTOPE LABELED BY AMINO ACID IN CULTURE (SILAC) STRATEGY TO ANALYZE HUMAN MIDDLE EAR EPITHELIAL CELLS (HMEEC) SECRETOME IN RESPONSE TO NTHI LYSATES
Stephanie Val (US)

11:43 - 11:50 AM
OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV): A RETROSPECTIVE MULTI-CENTER STUDY IN JAPAN -2) CLINICAL DIFFERENCES ACCORDING TO ANCAS-
Kaori Tateyama (Japan)

11:50 AM - 12:00 PM Q&A

12:00 PM **Lunch in Exhibit/Poster Hall**

1:30 PM **Panel 4 (B): Progress in understanding the role of viruses in OM pathogenesis**

Moderator: Janak Patel (US)

Panelists:
Janak Patel (US)
Terho Heikkinen (Finland)
Johanna Nokso-Koivisto (Finland)

2:30 PM **Podium 9: Immunology 1**

Moderator: Ann Hermansson (Sweden)

Speakers:

2:30 - 2:37 PM
AMPHIPHILIC Y-PGA NANOPARTICLES ADMINISTERED ON RAT MIDDLE EAR MUCOSA PRODUCE ADJUVANT-LIKE IMMUNOSTIMULATION IN VIVO
Ann Hermansson (Sweden)

2:37 - 2:44 PM
LACK OF NFκB PROLONGS PATHOGENIC RESPONSES AND PERMITS CO-INFECTION WITH NASOPHARYNGEAL BACTERIA DURING EXPERIMENTAL OTITIS MEDIA
Brian Nuyen (US)

2:44 - 2:51 PM
TLR4 DRIVES ACQUIRED CHOLESTEATOMA PATHOGENESIS BY PROMOTING LOCAL INFLAMMATION AND BONE DESTRUCTION
Yu Si (China)

2:51 - 2:58 PM
LYMPHOCYTES ASSOCIATED WITH ADAPTIVE IMMUNITY FROM THE ADENOIDS AND PERIPHERAL BLOOD OF CHILDREN FROM RURAL AUSTRALIA AND THE CORRELATION WITH CHRONIC OTITIS MEDIA OR ADENOID HYPERTROPHY
Jessica Browne (Australia)

2:58 - 3:05 PM
FUNCTIONAL DEFICITS OF CD4+ T CELLS IN YOUNG CHILDREN CONTRIBUTE TO THE RECURRENT OTITIS-PRONE CHILDREN
Saleem Basha (US)

3:05 - 3:15 PM Q&A

3:15 PM **Coffee Break in Exhibit/Poster Hall**

3:45 PM **Panel 5 (B): Pneumococcal Vaccine (PCV)**

Moderator: Stephen Pelton (US)

Panelists:
Stephen Pelton (US)
Michael Pichichero (US)
Ivo Vojtek (Belgium)

4:45 PM **Panel 7 (B): Microbial pathogenesis**

Moderator: Kevin Mason (US)

Panelists:
Jennelle Kyd (Australia)
Guanchun Bai (US)
Muneki Hotomi (Japan)

5:30 PM **Adjournment**

WEDNESDAY, JUNE 10 – 8:00 AM – 9:45 AM

CHERRY BLOSSOM BALLROOM
ALL ATTENDEES

8:00 AM **Plenary 3 (B): Vaccine**

Moderators: Lauren Bakaletz (US), Timothy Murphy (US)

8:00 - 8:05 AM
Introduction of Keynote Speaker by Lauren Bakaletz

Keynote Speaker:

8:05 - 8:30 AM Cecil Czerkinsky (Sweden)

8:30 - 8:35 AM Q&A

Speakers:

8:35 - 8:50 AM
CURRENT STATUS OF VACCINES FOR OTITIS MEDIA DUE TO NONTYPEABLE HAEMOPHILUS INFLUENZAE (NTHI)
Lauren Bakaletz (US)

8:50 - 9:05 AM
VACCINE DEVELOPMENT FOR MORAXELLA CATARRHALIS: RATIONALE, CHALLENGES AND CURRENT STATUS
Timothy Murphy (US)

9:05 - 9:20 AM
VACCINE POTENTIAL OF THE HMW1/HMW2 AND HIA PROTEINS OF NONTYPEABLE HAEMOPHILUS INFLUENZAE
Stephen Barenkamp (US)

9:20 - 9:35 AM
VIRAL VACCINES FOR OTITIS MEDIA
Tasnee Chonmaitree (US)

9:35 - 9:45 AM Q&A

9:45 AM **Coffee Break in Exhibit/Poster Hall**

WEDNESDAY, JUNE 10 – 10:15 AM – 5:30 PM

CHERRY BLOSSOM BALLROOM
CLINICAL SCIENCE

10:15 AM **Minisymposium 5 (C): Impact of OM on hearing and auditory function**

Moderators: Joseph Kerschner (US), Kenny Chan (US)

Speakers:

10:15 - 10:27 AM
IMPACT OF OTITIS MEDIA ON HEARING AND AUDITORY FUNCTION
Joseph Kerschner (US)

10:27 - 10:39 AM
OTITIS MEDIA AND HEARING LOSS IN EARLY PRIMARY SCHOOL GRADES: THE UNITED STATES EARLY CHILDHOOD LONGITUDINAL STUDY–KINDERGARTEN CLASS OF 2010–11 (ECLS–K:2011)
Howard Hoffman (US/NIDCD)

10:39 - 10:51 AM
A STRATEGY FOR IMPROVING PEDIATRICIANS DETECTION AND MANAGEMENT OF INFANTS "AT RISK" FOR SEVERE PATTERNS OF OTITIS MEDIA IN A TEACHING HOSPITAL
Andrés Sibbald (Argentina)

10:51 - 11:03 AM
DIFFERING SEASONALITIES OF HEARING MEASURES AND PARENT QUESTION RESPONSES REQUIRE SEASONAL ADJUSTMENT OF ANALYSES AND OF REFERRAL CRITERIA IN OM
Mark Haggard (UK)

11:03 - 11:15 AM Q&A

11:15 AM Podium 10: Vaccine 1

Moderator: Tal Marom (Israel)

Speakers:

11:15 - 11:22 AM
BACTERIOLOGY OF ACUTE OTITIS MEDIA IN YOUNG CHILDREN IN THE 7- AND 13-PNEUMOCOCCAL CONJUGATE VACCINES ERA IN CENTRAL ISRAEL
Tal Marom (Israel)

11:22 - 11:29 AM
DECREASE IN MYRINGOTOMIES TO THE PEDIATRIC PATIENTS WITH ACUTE OTITIS MEDIA AFTER INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINES IN JAPAN
Tatsuya Hayashi (Japan)

11:29 - 11:36 AM
REDUCED MIDDLE EAR INFECTION WITH NON-TYPEABLE H. INFLUENZAE, BUT NOT S. PNEUMONIAE, AFTER TRANSITION TO 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINE
Amanda Leach (Australia)

11:36 - 11:43 AM
SEROTYPES OF STREPTOCOCCUS PNEUMONIA IN 19 CASES OF ACUTE MASTOIDITIS IN SWEDEN IN RELATION TO PNEUMOCOCCAL VACCINATION
Frida Enoksson (Sweden)

11:43 - 11:50 AM
TRANSCUTANEOUS IMMUNIZATION WITH A TYPE IV PILUS AND OMP P5-TARGETED IMMUNOGEN BY BANDAID VACCINE PREVENTS THE ONSET OF NONTYPEABLE HAEMOPHILUS INFLUENZAE- INDUCED OTITIS MEDIA IN A POLYMICROBIAL MODEL OF DISEASE
Laura Novotny (US)

11:50 AM - 12:00 PM Q&A

12:00 PM Lunch in Exhibit/Poster Hall

1:30 PM Panel 8 (C): E Tube and Middle Physiology & Pathology

Moderators: Cuneyt Alper (US), William Doyle (US)

Panelists:
Cuneyt Alper (US)
William Doyle (US)
Samir Ghadiali (US)
Haruo Takahashi (Japan)

2:30 PM Podium 11: Vaccine 2/Diagnosis 1

Moderator: Snezana Andric Filipovic (Serbia)

Speakers:

2:30 - 2:37 PM
OTITIS MEDIA AND VACCINATION IMPACT – COMPARISON OF 7 AND 10 VALENT CONJUGATED PNEUMOCOCCAL VACCINATED COHORTS
Nikki Mills (New Zealand)

2:37 - 2:44 PM
Otopathogens Causing ACUTE OTITIS MEDIA IN THE 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ERA
Janet Casey (US)

2:44 - 2:51 PM
HEARING MAPS: CHILDREN'S PERCEPTIONS OF HEARING FUNCTIONALITY IN DIFFERENT ENVIRONMENTS
Carmel Capewell (UK)

2:51 - 2:58 PM
OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV): A RETROSPECTIVE MULTI-CENTER STUDY IN JAPAN – 4) AUDIOLOGICAL FINDINGS AND OUTCOME
Naohiro Yoshida (Japan)

2:58 - 3:05 PM
CAN LAYMAN PARENTS USE SPECTRAL GRADIENT ACOUSTIC REFLECTOMETRY RELIABLY?
Nora Erkkola-Anttinen (Finland)

3:05 - 3:15 PM Q&A

3:15 PM Coffee Break in Exhibit/Poster Hall

3:45 PM Podium 13: Diagnosis 2

Moderator: Paola Marchisio (Italy)

Speakers:

3:45 - 3:52 PM
CERUMEN IN CHILDREN: A NEGLECTED BUT FUNDAMENTAL PROBLEM
Paola Marchisio (Italy)

3:52 - 3:59 PM
OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV): A RETROSPECTIVE MULTICENTER STUDY IN JAPAN
Kan Kishibe (Japan)

3:59 - 4:06 PM
LOW PREDICTIVE VALUE OF R-VALUE OF TUBOMANOMETRY IN ASSESSING THE PRESENCE AND THE DEGREE OF MIDDLE EAR PRESSURE CHANGE WITH EUSTACHIAN TUBE OPENING
Jeehong Kim (US)

4:06 - 4:13 PM
SMARTPHONE-BASED FIELD SCREENING DEVICES ENABLING SCALEABLE AND STANDARDIZED DIAGNOSIS, REFERRAL, AND TREATMENT OF OTITIS MEDIA IN UNDERSERVED PATIENT COMMUNITIES IN INDIA AND BANGLADESH
Joseph Kerschner (US)

4:13 - 4:20 PM
CRANIOFACIAL MORPHOLOGY IN CHILDREN WITH AND WITHOUT OTITIS MEDIA
Allison Cullen Doyle (US)

4:20 - 4:27 PM
NONINVASIVE REAL-TIME OPTICAL MEASUREMENTS OF THE TYMPANIC MEMBRANE AND MIDDLE EAR FOR CHARACTERIZATION AND DIAGNOSIS OF OTITIS MEDIA
Guillermo Monroy (US)

4:27 - 4:34 PM
ASSESSMENT AND MANAGEMENT OF CHILDREN AND ADULTS WITH EUSTACHIAN TUBE DYSFUNCTION IN A SPECIALTY CLINIC SETTING
Beverly Richert (US)

4:34 - 4:45 PM Q&A

4:45 PM **Podium 15: Diagnosis 3**

Moderator: Sara Torretta (Italy)

Speakers:

4:45 - 4:52 PM
MEASURED TRANSMUCOSAL SPECIES EXCHANGE-CONSTANTS FOR THE HUMAN MIDDLE EAR
John Swarts (US)

4:52 - 4:59 PM
EUSTACHIAN TUBE FUNCTION IN 6-YEAR-OLD CHILDREN WITH AND WITHOUT A HISTORY OF MIDDLE-EAR DISEASE
Ellen Mandel (US)

4:59 - 5:06 PM
A METHOD TO QUANTITATIVELY DESCRIBE RELATIONAL MOVEMENTS OF EUSTACHIAN TUBE COMPONENTS RECORDED DURING TRANS-NASAL VIDEO-ENDOSCOPY
Selma Cetin-Ferra (US)

5:06 - 5:13 PM
OTITIS MEDIA AND CAREGIVER QUALITY OF LIFE: PSYCHOMETRIC PROPERTIES OF THE DANISH VERSION OF CAREGIVER IMPACT QUESTIONNAIRE
Christian Heidemann (Denmark)

5:13 - 5:20 PM
CLINICAL PRACTICE GUIDLINE FOR THE DIAGNOSIS AND MANAGEMENT OF OTITIS MEDIA WITH EFFUSION (OME) IN CHILDREN IN JAPAN -2015
Makoto Ito (Japan)

5:20 - 5:30 PM Q&A

5:30 PM Adjournment

WEDNESDAY, JUNE 10 – 10:15 AM – 5:30 PM

BALTIMORE 3-5
BASIC SCIENCE

10:15 AM Minisymposium 6 (B): Innate Immunity

Moderators: Allen Ryan (US), Allan Cripps (Australia)

10:15 - 10:20 AM
Introduction of Keynote Speaker by Allen Ryan

Keynote Speaker:

10:20 - 10:45 AM
THE GENETICS OF BITTER TASTE IN UPPER AIRWAY INFECTIONS
Noam Cohen (US)

10:45 - 10:50 AM Q&A

Speakers:

10:50 - 11:05 AM
CONTRIBUTIONS OF THE NOD-LIKE FAMILY OF INNATE IMMUNE RECEPTORS TO OTITIS MEDIA
Allen Ryan (US)

11:05 - 11:20 AM
INNATE IMMUNITY IN THE MIDDLE EAR
Allan Cripps (Australia)

11:20 - 11:35 AM
REGULATION OF INNATE IMMUNITY AND INFLAMMATION AND NOVEL ANTI-INFLAMMATORY STRATEGIES
Jian-Dong Li (US)

11:35 - 11:50 AM
IMMUNE DYSFUNCTION IN OTITIS PRONE CHILDREN
Michael Pichichero (US)

11:50 AM - 12:00 PM Q&A

12:00 PM **Lunch in Exhibit/Poster Hall**

1:30 PM **Panel 9 (B): Animal Model**

Moderator: Allan Ryan (US)

Panelists
Jae Hyang Lim (South Korea)
Stephen Wasserman (US)
Qing Zheng (US)
Alistair Harrison (US)

2:30 PM **Podium 12: Immunology 2**

Moderator: Sung Moon (US)

Speakers:

2:30 - 2:37 PM
RESPONSE OF COCHLEAR CELLS TO OTITIS MEDIA PATHOGENS
Sung Moon (US)

2:37 - 2:44 PM
PROTEOMIC CHARACTERIZATION OF MIDDLE EAR EFFUSION PROTEINS FROM CHILDREN WITH CHRONIC OTITIS MEDIA: IMPORTANCE OF NEUTROPHIL EXTRACELLULAR TRAPS IN THE EAR MUCOSAL IMMUNITY
Stephanie Val (US)

2:44 - 2:51 PM
LEUKOTRIENE B4 CONTRIBUTES TO NEUTROPHIL RECRUITMENT DURING OTITIS MEDIA
Kyung Wook Heo (US)

2:51 - 2:58 PM
DEFINING THE FUNCTIONAL EPITOPES OF INTEGRATION HOST FACTOR (IHF) TO DEVELOP A NOVEL BIOFILM-FOCUSED IMMUNOTHERAPEUTIC AGAINST NONTYPEABLE HAEMOPHILUS INFLUENZAE-INDUCED CHRONIC AND RECURRENT OTITIS MEDIA
Laura Novotny (US)

2:58 - 3:05 PM
A PHASE VARIABLE DNA METHYLTRANSFERASE FACILITATES ADAPTATION AND SURVIVAL OF NONTYPEABLE HAEMOPHILUS INFLUENZAE WITHIN THE MIDDLE EAR VIA ALTERED BIOFILM FORMATION
Kenneth Brockman (US)

3:05 - 3:15 PM Q&A

3:15 PM Coffee Break in Exhibit/Poster Hall

3:45 PM Podium 14: Microbiology 1

Moderator: Stephen Barenkamp (US)

Speakers:

3:45 - 3:52 PM
Resistance patterns OF STREPTOCOCCUS PNEUMONIAE ISOLATED FROM MIDDLE EAR FLUID IN CHILDREN WITH SEVERE ACUTE OTITIS MEDIA
Tal Marom (Israel)

3:52 - 3:59 PM
LACK OF MIDDLE EAR VIRULENCE OF STREPTOCOCCUS PNEUMONIAE 33F ISOLATES IN CHINCHILLAS IS ASSOCIATED WITH ABSENCE OF SPECIFIC TOXIN-ANTITOXIN SYSTEMS AND THE PNEUMOCOCCAL SERINE-RICH PROTEIN (PSRP) PATHOGENICITY ISLAND
Sabine Schnyder (US)

3:59 - 4:06 PM
Identifying determinants OF AI-2 QUORUM SIGNAL UPTAKE IN NONTYPEABLE HAEMOPHILUS INFLUENZAE 7P49H1
W. Edward Swords (US)

4:06 - 4:13 PM
BACTERIAL OPRF EXPRESSION HELPS IN THE SURVIVAL OF OTOPATHOGENIC PSEUDOMONAS AERUGINOSA INSIDE MACROPHAGES
Christopher Lisi (US)

4:13 - 4:20 PM
RISK FACTORS FOR PERSISTENT NASOPHARYNGEAL CARRIAGE OF STREPTOCOCCUS PNEUMONIAE
Paula Tähtinen (US)

4:20 - 4:27 PM
THE TYPE IV PILUS OF NONTYPEABLE HAEMOPHILUS INFLUENZAE IS MORE HIGHLY EXPRESSED IN BIOFILMS FORMED AT THE TEMPERATURE OF THE HUMAN NASOPHARYNX THAN AT 37°C, AND IS REQUIRED FOR BIOFILM TOWER FORMATION
Elaine Mokrzan (US)

4:27 - 4:34 PM
INCREASED MUCIN GENE EXPRESSION IS ASSOCIATED WITH HEARING LOSS IN PEDIATRIC OTITIS MEDIA PATIENTS
Justin Yan (US)

4:34 - 4:45 PM Q&A

4:45 PM **Podium 16: Microbiology 2**

Moderator: Anders P Hakansson (Sweden)

Speakers:

4:45 - 4:52 PM
PREDOMINANT BACTERIA AND VIRUSES LOCATED WITHIN THE UPPER RESPIRATORY TRACT AND MIDDLE EARS OF AUSTRALIAN URBAN CHILDREN EXPERIENCING OTITIS MEDIA
Chinh Ngo (Australia)

4:52 - 4:59 PM
UPPER RESPIRATORY TRACT VIRAL INFECTIONS, NASOPHARYNGEAL BACTERIAL COLONIZATION AND ACUTE OTITIS MEDIA IN THE FIRST YEAR OF LIFE
Tasnee Chonmaitree (US)

4:59 - 5:06 PM
EFFECT OF TNFa-308 AND IL-6-174 GENE POLYMORPHISMS ON NASOPHARYNGEAL COLONIZATION WITH OTOPATHOGENIC BACTERIA IN THE FIRST MONTHS OF LIFE
Janak Patel (US)

5:06 - 5:13 PM
INTRACELLULAR BACTERIAL COMMUNITY DEVELOPMENT IN NONTYPEABLE HAEMOPHILUS INFLUENZAE (NTHI) SURVIVAL AND PATHOGENESIS
Rachael Hardison (US)

5:13 - 5:20 PM
BIOFILM FORMATION BY NONTYPEABLE HAEMOPHILUS INFLUENZAE (NTHI) GROWING ON HUMAN NASOPHARYNGEAL CELLS
Robert Osgood (US)

5:20 - 5:30 PM Q&A

5:30 PM **Adjournment**

THURSDAY, JUNE 11 – 8:00 AM – 9:45 AM

CHERRY BLOSSOM BALLROOM
CLINICAL SCIENCE

8:00 AM **Minisymposium 7 (C): Developmental and learning sequelae of OM**

Moderators: Mark Haggard (UK), Jørgen Lous (Denmark)

Speakers:

8:00 - 8:18 AM
COMPREHENSIVE EVIDENCE-BASED MODEL FOR DEVELOPMENTAL IMPACT FROM SPECIFIC DISEASE FACETS IN OTITIS MEDIA
Mark Haggard (UK)

8:18 - 8:36 AM
DEVELOPMENTAL AND LEARNING SEQUELAE OF OTITIS MEDIA; REVIEW OF RESULTS FROM DANISH COHORT STUDIES
Jørgen Lous (Denmark)

8:36 - 8:54 AM
A REPORT CARD: ANALYSIS OF PUBLICATIONS CONCERNING OTITIS MEDIA 1875 TO 2015, AND CONSIDERATION OF THEIR EFFECTIVENESS
Robert Ruben (US)

8:54 - 9:12 AM
EAR INFECTION PREVALENCE AND RISK FACTORS IN PRE-SCHOOL AGED CHILDREN: THE UNITED STATES EARLY CHILDHOOD LONGITUDINAL STUDY–BIRTH COHORT: 2001 (ECLS–B:2001)
Chuan-Ming Li (US)

9:12 - 9:30 AM
RISK FACTORS FOR CHRONIC AND RECURRENT OTITIS MEDIA—A META-ANALYSIS
Yan Zhang (China)

9:30 - 9:45 AM Q&A

9:45 AM **Coffee Break in Cherry Blossom Foyer**

THURSDAY, JUNE 11 – 8:00 AM – 9:45 AM

BALTIMORE 3-5
BASIC SCIENCE

8:00 AM **Minisymposium 8 (B): Drug delivery to middle ear and innovative therapies**

Moderators: Steve Brown (UK), Anthony Campagnari (US)

8:00 - 8:05 AM
Introduction of Keynote Speaker by Steve Brown

Keynote Speaker:

8:05 - 8:30 AM
TRANS-TYMPANIC DELIVERY OF ANTIBIOTICS
Daniel Kohane (US)

8:30 - 8:35 AM Q&A

Speakers:

8:35 - 8:50 AM
NOVEL MOUSE MODELS OF CHRONIC OTITIS MEDIA (COME) IDENTIFY VEGF PATHWAYS AS A CRITICAL TARGET: TOWARDS NEW THERAPIES FOR OM
Steve Brown (UK)

8:50 - 9:05 AM
PHOTODYNAMIC THERAPY AND OTITIS MEDIA
Anthony Campagnari (US)

9:05 - 9:20 AM
THERAPEUTIC POTENTIAL OF ADENOVIRUS-MEDIATED DELIVERY OF β-DEFENSIN 2 FOR EXPERIMENTAL OTITIS MEDIA
Sung Moon (US)

9:20 - 9:35 AM
A NEW THERAPY ALLEVIATES STREPTOCOCCAL PEPTIDOGLYCAN POLYSACCHARIDE (PGPS)-INDUCED OTITIS MEDIA IN TLR2-DEFICIENT HOSTS
Qing Zheng (US)

9:35 - 9:45 AM Q&A

9:45 AM **Coffee Break in Cherry Blossom Foyer**

THURSDAY, JUNE 11 – 10:15 AM – 12:00 PM

CHERRY BLOSSOM BALLROOM
ALL ATTENDEES

10:15 AM **Plenary 4 (B): OMICS**

Moderators: Garth Ehrlich (US), Melinda Pettigrew (US)

Speakers:

10:15 - 10:30 AM
A MULTI-NEXT-GENERATION DNA SEQUENCING PLATFORM APPROACH TO STUDY BACTERIAL POPULATION EVOLUTION IN SITU
Garth Ehrlich (US)

10:30 - 10:45 AM
TRANSCRIPTIONAL PROFILING OF OTITIS MEDIA PATHOGENS: THE TRANSITION FROM COLONIZATION TO DISEASE
Melinda Pettigrew (US)

10:45 – 11:00 AM
A Proteomic CHARACTERIZATION OF CHRONIC OTITIS MEDIA: IS MUC5B FRIEND OR FOE?
Diego Preciado (US)

11:00 – 11:15 AM
DEFINING GENETIC RISK OF CHRONIC OTITIS MEDIA WITH EFFUSION AND/OR RECURRENT OTITIS MEDIA: A GENOME-WIDE ASSOCIATION FOLLOW-UP STUDY
Michele Sale (US)

11:15 – 11:25 AM Q&A

11:25 – 11:30 AM
Introduction of Keynote Speaker by Garth Ehrlich

Keynote Speaker:

11:30 – 11:55 AM
EXPLORING THE DARK MATTER OF THE HUMAN GENOME
Axel Visel (US)

11:55 AM – 12:00 PM Q&A

12:00 PM **Closing Remarks & Symposium Adjournment**

MONDAY SCIENTIFIC PRESENTATIONS

8:00 - 8:30 AM **MONDAY, JUNE 8**

CHERRY BLOSSOM BALLROOM

WELCOME & SPECIAL REMARKS

Welcome

Richard Rosenfeld, M.D., MPH, President, ISOM (US)

Special Remarks

Bracie Watson, Ph.D. Program Director, NIH/NIDCD (US)

Announcement of OM2017

Allan Cripps, Ph.D. (Australia)

Program Overview

Jian-Dong Li, M.D., Ph.D., Chair, Program Committee (US)

8:30 - 9:45 AM **MONDAY, JUNE 8**

CHERRY BLOSSOM BALLROOM

PLENARY SESSION 1 (C): CSOM

Moderators:

Tania Sih (Brazil)

Stephen Pelton (US)

Speakers:

Tania Sih (Brazil)

Stephen Pelton (US)

Ramon Jensen (Denmark)

Anna Stephen (Australia)

8:30 - 8:45 AM **MONDAY, JUNE 8**

OM2015190

IS CHRONIC SECRETORY OTITIS MEDIA A SOCIAL DISEASE?

Tania Maria Sih, M.D., Ph.D. *Presenter*

University Of Sao Paulo, ENT, Sao Paulo, SP, Brazil

Acute otitis media (AOM) when not judiciously managed could lead to a series of events, culminating in chronic secretory otitis media (CSOM), draining ears (persistent otorrhea) and hearing impairment. In poor rural areas, and also in rings of poverty that usually surrounds big cities, access to general health care is difficult and not always feasible. The prevalence of middle ear disease is high among certain populations, such as Inuits, Aborigines and Native Americans. Racial and ethnic factors as well as socio-economic conditions may contribute to this condition. Besides these populations, CSOM and otorrhea are very common in poor regions, either in rural as well in poor urban areas. Studies on the prevalence of CSOM in Angola, Brazil, Tanzania and Fillipines showed a close relation to poor socioeconomic living conditions. There is a strong relation between CSOM, draining ears and poverty. Chronic otitis media is more common among children in a socioeconomically underprivileged district than among those with better living conditions. Deficient hygiene and dietary habits, impaired immunological conditions and poor medical access make the clinical resolution of CSOM worse. In these cases, a cascade of middle ear events takes to CSOM. Aural toilette and eardrops with antimicrobials (quinolones are recommended) are usually the treatment of choice for CSOM. CSOM may also be accompanied by cholesteatoma, retraction pockets, granulomas with severe mucosal changes, total tympanic membrane perfurations, ossicular destructions, etc, mandating surgery for these conditions. If underprivileged population groups do not have easy access to clinical medical care, operating rooms are many times a utopia. Even with hospital access, the waiting lines for surgeries are often so long that very few patients can truly access treatment. Some pedagogical activities using Internet, creating / implementing Ear Care By YouTube for instance, are also very useful tools. In conclusion, health services should be improved not only in rural areas, but also in cities to facilitate treating and diagnosing acute otitis media in primary care. These improvements can help prevent hearing impairment caused by CSOM. The use of mHealth might also be a fruitful opportunity to decrease the burden of this disease.

8:45 - 9:00 AM **MONDAY, JUNE 8**

OM2015324

EPIDEMIOLOGY AND PATHOGENESIS OF CHRONIC SUPPURATIVE OTITIS MEDIA: IMPLICATIONS FOR PREVENTION AND TREATMENT REVISITED

Stephen I Pelton, M.D.[1] *Presenter*

Ron Dagan, M.D.[2]

[1]*Boston University, Pediatric Infectioius Disesaes/Pediatrics/School Of Medicine, Boston, MA, USA*
[2]*Soroka University Medical Center And The Faculty Of Health Sciences, Pediatric Infectious Diseases/Pediatrics/Health Sciences, Beer Sheva, Israel*

Chronic suppurative otitis media (CSOM) is a global burden on child health and a major impediment to future success in society as it is associated with mild to moderate hearing loss in 50% of cases. Its origins are multifactorial with early onset of middle ear disease, inadequate antibiotic treatment, recurrent respiratory tract infections and poor living conditions with poor access to medical care each contributing to the development of CSOM. Early onset of bacterial middle ear disease has the potential to initiate a cascade of events with the development of bacterial biofilms, persistent inflammation, chronic perforation with intermittent drainage and eventually disruption of the ossicular chan. Risk factors for early onset disease include genetic susceptibility, lack of breast feeding, early colonization with otopathogens, and impaired host defenses. This presentation will focus on the evolving understanding of how such risk factors contribute to the pathogenesis of early OM and subsequent progression to CSOM. It will focus on new strategies that offer the potential to modify the cascade of events and specifically the potential role of current and future vaccines to interrupt progression along the continuum.

9:00 - 9:15 AM **MONDAY, JUNE 8**

OM2015161

RECURRENT OTORRHEA IN CHRONIC SUPPURATIVE OTITIS MEDIA – IS BIOFILM THE MISSING LINK?

Ramon Gordon Jensen, Ph.D.[1] *Presenter*

Preben Homøe[2]

[1]*Copenhagen University Hospital, Department Of Otorhinolaryngology, Head And Neck Surgery, Copenhagen, 1366, Denmark*
[2]*Køge University Hospital, Department Of Otorhinolaryngology And Maxillofacial Surgery, Køge, 4600, Denmark*

Objective: Investigate if the same genotypes of bacteria are detected in repeated episodes of otorrhea in chronic suppurative otitis media, as a possible proof of dispersion from a biofilm.

Method: Population-based prospective case serie in a primary healthcare clinic in Nuuk, Greenland. Patients with more than 14 days of otorrhea were included consecutively. Samples for culturing and biofilm analysis were taken at enrollment. Participants were treated with daily saline irrigation and Ciprofloxacin eardrops for seven days. At any subsequent episode with otorrhea new samples were taken for biofilm analysis, culturing and subtyping.

Results: Biofilm was identified in otorrhea in 17 out of 21 (81%) participants at enrollment. Multispecies infections dominated with Nontypeable Haemophilus Influenzae (NTHI), Staphyloccocus aureus and anaerobes being the most frequent pathogens. After initial treatment 19 (90%) had dry ears. Median observation period was 140 days (range 14-260 days) where 13 participants had one or more recurrences. Median time to first recurrence was 60 days (range 14-197 days). Among the 13 with recurrence three individuals had the same genotype of bacteria at a subsequent episode. Another two had the same phenotype (NTHI). The remaining had new multispecies infections.

Conclusion: We confirmed a high rate of biofilm in CSOM. Multispecies biofilm could explain some of the reurrences. However, the clinical implication of biofilm presence might be of minor importance when treating with irrigation and Ciprofloxacin eardrops as recurrent episodes of otorrhea were dominated by new pathogens in each episode.

9:15 - 9:30 AM **MONDAY, JUNE 8**

OM2015332

COMMUNITY-LEVEL SOCIAL AND ENVIRONMENTAL RISK FACTORS ASSOCIATED WITH CHRONIC SUPPURATIVE OTITIS MEDIA IN 26 REMOTE ABORIGINAL COMMUNITIES IN NORTHERN AUSTRALIA

Anna Stephen *Presenter*

Amanda Leach
Federica Barzi
Matthew Stevens
Peter Morris

Menzies School Of Health Research, Darwin, NORTHERN TERRITORY, Australia

Aim: To investigate the relationship between prevalence of severe ear infection and social and environmental risk factors in remote Aboriginal communities.

Methods: Clinical data from a cross-sectional survey of 1346 children (6–30 months of age) from 26 communities were correlated with community-level social and environmental data from the Australian Census and the Community Housing and Infrastructure Survey. Risk factors assessed include: access to a child care facility, women's centre, swimming pool, ocean, doctor, nurse, Aboriginal Health Worker, an ENT specialist and an ear health program; distance to a hospital; mean family income; percentage of adults with no schooling;, mean number of people per dwelling; and number of permanent dwellings. Tympanometry and video-otoscopy were used in ear assessments. Random effects logistical modeling adjusting for age and clustering was used with a statistical significance of $P = 0.05$.

Results: Prevalence of tympanic membrane perforation (TMP) ranged from 0 to 47% (mean = 27%, SD = 11%). Factors found to be significantly associated with TMP in our multivariate model included: mean number of people per house ≥ 7 OR: 0.52(95%CI: 0.54 – 0.66), daily access to a doctor OR: 1.88(1.32 – 2.66), access to the ocean OR: 0.68(0.53 – 0.87) and access to a swimming pool OR: 0.41(0.27 – 0.63).

Conclusion: We found that access to the ocean, or a swimming pool, a mean household size ≥ 7 people and less than daily access to a doctor was associated with significantly lower odds of TMP. These findings suggest that there is potential for community wide interventions to prevent CSOM in remote Aboriginal communities.

9:45 - 10:15 AM **MONDAY, JUNE 8**

EXHIBIT HALL A

COFFEE BREAK IN EXHIBIT/POSTER HALL

10:15 - 11:15 AM **MONDAY, JUNE 8**

CHERRY BLOSSOM BALLROOM

MINISYMPOSIUM 1 (C): GLOBAL DIFFERENCES IN OM

Moderators:

Margaretha Casselbrant (US)

Vedantam Rupa (India)

Speakers:

Margaretha Casselbrant (US)

Vedantam Rupa (India)

Mahmood Bhutta (UK)

10:15 - 10:31 AM **MONDAY, JUNE 8**

OM2015199

OTITIS MEDIA FROM A GLOBAL PERSPECTIVE

Margaretha L Casselbrant, M.D.,Ph.D.[1,2] *Presenter*

[1]*University Of Pittsburgh School Of Medicine, Department Of Otolaryngology, Piitsburgh, PA, USA*
[2]*Children's Hospital Of Pittsburgh Of UPMC, Division Of Pediatric Otolaryngology, Pittsburgh, PA, USA*

Background: Otitis media in children is a worldwide problem and accounts for a substantial proportion of health care visits, complications, sequelae, and direct and indirect health care costs. However, the presenting signs and symptoms, as well as the course of the disease, may vary significantly between developed and developing countries. The main differences in the burden of disease across countries are caused by the frequency of suppurative complications such as mastoiditis, meningitis and intracranial abscesses and sequelae such as hearing loss due to chronic suppurative otitis media (CSOM). The hearing loss, which is preventable, may have long-term effects on early language development and learning and may prevent the child from reaching its full potential. Children in the poorest countries are at the highest risk during their first five years of life. WHO estimates that 65 to 330 million individuals suffer from CSOM and 50% of these individuals suffer from hearing impairment. While in the industrial countries there is an urgency to reduce the unnecessary prescription of antibiotics to prevent further increase in antibiotic resistance, prevention of complications and sequelae is of major importance in the developing countries.

Conclusions: Immunization with existing and future viral and bacterial vaccines may be the most promising means to affect disease burden and its consequences, both in developed and developing countries which will be discussed.

10:31 - 10:47 AM **MONDAY, JUNE 8**

OM2015091

EPIDEMIOLOGY OF ACUTE SUPPURATIVE OTITIS MEDIA IN THE FIRST 2 YEARS OF LIFE IN INDIAN INFANTS

Vedantam Rupa, M.D. , M.S., D.L.O.[1] *Presenter*

Rita Isaac [2]
Anand Manoharan [4]
Grace Rebekah, MSc[3]

[1]*Christian Medical College, Vellore, Otorhinolaryngology, Vellore, TAMIL NADU, India*
[2]*Christian Medical College, Vellore, RUHSA, Community Health, Vellore, TAMIL NADU, India*
[3]*Christian Medical College, Vellore, Biostatistics, Vellore, TAMIL NADU, India*
[4]*Pushpagiri Medical College, Microbiology, Thiruvalla, KERALA, India*

Background: Despite the fact that the prevalence of otitis media is high in India, there are no community – based studies regarding the epidemiology of acute suppurative otitis media (ASOM) in Indian children.

Objective: To study the epidemiology of acute suppurative otitis media (ASOM) in the first 2 years of life in a birth cohort

Method: We collected baseline sociodemographic data and followed up a birth cohort of 210 babies every month by performing otoscopy, clinical examination and nasopharyngeal swabbing to determine the presence of ASOM and colonization by S.pneumoniae. Babies were also seen at sick visits in between scheduled visits and similar examination was performed.

Results: Parents of babies were laborers (68.1%), had at least high school education (86.7%) and did not smoke (92.9%). Sixty babies (28.5%) experienced 212 episodes of ASOM [R.R= 2.63 (95% C.I. = 1.21-5.75)] with maximum incidence in the second half of the first year of life. All episodes of ASOM were associated with upper respiratory infection. Affected babies experienced 1-12 episodes of ASOM (mean=1.01). Most episodes occurred in winter (p=0.000). ASOM was also associated with nasopharyngeal colonization by S.pneumoniae (p=0.029). Serotype distribution in those with and without ASOM was significantly different (0.007).

Conclusion: The incidence of ASOM in Indian babies, although high, is somewhat less than in published Western studies suggesting possible asymptomatic disease. There is a strong association between ASOM incidence and winter season and S.pneumoniae colonization. Pneumococcal vaccination and public health measures may be required to reduce the burden of otitis media in this age group.

10:47 - 11:03 AM **MONDAY, JUNE 8**

OM2015295

EVOLUTIONARY FORCES IN OTITIS MEDIA: AN OVERVIEW AND AN EXPLANATION FOR THE HIGH PREVALENCE IN INDIGENOUS POPULATIONS

Mahmood F Bhutta, M.D.,Ph.D. *Presenter*

University College London, Ear Institute, London, United Kingdom

Heritability of recurrent acute otitis media (rAOM) in white infants is moderate and estimated at 0.49. In chronic otitis media with effusion (COME), time with effusion has high heritability of 0.73. Otitis media (OM) can also affect reproductive fitness. Global deaths from OM are estimated at 28,000 annually. Chronic OM can affect hearing, which will also affect reproductive fitness, although this is difficult to quantify. Because OM is heritable and can affect evolutionary fitness, it will be subject to natural selection. At first it may seem that this would mean OM should be rare in man, but it is not, and that is because of complex trade-offs in host-pathogen evolutionary co-dynamics. I will critically analyse selection forces that may determine susceptibility to OM, including those determining function of the middle ear, those affecting host immunity, and those affecting microbial colonization and pathogenicity. I review existing models of host-pathogen interaction to develop an understanding of the complex evolutionary landscape of middle ear infection and inflammation in man. Then, I will apply principles of population genetics to devise a new theory for the high prevalence of OM in certain indigenous populations: the Australian Aborigine, the Native American, the Inuit, and the Maori. I suggest high prevalence in such groups occurred as a result of colonization of previously isolated populations by Europeans in the 15th and 16th Centuries. This exposed them to new strains of bacteria to which their immune system had not evolved immunity, perturbing a previously stable host-pathogen co-evolutionary state.

11:15 AM - 12:00 PM **MONDAY, JUNE 8**

CHERRY BLOSSOM BALLROOM

PODIUM 1: TREATMENT 1

Moderator:

Anna Granath (Sweden)

Speakers:

Anna Granath (Sweden)
Mallory O'Neil (US)
Marisol Figueira (US)
Misha Verkerk (UK)
Thijs Van Dongen (Netherlands)

11:15 - 11:22 AM **MONDAY, JUNE 8**

OM2015302

EVIDENCE BASED TUBE TREATMENT-ARE WE WORKING ACCORDING TO PLAN? SWEDISH NATIONAL GUIDELINES AND NATIONAL REGISTRY FOR TUBE TREATMENT

Anna Granath, M.D.,Ph.D.[1] *Presenter*

Karin Stenfeldt, M.D.,Ph.D.[2]
Finn Jorgensen, M.D.,Ph.D.[4]
Ingrid Augustsson, M.D.,Ph.D.[3]
Claes Hemlin, M.D.,Ph.D.[1]
Sten Hellström, Professor[1]

[1]*Karolinska Institutet, Department Of Clinical Science, Intervention And Technology, Stockholm, Sweden*
[2]*SkÂne University Hospital, Department Of Audiology, Lund, Sweden*
[3]*Orebro University Hospital, Department Of Otorhinolaryngology, Orebro, Sweden*
[4]*Hallands Hospital Halmstad, Department Of Otorhinolaryngology, Halmstad, Sweden*

In 2008 the Swedish Council on Health Technology Assessment (SBU) initiated a systematic review on tube treatment in recurrent acute otitis media (rAOM) and otitis media with effusion (OME). Based on this report national guidelines for tube treatment were drawn up. As a result of this the national registry for tube treatment was revised and later rebooted in 2013. The treatment guidelines include recommendations for hearing tests before and after tube insertion in cases of OME. Data extracted from the new registry on hearing results and patients satisfaction are now being reviewed .There is still potential for improvement towards compliance to the guidelines and increased awareness on evidence based decision making in tube treatment.

11:22 - 11:29 AM **MONDAY, JUNE 8**

OM2015040

OTITIS MEDIA OUTCOMES DATABASE

Mallory B O'Niel, M.D. Presenter

Laura Cassidy
T. Roxanne Link, APNP
Joseph E Kerschner, FACS, FAAP

Medical College Of Wisconsin, Otolaryngology, Milwaukee, WI, USA

Objective: To implement a database for children with a diagnosis of otitis media (OM) to enable comparative outcomes and long-term prospective follow-up.

Method: A customized database was constructed to enroll all patients seen in consultation with a diagnosis of OM in a web-based format. Unique database fields include demographics, physical exam findings, risk factors, intervention, and long-term outcomes. Major surgical complications measured include: early extrusion, tympanic membrane perforation, retained tubes, chronic otorrhea, and cholesteatoma formation.

Results: 634 unique patients have been prospectively enrolled. 544 tubes have been followed from placement to extrusion. Outcomes demonstrate high prevalence of OM risk factors associated with surgical patients including 63% in daycare and 26% with a sibling requiring tympanostomy tubes. Identified complications include 1% developing perforations requiring surgical intervention, 2.6% requiring removal of retained tubes, 1% extruding early (<60 days), and 0.7% surgically removed for other complications. Cholesteatoma was identified in 0.56%, all had on going chronic ear disease.

Conclusion: Long-term, outcome driven investigations assessing the surgical management of OM are needed given the prevalence of this disease and the frequency of surgical intervention required. The current database represents the largest prospective cohort of patients enrolled and followed in this fashion and has generated data demonstrating a procedure associated with significant improvement in patient quality of life in the short-term with low complication rates in the long-term (~5%). This ongoing prospective investigation is providing data with the potential to be important in treatment algorithms, procedure justification and risk factor modification.

11:29 - 11:36 AM **MONDAY, JUNE 8**

OM2015073

EFFICACY OF SOLITHROMYCIN (CEM-101), FOR EXPERIMENTAL OTITIS MEDIA (EOM) DUE TO EITHER NONTYPEABLE HAEMOPHILUS INFLUENZAE (NTHI) AND STREPTOCOCCUS PNEUMONIAE (SP)

Marisol Figueira, M.D.[1] *Presenter*

Prabhavathi Fernandes[2]
Stephen I Pelton[1]

[1]*Boston University, Pediatrics, Boston, MA, USA*
[2]*Cempra, Inc, Chapel Hill, NC, USA*

Objective: To evaluate pharmacokinetics (PK), middle ear fluid (MEF) concentrations, and microbiologic efficacy of Solithromycin in a chinchilla model of EOM due to SP or NTHi.

Method: Plasma and MEF PK parameters (Cmax and AUC0-24) were determined on day1 and 3 after administration of 150mg/kg of Solithromycin via oral gavage daily for 3 days. Isolates with selected antimicrobial susceptibility patterns were inoculated directly into the middle ear (ME). Plasma and MEF were collected for Solithromycin PK studies and MEF cultures performed to determine efficacy.

Results: Solithromycin dosing resulted in the following PK parameters: Cmax and AUC0-24 were 2.2µg/ml and 27.4µg.h/ml in plasma and 1.7µg/ml and 28.2µg.h/ml, in extracellular MEF on day#1. By day#3, Cmax and AUC0-24 had increased to 4.5µg/ml and 54µg.h/ml in plasma and 4.8µg/ml and 98.6µg.h/ml in extracellular MEF, respectively. For NTHi EOM, 3 isolates with MIC/MBC [BCH:0.5/1; 1247:2/2 and 1213:4/4 µg/ml] were selected for study. On day#3 of therapy, Solithromycin sterilized the MEF in > 85% of animals infected with BCH1 and 1247. For NTHi 1213, >85% of MEF remained positive on day#3. Solithromycin sterilized the MEF in 100% of animals infected with SP331 (MIC:0.06µg/ml) and SPCP-645 (MLSB phenotype; MIC:0.125µg/ml). ME infection persisted in 60% of animals infected with CP-712 (M phenotype; MIC:0.5µg/ml).

Conclusion: In chinchilla model of EOM, Solithromycin at 150mg/kg/day for 3 days sterilized MEF in >85% animals challenged with NTHi isolates with MIC< 2µg/ml. Solithromycin sterilized EOM due to SP with MIC<0.125µg/ml. At the achieved Solithromycin exposures, sterilization of ME infection against both NTHi and SP was observed. Further evaluation of Solithromycin for treatment of respiratory tract infection, including AOM, is warranted.

11:36 - 11:43 AM **MONDAY, JUNE 8**

OM2015080

RANDOMISED TRIAL SHOWS SUPER-ADDED RAOM IN OME CASES BENEFITS SUBSTANTIALLY FROM VENTILATION TUBES

Misha Morsley Verkerk, MBBS[1] *Presenter*

Anne G M Schilder[1]
Snezana Andric Filipovic[2,3]
Helen Spencer[4]
Mark Haggard[4]

[1]*EvidENT, UCL Ear Institute, London, LONDON, United Kingdom*
[2]*Clinic Of ENT And Maxillofacial Surgery, Belgrade, BELGRADE, Serbia*
[3]*ENT Department, Mater Dei Hospital, Triq Dun KarmMsida, MSIDA, Malta*
[4]*MRC Multi-centre Otitis Media Study Group, Department Of Psychology, Cambridge, CAMBRIDGESHIRE, United Kingdom*

Introduction: Systematic review of ventilation tube (VT) treatment in typical recurrent acute otitis media (RAOM) cases (<3 years) has shown modest benefit. Hearing outcomes in the TARGET RCT of VTs for persistent otitis media with effusion (OME) have been published, but not other disease and developmental outcomes. Almost 30% of the generally older (3.25-6.75 years) OME cases show 'super-added' RAOM.

Objective: To determine the effect of VTs on markers of RAOM in a defined sample of children with OME.

Method: The RAOM score (6 scaled parent questionnaire items), including parental reports of AOM episodes in 3-month periods, was available for two baseline and two post-randomisation assessment visits. Of 376 children randomised in all, 334 gave data not requiring imputation. We performed linear regression for score data and logistic regression for episode count.

Results: Overall effects models gave mean VT effect sizes respectively of 0.77 SD (moderate-to-large; $p<0.0005$) and Odds-Ratio 2.91 ($p<0.0005$). Interaction with baseline was strong ($p=0.005$), with both effects about one third larger in those 50% of cases above median baseline (of approximately 3 episodes in 6-month baseline period).

Conclusion: Total score captures benefits of VTs more reliably than episode count, but benefit in these 'combined' cases equates to ~1 episode prevented: the similarity to findings in typical 'pure' RAOM augments the scanty evidence available. The effect modification provides an evidence base for VTs in OME cases with highly recurrent RAOM. These findings show a supplementary basis of benefits from VTs in OME.

11:43 - 11:50 AM **MONDAY, JUNE 8**

OM2015090

COST-EFFECTIVENESS OF TREATMENT FOR ACUTE OTORRHEA IN CHILDREN WITH TYMPANOSTOMY TUBES: A PRAGMATIC RANDOMIZED CONTROLLED TRIAL

Thijs M.A. Van Dongen, M.D.,Ph.D.[1] *Presenter*

Geert J.G.M. Van Der Heijden[1,2]
Roderick P Venekamp[1,3]
G. Ardine De Wit[1,4]
Anne G.M. Schilder[1,3]

[1]*University Medical Center Utrecht, Julius Center, Utrecht, Utrecht, Netherlands*
[2]*Academic Centre For Dentistry Amsterdam, Department Of Social Dentistry, Amsterdam, NOORD-HOLLAND, Netherlands*
[3]*University College London, Ear Institute, London, LONDON, United Kingdom*
[4]*National Institute Of Public Health And The Environment, Department Of Nutrition, Prevention And Care, Bilthoven, UTRECHT, Netherlands*

Background: Acute otorrhea is a common problem in children with tympanostomy tubes. We recently demonstrated that treatment with antibiotic-glucocorticoid eardrops is clinically superior to oral antibiotics and initial observation. The aim of this study was to assess the cost-effectiveness of these three common treatment strategies for this condition.

Methods: We performed an open-label pragmatic trial in which 230 children with acute uncomplicated tympanostomy-tube otorrhea were randomly allocated to receive either one of three treatments: hydrocortisone-bacitracin-colistin eardrops, oral amoxicillin-clavulanate suspension and initial observation (no assigned medication prescription to fill). Parents kept a daily diary capturing ear related symptoms, healthcare resource use and non-healthcare costs for 6 months. At 2 weeks and 6 months, the study doctor visited the children at home performing otoscopy. Using a societal perspective, the clinical outcomes treatment failure, (otoscopic presence of otorrhea at 2 weeks), and number of days with otorrhea as reported in the daily diary were balanced against the costs.

Results: Antibiotic-glucocorticoid eardrops were clinically superior to oral antibiotics and initial observation both at 2 weeks and 6 months. At 2 weeks, mean total cost per patient was US$42.43 for antibiotic-glucocorticoid eardrops, US$70.60 for oral antibiotics and US$82.03 for initial observation. At 6 months mean total cost per patient was US$368.20, US$420.73 and US$640.44, respectively. Because of the dominance of eardrops, calculating incremental cost-effectiveness ratios was redundant.

Conclusion: Antibiotic-glucocorticoid eardrops are clinically superior and cost less than oral antibiotics and initial observation in children with tympanostomy tubes who develop otorrhea.

12:00 - 1:30 PM **MONDAY, JUNE 8**

EXHIBIT HALL A

LUNCH IN EXHIBIT/ POSTER HALL

1:30 - 2:30 PM **MONDAY, JUNE 8**

CHERRY BLOSSOM BALLROOM

PANEL 1 (C): COMPLICATIONS TO AOM

Moderator:

Ann Hermannson (Sweden)

Panelists:

Ann Hermannson (Sweden)

Michal Luntz (Israel)

Anne Schilder (Netherlands)

1:30 - 2:30 PM **MONDAY, JUNE 8**

OM2015335

COMPLICATIONS OF ACUTE OTITIS MEDIA (AOM)

Anne Schilder[1] *Presenter*

Michal Luntz[2] *Presenter*

Ann Hermansson[3] *Presenter*

[1]*University College, London, United Kingdom*
[2]*University Of Haifa, Haifa, Israel*
[3]*University Of Lund, Lund, Sweden*

In the presentation the main complication to AOM, Acute Mastoiditis (AM) will be focused on. The new guidelines introduced in most countries during the last years, advocating a restricted use of antibiotic therapy in uncomplicated cases of AOM, have been feared to result not only in more cases of AM but also in more complicated cases with further complications intracranially. Thus we will present results from studies in the Netherlands and Sweden focusing on the number and severity of AM in relation to the use of antibiotic treatment of AOM and in relation to changes in microbiology over the years. The indications for treatment and the management of AM and its complications will be presented with background from these and several other studies. In the session there will be presented cases and time will be allowed for discussion of various steps in management of AM in different settings.

2:30 - 3:15 PM **MONDAY, JUNE 8**

CHERRY BLOSSOM BALLROOM

PODIUM 3: TREATMENT 2

Moderator:

Harvey Coates (Australia)

Speakers:

Harvey Coates (Australia)
Cuneyt Alper (US)
Juliane Banks (US)
Albert Park (US)
Huaili Jiang (China)

2:30 - 2:37 PM **MONDAY, JUNE 8**

OM2015170

INITIAL RESULTS OF A PILOT TRIAL OF TISSUE ENGINEERED MYRINGOPLASTIES IN WESTERN AUSTRALIA

Harvey Coates, FRACS[1,2] *Presenter*

Aanand Acharya[3]
Francis Lannigan[1,2]
Steve Rodrigues[2]
Paul Bumbak[2]
Gunesh Rajan[1,3]

[1]*The University Of Western Australia, Department Of Otolaryngology, Head And Neck Surgery, Perth, WESTERN AUSTRALIA, Australia*
[2]*Princess Margaret Hospital For Children, Department Of Otolaryngology, Head And Neck Surgery, Perth, WESTERN AUSTRALIA, Australia*
[3]*Fremantle Hospital, Perth, WESTERN AUSTRALIA, Australia*

Introduction: In view of over 100,000 Australian people with chronic tympanic membrane perforations a tissue engineered myringoplasty offers a simple potential alternative to conventional myringoplasty. Objective: To evaluate the safety and efficacy of new tissue engineering myringoplasty techniques using different scaffolds with basic fibroblast growth factor (b-FGF), in a pediatric and adult cohort.

Method: Prospective cohort study, designed into 4 groups: 1) topical use of b-FGF alone. 2) Topical use of b-FGF in combination with gelatin sponge. 3) Topical use of b-FGF in combination with silk fibroin scaffold. 4) Topical use of b-FGF in combination with collagen scaffold. To date, 18 adults and 12 children have been recruited from the Otolaryngology Departments of two major Western Australian Hospitals. The procedure is a modification of the technique devised by Kanemaru. The surgeries were performed under local and general anesthesia in adults and children, respectively. Serial video otoscopy and audiometry were performed post-operatively and results determined.

Results: Overall, there was a success rate in patient terms of 83%, with similar success rate in children. However, in terms of treatment, children required 1.3 treatments, on average, and adults 1.0. The major reason for the reduction in the success rate in children was related to post-operative infection or non-compliance with water precautions. There were no safety issues related to the procedure.

Conclusion: We are reporting the safety and efficacy of b-FGF combined with different scaffolds, in an effective and short procedure with comparable success to conventional myringoplasty, in both an adult and pediatric population.

2:37 - 2:44 PM **MONDAY, JUNE 8**

OM2015119

BALLOON DILATION IN REFRACTORY EUSTACHIAN TUBE DYSFUNCTION

Cuneyt Metin Alper, M.D.[1,2,3] *Presenter*

Miriam S Teixeira, M.D.,Ph.D.[1]
Tanya J Rath, M.D.[4]
Denise M Hall-Burton, M.D.[5,6]
Jenna A El-Wagaa[1]
Jeehong Kim, B.S.[7]
Juliane M Banks, B.S.[1]
J. Douglas Swarts, Ph.D.[1]
William J Doyle, Ph.D.[1]

[1]*University Of Pittsburgh School Of Medicine, Otolaryngology, Pittsburgh, PA, USA*
[2]*Children's Hospital Of Pittsburgh Of UPMC, Division Of Pediatric ENT, Pittsburgh, PA, USA*
[3]*University Of Pittsburgh School Of Medicine, Clinical And Translational Science Institute, Pittsburgh, PA, USA*
[4]*University Of Pittsburgh School Of Medicine, Department Of Radiology, Pittsburgh, PA, USA*
[5]*Children's Hospital Of Pittsburgh Of UPMC, Department Of Pediatric Anesthesiology, Pittsburgh, PA, USA*
[6]*University Of Pittsburgh School Of Medicine, Department Of Anesthesiology, Pittsburgh, PA, USA*
[7]*University Of Pittsburgh, School Of Medicine, Pittsburgh, PA, USA*

Introduction: Balloon dilation (BD) of the Eustachian tube (ET) is a new treatment for ET dysfunction (ETD).

Objective: Describe a research protocol to assess BDET efficacy for resolving refractory ETD.

Methods: Patients with unilateral or bilateral patent ventilation tubes (VT) inserted for otitis media with effusion are phone screened for eligibility and, if not disqualified, seen in the Middle Ear Physiology Laboratory. There, a thorough medical and otologic history is obtained including questionnaires for diagnosis of allergies, sinusitis and gastroesophageal reflux disease (GERD), a physical exam is performed including otoscopy, otoendoscopy, videoendoscopic examination of the nasopharynx and ET orifice at rest, during swallowing and other maneuvers, and ET function (ETF) is evaluated using tympanometry, sonotubometry, tubomanometry, inflation-deflation and forced-response testing. Subjects with confirmed ETD are placed on a treatment of topical nasal steroids and, where indicated, medications for allergies, sinusitis or GERD. After a minimum 4 week treatment, subjects undergo the above history, examination and testing sequence and, if their ETD

was refractory to treatment, undergo a CT scan with concurrent ETF testing to rule out cranial base anomalies, and then have unilateral BDET (1 min at 12 atm) under monitored anesthesia care. Subjects are examined and re-tested at 1, 3, and 6 months, with a repeat CT-ETF done at 3 months.

Conclusion: After the completion of this feasibility study, an efficacy trial will be conducted using objective test results and close follow-up. Recommendations regarding the use of BDET for clinical treatment of ETD will be based on those results. Supported in part by: NIH grant DC013167

2:44 - 2:51 PM **MONDAY, JUNE 8**

OM2015127

INTRANASAL RAGWEED CHALLENGE IN SENSITIZED ADULTS DOWNGRADES EUSTACHIAN TUBE FUNCTION

Juliane M Banks, B.S.[1] *Presenter*

J. Douglas Swarts, Ph.D.[1]
Todd M Wine, M.D.[2,3]
Michael S Cohen, M.D.[4,5]
William J Doyle, Ph.D.[1]

[1]*University Of Pittsburgh School Of Medicine, Otolaryngology, Pittsburgh, PA, USA*
[2]*Children's Hospital Colorado, Department Of Pediatric Otolaryngology, Aurora, CO, USA*
[3]*University Of Colorado School Of Medicine, Department Of Otolaryngology, Aurora, PA, USA* [4]*Massachusetts Eye And Ear Infirmary, Division Of Pediatric Otolaryngology, Boston, MA, USA*
[5]*Harvard Medical School, Department Of Otolaryngology, Boston, MA, USA*

Introduction: Past studies that used simple Eustachian tube (ET) function tests reported that intra-nasal challenge of atopic subjects with relevant allergens provoked ET opening failure.

Objective: This pilot study explored the ability of a modified pressure-chamber test to quantify the change in a continuous measure of ET function induced by experimental intra-nasal ragweed exposure in sensitized adults.

Methods: Double-blinded, placebo-controlled, cross-over, intra-nasal challenges with ragweed solution (1000 PNU) and vehicle were done at a minimum interval of 1 week on 16 otherwise healthy, ragweed allergic adults. Nasal symptoms were scored and summed after each challenge and then ET function was tested using a pressure-chamber protocol. There, chamber pressure was varied to create negative and positive middle ear (ME)-chamber pressure gradients and those gradients were measured before and after swallowing by tympanometry. Results were expressed as the fractional gradient equilibrated (FGE) which was calculated by dividing the change in gradient with swallowing by the pre-swallow gradient. For each outcome variable, paired results for the ragweed and placebo challenges were evaluated for significance using a 1-tailed, paired Student's t test.

Results: For persons, the ragweed total symptom score was significantly greater than the respective placebo score. For ears, the FGE recorded at negative ME-chamber pressure gradients was significantly less after the ragweed challenge as was the group FGE recorded at positive gradients when compared to the placebo challenge.

Conclusions: FGE, a continuous measure of ET function, is decreased during experimental nasal allergic reactions provoked by ragweed exposure in atopic adults. Supported in part by: NIH grant DC007667 and by the Hamburg and Eberly Endowments.

2:51 - 2:58 PM **MONDAY, JUNE 8**

OM2015166

EFFICACY DEMONSTRATED IN TWO PHASE 3 CLINICAL TRIALS OF INTRATYMPANIC EXTENDED-RELEASE CIPROFLOXACIN GEL IN CHILDREN WITH MIDDLE EAR EFFUSION UNDERGOING TYMPANOSTOMY TUBE PLACEMENT

Albert H Park[1] *Presenter*

Carl LeBel[2]

[1]*University Of Utah, Otolaryngology, Salt Lake City, UT, USA*
[2]*Otonomy, Inc., San Diego, CA, USA*

Objective: To investigate the safety and efficacy of a single administration of an extended-release gel of ciprofloxacin (OTO-201), in children requiring tympanostomy tube placement (TTP).

Method: Two prospective, randomized, double-blind, sham-controlled Phase 3 clinical trials; 532 children with confirmed middle ear effusion on the day of TTP were randomized to sham (TTP only) or OTO-201 (6 mg ciprofloxacin in hydrogel). Children were studied over a 29-day observation period. The main outcome measures were efficacy (assessed by the appearance of otorrhea, middle ear effusion culture/characterization, bacterial eradication, and safety (audiometry, otoscopy, tympanometry)).

Results: OTO-201 was highly effective in reducing the incidence of otorrhea ($p<0.001$) compared to sham, regardless of baseline middle ear effusion culture status or effusion type. Treatment with OTO-201 was effective in clearing bacteria from the middle ear and had no negative impact on hearing function, tube patency or other safety measures.

Conclusion: Phase 3 clinical trials demonstrated that a single intratympanic administration of OTO-201 is a safe and effective new treatment for otitis media at time of TTP. These data suggest that OTO-201, which affords sustained-exposure to ciprofloxacin, may reduce the risk of delivery and compliance challenges faced by the use of ear drops.

2:58 - 3:05 PM **MONDAY, JUNE 8**

OM2015233

COMPARATIVE EFFICACY AND SAFETY OF ANTIBIOTICS FOR PEDIATRIC ACUTE OTITIS MEDIA: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

Huaili Jiang *Presenter*

Zhigang Zhang

Sun Yat-Sen Memorial Hospital, Department Of Otolaryngology Head And Neck Surgery, Guang Zhou, GUANGDONG, China

Objective: To compare the efficacy and safety of different types of antibiotics for pediatric acute otitis media.

Method: Pubmed, Cochrane library and Embase were systematically searched to identify randomized controlled trials compared different types of antibiotics or antibiotics with a placebo for pediatric acute otitis media. The methodological quality of included studies was assessed according to criteria for risk of bias from Cochrane Handbook for Systematic Review of Interventions, and the quality of evidence was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation system (GRADE).

Results: A total of 34 randomized controlled trials (8687 patients) were included. No significant difference was found between the traditional meta-analysis and the network meta-analysis. Network meta-analysis revealed that antibiotics were more effective than the placebo for the treatment of PAOM. During 7 days therapy, ceftriaxone (relative risk [RR]: 0.75; 95% confidence interval [CI]: 0.19-1.46) and azithromycin (RR: 0.87; 95% CI: 0.12-2.41) were less effective than amoxicillin. From day 10-18, azithromycin was more effective than amoxicillin (RR: 1.93; 95% CI: 0.59-6.09) and amoxicillin-clavulanate (RR: 1.04; 95% CI: 0.71-1.44). Safety analysis indicated that diarrhea occurred mostly on cefaclor, vomiting on amoxicillin and rash on azithromycin respectively. The least frequency of adverse events was presented on ceftriaxone.

Conclusion: Antibiotics are more effective than placebo for treatment of PAOM both within 7 days and the period from day 10-18. Amoxicillin was the most effective antibiotic within 7 days therapy, followed by ceftriaxone, azithromycin and amoxicillin-clavulanate respectively. And from day 10-18, azithromycin tended to be the most one, followed by amoxicillin-clavulanate, ceftriaxone, cefaclor and amoxicillin. In terms of safety, ceftriaxone was best tolerated with the lowest incidence of diarrhea, vomiting and rash.

3:15 - 3:45 PM **MONDAY, JUNE 8**

EXHIBIT HALL A

COFFEE BREAK IN EXHIBIT/POSTER HALL

3:45 - 5:00 PM **MONDAY, JUNE 8**

CHERRY BLOSSOM BALLROOM

PANEL 2 (C): CONDUCTIVE HEARING LOSS IN NEWBORNS

Moderator:

Lisa Hunter (US)

Speakers:

Richard Rosenfeld (US)

Amanda Hall (UK)

Lisa Hunter (US)

Susan Nittrouer (US)

Albert Park (US)

3:45 - 5:00 PM **MONDAY, JUNE 8**

OM2015160

THE IMPACT OF CENTRALISATION OF CLEFT SERVICES ON MIDDLE EAR AND HEARING OUTCOMES OF 5 YEAR OLD CHILDREN WITH UNILATERAL CLEFT LIP AND PALATE

Amanda Hall[1] *Presenter*

Andrew Wills[2]
Andy Ness[2]
Jonathan Sandy[2]

[1]*University Hospitals Bristol NHS Foundation Trust, Children's Hearing Centre, Bristol, AVON, United Kingdom*
[2]*University Of Bristol, School Of Oral And Dental Sciences, Bristol, AVON, United Kingdom*

Objective: To compare middle ear and hearing outcomes pre- and post-centralisation of cleft services in the UK National Health Service.

Method: Two national multi-centre studies in the UK of five year olds born with non-syndromic unilateral cleft lip and palate approximately 12 years apart and treated within the UK National Health Service. Those in the original study were treated in a dispersed model of care with low volume operators. The children in the new study were treated in a more centralised, high volume operator healthcare system. A total of 227 out of 268 (84.7%) children had an audiological assessment. The median age was 5.6 (IQR: 5.4, 5.7) and 151 (66.5%) were boys. Questionnaire data and information from the medical notes were obtained.

Results: In the new study of centralised services, 43% of children received at least one set of grommets and this was a reduction of 17.6% compared to the previous study. There were no significant changes in hearing between the two studies. Middle ear differences will be discussed.

Conclusion: The implementation of centralised multi-disciplinary care does not appear to have had a marked impact on outcomes.

5:00 - 5:30 PM **MONDAY, JUNE 8**

CHERRY BLOSSOM BALLROOM

PODIUM 5: EPIDEMIOLOGY

Moderator:

Marie Gisselsson-Solen (Sweden)

Speakers:

Margaretha Casselbrant (US)

Marieke De Hoog (Netherlands)

Regie Lyn Santos-Cortez (US)

5:00 - 5:07 PM **MONDAY, JUNE 8**

OM2015134

INFORMATION ON COMORBIDITIES COLLECTED BY HISTORY IS POTENTIALLY USEFUL IN PREDICTING OTITIS MEDIA RISK IN CHILDREN

Margaretha L Casselbrant, M.D.,Ph.D.[1,2] *Presenter*

Ellen M Mandel, M.D. [1,2]
James T. Seroky, M.S.[2]
Beverly C. Richert, CRNP, PNP-BC[1,2]
William J Doyle, Ph.D.[2]

[1]*Children's Hospital Of Pittsburgh Of UPMC, Division Of Pediatric Otolaryngology, Pittsburgh, PA, USA*
[2]*University Of Pittsburgh School Of Medicine, Department Of Otolaryngology, Piitsburgh, PA, USA*

Introduction: The onset and evolution of the various otitis media (OM) expressions are believed to be conditioned by certain co-morbidities such as atopy, asthma, gastro-esophageal reflux-disease (GERD), and upper respiratory tract infection (URTI), among others.

Objective: Determine if a symptom/sign/state set for co-morbidities collected by history contains information useful to assigning a child's risks for chronic OM with effusion (COME) and for recurrent acute OM (RAOM).

Methods: Eighteen items related to the symptoms and expression of OM comorbidities collected by history from 141, 3-year old children at enrollment into a longitudinal study were analyzed using Principal Component Analysis (PCA) to identify their underlying factor-structure. Using well established criteria, this population was subdivided into 3 OM-referenced groups, Control (no past OM, n=45), COME (n=45) and RAOM (n=51), and Discriminant Analysis (DA) operating on the identified factors was used to define the best predictor set for pair-wise assignments.

Results: Eight, 5 multivariate and 3 univariate, factors captured 80% of the variance in the 18 items. DA showed that combinations of 3 (Factors 2,4,8 for the control-OME discrimination) and 4 (Factors 1,2,7,8 for the control-RAOM discrimination) factors had a control-OM assignment sensitivity of about 80% and specificity of 54%. For the COME-RAOM discrimination, a 3-factor combination (Factors 1,3,4) accurately assigned 65% of the COME and 73% of the RAOM children.

Conclusions: These results reproduce the coincidental (causal?) linkage previously reported between certain comorbidities and OM expressions in young children and suggest that specific comorbidity combinations contain information of relevance to assigning OM risk. Supported in part by: NIH grant DC007667

5:07 - 5:14 PM **MONDAY, JUNE 8**

OM2015140

EFFECTS OF EARLY ONSET ACUTE OTITIS MEDIA ON THE RISK OF ACUTE OTITIS MEDIA RECURRENCE AND HEALTHCARE RESOURCE USE: THE WHISTLER STUDY

Marieke L.A. De Hoog, Ph.D.[1] *Presenter*

Alexandre C Fortanier[1]
Roderick P Venekamp[1,2]
Cornelis K Van Der Ent[3]
Anne Schilder[2,4]
Roger A.M. Damoiseaux[1]
Henriette A. Smit[1]
Patricia Bruijning-Verhagen[1,5]

[1]*University Medical Center Utrecht, Julius Center For Health Science And Primary Care, Utrecht, Utrecht, Netherlands*
[2]*University Medical Center Utrecht, Otorhinolaryngology, Utrecht, Utrecht, Netherlands*
[3]*University Medical Center Utrecht, Paediatric Pulmonology, Utrecht, Utrecht, Netherlands*
[4]*University College London, EvidENT, Ear Institute, London, LONDON, United Kingdom*
[5]*National Institute Of Public Health And The Environment, Bilthoven, UTRECHT, Netherlands*

Introduction: Acute Otitis Media (AOM) at early age predispose to recurrent AOM (rAOM) at preschool age. We investigated whether age at first AOM episode is associated with AOM recurrences and related healthcare resource use during later childhood.

Methods: Children enrolled in the Wheezing-Illnesses-STudy-LEidsche-Rijn study with at least one AOM episode documented in the GP health record before two years of age were followed from birth through age six years. Data on GP-diagnosed AOM episodes and related GP consultations, antibiotic prescriptions and specialist referrals were retrieved. Regression models were used to model associations between age of initial AOM and subsequent AOM and healthcare resource use.

Results: 796 out of 2,026 children experienced a first AOM episode before age two years. Each month below the age of two at the time of first AOM increased the odds of developing rAOM (> 3 AOM episodes in 6 months or ≥4 in a year) by 8% (adjusted odds ratio (aOR):1.08;95%CI:1.04-1.09). For initial AOM episodes occurring before nine months, the odds for specialist referral increased by 23% (aOR:1.23;95%CI:1.08-1.38) and the cumulative 6-year GP-consultation rate by 9% (adjusted rate ratio:1.09; 95%CI:1.04-1.14) for each month decrease in age. No associations were found between age at onset and total number of subsequent AOM episodes or antibiotic prescriptions.

Conclusion: Children experiencing AOM at early age are at risk of developing rAOM with associated healthcare resource use, in particular when AOM occurs before the age of nine months. Preventing early onset AOM could therefore reduce disease burden of AOM and associated costs.

5:14 - 5:21 PM **MONDAY, JUNE 8**

OM2015057

RARE VARIANTS WITHIN A2ML1 CONFER SUSCEPTIBILITY TO OTITIS MEDIA

Regie Lyn Pastor Santos-Cortez, M.D.,Ph.D.[1] *Presenter*

Charlotte M Chiong[2,3]
Ma. Rina T Reyes-Quintos[2,3]
Eva Maria Cutiongco-de La Paz[7,8]
Kathleen A Daly[9]
Deborah A Nickerson[6]
Janak A Patel[10]
Michele M Sale[5]
Tasnee Chonmaitree[10]
Zubair M Ahmed[4]
Generoso T Abes, M.D. , M.P.H. [2,3]
Suzanne M Leal[1]

[1]*Baylor College Of Medicine, Center For Statistical Genetics, Department Of Molecular And Human Genetics, Houston, TX, USA*
[2]*University Of The Philippines Manila , National Institutes Of Health, Philippine National Ear Institute, Manila, Philippines*
[3]*University Of The Philippines College Of Medicine, Philippine General Hospital, Department Of Otorhinolaryngology, Manila, Philippines*
[4]*University Of Maryland, Department Of Otorhinolaryngology Head & Neck Surgery, School Of Medicine, Baltimore, MD, USA*
[5]*University Of Virginia, Center For Public Health Genomics, School Of Medicine, Charlottesville, VA, USA* [6]*University Of Washington, Department Of Genome Sciences, Seattle, WA, USA*
[7]*University Of The Philippines Manila, National Institutes Of Health, Institute Of Human Genetics, Manila, Philippines*
[8]*University Of The Philippines College Of Medicine, Philippine General Hospital, Department Of Pediatrics, Manila, Philippines*
[9]*University Of Minnesota, Department Of Otolaryngology, Head And Neck Surgery, Minneapolis, MN, USA*
[10]*University Of Texas Medical Branch, Division Of Pediatric Infectious Disease And Immunology, Department Of Pediatrics, Galveston, TX, USA*

Objective: Our aim is to identify rare genetic variants that predispose to nonsyndromic otitis media.

Method: DNA samples from a large indigenous Filipino pedigree with ~50% prevalence of otitis media were submitted for exome sequencing. Novel DNA variants shared by two affected relatives and predicted to be deleterious/damaging were Sanger-sequenced using DNA samples from 51 family members. Coding exons of A2ML1 were sequenced in (1) a case-control cohort with 123 otitis-prone and 118 non-otitis-prone children, and (2) probands from 143 families with chronic/

recurrent otitis media. The occurrence of A2ML1 variants was also screened in exome sequence data from 1,385 unrelated individuals and in >61,000 samples from the Exome Aggregation Consortium. A2ML1 expression in mouse middle ear was assessed using high-resolution confocal imaging.

Results: Exome sequencing revealed an A2ML1 duplication variant that co-segregates with otitis media within the indigenous Filipino pedigree, resulting in a statistically significant LOD score of 7.5. This variant was also identified in DNA samples from three otitis-prone European- and Hispanic-American children, and lies within a founder haplotype. Additionally three stop-gained and four missense variants were identified in DNA samples from six unrelated otitis-prone children. A2ML1 was immunolocalized to middle ear mucosa but not to inner ear, supporting middle ear specificity.

Conclusion: We present a rare genetic cause of susceptibility to nonsyndromic otitis media which affects 37 indigenous Filipino pedigree members and 3 individuals of Hispanic- or European-American descent. The occurrence of a founder haplotype suggests that specific populations with European or Hispanic admixture may be at risk for otitis media.

5:30 - 8:00 PM **MONDAY, JUNE 8**

EXHIBIT HALL A

POSTER RECEPTION

For a full list of posters, please see p. 289 of this program guide.

10:15 - 11:15 AM **MONDAY, JUNE 8**

BALTIMORE 3-5

MINISYMPOSIUM 2 (B): BIOFILM MANAGEMENT

Moderators:

W. Edward Swords (US)

Noboru Yamanaka (Japan)

Speakers:

W. Edward Swords (US)

Noboru Yamanaka (Japan)

Kevin Mason (US)

Larry McDaniel (US)

10:15 - 10:27 AM **MONDAY, JUNE 8**

OM2015308

POLYMICROBIAL BIOFILMS IN OTITIS MEDIA

W. Edward Swords, Ph.D. *Presenter*

Wake Forest School Of Medicine, Microbiology And Immunology, Winston-Salem, NC, USA

The introduction of culture independent assays for detection of microbes within clinical samples has dramatically changed our appreciation for the etiology of otitis media infections. In our work, we have asked how polymicrobial infection impacts the course, severity and therapeutic outcomes for otitis media infections. Our published work has shown that Moraxella catarrhalis utilizes soluble quorum signals from other bacterial species in order to coordinate its persistence within biofilm communities. I will discuss our latest work on mechanisms for interspecies quorum signaling/sensing between M. catarrhalis and other bacterial species, including identification of the factors which mediate uptake and regulation of gene expression.

10:27 - 10:39 AM **MONDAY, JUNE 8**

OM2015071

PATHOGENESIS OF BIOFILM OTITIS AND TREATMENT STRATEGIES

Noboru Yamanaka *Presenter*

Shin Takei
Muneki Hotomi

Wakayama Medical University, Otolaryngology-Head & Neck Surgery, Wakayama, Japan

Objective: 1) To clarify the role of biofilm on persistent and/or reflactory clinical outcome of acute otitis media (AOM). 2) To study biofilm formations of otitis pathogens, especially nontypeable H.influenzae (NTHi) and to evaluate clinical impacts of biofilm formations on clinical pictures of AOM. 3) To develop appropriate parameter of anti-biofilm activiy of antimicrobial agents and to study anti-biofilm activities of commonly used antibiotics for AOM. 4) To make proposals of treatment strategies against biofilm otitis.

Method: We investigated biofilm formation of NTHi by the crystal violet dye assay, the 96-well pin-replicator assay with confocal laser scanning microscopy, and scanning electromicroscopy (SEM). To study anti-biofilm activities of antibiotics, we developed a parameter, minimal biofilm eradication concentration (MEBC) as the concentration required to kill a bacteria in biofilms.

Results: Clinical NTHi isolates from AOM adhered and began to aggregate forming microcolonies within 2 hours of incubation, and after 18 hours of incubation a matured biofilm was observed on the plate. The level of biofilm formation by NTHi was significantly higher in AOM cases not improved by AMPC than those improved by AMPC. The MBEC study suggested that ß-lactams such as AMPC and oral cephalosporin were not effective to bacteria in biofilm even with high-dose administration. Contrarily, TFLX, LVFX, CAM and AZM were highly effective to NTHi biofilms.

Conclusion: Putting together low MBECs and antibiofilm effects validated by SEM study, CAM, AZM, TFLX and LVFX are highly recommended as therapeutic antimicrobial agents against biofilm otitis media.

10:39 - 10:51 AM **MONDAY, JUNE 8**

OM2015326

NUTRITIONAL INFLUENCE ON BIOFILM ARCHITECTURE AND INTRACELLULAR BACTERIAL COMMUNITY DEVELOPMENT OF NONTYPEABLE HAEMOPHILUS INFLUENZAE: A LINK TO PERSISTENCE?

Kevin Michael Mason, Ph.D. [1,2] **Presenter**

[1]*The Research Institute At Nationwide Children's Hospital, Center For Microbial Pathogenesis, Columbus, OH, USA*
[2]*Ohio State University, College Of Medicine, Columbus, OH, USA*

Nontypeable Haemophilus influenzae (NTHI) is a fastidious commensal of the human nasopharynx and pathogen of the upper and lower respiratory tracts. Nasopharyngeal and middle ear microenvironments differ in nutrient availability, specifically the essential iron containing compound heme. Host sequestration of essential nutrients at privileged sites, termed nutritional immunity, serves to limit microbial outgrowth. Thus, transition of NTHI from commensal to pathogen life-style (i.e, otitis media) coincides with diminished availability of essential nutrients. Previous work from our laboratory demonstrates that fluctuations in heme-iron availability, however, influences biofilm formation and architecture concurrent with development of intracellular bacterial communities in middle ear epithelial cells. Our data suggest that heme-iron limitation potentiates the pathogenic potential of NTHI and development of a persister cell phenotype that promotes NTHI survival in the hostile host environment. Pathogen adaptation to nutrient limitation coincides with suppression of inflammatory indicators, such as edema, capillary vasodilation, and proinflammatory cytokine production. Further, our novel examination of the host-bacterial proteome and metabolome begins to now illuminate the dynamic orchestration of the host-pathogen interaction in the infectious disease model of otitis media. Nutrient limitation, therefore, triggers a bacterial pathoadaptive lifestyle to equip survival in the host, a paradoxical response to host nutritional immunity. Since maintenance of biofilm structure and intracellular NTHI communities may be associated with chronic infection, strategies to manage biofilm growth or dispersal coincident with inhibition of intracellular community development will augment current approaches to thereby enhance the therapeutic outcomes of diseases such as otitis media.

10:51 - 11:03 AM **MONDAY, JUNE 8**

OM2015182

PATHOGENESIS OF NONENCAPSULATED STREPTOCOCCUS PNEUMONIAE IN EXPERIMENTAL OTITIS MEDIA

Larry S. McDaniel, Ph.D. *Presenter*

University Of Mississippi Medical Center, Microbiology And Immunology, Jackson, MS, USA

Objective: Nonencapsulted Streptococcus pneumoniae (NESp) are becoming an important cause of upper respiratory infections such as otitis media (OM). One study found that as many as 8% of OM isolates were NESp. However, very little is known about how this genetically diverse emerging human pathogen causes disease. The purpose of our study was to use the chinchilla model of OM to identify virulence factors of NESp that allow these pneumococci to cause disease. We have focused our studies on NESp in which the capsule polysaccharide synthesis (cps) locus has been replaced by genes encoding novel proteins.

Method: A chinchilla model of OM was used, and the animals were challenged by intrabullar injection. Infection was assessed through bacterial enumeration, and the pathological affects were determined using a scoring scale. An adhesion-invasion assay using human epithelial cell lines was performed. Allelic replacement was used to create specific pneumococcal mutants that were subsequently genetically complemented.

Results: NESp strains containing pneumococcal surface protein K (PspK) caused OM in the chinchilla. Deletion of PspK from NESp significantly reduced the level of infection. Furthermore, expression of PspK in an avirulent NESp resulted in virulence. Also, deletion of AliC and AliD from NESp reduced the ability of NESp to cause OM.

Conclusion: We found that PspK is a NESp-specific virulence factor. However, other factors of NESp contribute to virulence. Understanding the virulence of NESp is essential since the current pneumococcal capsular polysaccharide vaccines do not target these pneumococci.

11:15 AM - 12:00 PM **MONDAY, JUNE 8**

BALTIMORE 3-5

PODIUM 2: ANIMAL & CELL MODEL/ GENETICS

Moderator:

Qing Zheng (US)

Speakers:

Derek Hood (UK)

Yan Zhang (China)

Shirng-Wern Tsaih (US)

Rahul Mittal (US)

Mahmood Bhutta (UK)

11:15 - 11:22 AM **MONDAY, JUNE 8**

OM2015254

THE JUNBO MUTANT MOUSE; A TRANSLATIONAL MODEL FOR NTHI MIDDLE EAR INFECTION

Derek William Hood, Ph.D.[1] Presenter

Jiewu Yang[1]
Tom Purnell[1]
Sara Wells[3]
Michael Cheeseman[2]
Steve Brown[1]

[1]MRC Harwell, Mammalian Genetics Unit, OXFORD, OXFORDSHIRE, United Kingdom
[2]University Of Edinburgh, Roslin Institute And Royal (Dick) Veterinary College, Edinburgh, LOTHIAN, United Kingdom
[3]MRC Harwell, Mary Lyon Centre, Oxford, OXFORDSHIRE, United Kingdom

Objective: To develop the Junbo mouse as a model for otopathogen infection and translational studies; the Junbo mouse middle ear (ME) can be infected at high efficiency following intranasal (IN) inoculation with non-typeable Haemophilus influenzae (NTHi).

Method: The heterozygote mutant Junbo mouse (Jbo/+) spontaneously develops otitis media characterised by chronic middle ear (ME) inflammation under specific pathogen free conditions. A single IN inoculation of Jbo/+ mice with different wild-type NTHi strains establishes infection in a significant proportion (up to 90%) of ME achieving high titres (107-108 CFU ml-1) in bulla fluids that can remain up to at least 56 days post-inoculation. Junbo mice were immunized with killed NTHi bacteria (162sr, 176sr or 375sr) then infected IN by strain 162sr; resultant immune sera were analysed in vitro.

Results: Mice immunized with the homologous strain showed significant protection (greatly reduced ME infection and NP carriage rates) compared to non-immunized controls, the titre achieved in the small proportion of NTHi culture-positive ME was reduced. Mice immunized with heterologous NTHi strains then infected by NTHi 162sr did not show significant protection indicated by ME infection rates but NTHi ME titres attained were lower. The pattern of serum antibodies raised varied greatly between individual mice. In vitro analysis of immune sera identified lipopolysaccharide (LPS) as a major factor influencing NTHi killing.

Conclusion: LPS plays a role in the in vivo survival of NTHi in the Jbo/+ mouse ME. Differences in LPS structure can considerably influence the outcome of in vitro killing assays on NTHi.

11:22 - 11: 29 AM **MONDAY, JUNE 8**

OM2015052

PATHOLOGICAL FEATURES IN A NEW MOUSE MODEL OF HUMAN OTITIS MEDIA AND EXPRESSION OF TOLL-LIKE RECEPTOR 2 AND 4 IN HUMAN CHRONIC OTITIS MEDIA

Yan Zhang, M.D.,Ph.D.[1] Presenter

Min Xu[1]
Qingyin Zheng, M.D.,Ph.D.[1,2]

[1]Second Hospital, Xi'an Jiaotong University School Of Medicine, Otolaryngology HNS, Xi'an, SHAANXI, China
[2]Case Western Reserve University School Of Medicine, Otolaryngology HNS, Cleveland, OH, USA

Objective: Genetic predisposition is recognized as an important pathogenetic factor in otitis media (OM) and associated diseases. Mutant Lmna mice heterozygous for the disheveled hair and ears allele (Lmna(Dhe/+)) exhibit early-onset, profound hearing deficits and other pathological features mimicking human laminopathy associated with the LMNA mutation. Toll-like receptor (TLR) 2 and TLR4 signaling pathways may be involved in the inflammation of human OM.

Method: We assessed the effects of the Lmna(Dhe/+) mutation on development of OM and pathological abnormalities characteristic of laminopathy. We further stained the TLR 2 and TLR4 both in human paraffin sections of chronic OM and controls.

Results: Malformation of the eustachian tube, accompanied by OM, were observed in all of the Lmna(Dhe/+) mice as early as postnatal day P12. Scanning electronic microscopy revealed ultrastructural damage to the cilia in middle ears that exhibited OM. Hearing assessment revealed significant hearing loss, paralleling that in human OM. Expression of NF-κB, TNF-α, and TGF-β was up-regulated in the ears or in the peritoneal macrophages of Lmna(Dhe/+) mice. Rugous, disintegrative, and enlarged nuclear morphology of peritoneal macrophages and hyperphosphatemia were found in Lmna(Dhe/+) mutant mice. Expression of TLR 2 and 4 were different between human OM and controls.

Conclusion: These features resemble the pathology of human laminopathies, possibly revealing some profound pathology, beyond OM, associated with the mutation. The Lmna(Dhe/+) mutant mouse provides a novel model of human OM and laminopathy. The signaling of TLR 2 and TLR 4 may contribute to the pathogenesis of human OM.

11:29 - 11:36 AM **MONDAY, JUNE 8**

OM2015079

A TRANSCRIPTOME-WIDE VIEW OF ACUTE OTITIS MEDIA HOST RESPONSE IN THE CHINCHILLA ANIMAL MODEL

Shiring-Wern Tsaih[1] *Presenter*

Alexander Stoddard, M.S.[1,2]
Pawjai Khampang, M.S.[1]
Wenzhou Hong, DVM[1]
Angela Lemke, B.S.[2]
Michael Tschannen, B.S.[2]
Michale Flister[2]
Joseph Kerschner, FACS, FAAP[1]

[1]*Medical College Of Wisconsin, Otolaryngology And Communication Sciences, Milwaukee, WI, USA*
[2]*Medical College Of Wisconsin, Human Molecular Genetics Center, Milwaukee, WI, USA*

Introduction: The chinchilla provides an excellent model for the study of otitis media (OM) but has been limited by a lack of genomic reference data. The recently completed high-quality draft chinchilla genome assembly and functional annotation provide new opportunities utilizing this model. While RNA-seq assays without prior knowledge the whole transcriptome of any given animal model system, including enabling identification and quantification of alternatively spliced transcripts, a genome reference greatly aids in validating and interpreting the data.

Objective: To perform a transcriptome-wide assessment of the chinchilla in response to an acute OM pathogen. Method: Following infection with TIGR4 Streptococcus pneumoniae, the genome-wide transcriptional response of the chinchilla middle ear mucosa was assessed over a short time-course. RNA-seq data was generated from young adult animals in 3 pools, an uninfected control group, and two groups at days 3 and 17 post transbullar inoculation.

Results: The transcriptome-wide changes were compared to previously identified responses including the induction of mucin genes, acute inflammatory response mediators including S100a8 and S100a9, cytokines such as IL-1b and TNF-a, complement components and other members of stress and defense response pathways. Utilization of this approach demonstrated important differences in each of these areas of interest, between infected and control animals as well as animal to animal variability.

Conclusion: The recently sequenced chinchilla genome is well-suited to techniques such as RNA-seq. These experiments will provide ground-breaking insights into host responses to better understand the pathophysiology of OM in an ideal animal model of OM.

11:36 - 11:43 AM **MONDAY, JUNE 8**

OM2015164

ROLE OF NEUTROPHIL EXTRACELLULAR TRAPS IN THE PATHOGENESIS OF PSEUDOMONAS AERUGINOSA INDUCED OTITIS MEDIA

Rahul Mittal, Ph.D. *Presenter*

Robert Gerring
M'hamed Grati
Xue-Zhong Liu

University Of Miami Miller School Of Medicine, Otolaryngology, Miami, FL, USA

Introduction: Otitis media (OM) is a major health problem and occurs with a high incidence in both developed and developing countries. One form of this disease, chronic suppurative otitis media (CSOM) is defined as an inflammatory disorder of the middle ear with tympanic membrane perforation and drainage. The most commonly isolated bacteria in CSOM is Pseudomonas aeruginosa (PA). Objective: The interaction of otopathogenic PA with neutrophils is not known. Neutrophils are the first line of defense against pathogens and form neutrophil extracellular traps (NETs) in response to bacterial infection. These NETs are also hypothesized to be determinants of bacterial persistence. The objective of this research is to characterize the role of NETs in the pathogenesis of PA induced OM.

Methods: Neutrophils were isolated from healthy human blood samples and infected with PA. Gentamicin protection assays were used to quantify the extent of bacterial invasion and survival within neutrophils. A mouse model of PA induced OM was established to examine NET formation. Scanning, transmission, and confocal microscopy were used to determine the presence of NET formation.

Results: There was neutrophil invasion and formation of NETs in vitro as well as in mouse model of PA induced OM. Disruption of NET formation by a small molecule lead to decreased invasion and enhanced clearance of bacteria in mouse model.

Conclusion: This study suggests that NETs play an important role in the pathogenesis of PA induced OM. Targeting NETs can open up new avenues to design novel therapeutic modalities against OM.

11:43 - 11:50 AM **MONDAY, JUNE 8**

OM2015044

THE FIRST LARGE-SCALE ASSOCIATION STUDY FOR CHRONIC OTITIS MEDIA IDENTIFIES ASSOCIATION WITH THE LOCI TGIF1 AND FBXO11

Mahmood F Bhutta, M.D.,Ph.D.[1,2,3] *Presenter*

Steve DM Brown[3]
Anuj Goel[4]
Martin Farrall[4]
Martin Burton[2]

[1]*University College London, Ear Institute, London, United Kingdom*
[2]*University Of Oxford, Nuffield Dept Of Surgical Sciences, Oxford, United Kingdom*
[3]*MRC Harwell, MGU, Oxfordshire, United Kingdom*
[4]*Wellcome Trust Centre For Human Genetics, Cardiovascular Genetics, Oxford, United Kingdom*

Introduction: Susceptibility to chronic otitis media (OM) is highly heritable. Several association studies for OM have been reported, but most have been significantly underpowered, all have focused on acute rather than chronic otitis media, some have had poor phenotype definition, and many have not appropriately selected candidate genes for association testing.

Objective: To undertake the first well powered genetic association study on chronic OM, on candidate loci inferred from non-syndromic mouse models.

Method: We analysed 1269 nuclear families (>4,000 individuals) recruited from across the UK. Phenotype was defined as a child having grommet insertion for COME, with effusion confirmed at operation. Using Haploview we derived 53 tagging single nucleotide polymorphisms (SNPs) for the loci FBXO11, EVI1, TGIF1 and NISCH (candidate loci derived from mouse models), with r2 set to >0.8. Sequencing data were analysed using PLINK, excluding individuals with genotyping success <80%, and SNPs with genotyping success <95% or departure from Hardy-Weinberg Equilibrium at p<1e4. Association was determined using the TDT test.

Results: We found increased risk of disease with polymorphism at rs881835 (p<0.006, OR 1.39) and rs1962914 (p<0.007, OR 1.58) in TGIF1, and also for rs10490302 (p<0.017, OR 1.17) and rs2537742 (p<0.038, OR 1.16) in FBXO11. We will present results of replication in a Finnish cohort (due to complete Feb 2015).

Conclusion: This is the first large-scale association study for chronic OM. The loci TGIF1 and FBXO11 convey risk of disease, implicating TGF-beta signalling as a key pathway in chronic OM, and a potential target for future therapy.

12:00 - 1:30 PM **MONDAY, JUNE 8**

EXHIBIT HALL A

LUNCH IN EXHIBIT/ POSTER HALL

1:30 - 2:30 PM **MONDAY, JUNE 8**

BALTIMORE 3-5

SPECIAL NIH WORKSHOP: NIH FUNDING OPPORTUNITIES & GRANT REVIEW

Speakers:

Bracie Watson (US), NIH/NIDCD

Alberto Rivera-Rentas (US), NIH/NIDCD

Alexander Politis (US), NIH/CSR

2:30 - 3:15 PM **MONDAY, JUNE 8**

BALTIMORE 3-5

PODIUM 4: PATHOGENESIS

Moderator:

Wenzhou Hong (US)

Speakers:

Wenzhou Hong (US)
Joseph Kerschner (US)
Joseph Jurcisek (US)
Apoorva Mulay (UK)
Justo Torres-Rodriguez (US)

2:30 - 2:37 PM **MONDAY, JUNE 8**

OM2015082

ROLES OF LUXS/AI-2 QUORUM SENSING REGULATION IN PNEUMOCOCCAL BIOFILM FORMATION, GENE EXPRESSION AND PATHOGENICITY IN OTITIS MEDIA

Wenzhou Hong, Ph.D.[1] *Presenter*

Pawjai Khampang[1]
Jorge E Vidal[2]
Joseph E Kerschner[1]

[1]*Medical College Of Wisconsin, Otolaryngology, Milwaukee, WI, USA*
[2]*Emory University School Of Medicine, Hubert Department Of Global Health, Atlanta, GA, USA*

Introduction: Quorum sensing (QS) is an autonomous process of cell to cell communication that allows bacteria to adjust their metabolism and behaviors in response to cell density in the vicinity environment. QS plays critical roles in bacterial fitness and pathogenicity. Streptococcus pneumoniae (Spn), one of major pathogen of otitis media, uses multiple QS systems to regulate its activities. However, the functions of these QS regulations in pathogenesis of otitis media have not been well defined.

Objective: To investigate the effects of LuxS/AI-2 QS regulation on pneumococcal survival, biofilm formation, gene expression and pathogenicity. Method: Spn strain TIGR4 and its isogenic mutant TIGR4luxS- were used in in vitro and in vivo experiments. Biofilms were visualized by confocal laser scanning microscopy following live/dead staining. Viable bacteria within biofilms and gene expressions were measured. Chinchilla middle ear infections were performed to investigate the role of LuxS/AI-2 QS regulation in the pathogenicity of Spn.

Results: Inactivation of luxS gene significantly decreased pneumococcal biofilm formation in vitro. Compared to wild type strain TIGR4, thinner biofilm structures ($P<0.01$) and less viable cells ($P<0.01$) were observed in the biofilms of TIGR4luxS-. Inactivation of luxS gene also down regulated the expressions of pneumolysin and autolysin. Inactivation of luxS gene didn't impair pneumococcal survival and persistence in chinchilla middle ear but attenuated Spn to elicit inflammation.

Conclusion: LuxS/AI-2 QS regulation contributes to pneumococcal biofilm formation and virulence but is not essential for bacterial survival and persistence in vivo.

2:37 - 2:44 PM **MONDAY, JUNE 8**

OM2015084

IMPACT OF EXPERIMENTAL OTITIS MEDIA TREATMENT ON CHINCHILLA MUCIN GENES

Joseph E Kerschner, M.D.[1] *Presenter*

Wenzhou Hong[1]
Pawjai Khampang, M.S. [1]
Alexander J Stoddard, M.S. [1]
Alexander C Mackinnon[2]

[1]*Medical College Of Wisconsin, Otolaryngology And Communication Sciences, Milwaukee, WI, USA*

[2]*Medical College Of Wisconsin, Pathology, Milwaukee, WI, USA*

Objective: To assess the gel-forming mucin (GFM) responses to OM pathogens in relationship to middle ear mucosal changes and antibiotic treatment.

Method: Transbullar infection in the chinchilla model by Nontypeable Haemophilus influenzae or Streptococcus pneumonia was used to assess the impact of antimicrobial treatment on MEM changes and mucin gene expression at specific time points.

Results: Single bacterial OM demonstrated measurable changes in the mucosal hypertrophy and inflammatory cells infiltrates in the chinchilla middle ear. Gel forming mucins, Muc5AC, Muc5B and Muc19, were increased by day 3 and were at the highest level on day 10 post inoculation. On day 17 post inoculation, all three GFMs lowered toward basal level. Treatment with ceftriaxone cleared the bacteria in the middle ear lavage, rapidly alleviated MEM changes and significantly facilitated the reduction of GFM to basal expression by day 10 post inoculation.

Conclusion: GFM response to single bacterial OM infection is associated with significant mucosal changes in the middle ear. Antibiotic treatment facilitates return of these changes and GFM production to normal level and may have important implications in considering therapy for certain patient populations.

2:44 - 2:51 PM **MONDAY, JUNE 8**

OM2015156

INTEGRATION HOST FACTOR AND EXTRACELLULAR DNA ARE RELEASED BY NON-TYPEABLE HAEMOPHILUS INFLUENZAE DURING GROWTH AND BIOFILM FORMATION

Joseph Angelo Jurcisek, B.S.[1,2] *Presenter*

Steven D Goodman[1,2]
Cynthia Whitchurch[3]
Lauren O Bakaletz[1,2]

[1]*Nationwide Children's Hospital, Center For Microbial Pathogenesis, Columbus, OH, USA*
[2]*Ohio State University, College Of Medicine, Columbus, OH, USA*
[3]*The Ithree Institute, University Of Technology Sydney, Sydney, NEW SOUTH WALES, Australia*

Objective: Nontypeable Haemophilus influenzae (NTHI) is a causative agent of multiple respiratory tract diseases including otitis media (OM). Biofilms formed by NTHI play a central role in the chronicity, recurrence and resistance to treatment of these diseases; therefore, the development of therapeutic biofilm-targeted measures is essential. Extracellular DNA (eDNA) is an abundant component of NTHI biofilm matrices; moreover, Integration Host Factor (IHF), a DNABII family member, is found at virtually all eDNA vertices and is thus critical for the structural integrity of these biofilms. We therefore wanted to begin to elucidate the mechanism(s) and kinetics by which IHF and DNA are released by NTHI yet remain accessible to biofilm matrix formation.

Method: We hypothesized that IHF and DNA were not likely released from the cells by way of vesicle extrusion as this would inhibit their availability to the extracellular milieu but rather they are released from a discrete subpopulation of enlarged thin membraned cells when these cells lyse, as has been observed with Pseudomonas aeruginosa. We utilized time-lapse fluorescent microscopy as well as immuno-TEM.

Results: We demonstrated these large cells forming and lysing with the release of DNA as well as associated DNABII protein into the extracellular milieu.

Conclusion: Understanding the mechanism by which these two critical biofilm matrix components are released by NTHI will allow a much greater understanding of biofilm formation by NTHI and as such contribute to our development of novel biofilm-targeted therapeutic approaches for patients with chronic OM. This work was funded by NIH R01 DC011818 to SDG and LOB

2:51 - 2:58 PM **MONDAY, JUNE 8**

OM2015191

ISOLATION AND CHARACTERIZATION OF MIDDLE EAR AND NASAL EPITHELIAL CELLS FOR DEVELOPMENT OF AN IN VITRO OTOPATHOGENIC INFECTION MODEL

Apoorva Mulay, MSc[1,2] *Presenter*

Michael Cheeseman[3]
Steve Brown, FMedSci[2]
Derek Hood[2]
Khondoker Akram, MBBS[1]
Lynne Bingle[1]
Colin Bingle[1]

[1]*University Of Sheffield, Infection And Immunity, Sheffield, SOUTH YORKSHIRE, United Kingdom*
[2]*Medical Research Council, Mammalian Genetics Unit, Harwell, OXFORDSHIRE, United Kingdom*
[3]*University Of Edinburgh, The Roslin Institute And Royal (Dick) School Of Veterinary Studies, Edinburgh, MIDLOTHIAN, SCOTLAND, United Kingdom*

Introduction: Secretory innate immunity molecules play an important role in middle ear (ME) protection and epithelial abnormalities are commonly implicated in pathogenesis of Otitis media (OM). SNPs in BPIFA1, the predominant member of BPI fold containing family of putative innate defence proteins, have been associated with OM. We have previously shown that BPIFA1 is expressed in the ME and nasal passages of Wt mice and its expression decreases with OM development in the Junbo model of chronic OM.

Objective: To develop an in vitro otopathogenic infection model in order to investigate the role of BPIFA1 in nasopharynx and ME. Method: We isolated and cultured murine ME and nasal cells at Air Liquid Interface (ALI). We characterised the cell populations by RT-PCR, Immunofluorescence Confocal Microscopy and Western blotting.

Results: Both nasal and ME epithelial cells undergo differentiation within 14 days at ALI. We detected presence of epithelial markers like keratin, Muc5B (mucin cells), FoxJ1 and Tekt1 (ciliated cells) in our model, replicating the in vivo situation. We also detected intracellular and secreted BPIFA1. BPIFA1-/- cells were morphologically similar to Wt cells. The system was readily infected by the human otopathogen,NTHi in a dose and time dependent manner. We are presently determining if the BPIFA1 loss increases cell susceptibility to NTHi infection.

Conclusion: We have developed a novel in vitro primary epithelial culture system that can be widely applied as a tool to study host response to otopathogens, to help us better understand the role of innate defence molecules in OM pathophysiology.

2:58 -3:05 PM **MONDAY, JUNE 8**

OM2015216

COMPUTATIONAL ANALYSIS OF SONOTUBOMETRY AND EUSTACHIAN TUBE FUNCTION

Justo Torres-Rodriguez, B.S. *Presenter*

Samir Ghadiali

Ohio State University, Biomedical Engineering, Columbus, OH, USA

Objective: Sonotubometry is a non-invasive test of Eustachian tube (ET) function that measures sound transmission within the ET during swallowing. Currently, sonotubometry readings can only be indirectly associated with the biomechanical mechanics of ET dysfunction. We have developed a novel computational model of the sonotubometry test and have used these models to directly correlate tensor and levator veli palatini muscle forces (FTVP and FLVP) with specific sonotubometry readings.

Methods: Finite element techniques were used to simulate tissue deformation and sound transmission in an adult patient's ET. A pure-tone sound wave was applied at the nasopharynx and time-dependent changes in sound levels at the middle ear were recorded for a wide range of FTVP and FLVP values.

Results: Computational results compared well with clinical sonotubometry readings. Peak sound levels correlated with maximum lumen opening and the sound curve's width at 50% amplitude (50% width) correlated with the duration of opening. Increasing FTVP resulted in increased peak sound levels and 50% widths. Interestingly, increasing FLVP did not alter peak sound levels but did result in a significant decrease 50% width and a faster closing of the ET.

Conclusions: Computational models of sound transmission in the ET during sonotubometry indicate that reduced 50% width is correlated with faster lumen closing due to elevated LVP muscle contraction. Ongoing simulations are being used to investigate how other biomechanical factors correlate with sonotubometry readings. These models may lead to novel ways to diagnose the mechanisms of ET dysfunction from sonotubometry readings. Supported by NIH-DC007667 and NSF-DGE1343012.

3:15 - 3:45 PM **MONDAY, JUNE 8**

EXHIBIT HALL A

COFFEE BREAK IN EXHIBIT/POSTER HALL

3:45 - 5:30 PM **MONDAY, JUNE 8**

BALTIMORE 3-5

WORKSHOP 1 (B): CHINCHILLA GENOMICS

Speakers:

Mary Shimoyama (US)

Joseph Kerschner (US)

3:45 - 5:30 PM **MONDAY, JUNE 8BALTIMORE 3-5**

OM2015011

AN OTITIS MEDIA RESEARCHER'S GUIDE TO CHINCHILLA GENOMICS: BACKGROUND, APPLICATIONS, TOOLS, AND OPPORTUNITIES

Mary Shimoyama[4] *Presenter*

Joseph Kerschner[1] *Presenter*

Alexander Stoddard, M.S.[1,4]
Lauren Bakaletz[2]
Garth D. Ehrlich[3]

[1]*Medical College Of Wisconsin, Otolaryngology And Communication Sciences, Milwaukee, WI, USA*
[2]*Nationwide Children's Hospital, Columbus, OH, USA*
[3]*Drexel University College Of Medicine, Philadelphia, PA, USA*
[4]*Medical College Of Wisconsin, Human Molecular Genetics Center, Milwaukee, WI, USA*

The chinchilla provides an excellent model for the study of otitis media (OM) but has been limited by a lack of molecular and genomic tools. The recently completed high-quality draft genome assembly for the chinchilla and its annotation now provide excellent opportunities for the scientific exploitation of this model, applying both traditional assays to individual genes and enabling genome-scale studies including RNA-seq and proteomics. These data are now publically available; however, it is necessary for the community of chinchilla researchers to enhance their understanding and utilization of these data for their potential to be realized. Attendees at all levels of genomics expertise will benefit from this workshop. This workshop will present an overview of the generation of the raw sequence and its assembly into a 2.39 Gbase draft genome. Interrogation of this genome utilizing NCBI Entrez Gene, BLAST and primer design services for the chinchilla data will be presented. Methods for validating particular gene models of interest will be demonstrated including visualization of public RNA-seq data, and the examination of syntenic relationships using the genome browsers available at the NCBI and the chinchilla genome database at http://ngc.mcw.edu. Workshop attendees will also gain familiarity with the tools to query the functional data inferred for many chinchilla gene models. At the whole genome scale the necessary steps will be discussed to align, quantify, detect differential expression, functionally annotate, and visualize a chinchilla RNA-seq experiment. The ability to extend these methods to analysis of host and pathogen genome wide responses will be discussed.

5:30 - 8:00 PM **MONDAY, JUNE 8**

EXHIBIT HALL A

POSTER RECEPTION

For a full list of posters, please see p. 289 of this program guide.

TUESDAY SCIENTIFIC PRESENTATIONS

8:00 - 9:45 AM **TUESDAY, JUNE 9**

CHERRY BLOSSOM BALLROOM

PLENARY SESSION 2 (C): CURRENT CLINICAL PRACTICE GUIDELINES FOR OM

Moderator:

Richard Rosenfeld (US)

Speakers:

Sten Hellström (Sweden)

Richard Rosenfeld (US)

Roger Damoiseaux (Netherlands)

Paola Marchisio (Italy)

David Tunkel (US)

8:00 - 8:18 AM **TUESDAY, JUNE 9**

OM2015299

SWEDISH NATIONAL GUIDELINES FOR MANAGEMENT OF AOM

Sten Hellström, M.D.,Ph.D. *Presenter*

Department Of Audiology And Neurotology, CLINTEC, KI, Stockholm,Sweden

Introduction: To keep up with an increasing knowledge of the natural course and pathogenesis of AOM and an increasing antimicrobial resistance problems the Swedish Health Authorities have initiated consensus conferences with production of guidelines on this subject in 1991, 2000 and 2010. The guidelines have focussed on diagnostics, etiology, antibiotic treatment, complications and follow up.

Objective: The objective is to present the hallmarks of the 2010 Swedish guidelines or recommendations for diagnostics, treatment and follow up of AOM. The experts involved in the development of the guidelines represented otorhinolaryngology, family medicin, bacteriology and pediatrics.

Results: In brief the guidelines put pressure on an adequate diagnosis and an active expectans or appropriate antibiotic treatment. In children between one year of age up to twelve with AOM active expectans is recommended and children should only be treated with antibiotics if complicating factors occur. The treatment drug of choice is penicillin V. A follow up procedure at 3 months should be considered but is not mandatory eg in unilateral AOM in a child with a known normal hearing.

Discussion: Twentyfive years with national guidelines for AOM, including similar aspects of diagnostics and a restrict antibiotic policy, are now quite well adopted by the Swedish physicians. Despite the altered antibiotic policy any increasing rates of complications have not been observed. However, still there appears to be an over-consumption and use of broad-spectrum antibiotics.

8:18 - 8:36 AM **TUESDAY, JUNE 9**

OM2015177

CURRENT GUIDELINES FOR OTITIS MEDIA

Richard Rosenfeld, M.D. *Presenter*

SUNY Downstate Medical Center, Department Of Otolaryngology, Brooklyn, NY, USA

This plenary session will summarize current national guidelines for otitis media, emphasizing consensus, controversies, and opportunities for quality improvement. After an introduction by the moderator, each panelist will give a brief (up to 8 minutes) presentation followed by a group discussion and debate. The US otitis media with effusion guideline, which is currently undergoing a multidisciplinary update, will be discussed by Richard Rosenfeld. Guidelines on acute otitis media from Italy, Sweden, and The Netherlands, will be presented by Paola Marchisio, Sten Hellström, and Roger Damoiseaux, respectively. The US tympanostomy tube guideline will be discussed by David Tunkel. The goal of the session will be to illuminate best practices and to promote a lively debate about opportunities for collaboration, quality improvement, and regional adaptation.

8:36 - 8:54 AM **TUESDAY, JUNE 9**

OM2015064

THE DUTCH AOM GUIDELINE IN A HISTORIC PERSPECTIVE

Roger Damoiseaux, M.D.,Ph.D. , Professor *Presenter*

UMC Utrecht, Julius Center For Health Sciences And Primary Care, Utrecht, Netherlands

In the Netherlands until 1980 AOM was treated with paracentesis. Only in 20% of all episodes antibiotics were used. The studies of van Buchem showed that paracentesis was not effective as a treatment of AOM. Treatment from 1980 onwards was for symptomatic relief only. Van Buchem included only children more than two years of age, but even in the younger children antibiotics were used in a minority. The first guideline on AOM in 1990 advised to start antibiotics immediately in children less than 6 months, after 1 day in children less than two years and after 3 days in older children if no improvement occurred. In this climate it was easy to perform a placebo controlled RCT in children less than 2 years of age. The effect of antibiotics was moderate (NNT=7) and the first revision of the guideline in 1999 advised also for children between 6 months and 2 years to wait for 3 days to start with antibiotics if no improvement occurred. Rovers showed in an IPD meta-analysis that children less than 2 years of age with bilateral AOM and children presenting with otorhoe had the best effect of antibiotics on pain and fever. More recent trials showed no different results on symptomatic outcomes. The latest revision of the guideline in 2014 advises to give proper symptomatic treatment and to start antibiotics immediately in children less than 6 months, and to consider antibiotics in children less than 2 years with bilateral AOM and those presenting with otorhoe.

8:54 - 9:12 AM **TUESDAY, JUNE 9**

OM2015112

THE ITALIAN GUIDELINE ON ACUTE OTITIS MEDIA

Paola Marchisio, M.D. *Presenter*

University Of Milan, Department Of Pathophysiology And Transplantation, Milan, Italy

Almost 1,000,000 cases of acute otitis media (AOM) are diagnosed in Italian children every year. In 2010 the first Italian AOM guideline, shared by pediatricians (PEDs) and otolaryngologists (ENTs), was published with several key points. The diagnosis of AOM must be certain and based on acute symptoms plus inflammation of the eardrum plus evidence of middle ear effusion. Pneumatic otoscopy is strongly recommended and ear wax should be removed. Treatment should limit symptoms and eradicate bacteria. Only systemic analgesics (paracetamol or ibuprofen) are recommended. Antibiotics should be prescribed immediately for severe cases of AOM, in children < 2 years with bilateral AOM, and in the case of otorrhea. In all other cases, in agreement with the parents, watchful waiting is possible and antibiotics should be given if worsening. Amoxicillin is the first choice for mild AOM, without complications and in patients not at risk of drug-resistant bacteria and without a history of recurrences whereas amoxicillin plus clavulanic acid should be used for AOM with otorrhea or severe symptoms and/or in children at risk of drug-resistant bacteria or with a history of recurrences. In 2012 PEDs and ENTs were interviewed about how they managed AOM. First-line antibiotics were appropriately chosen by the majority of PEDs and ENTs, but ENTs were significantly more likely than PEDs to report prescribing decongestants, mucolytics, anti-inflammatory drugs, and steroids. This finding highlights the need for continuing educational strategies aimed at PEDs and ENTs to improve their compliance with evidence-based guidelines for AOM treatment.

9:12 - 9:30 AM **TUESDAY, JUNE 9**

OM2015063

A BRIEF INTRODUCTION TO THE AAOHNS TYMPANOSTOMY TUBE CLINICAL PRACTICE GUIDELINE

David Eric Tunkel, M.D. *Presenter*

Johns Hopkins University SOM, Pediatric Otolaryngology, Baltimore, MD - MARYLAND, USA

Objective: The AAOHS developed a clinical practice guideline (CPG) on tympanostomy tubes in children that was published in 2013. This invited presentation will describe a few of the action statements included in this document to help advance acceptance and implementation.

Method: This CPG was a multidisciplinary evidence-based document developed using a defined process published in the AAOHNS CPG development manual.

Results: The tympanostomy tube CPG most notably contains action statements that recommend against the use of tympanostomy tubes for children with short-term otitis media with effusion (OME) and for children who have a history of recurrent acute otitis media but have normal ear exam at the time of evaluation for surgery. The concept of an “at-risk” child who is rarely included in randomized controlled trial of interventions for otitis media, but may have greater consequence from middle ear disease, is discussed in this CPG. Tubes are recommended for children with long-term OME and hearing difficulties, and are an option for children with OME and symptoms that are likely attributable to ear disease (vestibular problems, otalgia, etc.).

Conclusion: This guideline provides action statements that give guidance on the use of tubes for children who will likely receive hearing and quality of life benefits. The CPG will help reduce the use of tympanostomy tubes for children who are unlikely to benefit from surgery.

9:45 - 10:15 AM **TUESDAY, JUNE 9**

EXHIBIT HALL A

COFFEE BREAK IN EXHIBIT/POSTER HALL

10:15 - 11:15 AM **TUESDAY, JUNE 9**

CHERRY BLOSSOM BALLROOM

MINISYMPOSIUM 3 (C): COMPLEMENTARY AND ALTERNATIVE THERAPY FOR OM

Moderators:

Sujana Chandrasekhar (US)

Tulio Valdez (US)

Speakers:

Sujana Chandrasekhar (US)

Takashi Hirano (Japan)

Ruth Thornton (Australia)

Zhigang Zhang (China)

10:15 - 10:27 AM **TUESDAY, JUNE 9**

OM2015337

INTRANASAL SURFACTANT FOR OTITIS MEDIA

Sujana S Chandrasekhar *Presenter*

Alan J Mautone

New York Otology, New York, NY, USA

Otitis Media remains a vexing problem. Neither antibiotics, systemic analgesics, decongestants, antihistamines, nor intranasal steroids target the actual cause, dilatory Eustachian tube dysfunction. Surfactants are present ubiquitously in the body. In OM, the surfactants responsible for proper ET opening are deficient, leading to mucosal apposition at its nasopharyngeal end and secondary fluid entrapment in the middle ear. Bacterial superinfection of that fluid is AOM. 'De-sticking' of the ET and natural clearance of the ME fluid can take several painful days to even begin. We have formulated a synthetic surfactant composed of dipalmitoylphosphatidylcholine (DPPC) and cholesterol palmitate (CP) which, when delivered to the front of the nose as a dry powder through a metered dose inhaler, effectively 'de-sticks' and opens the ET in animals with normal ears, with OME, and with bacterial AOM. Endoscopic videos of adult humans with and without OME show the opening of the ET within 5 to 10 minutes after anterior intranasal application of this surfactant. An individual with a month-long OME showed clinical and audiometric resolution of conductive hearing loss within 20 minutes of using this intranasal surfactant. We postulate that use of this surfactant nasal spray will alleviate pain and discomfort within a few minutes and promote natural resolution of the OM and CHL by addressing the ET dysfunction directly. We will present this robust animal data and the anecdotal human data, and the plan for clinical trials which the FDA has approved to begin.

10:27 - 10:39 AM **TUESDAY, JUNE 9**

OM2015037

EFFECT OF ANTI-CD25 MONOCLONAL ANTIBODY ON CHRONIC OTITIS MEDIA IN MICE MODEL

Takashi Hirano, M.D., Ph.D. *Presenter*

Satoru Kodama, M.D., Ph.D.
Munehito Moriyama, M.D.
Tarou Iwasaki, M.D.
Yoshinori Kadowaki, M.D.
Toshiaki Kawano, M.D., Ph.D.
Masashi Suzuki, M.D., Ph.D.

Oita University, Faculty Of Medicine, Otolaryngology, Yufu, Oita, Japan

Objective: Chronic otitis media (COM) is associated with hearing loss, delayed speech development, permanent middle ear damage, and mucosal changes. The etiology and pathogenesis of COM are not fully understood. Previously, we reported a murine model of COM with persistent nontypeable Haemophilus influenza (NTHi) infection by using an eustachian tubal block for 2 months, and CD4+CD25+forkhead box P3 (FoxP3)+ regulatory T cells are assumed to confer infectious tolerance to NTHi in the middle ear. In this study, we investigated the effect of anti-CD25 monoclonal antibody on COM.

Method: Mice were transbullary inoculated with 10μ l (1.0 × 107 cfu) of live NTHi suspension. At 2 week after the inoculation, anti-CD25 monoclonal antibodiy was injected intraperitoneally after confirming OM, and this antibody was injected 3 times at the interval of 2 weeks. At 2 months after the inoculation, the mice were monitored otomicroscopically, and the samples of middle ear effusions (MEE) were obtained by myringotomy and washing with physiologic saline. Supernatants were harvested and cytokine levels from a pooled sample were measured by a Multiplex assay.

Results: MEE was induced in all mice. As far as the characteristics of MEE, the ratio of serous effusions increased in CD25 treated mice and bacterial culture positive ratio in MEE was significantly diminished in CD25 treated mice when compared to non-treated mice. The number of neutrophils and concentration of inflammatory cytokines in MEE decreased in CD25 treated mice when compared to non-treated mice.

Conclusion: Administration of anti-CD25 monoclonal antibody tend to improve the chronic inflammation in the middle ear. New strategy will be develop against chronic inflammatory diseases with NTHi infection by using our mice model.

10:39 - 10:51 AM **TUESDAY, JUNE 9**

OM2015196

BREAKING DOWN THE NETS – NO EVIDENCE OF OTOTOXICITY WHEN DORNASE ALFA IS ADMINISTED AT THE TIME OF VENTILATION TUBE INSERTION

Ruth B Thornton[1,2] *Presenter*

Stephanie Jeffares[2]
Shyan Vijayasekaran, FRACS[1,3]
Harvey Coates, FRACS[1,2,3]
Peter Richmond, FRACP[1,2,3]

[1]*University Of Western Australia, School Of Paediatrics And Child Health, Crawley, WA, Australia*
[2]*Telethon Kids Institute, Wesfarmers Centre For Vaccines And Infectious Diseases, Subiaco, WA, Australia*
[3]*Princess Margaret Hospital For Children, Subiaco, WA, Australia*

Objective: Neutrophil-derived DNA in the form of NETs comprises a large proportion of middle ear effusion (MEE). Bacteria can reside within the DNA in the form of biofilms, representing an infectious reservoir. Dornase alfa is a DNase used in treating cystic fibrosis and can digest the DNA in MEE. This study aims to determine the safety and efficacy of Dornase alfa at the time of ventilation tube insertion (VTI) in children with chronic otitis media to prevent complications following surgery and reduce the need for repeat VTI surgery.

Method: Children aged between 6months and 5years undergoing bilateral VTI were recruited. Subjects acted as their own internal control and ears were randomised to receive 1 ml of Dornase alfa or a placebo (sterile 0.9% NaCl) prior to VTI. A 5 day diary card following surgery was kept. Audiometry, tympanometry, questionnaire and video-otoscopy were conducted at their post-surgical visit.

Results: 60 children were recruited, 19 had surgery for rAOM only, 14 for OME only and 27 for both. 58 had adenoidectomy and VTI, 2 children had VTI alone. Audiometry showed no evidence of ototoxicity with improvements observed in post-surgery hearing tests. Five children experienced fever in the 2 days following surgery. 60% of children experienced some degree of ear pain the day following surgery, this was often bilateral and was reduced to 15% by day 5. 20% experienced ear discharge in the day following surgery, this was reduced to 10% by day 5. No SAE's related to the investigational product were recorded.

Conclusion: Administration of Dornase alfa into the middle ear at the time of VTI was safe with no evidence of ototoxicity or increased infection.

10:51 - 11:03 AM **TUESDAY, JUNE 9**

OM2015231

CARTILAGE MYRINGOPLASTY COMBINED WITH TYPE TYMPANOPLASTY III IN THE TREATMENT OF ADHESIVE OTITIS MEDIA

ZG Zhang, M.D. *Presenter*

Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Department Of Otolaryngology Head And Neck Surgery, Guangzhou, GUANGDONG, China

Object: To investigate the surgical techniques and the therapeutic effect o f adhesive otitis media.

Methods: 106 patients of adhesive otitis media underwent surgical treatment were retrospectively analyzed.The adhesive tympanic membranes and scars were removed, as well as malleus and incus. Type III tympanoplasty and the myringoplasty with full-thickness tragus cartilages were performed.

Results: 4-6 weeks after surgery, all the patients obtained dry ear and anatomically normal but a slightly thicker tympanic membranes with poor movement. Membranes improved to normal and obtained good m ovement after more than 1 year follow -up without perforation in all cases. Acoustic immittance tests showed all tympanogram curve are “As”type. The average values of A-B Gap in pure tone were 38.8 dB with the increase of 15.7dB in 3 months after surgery and 25.4 dB with the increase o f 28.5 dB in 1 year a fter surgery.

Conclusion: Cartilage myringoplasty combined with type tympanoplasty in the treatment of adhesive otitis media obtains good therapeutic effect and has significant clinical application values.

11:15 AM - 12:00 PM **TUESDAY, JUNE 9**

CHERRY BLOSSOM BALLROOM

PODIUM 6: TREATMENT 3

Moderator:

Shi-Nae Park (South Korea)

Speakers:

Richard Rosenfeld (US)

Miriam Teixeira (US)

Vishakha Sabharwal (US)

Amanda Leach (Australia)

Maojin Liang (China)

11:15 - 11:22 AM **TUESDAY, JUNE 9**

OM2015176

OFFICE INSERTION OF TYMPANOSTOMY TUBES WITHOUT ANESTHESIA IN YOUNG CHILDREN: SAFETY, TECHNIQUE, AND EXPERIENCE MANAGEMENT

Richard Rosenfeld, M.D. Presenter

SUNY Downstate Medical Center, Department Of Otolaryngology, Brooklyn, NY, USA

Objective: Discuss safety, technique, and experience management for tympanostomy tube insertion without anesthesia in the office setting for young children.

Methods: Case series building upon a previously reported case-control study showing no difference in outcomes for tympanostomy tube insertion in the office vs. operating room. Tubes were inserted without anesthesia while an assistant restrained the child's head and the body was immobilized in a papoose board. A parent was present and was encouraged to feed the child immediately after. Audiometry was performed before and after the procedure.

Results: Bilateral office insertion of tubes was performed in 76 children aged 4 to 18 months (mean 12.5) over 3.5 years, building upon experience with an additional 46 children in the earlier case-control study. The primary indications for tubes was recurrent acute otitis media, persistent acute otitis media, or both. Most procedures were completed within 5 to 7 minutes. All tubes were successfully placed except for one child with mild canal stenosis that required rescheduling for the operating room. There were no cases of hearing loss, ossicular injury, or inadvertent damage to the tympanic membrane. One tube extruded in 2 weeks and was replaced in the office. Most children were calm within a few minutes and no parent reported any persistent impact of the experience on their child's behavior.

Conclusions: Office insertion of tubes can be a safe alternative to traditional operating room insertion. Special considerations for patient selection, insertion technique, and managing the experience for patients and families will be discussed.

11:22 - 11:29 AM **TUESDAY, JUNE 9**

OM2015198

EFFECTS OF OXYMETAZOLINE ON THE BLOOD TO MIDDLE-EAR GAS EXCHANGE-RATE

Miriam Scarpin Teixeira, M.D. , PhD[1] *Presenter*

Cuneyt M Alper, M.D.[1,3,5]
Jenna A El-Wagaa[1]
James T Seroky, M.S.[1]
Narmin Helal, DDS, CAGs[2,4]
Brian S Martin, DMD, MS[2,4]
Brendan M Cullen-Doyle, B.S.[6]
William J Doyle, Ph.D.[1]

[1]*University Of Pittsburg School Of Medicine, Department Of Otolaryngology, Pittsburgh, PA, USA*
[2]*University Of Pittsburg School Of Dental Medicine, Division Of Pediatric Dentistry, Pittsburgh, PA, USA*
[3]*Children's Hospital Of Pittsburgh Of UPMC, Department Of Pediatric Otolaryngology, Pittsburgh, PA, USA*
[4]*Children's Hospital Of Pittsburgh Of UPMC, Department Of Dentistry, Piitsburgh, PA, USA*
[5]*University Of Pittsburg School Of Medicine, Clinical And Translational Science Institute, Pittsburgh, PA, USA*
[6]*University Of Pittsburgh School Of Public Health, Department Of Human Genetics, Pittsburgh, PA, USA*

Introduction: Pharmacological modulation of the middle ear (ME) trans-mucosal gas exchange-rate is a feasible approach to lowering the trans-Eustachian tube gas-transfer rate required to stabilize ME pressure.

Objective: Determine if topical, nasal application of a vasoconstrictor decreases the blood to ME exchange-rate of the perfusion-limited gas, Nitrous Oxide (N2O). Design: Randomized, double-blind, crossover study.

Methods: Twenty adult subjects completed paired experimental sessions, identical but for pretreatment with a nasal spray containing either Afrin® (Oxymetazoline) or saline (placebo). At each session, they were fitted with a non-rebreathing mask and breathed room-air for 20 minutes (acclimation period), 50% N2O:50% O2 for 20 minutes (experimental period) and 100% O2 for 10 minutes (recovery period). Throughout, heart-rate, blood-pressure and O2-saturation were monitored and bilateral ME pressure was recorded by tympanometry every minute. The primary outcome was the slope of the ME pressure-time function for the experimental period which estimates the blood to ME N2O exchange-rate. Using repeated measures ANOVA, the effects of Treatment and Period on the vital-signs measures and of Treatment and Ear (left/right) on the measured slopes were evaluated for statistical significance.

Results: The analysis documented a significant effect of Period on O2-saturation (Period 2>Period 1, P=0.03) and of Treatment on Blood-Pressure (Active>Placebo, P<0.02) and on the ME pressure-time slope (Placebo>Active, P=0.05).

Conclusion: The exchange-rate across the ME mucosa of perfusion-limited gases can be modulated by topical treatment of the nasal mucosa with Oxymetazoline. The significance of this observation for ME pressure-regulation and disease risk is discussed. Supported by NIH Grant DC007667

11:29 - 11:36 AM **TUESDAY, JUNE 9**

OM2015186

EFFICACY OF TRANSTYMPANIC CIPROFLOXACIN GEL FORMULATION AGAINST EXPERIMENTAL OTITIS MEDIA IN A CHINCHILLA MODEL DUE TO NON TYPABLE HEMOPHILUS INFLUENZA

Vishakha Sabharwal, M.D.[1] *Presenter*

Rong Yang[2]
Daniel Kohane[2]
Stephen Pelton[1]

[1]*Boston University, Division Of Pediatrics Infectious Diseases, Boston, MA, USA*
[2]*Harvard School Of Medicine, Brookline, MA, USA*

Introduction: Prolonged and subsequent systemic exposure to antibiotics as treatment of acute otitis media is partially responsible for the emergence of drug-resistant strains of pathogenic bacteria. Transtympanic drug delivery of antibiotics directly to the middle ear has the potential to provide local bioavailability sufficient to achieve sterilization while minimizing systemic antibiotic exposure.

Objective: To evaluate pharmacokinetics (PK), middle ear fluid (MEF) concentrations, and microbiologic efficacy of ciprofloxacin gel formulation for the sustained trans-tympanic delivery in a chinchilla model of experimental otitis media (EOM) against non typable haemophilus influenza(NTHi) isolates.

Methods: Isolates with selected antimicrobial susceptibility patterns were inoculated directly into the chinchilla middle ear. Plasma and MEF were collected for transtympanic ciprofloxacin PK studies and MEF cultures performed once animals developed otitis to determine efficacy. Minimum inhibitory concentration (MIC) and minimum bactericidal concentration for NTHi was determined by microtiter dilution.

Results: In chinchilla model of EOM, one deposition of ciprofloxacin-containing gel (1mg/ml) onto the tympanic membrane sterilized MEF in >85% of animals challenged with NTHi isolates with MIC ≤0.006µg/ml while the untreated ears still had middle ear infection by day 7 after inoculation. There was no evidence of systemic absorption of ciprofloxacin in the chinchilla plasma 24 hours after drug administration.

Conclusion: Transtympanic drug delivery is potentially a highly promising alternative to oral antibiotics for treatment of otitis media. The localized antibiotic delivery directly to the middle ear enhances the local bioavailability of drug while minimizing systemic antibiotic exposure thus reducing the selective pressures for antibiotic resistance.

11:36 - 11:43 AM **TUESDAY, JUNE 9**

OM2015331

ANTIBIOTICS FOR ASYMPTOMATIC ACUTE OTITIS MEDAI (AAAOM): WILL THIS PREVENT POOR OUTCOMES IN AUSTRALIAN ABORIGINAL CHILDREN?

Amanda J Leach[1] *Presenter*

Christine Wigger[1]
Jemima Beissbarth[1]
Heidi Smith-Vaughan[1]
Ruth Lennox[1]
Susan McMinn[1]
Andre Wattiaux, [2]
Mark Chatfield[1]
Cate Wilson[1]
Peter S Morris[1,2]

[1]*Menzies School Of Health Research, Darwin, NORTHERN TERRITORY, Australia*
[2]*Royal Darwin Hospital, Darwin, NORTHERN TERRITORY, Australia*

Background: Around 20% of young Australian Aboriginal children living in remote regions have tympanic membrane perforations. More effective treatments of acute otitis media (AOM) are needed. Placebo-controlled randomised trials have shown that antibiotics will reduce the risk of perforation. However, none of the studies have addressed asymptomatic AOM.

Methods: Aboriginal children aged 6 months to 6 years living in rural and remote communities were screened. After consent, children with a diagnosis of asymptomatic AOM were randomised to either two single weekly doses of azithromycin (30mg/kg) or placebo. The primary outcome was failure to cure AOM (based on antibiotic prescription and/or persistent bulging) at end of therapy. Nasal carriage of OM pathogens was also measured.

Results: We were able to follow up 127 of 148 randomised children (86%). Most children (>80%) had Streptococcus pneumoniae or non-capsular Haemophilus influenza (NCHi) at baseline. S pneumonia carriage was reduced at follow up while NCHI carriage remained high. Overall, 55% of children had clinical failure (mainly persistent bulging of the TM). Very few children (<10%) progressed to perforation. The study will be unblinded in March 2015.

Conclusion: Asymptomatic bulging and perforation of the tympanic membrane are both common in Australian Aboriginal children living in the Northern Territory. Weekly azithromycin for 2 doses was well tolerated. While most children with asymptomatic bulging do not develop AOMwiP in the 4 weeks after diagnosis, bulging of the tympanic membrane and carriage of bacterial pathogens persists. The impact of azithromycin on these outcomes will be described.

11:43 - 11:50 AM **TUESDAY, JUNE 9**

OM2015286

EFFICACY OF EUSTACHIAN BALLOON DILATION ON REFRACTORY CHRONIC OTITIS MEDIA WITH EFFUSION

Maojin Liang, M.D. *Presenter*

Hao Xiong
Zhigang Zhang
Suijun Chen
Yaodong Xu
Yongkang Ou
Haidi Yang
Yiqing Zheng

Sun Yat-Sen Memorial Hospital, Department Of Otolaryngology, Guangzhou, GUANGDONG, China

Objective: It's long to be a clinical challenge to deal with the refractory chronic otitis media with effusion (COME). Our present study was to evaluate the efficacy of Balloon dilation of Eustachian Tube (BET) and also the intra- and post-operation management.

Method: Fifty-six ears (thirty-nine patients) with refractory COME were included. R-value in tubomanometry (TMM) and Impedance audiometry were admitted to confirm Eustachian tube dysfunction (ETD). Balloon dilation of Eustachian Tube (BET) was performed and tympanic puncture was admitted according to the middle ear condition during the operation and the following-up. The main outcomes included the middle ear effusion, R-value in TMM, and tympanogram. And the following-up periods were 6 months.

Results: Forty-eight (85.7%) ears were admitted BET and synchronous tympanic puncture. Among which twenty (41.6%) ears did not need further management during the 6-month following-up, and twenty-five (52.1%) ears had recurrent effusion and were admitted tympanic puncture and then recovered, but the other three (6.2%) ears needed further grommet insertion. Eight (14.3%) ears were performed simple BET, no recurrence was found at the 6-month following-up, except for that two ears needed tympanic puncture for once within two weeks post operation. And the R-value and tympanogram significantly improved at the 6-month post operation. Overall, the effective rate of BET on refractory COME was 94.6%.

Conclusion: Balloon dilation of Eustachian Tube (BET) was an ideal way for the refractory chronic otitis media with effusion, and the intra- and post-operation tympanic puncture might also be helpful.

12:00 - 1:30 PM **TUESDAY, JUNE 9**

EXHIBIT HALL A

LUNCH IN EXHIBIT/ POSTER HALL

1:30 - 2:30 PM **TUESDAY, JUNE 9**

CHERRY BLOSSOM BALLROOM

PANEL 3 (C): DIAGNOSIS

Moderator:

Mark Haggard (UK)

Speakers:

Mark Haggard (UK)

Yasuaki Harabuchi (Japan)

Sun Jianjun (China)

Snezana Andric Filipovic (Serbia)

1:30 - 2:30 PM **TUESDAY, JUNE 9**

OM2015096

COMBINED DIAGNOSIS OF OME WITH RAOM (2): DIAGNOSIS FROM MEASUREMENTS AND PARENTAL QUESTIONNAIRES OUTPERFORMS THE CLINICIANS ON WHICH IT IS BASED

Mark Pergrine Haggard, Ph.D.[1] *Presenter*

Snezana Andric Filipovic, [2,3]
Helen Spencer, MSc[1]

[1]*University Of Cambridge, Psychology, Cambridge, ENGLAND, United Kingdom*
[2]*Mater Dei Hospital, ENT, Valletta, MALTA, Malta*
[3]*Clinical Ceter Of Serbia, ENT And Maxillofacial Surgery, Belgrade, Serbia*

Objective: Diagnosis in OME and (R)AOM) has concentrated on cut-offs in clinician-judged ratings from otoscopic examination, but consistency and accuracy are hard to deliver routinely. The entire concept may be flawed (current ear state or child proclivity ?) and lack an appropriate 'gold standard', but pragmatic solutions are required for training and professional/public communication.We sought to compare clinician 3-way diagnosis (RAOM, OME, combined) with an optimum formula based on clinician diagnosis, using tympanometry and scaled parental questions on history, acute infections (RAOM) and reported hearing problems (RHD).

Method: Using discriminant function analysis (DFA) with the four variables most strongly differing between clinician diagnoses on 1449 Eurotitis-2 cases, we developed optimum classifiers for the 2 dimensions needed to separate the 3 clinician diagnoses. Age added only marginally so was dropped. Modestly related variables HL and URTI provided validation paradigms.

Results: Neither physicians nor algorithm had particular difficulty with "combined" diagnosis. Overall agreement was good (65.5 %). However, the algorithm performed almost twice as well In subsequent validation predicting HL (partial eta-squared 0.174 vs 0.090) and URTI (0.034 vs 0.020) from diagnostic category.

Conclusions: Formal optimum classification rules for OM diagnoses have not been available till now. Using continuous measures, the formula classifies consistently. It Is useful in cases without clinician diagnosis, for clinic episode statistics, or for multi-center clinical research eg standardised diagnosis without biases or individual differences among clinicians. The information used is similar and clinically conventional, but the measurement and algorithm combination are more precise.

1:30 - 2:30 PM **TUESDAY, JUNE 9**

OM2015214

CLINICAL FEATURES, DIAGNOSTIC AND TREATMENT STRATEGIES OF OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV)

Yasuaki Harabuchi, M.D.,Ph.D.[1] *Presenter*

Naohiro Yoshida, M.D.,Ph.D.[2]
Kan Kishibe[1]
Yuka Morita[4]
Kaori Tateyama[3]
An OMAAV Working Group Of The Japan Otological Society[5]

[1]*Asahikawa Medical University, Department Of Otolaryngology-Head And Neck Surgery, Asahikawa, Japan*
[2]*Jichi Medical University Saitama Medical Center, Saitama, Japan*
[3]*Oita University Faculty Of Medicine, Oita, Japan*
[4]*Niigata University Faculty Of Medicine, Niigata, Japan*
[5]*Japan Otological Society, Tokyo, Japan*

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis often initially involves middle ear and presents otological symptoms. Such ear disease is recently called otitis media with ANCA-associated vasculitis (OMAAV) in Japan. Recently, the OMAAV working group of Japan Otological Society performed nationwide survey. A total of 297 patients (86 males and 211 females with age ranged from 13 to 89 years), who were diagnosed OMAAV at 65 departments of otolaryngology, were registered in this survey. PR3-ANCA-positive was in 67 (23%) patients, MPO-ANCA-positive was in 159 (54%), both ANCA-positive in 15 (5%), and both ANCA-negative was in 52 (17%). A definitive histological diagnosis of AAV was seen in only 54 (30%) of 179 patients tested. Of 604 ears, 475 (78%) showed rapid progression of sensory hearing loss. Throughout clinical course, relapse occurred in 125 (43%) patients. lung and kidney involvements were seen in 113 (38%) and 77 (26%) patients respectively, facial nerve palsy and hypertrophic pachymeningitis were done in 94 (32%) and 74 (25%) patients respectively. In 480 ears tested, each 30% showed complete or partial recovery (<10dB), and the remaining 40% showed no change or worse. Each 4 patients died of the disease (3 were basial arteritis) or of treatment-related disease. Multivariate analysis showed that treatment with steroid plus immunosuppression regents was an independent favorable prognostic factor for hearing and survival. On the basis of the findings, the speaker propose diagnostic and treatment strategies of OMAAV.

1:30 - 2:30 PM **TUESDAY, JUNE 9**

OM2015066

INTRODUCTION OF THE GUIDLINE ON OTITIS MEDIA IN CHINA

Sun Jianjun Presenter

Center Of Otolarygology Head And Neck Surgery PLA, Navy General Hospital, Beijing, BEIJING, China

Clinical Classification: 1. Otitis Media with Effusion 2. Purulent Otitis Media (POM) 2.1 Acute Purulent Otitis Media (aPOM) 2.2 Chronic Purulent Otitis Media (cPOM)?(1) Inactive Stage?(2) Active Stage 3. Middle Ear Cholesteatoma 4.Special Subtypes 4.1 Otitis Media Tuberculus 4.2 Aids Associated Otitis Media 4.3 Syphilitic Otitis Media 4.4 Fungus Otitis Media 4.5 Necrotic Otitis Media 4.6 Radiation Otitis Media 4.7 Baro-traumatic Media

Complications: 1.Extracranial Complications 1.1 Extratemporal Complications?(1) Periotic Subperiosteal Abscess?(2) Bezold Abscess?(3) Mouret Abscess 1.2 Intratemporal Complications?(1) Peripheral Facial Nerve Paralysi?(2) labyrinthitis: a. Labyrinthine fistula?b. purulent labyrinthitis? (3) apicitis pyramidalis 2. Intracranial Complications 2.1 Extradural Abscess 2.2 Subdural Abscess 2.3 Meningitis 2.4 Sigmoideus Sinus Thrombophlebitis 2.5 Brain Abscess?(1) Cerebral Abscess?(2) Cerebellar Abscess 2.6 Hydrocephalus

Sequela: Middle Ear Atelectasis/Adhesive Otitis Media Tympanosclerosis Cholesterin Granuloma of Middle Ear Masked Otitis Media

Surgery Categorizing: 1.Tympanoplasty Type I?Simple Tympanoplasty (unnecessary reconstruction of ossicular chain) Type II?Movable Footplate, Presence of the Stapes Suprastructure Type III?Movable Footplate, Absence of the Stapes Suprastructure 2. Excision of Lesion of Middle Ear 2.1 Mastoidotomy 2.2 Radical Mastoidectomy 2.3 Modified Radical Mastoidectomy (Bondy Surgery) 3. Excision of Lesion of Middle Ear + Tympanoplasty 3.1 Intact Canal Wall Mastoidectomy with Tympanoplasty 3.2 Open Mastoidectomy with Tympanoplasty 3.3 Intact-Bridge Mastoidectomy with Tympanoplasty 3.4 Atticotomy with Tympanoplasty 4. Other Types of Surgery for Otitis Media 4.1 Tympanotomy 4.2 Plasty of Cavity of Concha 4.3 Canaloplasty of External Auditory Meatus 4.4 Reconstruction of Posterior Wall of the External Auditory Canal 4.5 Mastoid Cavity Constriction 4.6 Middle Ear Sealing

1:30 - 2:30 PM **TUESDAY, JUNE 9**

OM2015072

PARENTALLY REPORTED HEARING DIFFICULTIES, HL AND TYMPANOMETRY SHOW GOOD CORRELATION AND SHARE DETERMINANTS IN OTITIS MEDIA

Snezana Andric Filipovic, M.D.,AuD[1,2] Presenter

Paola Marchisio, M.D.,Ph.D.[3]
Helen Spencer, MSc[4]
Mark Haggard, Ph.D.[4]

[1]Clinical Centre Of Serbia, Clinic Of ENT And Maxillofacial Surgery, Belgrade, Serbia
[2]Mater Dei Hospital, ENT Department, Msida, Malta
[3]University Of Milan, Department Of Pathophysiology And Transplantation, Milan, Italy

[4]University Of Cambridge, UK, Department Of Psychology, Cambridge, United Kingdom

Introduction: Various measures of hearing have been used in OM as disease markers or impact proxies, but there is little clarity about their interrelations, respective determinants, or possibilities for combining to maximise generalisability and reliability

Objective: We sought to establish similarities and differences in pattern of determinants for hearing level (HL), ACET (published HL-mapping of binaural tympanometry) and RHD (scaled parentally reported hearing items, four here); also to explore combinations

Method: In the Eurotitis-2 secondary care database, 1400 OM cases had all three hearing measures, with N>2160 for single measures. Generalised Linear Models tested prediction of each by eight determinants (recruiting centre, age, sex, maternal education (proxy SES), diagnosis (RAOM/OME), length of history, and seasonality, modelled as sine and cosine of month

Results: Results concern severity of presentation, not disease occurrence. Moderate inter-correlations underpinned similarity of determinant pattern for all measures. Centre, length of history and diagnosis (OME, RAOM, combined) predicted the measures very strongly; age, SES, and winter season were strong predictors, but sex was pervasively null. RHD's pattern had later annual peak severity than HL's and ACET's, but only centre and history predicted the discrepancy (RHD-HL) strongly.

Conclusion: The six strong determinants provide obligatory adjustment terms to any analyses of effects on hearing in OM. Combinations have good properties eg RHD with tympanometry, for case triage where HL is not available. RHD particularly reflects length of history; so in a fluctuating condition its 'smoothing' may indicate treatment needs better than threshold measured objectively on an arbitrary occasion.

2:30 - 3:15 PM **TUESDAY, JUNE 9**

CHERRY BLOSSOM BALLROOM

PODIUM 8: TREATMENT 4

Moderator:

Sten Hellström (Sweden)

Speakers:

Sten Hellström (Sweden)
Sun Jianjun (China)
Samir Ghadiali (US)
Karin Stenfeldt (Sweden)
Christian Heidemann (Denmark)

2:30 - 2:37 PM **TUESDAY, JUNE 9**

OM2015307

A DELAYED HEALING OF TYMPANIC MEMBRANE PERFORATIONS IN DIABETIC MICE CAN BE CURED BY PLASMINOGEN

Sten OM Hellström, M.D.,Ph.D.[1] *Presenter*

Mahsa Fallah[2]
Elin Kallin[2]
Hege Boja[2]
Yongzhi Guo[2]
Lina Ny[2]
Malgorzata Wilczynska[2]
Tor Ny[2]

[1]*Department Of Audiology And Neurotology, CLINTEC, Stockholm, Sweden*
[2]*Department Of Medical And Biochemistry And Biophysics, Umeå University, Umeå, Sweden*

Introduction: The blood plasma protein plasminogen has been shown to be a potent pro-inflammatory regulator of wound healing. In mice and rats, chronic tympanic membrane (TM) perforations, can be healed through administration of plasminogen, irrespective of intravenous or local injections or topically applied.

Objective: In diabetes a poor wound repair or healing is commonly observed as a clinical manifestation and TM perforations in diabetic rats seem to have a delayed healing. The present study aimed at investigating if this delayed can be cured by administration of plasminogen.

Method: The study was performed in diabetic db/db mice, with a perforation occupying one quadrant of the TM obtained by a myringotomy lancet, and by intravenous injection of plasminogen.

Results: Perforations of diabetic mice showed a delayed closure compared to control heterozygous +/- littermates. Fifteen days after the perforation all controls showed a perfectly thin, healed TM, whereas only 1 of 7 TMs of the diabetic mice was healed. Immunocytochemical studies showed that the diabetic mice have a disturbed migration of keratinocytes, although accumulating neutrophils in the perforation border indicate an active inflammatory reaction. When treated by plasminogen, 12 out of 16 TM perforations were closed, whereas only 7 of 25 in the PBS-treated group.

Discussion: Our study showed that treatment with plasminogen will improve the healing of TM perforations in diabetic mice and cause closure times comparable to those of normal wild-type mice. This experimental study will be one important observation justifying clinical studies in progress.

2:37 - 2:44 PM **TUESDAY, JUNE 9**

OM2015095

INTACT EXTERNAL CANAL SLEEVE FLAP TECHNIQUE - A NEW MODIFIED TECHNIQUE OF OUTER SURFACE GRAFTING FOR TYMPANIC MEMBRANE RECONSTRUCTION BY POSTAURICULAR APPROACH

Sun Jianjun *Presenter*

Center Of Otolaryngology Head And Neck Surgery PLA, Navy General Hospital, Beijing, BEIJING, China

Objective: To introduce a new modified technique to repair perforation of tympanic membrane - intact external canal sleeve flap technique and evaluate its clinical value.

Method: The intact external canal sleeve flap technique involves eight steps: (1) postauricular incision and exposure; (2) removal of the temporalis fascia for use; (3) elevation of the canal flap with vascular strip including the epithelia on the surface of residual tympanic membrane; (4) enlargement of the ear canal; (5) placement of the fascia on the outer surface of tympanic membrane remnant; (6) replacement of the sleeve canal flap; (7) closure of the postauricular incision; (8) packing the ear canal. This technique was applied to treat patients with tympanic membrane perforation from OME and/or trauma of middle ear. Its clinical outcomes and application value were analyzed retrospectively.

Results: Intact external canal sleeve flap technique was conducted in 219 cases. The reconstructed tympanic membrane healed in 216/219 cases ?98.6%? in the period of follow-up of 6-36 months.

Conclusion: The advantages of sleeve flap technique are as follow: (1) It allows preservation of intact meatus skin, which ensures the blood supply for tympanic grafting and leads to shorter healing time. (2) Because of the excellent exposure, the process to enlarge the external canal is easier. (3) Blunting in the anterior sulcus and lateralization of the graft material can be well avoided. (4) A higher chance of hearing improvement could be obtained. Therefore the intact external canal sleeve flap technique is a valuable method for tympanic membrane reconstruction.

2:44 - 2:51 PM **TUESDAY, JUNE 9**

OM2015304

COMPUTATIONAL MODELING OF SURFACTANT THERAPY ON EUSTACHIAN TUBE FUNCTION

Samir Ghadiali, Ph.D.[1] *Presenter*

Jennifer Malik, B.S. [1]
Natalia Higuita-Castro[1]
John Douglas Swarts[2]
Cuneyt Alper[2]

[1]*Ohio State University, Biomedical Engineering, Columbus, OH, USA*
[2]*University Of Pittsburgh Medical Center, Piitsburgh, PA, USA*

Objective: Elevated surface tension forces have been shown to play a role in Eustachian tube (ET) dysfunction. Unfortunately, surfactant therapy, which theoretically reduces surface tension forces, has not been successful in treating chronic Otitis Media. In this study, we developed a computational model of ET function that accounts for surface tension dynamics and have used this model to investigate how uniform and non-uniform delivery of surfactants alters the biomechanics of ET opening.

Methods: Computational fluid dynamic (CFD) techniques were used to simulate the movement of air-liquid interfaces within the lumen during ET opening. The muscle forces required to open the ET were then quantified as a function of the air-liquid surface tension at the middle ear (ME) or nasopharyngeal (NP) orifice. Uniform surfactant delivery was simulated by concurrently reducing both ME and NP surface tension while non-uniform delivery was simulated by altering only the NP surface tension.

Results: Preliminary results indicate that the force required to open the ET is a strong function of both the ME and NP surface tension. Interestingly, although modest, concurrent reductions in both the ME and NP surface tension significantly reduced the force required to open the ET, reducing the NP surface tension only did not significantly reduce the opening force.

Conclusions: Computational models indicate that uniform surfactant delivery to both the ME and NP might be required to effectively treat ET dysfunction. Therefore, development of novel uniform surfactant delivery techniques may lead to more effective therapies for ET dysfunction. Supported by NIH-DC007667.

2:51 - 2:58 PM **TUESDAY, JUNE 9**

OM2015309

COMPARISON BETWEEN THE ADULT AND CHILD MASTOIDITIS PATIENT – IS THERE A DIFFERENCE IN CLINICAL APPEARANCE?

Karin Stenfeldt, M.D.,Ph.D.[1] *Presenter*

Frida Enoksson, M.D.[2]
Joacim Stalfors, Associate Professor[6]
Malou Hultcrantz, Professor[4]
Ann Hermansson, Associate Professor[3]
Anita Groth, Associate Professor[5]

[1]*Department Of Audiology, Skåne University Hospital, Lund, , Sweden*
[2]*Department Of Otorhinolaryngology, Helsingborg Lasarett, Helsingborg, Sweden*
[3]*Department Of Otorhinolaryngology, Skåne University Hospital, Lund, Sweden*
[4]*Department Of Otorhinolaryngology, Karolinska University Hospital, Solna, Sweden*
[5]*Strama, Lund, Sweden*
[6]*Department Of Otorhinolaryngology, Sahlgrenska University Hospital, Göteborg, Sweden*

Objective: The clinical course of mastoiditis in adults is compared to that of the child. The aim of this study was to find out if acute mastoiditis in the adult patient has special characteristics that are important to consider.

Method: Records from patients treated for acute mastoiditis in Sweden 1993 to 2007 were collected. Data from patients over 18 years old were compared to the age group 0-23 months.

Results: 78 adult mastoiditis patients were included. The youngest was 18 and the oldest 87 years, median age 41. 325 children 0-23 months were included. Highly significant differences were revealed when comparing the groups: In the adult group, 64 % were women, compared to 39 % girls in the child group. 58 % of adults compared to 16 % of children had ear discharge at time of admittance. 32 % of adults had fever, compared to children: 67 %. 31 % of adults had protruding ear, which was the case in 92 % of children. 45 % of adults had swelling and 59 % redness behind the ear compared to 68 % and 91 % of children respectively. The causal agent was Pneumococci in 10 % of adults and 42 % of children and Group A Streptococci in 18 % of adults versus 3.5 % of children. In 50 % of the adults and 18.5 % of children, mastoidectomy was performed.

Conclusion: Acute mastoiditis in the adult population differs in many aspects regarding clinical appearance compared to that of the child.

2:58 - 3:05 PM **TUESDAY, JUNE 9**

OM2015317

CAREGIVER QUALITY OF LIFE AND DAILY FUNCTIONING IN RELATION TO VENTILATING TUBE TREATMENT

Christian Hamilton Heidemann, M.D.,Ph.D.[1,2] *Presenter*

Henrik Hein Lauridsen, Ph.D. , M.Sc.[3]
Anette Drøhse Kjeldsen, M.D.,Ph.D. [1,2]
Christian Emil Faber, M.D.,Ph.D. [1,2]
Eva Carlotte Jung Johansen, M.D.,Ph.D.[4]
Christian Godballe, M.D.,Ph.D. [1,2]

[1]*Odense University Hospital, Dept. Of ENT - Head & Neck Surgery, Odense, 5000, Denmark*
[2]*University Of Southern Denmark, Faculty Of Health Science, Odense, 5000, Denmark*
[3]*University Of Southern Denmark, Research Unit For Clinical Biomechanics, Odense, 5000, Denmark*
[4]*ENT Private Clinic, Odense, 5000, Denmark*

Objective: Caregiver quality of life and daily functioning may improve after ventilating tube treatment in children with otitis media. The aims of this study are to assess possible changes in caregiver quality of life and daily functioning in relation to ventilating tube treatment and to investigate possible predictors for clinical success.

Method: Four hundred ninety-one families were enrolled in the study. The Caregiver Impact Questionnaire was applied in the assessment of caregiver quality of life. Caregivers completed questionnaires at baseline and at 1, 3, 6, 12, and 18 months' follow-up. Variables on caregiver daily functioning comprised 4 weeks' history of number of interrupted nights, absenteeism, cancelled social activities, and doctor visits as a result of otitis media in the child.

Results: Response rates ranged from 96% to 79%. Significant improvements in disease-specific quality of life were seen after treatment. The poorest baseline quality of life was found in caregivers of children with recurrent acute otitis media. Significant improvements were found on all variables on daily functioning. Predictors for caregiver-perceived clinical success included child sex, number of interrupted nights, doctor visits, absenteeism, and cancelled social activities.

Conclusion: Results of this study support the notion that caregivers of children with otitis media with defined surgical indications improve their quality of life and daily functioning after ventilating tube treatment. Factors related to caregiver functioning and disease severity were found to be associated with caregivers experiencing important improvements after treatment.

3:15 - 3:45 PM **TUESDAY, JUNE 9**

EXHIBIT HALL A

COFFEE BREAK IN EXHIBIT/POSTER HALL

3:45 - 4:45 PM **TUESDAY, JUNE 9**

CHERRY BLOSSOM BALLROOM

WORKSHOP 2 (C): OM GUIDELINES

Speakers:

Richard Rosenfeld (US)

Stephanie Jones (US), AAO-HNS

3:45 - 4:45 PM **TUESDAY, JUNE 9**

OM2015081

UNDERSTANDING OTITIS MEDIA GUIDELINES: AN INTERACTIVE WORKSHOP FOR USERS, CLINICIANS, AND DEVELOPERS

Richard Rosenfeld, M.D.[1]

Stephanie Jones[2]

[1]*SUNY Downstate Medical Center, Department Of Otolaryngology, Brooklyn, NY, USA*
[2]*American Academy Of Otolaryngology - Head & Neck Surgery, Alexandria, VA, USA*

Objective: This 60-minute workshop will allow participants to (a) achieve greater insight into what makes an otitis media clinical practice guideline valid and trustworthy, (b) understand the value of guideline action statements (recommendations) and their limitations, and (c) participate in a discussion of challenges and opportunities in crafting multidisciplinary, evidence-based guidelines for otitis media.

Method: A presentation will be given by the instructors with ample opportunity for audience engagement and exchange of ideas. Emphasis is placed on valid and trustworthy guideline methodology that adheres to standards from the US Institute of Medicine and the Guideline International Network.

Results: The guideline methodology in this workshop has been used by professional medical societies in pediatrics and otolaryngology to create multidisciplinary guidelines on acute otitis media, otitis media with effusion, and tympanostomy tubes. The guidelines have been widely cited nationally and internationally as examples of best clinical practice. Examples from these guidelines will be used to illustrate the principles of successful guideline development and implementation.

Conclusion: Otitis media guidelines can be used, developed, and implemented most effectively when the underlying methodology is transparent, trustworthy, and efficient. Participants in this workshop will emerge with a better understand of what constitutes a valid otitis media guideline and how it can be used to improve patient care.

4:45 - 5:30 PM **TUESDAY, JUNE 9**

CHERRY BLOSSOM BALLROOM

PANEL 6 (C): FAMILY MEDICINE

Moderator:

Jørgen Lous (Denmark)

Speakers:

Jørgen Lous (Denmark)

Johanna Uitti (Finland)

Snezana Andric Filipovic (Serbia)

4:45 - 5:30 PM **TUESDAY, JUNE 9**

OM2015178

PRESCHOOL CHILDREN IN OUT-OF-HOURS PRIMARY CARE SERVICES – A POPULATION-BASED STUDY OF COMPLAINTS, PROVIDED CARE, AND PATIENT SATISFACTION

Jørgen Lous, M.D., DMSc[1] *Presenter*

Grete Moth, Ph.D. , MHSc[2]
Linda Huibers, M.D.,Ph.D.[2]
Peter Vedsted, M.D.,Ph.D.[2]
Morten Bondo Christensen, M.D.,Ph.D.[2]

[1]*University Of Southern Denmak, Research Unit For General Practice/ Department Of Public Health, 5000 Odense C, Denmark*
[2]*Aarhus University, Reseach Unit For General Practice, Department Of Publich Health, DK-8000 Aarhus C, Denmark*

Introduction: Large shares of calls to the out-of-hours (OOH) primary care services regard young children; this group also tends to attend emergency treatment for non-urgent medical problems. Objective: The aim was to examine the characteristics of OOH primary care contacts for young children aged 0-5 years regarding diagnosis, provided care and parental satisfaction.

Method: Analyses were based on selected data from a population-based cross-sectional survey (LV-KOS) on “reasons for encounter” and “disease patterns” performed in the Central Region Denmark. Included GPs filled out electronic questionnaires in the computerized patient record system on a wide range of GP-assessed contact characteristics. Patients (parents) received a postal questionnaire on their experience with the contact and perceived severity of the health problem.

Results: The parents found the presented health problem “potentially severe” twice as often as the GPs. The most common diagnoses were respiratory tract infection without ear disease (n=979, 41%) and ear disease (n=370, 16%) of which 291 (79%) were diagnosed as acute otitis media, 45 (12%) were diagnosed as otitis media with effusion, and 23 (6%) were simply ear pain without further diagnosis. Antibiotics (primarily penicillin V) were prescribed to 225 children (61%) with diagnosed ear disease or ear symptoms. Parental satisfaction with consultations (OOH clinic consultation or home visit) was generally rated high.

Conclusion: Parents tend to overrate the potential severity of a health problem among young children when consulting the OOH services. The high proportion of antibiotic prescriptions suggests room for improvement in rational antibiotic use.

4:45 - 5:30 PM **TUESDAY, JUNE 9**

OM2015045

CAN THE VALIDATED PAIN SCALES DIFFERENTIATE CHILDREN WITH ACUTE OTITIS MEDIA FROM CHILDREN WITHOUT ACUTE OTITIS MEDIA?

Johanna Marjukka Uitti, M.D.[1,2] *Presenter*

Sanna Salanterä[3]
Miia K Laine, [1]
Paula A Tähtinen[1,4,5]
Aino Ruohola[1,2]

[1]*Turku University Hospital, Department Of Paediatrics And Adolescent Medicine, Turku,Finland* [2]*University Of Turku, Department Of Paediatrics And Adolescent Medicine, Turku, Finland*
[3]*University Of Turku, Department Of Nursing Science, Turku, Finland*
[4]*Boston Medical Center, Division Of Pediatric Infectious Diseases, Boston, MA, USA*
[5]*Boston University, School Of Medicine, Boston, MA, USA*

Objective: Ear pain is considered as an important sign of acute otitis media (AOM). However, in preverbal children, the assessment of ear pain is challenging. We studied, whether the validated pain scales could differentiate children with AOM from children without AOM.

Method: Children aged 6 to 35 months with acute symptoms suggestive of AOM were eligible. Children's pain was assessed by the parents with the Faces Pain Scale-Revised (FPS-R) and the Face, Legs, Activity, Cry, Consolability (FLACC) Behavioral Scale, both scales ranging from 0 to 10, respectively. The scores from 0-3 were classified as no pain and the scores 4-10 as having pain, respectively.

Results: Of 426 children, 201 (47%) had AOM. The median scores with both the FPS-R and the FLACC Scale were 6.0 in children with and without AOM, respectively. Assessed with the FPS-R, the children with AOM had more often pain (scores from 4 to 10) compared to the children without AOM (90% vs. 83%, P=0.037) and the age-adjusted odds ratio (OR) for AOM was 1.90 (95% confidence interval [CI], 1.06-3.40; P=0.031) for the children with pain. Assessed with the FLACC Scale, the occurrence of pain did not differ between children with and without AOM (91% vs. 88%, P=0.247) and the age-adjusted OR for AOM was 1.52 (95% CI, 0.81-2.85; P=0.197) for the children with pain.

Conclusion: Among children whose parents suspected AOM, the FPS-R or the FLACC Scale cannot differentiate children with AOM from those without AOM.

4:45 - 5:30 PM **TUESDAY, JUNE 9**

OM2015088

COMBINED DIAGNOSIS OF OME WITH RAOM: (1) COHERENT USE BY PHYSICIANS IN SECONDARY CARE

Snezana D. Andric Filipovic, M.D.,AuD[1,2] Presenter

Zsuzsanna Csakanyi, M.D.,Ph.D.[3]
Misha Verkerk, M.D.[4]
Helen Spencer, , MSc[5]
Mark Haggard, Ph.D.[5]
Ian Williamson[6] & Eurotitis-2 study group

[1]Clinical Centre Of Serbia Pasterova Bb Belgrade, Serbia and Montenegro
[2]Mater Dei Hospital Msida Msida 2090, Malta
[3]Heim Pal Children's Hospital, Budapest Üllői Boulevard Budapest, Hungary
[4]Ear Institute London Gower Street London, United Kingdom
[5]University Cambridge Downing Street CB2 3EB Cambridge, United Kingdom
[6]Department of General Practice, University of Southampton, UK

Introduction: The overlap in histories and aetiology of RAOM and OME is widely acknowledged, but predominant clinical practice reflects pressures for single diagnoses, despite their limited usefulness for referral and treatment decisions in OM.

Objective: We wished to determine the coherence achievable by clinicians in allocating a third, combined diagnostic category when requested, plus the correlates and frequency of the combined OME+RAOM subset.

Method: A sub-sample of 1449 cases in the Eurotitis-2 study gave diagnosis information with complete other relevant data. Parent questionnaires (OM8-30 or OMQ-14) provided scores from scaled items on relevant aspects of OM presentation: RAOM signs and symptoms, reported hearing (RHD) and developmental impact. Differences were expressed as SD effect sizes.

Results: 53.3% of cases were pure OME, 19.5% RAOM, with 27.3% combined. There were no univariate age, sex or SES differences with diagnosis. Combined cases were slightly 'worse' than 'pure' RAOM diagnosis in all presentation facets, with only the RAOM score itself giving moderate-to-large effect size (>0.5 SD.). Pure RAOM was milder than OME or Combined, with four large effect sizes much as expected: for tympanometry, HL, RHD and length of history.

Conclusion: Combined cases are much more adversely affected than 'pure' RAOM, slightly more than OME. The relative frequencies will differ with local referral practices but show that 'combined' is not uncommon. Given the obstacles in training, visualisation and standardisation with conventional otoscopy-centred diagnosis, use of the third category and use of questionnaire information on RHD, length of history and RAOM can be recommended.

10:15 - 11:15 AM **TUESDAY, JUNE 9**

BALTIMORE 3-5

MINISYMPOSIUM 4 (B): PATHOGENESIS/ GENETICS

Moderators:

Mahmood Bhutta (UK)

Anna Granath (Sweden)

Speakers:

Mahmood Bhutta (UK)

Anna Granath (Sweden)

Xuezhong Liu (US)

Jizhen Lin (US)

10:15 - 10:27 AM **TUESDAY, JUNE 9**

OM2015294

THE PHENOTYPE LANDSCAPE OF OTITIS MEDIA

Mahmood F Bhutta, M.D.,Ph.D. *Presenter*

University College London, Ear Institute, London, United Kingdom

Otitis media (OM) represents a complex set of clinically defined discrete disease phenotypes. Epidemiological and pathological data suggest that in fact inflammation of the middle ear occurs on a continuum of disease. Here I review data selected from several large-scale epidemiological studies of OM in the developed world. I apply mathematical modelling and imputation to better characterise the incidence of OM, looking specifically at the example of a two-year old white child in a developed world environment. Next, I extract and extrapolate relevant data to define and map the interrelation of OM phenotypes, including the relationship of upper respiratory tract infection to acute OM (AOM), of AOM to OM with effusion, and of recurrent OM to chronicity of effusion. I combine these mathematical models to represent OM graphically as a 3-dimensional continuum: a 'landscape of disease'. This is a conceptual model of middle ear inflammation, akin to the landscape approach to phenotypes exploited in the field of population genetics. Finally, I look at factors that may influence the nature of this landscape, including gender, age, environmental factors, and medical interventions. The novel nosology of OM presented here provides an overview of the spectrum and inter-relation of middle ear inflammatory phenotypes. This approach may enable clinicians and researchers to better conceptualise middle ear inflammation in its various forms, although I will also discuss the limitations of this approa

10:27 - 10:39 AM **TUESDAY, JUNE 9**

OM2015301

NITRIC OXIDE IN THE HUMAN MIDDLE EAR MILIEU

Anna Granath, M.D.,Ph.D.[1] *Presenter*

Eddie Weitzberg, Professor[2]
Lars-Olaf Cardell, Professor[1]

[1]*Karolinska Institutet, Department Of Clinical Science, Intervention And Technology, Stockholm, Sweden*
[2]*Karolinska Institutet, Department Of Physiology And Pharmacology, Stockholm, Sweden*

Objective: Presence of nitric oxide synthases (eNOS and iNOS) has been described in human middle ear mucosa but not direct measurements of gaseous nitric oxide (NO).The objective was to investigate the representation of NOS in human middle ear mucosa and if gaseous NO is present in the human middle ear.

Method: Samples of middle ear mucosa from patients with chronic otitis and healthy controls were assessed for NOS using real-time PCR. NO in middle ear gas samples from patients with chronic otitis or tubulated tympanic membranes was detected with chemilumenescense.

Results: eNOS was detected in the middle ear mucosa of all tested samples. Patients with chronic otitis expressed reduced levels of eNOS compared to controls. The expression of iNOS was generally low. Gas sampled from the middle ear generally contained more gaseous NO than gas sampled in the ear canal close to the intact tympanic membrane of the contralateral ear and room air.

Conclusion: The presented data indicate that NO contributes to the middle ear gas milieu and that it might be produced locally. NO and the regulation thereof might play a role in the development of chronic otitis. Reduced eNOS expression in samples from middle ears with chronic otitis indicates that there is such a connection. Further studies of NO and its metabolites in the human middle ear milieu are warranted.

10:39 - 10:51 AM **TUESDAY, JUNE 9**

OM2015274

UNRAVELING THE GENETICS/GENOMICS OF OTITIS MEDIA

Xue Zhong Liu, M.D.,Ph.D. *Presenter*

University Of Miami - Miller School Of Medicine, Otolaryngology, Miami, FL, USA

Otitis media (OM) is the most common cause for clinical consults in the United States and affects a huge proportion of the global population. OM continues to be one of the most challenging diseases in the medical field due to its diverse host targets and wide range of clinical manifestations. As a complex trait, many environmental risk factors have been linked to OM., However twin and family studies have shown evidence of significant genetic contribution to susceptibility to OM. Advances in targeted DNA enrichment and next generation sequencing technologies provide unprecedented opportunities for massive analysis of DNA variation throughout the genome and have enabled low cost and accurate screening of the entire set of human coding genes or 'exome'. Exome sequencing is now beginning to expedite disease-causing genes discovery in complex and multifactorial disorders such as presbycusis and OM. Identification of gene variants that predispose to OM is an important means to better understand the pathophysiology of OM. The whole genome sequencing of patients and microbes will provide deeper insights into molecular mechanisms. Comprehensive genomic data from individuals with OM and pathogens will deepen the knowledge and accelerate progress in deciphering the molecular basis of OM. The presentation is to focus on the approaches to identifying genetic factors in host susceptibility to pathogens, and to update current status of genetics/genomics status of OM.

10:51 - 11:03 AM **TUESDAY, JUNE 9**

OM2015329

ADAPTIVE IMMUNITY IN THE MIDDLE EAR MUCOSA OF THE MUTANT MICE WITH KNOCKOUT OF ID1 AND/OR ID3

Jizhen Lin *Presenter*

Qing Y Zheng

University Of Minnesota, Department Of Otolaryngology, Minneapolis, MN, USA

Objective: The study was designed to investigate the adaptive immunity of the middle ear with chronic otitis media (COM) in animals.

Method: The mutant mice with knockout of the inhibitor of DNA-binding protein genes (Id1 and/or Id3) were used for the studies of the innate and adaptive immunity in the middle ear with COM.

Results: The mutant mice with the Id1 gene knockout (Id1-/-) developed naturally occurring COM in approximately 25% of animals whereas the mutant mice with the both Id1 and Id3 gene knockout (i.e., Id1-/- Id3-/+) developed the same type of COM in approximately 75% of animals. The both Id1-/- and Id1-/- Id3-/+mutant mice reduced the expression of the programmed death-1 (PD-1, an activation marker of CTLs) on the surface of CTLs but increased the expression of the programmed death ligand-1 (PD-L1, an immune protein that inhibits the activity of CTLs) in the middle ear mucosa. The production of interleukin-2 (IL-2) was significantly reduced in the CTLs in the mutant mice. In addition, Id1 inhibited the production of mucins in the cultured middle ear epithelial cells and immune/inflammatory cytokines such as interleukin-8 (IL-8), interferon-gamma (IFNg), tumor necrosis factor-alpha (TNFa), and vascular epithelial growth factor (VEGF).

Conclusion: The middle ear of the mutant mice (both Id1-/- and Id1-/- Id3-/+) developed naturally occurring COM in approximately 25-75% of animals which are associated with the suppression of CTLs activity. Immunotolerance and mucin production disorder co-exist in the middle ear mucosa with the Id family genes being knocked out.

11:15 AM - 12:00 PM TUESDAY, JUNE 9

BALTIMORE 3-5

PODIUM 7: PATHOGENESIS 2

Moderator:

Mahmood Bhutta (UK)

Speakers:

Natalia Higuita-Castro (US)
Saori Takeda (Japan)
Huaili Jiang (China)
Stephanie Val (US)
Kaori Tateyama (Japan)

11:15 - 11:22 AM **TUESDAY, JUNE 9**

OM2015291

EFFECT OF SUB-AMBIENT MIDDLE EAR PRESSURE AND HYPOXIC CONDTIONS ON PRO-INFLAMMATORY SIGNALING AND MUCIN GENE EXPRESSION

Natalia Higuita-Castro, Ph.D. *Presenter*

Samir Ghadiali, Ph.D.

Ohio State University, Biomedical Engineering, Columbus, OH, USA

Objective: Eustachian tube (ET) dysfunction leads to sub-ambient middle ear (ME) pressures and hypoxic conditions in the ME. Although these biophysical changes may lead to further ET dysfunction, it is not known if changes in ME pressure and gas composition directly alter inflammatory signaling and mucin production. The objective of this study was to investigate how sub-ambient pressures and hypoxic conditions influence mucin production and inflammatory signaling in respiratory epithelial cells.

Methods: A549 lung epithelial cells and primary human nasal epithelial cells were cultured in transwell inserts at an air-liquid interface to form a polarized epithelium. Cells were then exposed to either sub-ambient pressures (-25cmH2O) or hypoxic conditions (6% O2, 5% CO2) for 24 hours. Control conditions were defined as atmospheric pressure and normoxic conditions (21% O2, 5% CO2). ELISA was then used to measure the secretion of pro-inflammatory cytokines (IL6 and IL8) as well as the secretion of mucin-5AC into the media. All data was analyzed via ANOVA.

Results: Preliminary results in A549 cells indicates that although sub-ambient pressures resulted in a 3-fold increase in IL6 and IL8 secretion ($p<0.01$), negative pressures did not significantly alter MUC5AC secretion ($p=0.2$). However, hypoxic conditions resulted in a significant 1.5-fold increase in MUC5AC secretion ($p<0.01$) and no significant change in IL6 and IL8 levels.

Conclusions: Respiratory epithelial cells alter pro-inflammatory cytokine and mucin secretion in response to changes in ME pressure and gas composition. Ongoing mechanistic studies may lead to novel ways to regulate ME inflammation during ET dysfunction. Supported by NIH-DC007667.

11:22 - 11:29 AM **TUESDAY, JUNE 9**

OM2015235

REDUCTION CAPSULAR PRODUCTION OF S.PNEUMONIAE BY SUB-MIC LEVELS OF CLARITHROMYCIN

Saori Takeda, M.D. *Presenter*

Muneki Hotomi
Masamitsu Kono
Yorihiko Ikeda
Akihisa Togawa
Noboru Yamanaka

Wakayama Medical University, Otorhinolaryngology, WAKAYAMA, WAKAYAMA, Japan

Objective: Streptococcus pneumoniae, a leading cause of acute otitis media (AOM), undergoes spontaneous intra-strain phase variations such as transparent or opaque in colony morphology depending on the capsular production. However, there is little information about the pneumococcal phase variation after antimicrobial treatment. In this study, we evaluate pneumococcal phase variation treated with sub-MIC levels of clarithromycin (CAM).

Method: We evaluated effects of sub-MIC levels of CAM on pneumococcal capsular production by planktonic culture methods and co-culture method with human cells (Detroit 562 cells). S.pneumoniae L82016 strain (serotype 6B) and BG7322 (serotype 6A) were grown at mid-log phase was evaluated for their growth, phase variation and amount of capsular polysaccharides with or without sub-MIC levels of CAM. Pneumococcal phase variation was determined on Trypticase soy agar (TSA) plates with 6300 U/plate catalase under the phase contrast microscopy. The effect of sub-MIC levels of CAM on capsular production was further evaluated.

Results: The sub-MIC levels of CAM reduced the ratio of opaque phase variants as well as the amount of capsular polysaccharide of pneumococcal cells without inhibition of pneumococcal growth by both planktonic culture systems and co-culture systems with Detroit562 cells.

Conclusion: The current results suggested that sub-MIC levels of CAM reduced the opaque variant that is more highly adapted to middle ear rather than the transparent variant. Furthermore, sub-MIC levels of CAM reduced the capsule of inter-cellular invaded pneumococci. The effect of CAM against pneumococcal phase variation will suggest that CAM would reduce the virulence of pneumococci.

11:29 - 11:36 AM **TUESDAY, JUNE 9**

OM2015229

THE EXPRESSION OF TREM-2 AND ITS BONE DESTRUCTION IN MIDDLE EAR CHOLESTEATOMA

Huaili Jiang, M.D. *Presenter*

Yu Si
Zhigang Zhang

Sun Yat-Sen Memorial Hospital, Department Of Otolaryngology Head And Neck Surgery, Guang Zhou, GUANGDONG, China

Objective: to explore the distribution of Triggering receptor expressed on myeloid cells 2(TREM-2) and its correlation with inflammatory cytokines, matrix metalloproteinases(MMPs) and osteoclasts in middle ear cholesteatoma (MEC).

Methods: we detected the expression level of TREM-2, IL-1β, IL-6, MMP-2, MMP-8 and MMP-9 in MEC compared with normal skin of external auditory canal(NSC). Then we established an animal model to imitate the process of bone destruction by middle ear cholesteatoma. Real-time PCR, Immunohistochemistry and Tartrate Resistant Acid Phosphataste(TRAP) were applied.

Results: Immunohistochemistry revealed that compared with the expression of TREM-2 in NSC group, that of MEC group was positive. Real-time PCR also indicated that TREM-2 expressing in MEC group was significantly higher than that of in NSC group ($p=0.001$). Similar with that, IL-1β, IL-6, MMP-2, MMP-8, MMP-9 were up-regulated in MEC group. TRAP staining demonstrated that there were lots of active osteoclasts in MEC, however they were absent in NSC.

Conclusions: the up-regulation of TREM-2 in MEC may correlated with increase of inflammatory cytokines, MMPs and the activation of osteoclasts, which induced the process of temporal bone destruction.

11:36 - 11:43 AM **TUESDAY, JUNE 9**

OM2015262

STABLE ISOTOPE LABELED BY AMINO ACID IN CULTURE (SILAC) STRATEGY TO ANALYZE HUMAN MIDDLE EAR EPITHELIAL CELLS (HMEEC) SECRETOME IN RESPONSE TO NTHI LYSATES

Stephanie Val, Ph.D.[1] *Presenter*

Kristy Brown[2]
Diego Preciado[1]

[1]*Children's National Medical Center, Sheikh Zayed Institute For Pediatric Surgical Innovation, Washington, DC, USA*
[2]*Children's National Medical Center, Center For Genetic Medicine, Washington, DC, USA*

Objective: This study aims at characterizing the secretome of HMEEC-1 and to evaluate its regulation in response to NTHi lysates.

Method: We labeled HMEEC-1 with heavy isotopes of arginine and lysine to obtain a spike-in standard. The spike-in standard was mixed with the conditions of interest (control or treated 24hrs, secretions recovered 24hrs or 48hrs) and separated by SDS-PAGE. Peptides generated by in-gel digestion were analyzed by LC-MS/MS.

Results: 767 proteins were detected by MS in HMEEC secretions at both 24hrs and 48hrs. The more abundant proteins detected were components of the extracellular matrix: fibronectin and laminins; and cytoskeleton binding proteins: filamin-A, filamin-B, plectin, gelsolin … Complement C3, heath shock proteins and Ubiquitin were secreted by HMEEC, proteins participating to the immune response. An analysis using IPA showed the high upregulation of Neutrophil gelatinase associated lipocalin in response to NTHi lysates, protein that limits bacterial infection. Extracellular matrix remodeling proteins were regulated: MMP1, Serpin H1, ECM1 (upregulated) and Collagen 7 (downregulated). Ingenuity Pathway Analysis (IPA) showed that these proteins were associated to Integrin Linked Kinase, Tight junction signaling pathways and the inhibition of metalloproteases. The upstream regulators found by IPA were TNF, lipopolysaccharide and JUN all related to NFkB transcription factor activation.

Conclusion: In conclusion, we have characterized the secretome of HMEEC in response to NTHi lysates treatment that show a remodeling of the extracellular matrix of the epithelium, that might be implicated in the metaplasia of the middle ear epithelium in OM.

11:43 - 11:50 AM **TUESDAY, JUNE 9**

OM2015035

OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV): A RETROSPECTIVE MULTI-CENTER STUDY IN JAPAN -2) CLINICAL DIFFERENCES ACCORDING TO ANCAS-

Kaori Tateyama, M.D.[1] *Presenter*

Naohiro Yoshida, M.D.,Ph.D.[4]
Kan Kishibe, M.D.,Ph.D.[2]
Yuka Morita, M.D.,Ph.D.[3]
Yukiko Iino, M.D.,Ph.D.[4]
Masashi Suzuki, M.D.,Ph.D.[1]
OMAAV Working Group Of The Japan Otological Society, [5]
Yasuaki Harabuchi, M.D.,Ph.D.[2]

[1]*Oita University Faculty Of Medicine, Otolaryngology Head And Neck Surgery, Yufu, OITA, Japan*
[2]*Asahikawa Medical University, Otolaryngology Head And Neck Surgery, Asahikawa, HOKAIDDO, Japan*
[3]*Niigata University Faculty Of Medicine, otolaryngology Head And Neck Surgery, Niigata, NIIGATA, Japan*
[4]*Jichi Medical University Saitama Medical Center, Otolaryngology, Oomiya, SAITAMA, Japan*
[5]*Japan Otological Society, Minato-Ku, TOKYO, Japan*

Objective: Otitis media with ANCA (antineutrophil cytoplasmic antibody) associated vasculitis (OMAAV) are intractable conditions that are resistant to conventional treatment. In the present study, we examined the clinical differences according to ANCA subtype.

Methods: A total of 297 patients were registered in the nationwide surveys. Patients were divided into three groups : PR3-ANCA positive group (67 cases, 23%), MPO-ANCA positive group (159 cases, 54%) and ANCA negative group (52 cases, 17%). Both ANCA positive (15 cases, 5%) and ANCA unmeasured patients were excluded. Clinical data were collected and compared among the three groups (Ryan's multiple comparison methods).

Results: No significant differences among groups were found in the clinical findings and the major clinical symptoms on the initial visit. Over the whole course of the follow-up period, PR3-ANCA positive group had significantly higher rate of the nose involvement (PR3= 65.7% vs MPO=26.4%, p=0.000)(PR3= 65.7% vs ANCA negative=38.5%, p=0.003) and the lung involvement (PR3= 52.2% vs ANCA negative=23.1%, p=0.001), while ANCA negative group had significantly higher rate of hypertrophic pachymeningitis (PR3= 14.9% vs ANCA negative=44.2%, p=0.000)(MPO=20.8 % vs ANCA negative=44.2%, p=0.001). Rate of relapes was significantly higher in PR3-ANCA positive group (PR3= 53.7% vs MPO=36.5%, p=0.017).

Conclusion: Over the course of the follow-up period, PR3-ANCA positive group had significant higher rate of nose and lung involvement, and had a higher rate of relapse. ANCA negative group had significantly higher rate of hypertrophic pachymeningitis. These findings may allow for better characterization of pathologies and eventually assist in improving the clinical utility of OMAAV diagnostic criteria.

12:00 - 1:30 PM **TUESDAY, JUNE 9**

EXHIBIT HALL A

LUNCH IN EXHIBIT/ POSTER HALL

1:30 - 2:30 PM **TUESDAY, JUNE 9**

BALTIMORE 3-5

PANEL 4 (B): PROGRESS IN UNDERSTANDING THE ROLE OF VIRUSES IN OM PATHOGENESIS

Moderator:

Janak Patel (US)

Speakers:

Janak Patel (US)

Terho Heikkinen (Finland)

Johanna Nokso-Koivisto (Finland)

1:30 - 2:30 PM **TUESDAY, JUNE 9**

OM2015321

ASYMPTOMATIC VIRAL UPPER RESPIRATORY INFECTION: EFFECT ON ACUTE OTITIS MEDIA

Janak A Patel, M.D.[1] *Presenter*

[1]*University Of Texas Medical Branch, Pediatric Infectious Diseases, Galveston, TEXAS, USA*

Advances in molecular testing, such as use of polymerase chain reaction assays, have increased the detection of viruses in the upper respiratory tract in asymptomatic individuals. In case-control studies, respiratory viruses were detected in 58-90% of symptomatic upper respiratory tract infection (URI) cases and 28-52% of asymptomatic controls. Positive PCR results in asymptomatic children may indicate acute asymptomatic viral infection, recent symptomatic infection with residual shedding, or viral persistence from past infection. Until recently, it was not clear if asymptomatic URI was associated with the development of acute otitis media (AOM). In our recent studies, we have found that asymptomatic URI is more common in younger infants than older infants. Rhinovirus is the most commonly detected virus in both symptomatic and asymptomatic infants. Prolonged presence of bocavirus may partially explain a lack of association between symptoms and this virus detection. Our finding that asymptomatic viral infection did not lead to AOM highlights the fact that a necessary step in the pathogenesis of AOM is an inflammation of the nasopharynx and the Eustachian tubes severe enough to cause URTI symptoms and associated Eustachian tube dysfunction. We also show a strong correlation between expression of URI symptoms and high viral load, however, the development of AOM was not associated with a higher viral load.

1:30 - 2:30 PM **TUESDAY, JUNE 9**

OM2015290

UPDATE ON VIRAL-BACTERIAL INTERACTIONS IN ACUTE OTITIS MEDIA

Terho Heikkinen, M.D.,Ph.D.[1] *Presenter*

[1]*University Of Turku, Department Of Pediatrics, Turku, Finland*

Research into the role of viruses in acute otitis media (AOM) has produced strong evidence for the crucial role of respiratory viruses in the etiology and pathogenesis of this disease. In most cases, respiratory virus infection initiates the whole cascade of events that eventually leads to the development of AOM. Recent studies in children have demonstrated that viral infection and viral load are significantly associated with the nasopharyngeal detection and colonization density of AOM bacterial pathogens. With the use of PCR-based techniques for the detection of bacteria and viruses directly in the middle-ear fluid, bacteria have been found in 90% and viruses in 70% of AOM cases, indicating that in at least two-thirds of children AOM is a combined bacterial-viral infection. Increasing knowledge of the contribution of viruses and viral-bacterial interaction to the pathogenesis of AOM will likely have an impact on the future management and prevention of this condition.

1:30 - 2:30 PM **TUESDAY, JUNE 9**

OM2015300

ROLE OF HUMAN BOCAVIRUS AND HUMAN METAPNEUMOVIRUS IN ACUTE OTITIS MEDIAE

Johanna Nokso-Koivisto[1] *Presenter*

[1]*Helsinki University Hospital, Department Of Otorhinolaryngology, Helsinki, Finland*

Acute otitis media (AOM) occurs as a complication of viral upper respiratory tract infection (URI). Multiple respiratory viruses of hundreds of different serotypes can cause URI. Modern molecular methods have made it possible to detect new viruses such as human bocavirus type 1 (HBoV1) and human metapneumovirus (HMPV). HBoV1 is a parvovirus that was first discovered in 2005. Active HBoV1 infection as documented by serology has been associated with AOM development and HBoV1-DNA has been detected in the middle ear fluid of children with AOM. Also high proportion of HBoV1-associated URI episodes complicated by AOM has been reported. However, HBoV1 shedding can persist in the nasopharynx for a long period and the overall significance of this virus in respiratory infections and AOM is still unclear. HMPV was first identified in 2001. It is a respiratory virus that belongs to the Paramyxoviridae family, subfamily Pneumovirinae, along with RSV. It has been shown that HMPV is prevalent and infects almost all children by the age 5 years causing URI and lower respiratory infections. During AOM, HMPV has been detected in nasopharyngeal aspirate samples and in middle ear fluids, and there have been reports of high rate of concomitant AOM during URI due to HMPV. However, HMPV seems to have low tendency to induce AOM compared to phylogenetically and clinically closely related, ototropic RSV.

2:30 - 3:15 PM **TUESDAY, JUNE 9**

BALTIMORE 3-5

PODIUM 9: IMMUNOLOGY

Moderator:

Ann Hermansson (Sweden)

Speakers:

Ann Hermansson (Sweden)
Brian Nuyen (US)
Yu Si (China)
Jessica Browne (Australia)
Saleem Basha (US)

2:30 - 2:37 PM **TUESDAY, JUNE 9**

OM2015043

AMPHIPHILIC Y-PGA NANOPARTICLES ADMINISTERED ON RAT MIDDLE EAR MUCOSA PRODUCE ADJUVANT-LIKE IMMUNOSTIMULATION IN VIVO

Ann Hermansson, M.D.,Ph.D. , Associate Professor[1] *Presenter*

Johan Nilsson[1]
Lennart Greiff[1]
Per Caye-Thomasen [2]
Ann Hermansson[1]

[1]*Dept Of ENT, University Of Lund, Lund, Sweden*
[2]*Department Of Otorhinolaryngology, Head & Neck Surgery, Copenhagen University Hospital, Copenhagen, Denmark*

Objective: To examine effects of topical mucosal administration of γ-PGA-Phe NPs as a potentially combined antigen delivery system and adjuvant

Method: γ-PGA-Phe NPs were administered on rat middle ear mucosa in a sham-controlled design and the response was monitored, focusing on soluble markers in mucosal surface liquids and on overall histopathology

Results: γ-PGA-Phe NPs produced a dose- and time-dependent inflammatory response characterized by generation of proinflammatory cytokines (IL-1α, IL-1β, IL-6, MIP-1α, and TNF-α) and associated histopathological changes

Conclusion: Amphiphilic biodegradable nanoparticles (NPs) composed of poly(γ-glutamic acid) conjugated with L-phenylalanine ethylester (γ-PGA-Phe NPs) applied on the rat middle ear mucosa produce an inflammatory type 1 response. The observation is of relevance for the use of γ-PGA-Phe NPs as a concomitant antigen delivery system and adjuvant measure in the context of vaccinations.

2:37 - 2:44 PM **TUESDAY, JUNE 9**

OM2015065

LACK OF NFκB PROLONGS PATHOGENIC RESPONSES AND PERMITS CO-INFECTION WITH NASOPHARYNGEAL BACTERIA DURING EXPERIMENTAL OTITIS MEDIA

Brian Anthony Nuyen, B.S.[1] *Presenter*

Xinwei Liu, B.S.[2]
Chang Cho[1]
Kwang Pak, B.S.[1]
Stephen I. Wasserman, M.D.[3]
Allen F. Ryan, Ph.D. [1]

[1]*University Of California - San Diego, Surgery/Otolaryngology, La Jolla, CA, USA*
[2]*University Of Central Florida, School Of Medicine, Orlando, FL, USA*
[3]*University Of California - San Diego, Medicine/Allergy&Immunology, La Jolla, CA, USA*

Objective: NFκB, a dimeric transcription factor composed of p50 (NF-κB1) and p65 (RelA) subunits, is a central orchestrator of many immune/inflammatory processes, including innate immune responses activated by Toll-like receptors (TLRs) and NOD-like receptors (NLRs).

Method: We assessed middle ear expression of genes related to NFκB signaling in OM, using arrays generated from mice undergoing acute nontypeable Haemophilus influenzae (NTHi) infection. We also evaluated OM in mice deficient in the nfkb1 gene.

Results: Many NFκB activating genes were up-regulated 6-24 hours after NTHi inoculation. Inhibitory genes tended to be up-regulated at 24-72 hours. NFκB1-/- deficient mice demonstrated a significantly prolonged inflammatory course, and markedly delayed bacterial clearance, when compared to wildtypes. NFκB1 deletion resulted in decreased phagocytic capacity of macrophages, although intracellular killing ability was unhampered. Finally, lack of NFκB1 was permissive for a native murine pathogen (Klebsiella sp.) to invade the ME during OM

Conclusion: Our results suggest that NFκB plays a critical role in the normal resolution of OM. This is consistent with its position downstream from both TLRs and NLRs as a major mediator of innate immunity. The observed deficient in uptake of NTHi by NFκB1-deficient macrophages is consistent with the participation of innate immune receptors in phagocytosis. The unexpected appearance of Klebsiela in middle ears of NTHi-infected NFκB1-/- mice indicates that this transcription factor plays a role in preventing the passage of pathogens from the nasopharynx through the Eustachian tube during OM. (Supported by a HHMI Medical Research Fellowship and NIH/NIDCD grants DC000129, DC006297 and DC012595.)

2:44 - 2:51 PM **TUESDAY, JUNE 9**

OM2015221

TLR4 DRIVES ACQUIRED CHOLESTEATOMA PATHOGENESIS BY PROMOTING LOCAL INFLAMMATION AND BONE DESTRUCTION

Y Si, M.D. *Presenter*

YQ Zheng
ZG Zhang

Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Department Of Otolaryngology Head And Neck Surgery, Guangzhou, GUANGDONG, China

Acquired cholesteatoma is a chronic inflammatory disease characterised by both hyperkeratinised squamous epithelial overgrowth and bone destruction.Toll-like receptor 4 (TLR4) activation and subsequent inflammatory cytokine production are closely associated with inflammatory bone disease. However, the expression and function of TLR4 in cholesteatoma remain unclear. Here, we observed inflammatory cellinfiltration of the matrix and prematrix ofhuman acquired cholesteatoma, as well as dramatically increased expression of TLR4 and the pro-inflammatory cytokines TNF-α and interleukin (IL)-1β.TLR4 expression in human acquired cholesteatoma correlated with the disease severity; the number of TLR4-positive cells increased as the degree of cholesteatoma invasion, bone destruction and hearing loss increased. Moreover, TLR4 deficiency was protective against experimental acquired cholesteatoma-driven bone destruction and hearing loss, reducing local tumour necrosis factor (TNF)-α and IL-1β expression and impairing osteoclast formation by diminishing expression of the osteoclast effectors receptor activator of nuclear factor (NF)-κB ligand (RANKL) and tartrate-resistant acid phosphatase (TRAP). However, TLR4 deficiency had no effect on antimicrobial peptide, inducible nitric oxide synthase (iNOS) or BD-2 expression or bacterial clearance. Therefore, TLR4 promotes cholesteatoma-induced bone destruction and deafness by enhancing inflammatory responses and osteoclastogenesis.

2:51 - 2:58 PM **TUESDAY, JUNE 9**

OM2015249

LYMPHOCYTES ASSOCIATED WITH ADAPTIVE IMMUNITY FROM THE ADENOIDS AND PERIPHERAL BLOOD OF CHILDREN FROM RURAL AUSTRALIA AND THE CORRELATION WITH CHRONIC OTITIS MEDIA OR ADENOID HYPERTROPHY

Jessica Browne, B.Sc(Hons)[1] *Presenter*

Evan Matthews[1]
Andrew Taylor-Robinson[1]
Jennelle Kyd[2]

[1]*CQUniversity Australia, Health Sciences, Rockhampton, QLD, Australia*
[2]*Swinburne University Of Technology, Faculty Of Science, Engineering And Technology, Hawthorn, VIC, Australia*

Objective: Adenoidectomy is often used to manage chronic OM and how it contributes to improving OM is not well identified. This study aimed to identify factors that influence lymphocyte subsets from the blood and adenoids of children with and without chronic OM. It reports the association between adenoid and blood lymphocytes removed from children from an Australian rural community for either chronic OM or hypertrophy.

Method: 40 children aged 2 to7 years undergoing adenoidectomy in Rockhampton, Queensland were recruited. Background and clinical information was collected. B cell(CD19+), T cells(CD3+), T helper cells(CD3+CD4+), cytotoxic T cells(CD3+CD8+) and Treg cells(CD3+CD4+CD25hi+CD127lo+FoxP3+) were extracted from the blood and adenoids and analysed by multi-colour flow cytometry.

Results: Percentage of PBMC derived B cells cells ($p<0.05$) and Th cells ($p<0.005$) moderately, negatively correlated with age. Th cell percentages in children ≤3 years were higher than in children ≥4 years ($p<0.005$), and in children who did not attend daycare ($p<0.005$). PBMC derived Treg cells ($p<0.05$) had a moderate, positive correlation with daycare attendance. Age and daycare attendance did not influence lymphocyte percentages derived from the adenoid. Gender was significant for PBMC derived Tregs cells ($p<0.05$), but not in adenoid lymphocytes. Smoking exposure, birth order and number of children living in the household did not significantly influence lymphocyte subsets in the adenoid or blood.

Conclusion: In this population and within the two clinical groups, there were several moderate correlations associated with the child's clinical condition. The lymphocyte populations in the adenoid were not deficient in the OM group.

2:58 - 3:05 PM **TUESDAY, JUNE 9**

OM2015256

FUNCTIONAL DEFICITS OF CD4+ T CELLS IN YOUNG CHILDREN CONTRIBUTE TO THE RECURRENT OTITIS-PRONE CHILDREN

Saleem Basha *Presenter*

Matthew Morris
Michael Pichichero

Rochester General Hospital, Research Institute, Rochester, NY, USA

Objective: Our group seeks a more precise explanation for immunologic dysfunction that causes children to be prone to repeated episodes of acute otitis media (AOM). In our prospective, NIDCD-supported, longitudinal study, we have identified a subset of stringently-defined otitis prone (sOP) children who experience recurrent otitis media despite tympanocentesis drainage and individualized antibiotic treatment. These sOP children do not develop protective antibody responses to several AOM vaccine candidate protein antigens after exposure to Streptococcus pneumoniae and Haemophilus influenzae during nasopharyngeal colonization and AOM episodes. Efficient generation of protective antibodies from B-cells depends on the function of CD4+ T cells. Therefore we sought to understand the function and phenotypes CD4+T cells in sOP children compared to non-OP (NOP) children.

Method: Peripheral blood mononuclear cells (PBMC) were stimulated with anti-CD3 & anti-CD28 beads to induce global T-cell receptor stimulation. The memory (CD45-) and naïve (CD45+) CD4 T-cell responses were studied by intracellular cytokines analysis and flow cytometry. Th1 and Th2 activity will be measured by expression of the cytokines IFNγ, IL-2, TNF-α and IL-4.

Results: sOP children had a significantly lower percentage of activated CD69+ T cells compared to NOP children. We also found significant differences in the frequencies of activated memory T cells and polyfunctional Th1 responses (IFNγ+ TNF-α+) in sOP children.

Conclusion: sOP children have functionally defective T cells, which may impair the functional responses of antibody secreting B cells, rendering these children susceptibile to recurrent infections. Supported by NIDCD RO1 08671.

3:15 - 3:45 PM **TUESDAY, JUNE 9**

EXHIBIT HALL A

COFFEE BREAK IN EXHIBIT/POSTER HALL

3:45 - 4:45 PM **TUESDAY, JUNE 9**

BALTIMORE 3-5

PANEL 5 (B): PNEUMOCOCCAL VACCINE (PCV)

Moderator:

Stephen Pelton (US)

Speakers:

Stephen Pelton (US)

Michael Pichichero (US)

Ivo Vojtek (Belgium)

3:45 - 4:45 PM **TUESDAY, JUNE 9**

OM2015268

MULTIPLE NON-VACCINE SEROTYPES OF STREPTOCOCCUS PNEUMONIAE EMERGE DURING THE 7-VALENT (PCV7) AND 13-VALENT (PCV13) PNEUMOCOCCAL CONJUGATE VACCINATION – ROCHESTER, NY – 2006-2014

Michael Pichichero[2] *Presenter*

Ravinder Kaur[1,2]
Janet Casey[1]

[1]*Legacy Pediatrics, Rochester, NY, USA*
[2]*Rochester General Hospital Research Institute, Rochester, NY, USA*

Objective: A 13-valent pneumococcal conjugate vaccine (PCV13) was introduced in the U.S. in 2010, replacing the 7-valent (PCV7) product. PCV13 included all PCV7 serotypes plus six additional serotypes (1, 3, 5, 6A, 7F & 19A). We prospectively monitored S. pneumoniae (Spn) serotypes colonizing the nasopharynx (NP) for 9 consecutive years (2006-2014).

Method: NP samples were obtained for Spn identification from prospectively followed healthy children at 6-30 months of age. A total of 994 visits during the PCV7 and 1498 visits during the PCV13 era were included from 538 enrolled children. Serotyping and multi-locus sequence typing (MLST) types of each Spn were determined.

Results: A total of 803 Spn were isolated. 327 Spn were identified in the PCV7 era and 476 in the PCV13 era. There was no difference in the prevalence of Spn NP colonization comparing the PCV7 and PCV13 eras. The 12 most common non-vaccine serotypes identified during the PCV7 and PCV13 eras are shown in the figure. The most common MLST types found (>20 isolates) in the PCV7 era were ST320, ST199 and ST62 while in the PCV13 era were ST558, ST439, ST432, ST199 and ST62. In addition ST36, ST448, ST1840 and ST3280 were observed only during PCV13 era (≥6 isolates).

Conclusion: PCV13 has rapidly reduced NP colonization by serotypes included in the vaccine (e.g., 19A and 6A) but new serotypes such as 35B, 21, 23A, 23B, 15A, 15B & 15C have rapidly emerged as NP colonizers. The MLST data suggest mostly unmasking of new strains rather than capsular switching. Supported by NIDCD R01 08671.

3:45 - 4:45 PM **TUESDAY, JUNE 9**

OM2015108

REDUCTIONS IN OTITIS MEDIA AFTER IMPLEMENTATION OF THE 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D-CONJUGATE VACCINE IN NATIONAL IMMUNIZATION PROGRAMS: A REVIEW OF POST-MARKETING STUDIES

Ivo Vojtek, Ph.D. *Presenter*

Bernard Hoet, Ph.D.

GSK Vaccines, Wavre, BRABANT WALLON, Belgium

Introduction: Streptococcus pneumoniae and non-typeable Haemophilus influenzae (NTHi) are major bacterial pathogens causing otitis media (OM). The 10-valent pneumococcal NTHi protein D-conjugate vaccine (PHiD-CV), designed to protect against pneumococcal and NTHi diseases and licensed outside the US in 130 countries, has demonstrated efficacy against invasive pneumococcal disease, pneumonia and acute OM.

Objective: To review PHiD-CV's impact on OM after its implementation in national immunization programs.

Methods: Review of OM surveillance data from Brazil, Iceland, Canada, Australia.

Results: A time-series database analysis in Goiania, Brazil (3+1-PHiD-CV-schedule since 2010), indicated 45% (95%CI: 43%-46%) lower rates of all-cause OM visits in 2-23-month-olds post-PHiD-CV-vaccination (6/2011-8/2013) versus pre-vaccination (5/2008-5/2010).1 In Iceland (2+1-PHiD-CV-schedule since 2011), the annual incidence of acute OM hospital visits/admissions between 1/2008-12/2013 was 24% (95%CI: 15%-33%) lower in <2-year-olds born post-PHiD-CV-implementation (2011) versus pre-implementation (2008-2010).2 In a study in <2-year-olds in Quebec, Canada (2+1-PHiD-CV-schedule replacing 7-valent pneumococcal CRM197-conjugate vaccine [7vCRM] in 2009), comparing PHiD-CV- and 7vCRM-eligible children, no consistent differences in OM visit frequencies between both vaccines were reported.3 Physician OM claims in this study may not be truly OM-specific, thereby obscuring possible differences. OM surveillance in <36-month-olds in Indigenous communities in Australia's Northern Territories (3+1-PHiD-CV-schedule replacing 7vCRM in 10/2009) between 9/2008 and 12/2012 showed a 12% (95%CI: 5%-19%) absolute risk reduction in suppurative OM in PHiD-CV-vaccinated versus 7vCRM-vaccinated children.

Conclusion: In post-marketing OM studies, PHiD-CV has shown a positive impact on OM across several regions with different epidemiology and standards of care. 1Sartori, ISPPD-2014; 2Sigurdsson, ESPID-2014; 3De Wals, ESPID-2013; 4Leach, BMC Pediatrics-2014

4:45 - 5:30 PM **TUESDAY, JUNE 9**

BALTIMORE 3-5

PANEL 7 (B): MICROBIAL PATHOGENESIS

Moderator:

Kevin Mason (US)

Speakers:

Jennelle Kyd (Australia)

Guanchun Bai (US)

Muneki Hotomi (Japan)

4:45 - 5:30 PM **TUESDAY, JUNE 9**

OM2015248

POLYMICROBIAL COLONISATION ASSOCIATED WITH CHRONIC OTITIS MEDIA CORRELATES WITH MICROBIAL CONDITIONS IN VITRO THAT INCREASE ADHERENCE, BIOFILM FORMATION AND REDUCED PRO-INFLAMMATORY RESPONSES WITH RESPIRATORY EPITHELIAL CELLS

Jennelle Maree Kyd, Ph.D.[1] *Presenter*

Jessica Browne, B.Sc(Hons)[2]
Ajay Krishnamurthy[1]
Evan Matthews[2]

[1]*Swinburne University Of Technology, Faculty Of Science, Engineering And Technology, Hawthorn, VIC, Australia*
[2]*CQUniversity Australia, Health Sciences, Rockhampton, QLD, Australia*

Objective: Polymicrobial colonisation load has been identified as a significant risk factor for AOM and particularly recurrent and chronic OM. This study aimed to investigate the bacterial factors that contribute to increased biofilm, adherence and modification of inflammation in vitro using respiratory epithelial cells and compare to adenoidal and nasopharyngeal colonisation patterns in OM and non-OM children to understand the significance of the colonisation patterns to clinical condition.

Method: Human respiratory epithelial cell lines were used to study single and multiple combinations of Streptococcus pneumonia, Moraxella catarrhalis and nontypable Haemophilus influenzae inoculation conditions with and without viral infection. Adherence, biofilm formation and Interleukin-6 and IL-8 responses were measured. Clinical microbiology was measured on adenoid biopsies and nasopharyngeal aspirates from children 2 to 7 years of age, with or without chronic otitis media.

Results: Polymicrobial combinations in vitro and particularly a pre-viral infection significantly increased S. pneumoniae, M. catarrhalis and NTHi adherence and biofilm formation in specific combinations of co-culture and epithelial cell type ($p<0.05$) and reduction in the production of IL-6 and IL-8. Epithelial cell contact was a significant contributor to rapid upregulation of biofilm formation. M. catarrhalis positive adenoid biopsies and nasopharyngeal aspirates positively correlated with presence of S. pneumoniae cultures ($p<0.05$); and S. pneumoniae positively correlated with NTHi ($p<0.005$).

Conclusion: Certain polymicrobial infections conditions are associated with chronic OM and in vitro, specific conditions can be shown to augment bacterial adherence and biofilm formation as well as reduce the pro-inflammatory cytokine responses by epithelial cells.

4:45 - 5:30 PM **TUESDAY, JUNE 9**

OM2015279

ROLE OF CYCLIC DI-AMP IN PNEUMOCCAL BIOLOGY AND PATHOGENESIS

Guangchun Bai, M.D.,Ph.D. *Presenter*

Albany Medical College, Center For Immunology And Microbial Disease, Albany, NY, USA

It has been reported that two DHH subfamily 1 proteins in Streptococcus pneumoniae play an important role in several infection models including otitis media and pneumonia. However, the molecular basis remains unclear. In our study, we have demonstrated that both proteins possess cyclic di-AMP (c-di-AMP) phosphodiesterase activity. c-di-AMP was recognized only recently as a potential new second messenger and has been shown to play important roles in bacterial biology and pathogenesis. This dinucleotide is synthesized enzymatically from two molecules of ATP or ADP by diadenylate cyclase and cleaved to pApA or AMP by distinct c-di-AMP phosphodiesterases. We have shown that S. pneumoniae encodes a diadenylate cyclase, dacA, which is an essential gene. The two DHH subfamily 1 proteins, Pde1 and Pde2, cleave c-di-AMP to pApA and AMP, respectively. Deletion of either pde1 or pde2 elevates bacterial c-di-AMP levels, reduces bacterial chain length, and enhances pneumococcal sensitivity to several stress conditions. We have also identified a c-di-AMP binding protein (CabP) in S. pneumoniae by using c-di-AMP affinity chromatography. Our results revealed that CabP plays a role in potassium uptake through a direct interaction with a potassium transporter. Deletion of either cabP or the potassium transporter-encoding gene in pneumococcus abolishes bacterial growth in media with low concentrations of potassium. c-di-AMP impairs potassium uptake by abolishing the interaction between CabP and the potassium transporter. Our future work will explore the role of c-di-AMP and CabP in the stress response of pde mutants and other signaling cascades mediated by c-di-AMP in S. pneumoniae.

4:45 - 5:30 PM **TUESDAY, JUNE 9**

OM2015204

WHY THE CO-COLONIZATION WITH S. PNEUMONIAE AND H. INFLUENZAE LEADS INTRACTABLE ACUTE OTITIS MEDIA?

Muneki Hotomi, M.D.,Ph.D. *Presenter*

Masanobu Hiraoka
Masamitsu Kono
Shunji Tamagawa
Saori Takeda
Shigeki Tsuchihashi
Noboru Yamanaka

Wakayama Medical University, Otorhinolaryngology-Head And Neck Surgery, Wakayama-shi, WAKAYAMA, Japan

Objectives: Streptococcus pneumoniae and nontypeable Haemophilus influenzae (NTHi) are the most common pathogens responsible for 19-74% and 16-61% of episodes of acute otitis media (AOM), respectively. AOM caused by S. pneumoniae alone has been associated with much severe clinical course, compared with AOM caused by NTHi alone. However, as shown in several studies, polymicrobial infections with S. pneumoniae and NTHi often brought on recurrent and persistent episodes of AOM.

Methods: S. pneumoniae and NTHi were cultured with human epithelial cell Detroit 562 cell by co-culture method. Briefly, Detroit562 cell was cultured until the confluent phase. S. pneumoniae and NTHi were inoculated on the Detroit562 cell and incubated at 37?C at 5% CO2 atmosphere. The morphological changes of both pathogens were observed in microscopic video shoots.

Results: S. pneumoniae invaded to the cell-to-cell junctions of Detroit562 cells and varied its phase from transparent to opaque. In contrast, NTHi adhered on the Detroit562 cells and formed biofilm.

Conclusion: Recurrent/Intractable AOM is associated with persistent, often mixed, infections with S. pneumoniae and NTHi. NTHi frequently produces biofilm and resides in the adenoid and middle ear mucosa. The current ex-vivo study indicated that S. pneumoniae and NTHi co-related with each other and persisted efficiently onto and into the cultured human epithelial cells. Mix infections of S. pneumoniae and NTHi allow both organisms to promote biofilm formation and/or persistence in cell-to cell junctions.

WEDNESDAY SCIENTIFIC PRESENTATIONS

8:00 - 9:45 AM **WEDNESDAY, JUNE 10**

CHERRY BLOSSOM BALLROOM

PLENARY 3 (B): VACCINE

Moderators:

Lauren Bakaletz (US)

Timothy Murphy (US)

Keynote Speaker:

Cecil Czerkinsky (Sweden)

Speakers:

Lauren Bakaletz (US)

Timothy Murphy (US)

Stephen Barenkamp (US)

Tasnee Chonmaitree (US)

8:35 - 8:50 AM **WEDNESDAY, JUNE 10**

OM2015150

CURRENT STATUS OF VACCINES FOR OTITIS MEDIA DUE TO NONTYPEABLE HAEMOPHILUS INFLUENZAE (NTHI)

Lauren O. Bakaletz, Ph.D. *Presenter*

The Research Institute At Nationwide Children's Hospital And The Ohio State University College Of Medicine, Center For Microbial Pathogenesis, Columbus, OH, USA

In 2006, the POET study demonstrated for the first time that one could immunize parenterally against OM due to NTHI. In that study, NTHI outer membrane protein D (or PD) was conjugated to11 distinct pneumococcal capsular polysaccharides (Pnc-PD). Efficacy vs. AOM due to Streptococcus pneumoniae was ~57%, a result very similar to that shown by the already licensed PCV7. However, the efficacy against all AOM was 34%, far greater than the 6-7% reported for PCV7. Moreover, POET data revealed that Pnc-PD showed 35.3% efficacy vs. AOM due to NTHI, and a 41.4% reduction in NP carriage of NTHI, a result attributed to the inclusion of an NTHI-specific antigen in the vaccine formulation. Since the POET study, and following release of a 10-valent version of Pnc-PD (PHiD-CV), an additional study demonstrated no effect on NP colonization by NTHI in the second year of life. Moreover, Smith-Vaughan et al. reported the absence of the gene that encodes PD in ~19% of multiple carriage and disease isolates of NTHI. The inability of ~19% of NTHI isolates to express the single NTHI antigen targeted by PHiD-CV helps to explain the limited ~35% efficacy against AOM due to NTHI in the POET study. Thus, despite initial enthusiasm and continued optimism as to our ability to develop a broadly effective vaccine for NTHI-induced OM, it is a broadly held view that these vaccines cannot be reliant upon any single antigen due to the vast heterogeneity of NTHI. Recent progress towards achieving this goal will be discussed.

8:50 - 9:05 AM **WEDNESDAY, JUNE 10**

OM2015314

VACCINE DEVELOPMENT FOR MORAXELLA CATARRHALIS: RATIONALE, CHALLENGES AND CURRENT STATUS

Timothy F. Murphy, M.D. *Presenter*

State University Of New York At Buffalo, Clinical And Translational Research Center, Buffalo, NY, USA

Moraxella catarrhalis causes approximately 10 to 20% of episodes of acute otitis media based on cultures of middle ear fluid. However, the burden of M. catarrhalis in otitis media is underestimated by relying on culture alone which detects exclusively planktonic bacteria. Based on results of analysis of middle ear fluids using state-of-the-art imaging and molecular techniques to detect biofilms, a much larger proportion of middle ear fluids from children with acute otitis media and otitis media with effusion contain M. catarrhalis than is detected by culture. Thus, prevention of otitis media by immunization will require vaccines that are directed at all three pathogens, including nontypeable Haemophilus influenzae, Streptococcus pneumoniae and M. catarrhalis. A promising approach to vaccine development for M. catarrhalis is to identify conserved, surface-exposed proteins that will generate functional immune responses and induce enhanced clearance in the mouse pulmonary clearance model. This approach parallels the observation that protein D, a conserved, surface protein of H. influenzae induces protective responses to otitis media in children. An important area for future study is to characterize the elements of a protective immune response and identify a correlate of protection. Several surface proteins of M. catarrhalis are in various stages of development as vaccine antigens. A vaccine against M. catarrhalis has the potential to prevent both acute and chronic forms of otitis media that cause substantial morbidity in otitis-prone children.

9:05 - 9:20 AM **WEDNESDAY, JUNE 10**

OM2015008

VACCINE POTENTIAL OF THE HMW1/HMW2 AND HIA PROTEINS OF NONTYPEABLE HAEMOPHILUS INFLUENZAE

Stephen J Barenkamp, M.D. *Presenter*

Linda E Winter, B.S.Ed.

Saint Louis University School Of Medicine, Department Of Pediatrics, St. Louis, MO, USA

Objective: The HMW1/HMW2 and Hia proteins are highly immunogenic adhesins of nontypeable Haemophilus influenzae (NTHi). Approximately 75% of NTHi express HMW1/HMW2 adhesins and 25% express an Hia adhesin. Our objective was to assess the ability of antisera raised against purified HMW1/HMW2 proteins and against outer membrane vesicles of NTHi over-expressing Hia to mediate opsonophagocytic killing of a large panel of NTHi.

Methods: Native HMW1/HMW2 proteins were purified from four HMW1/HMW2-expressing NTHi. Outer membrane vesicles (OMV) were prepared from two prototype NTHi engineered to overexpress Hia proteins. Immune sera were raised in guinea pigs and the resulting antisera were assessed for their ability to mediate killing of NTHi in an opsonophagocytic assay with HL-60 phagocytic cells.

Results: The four HMW1/HMW2 antisera mediated killing, respectively, of 22 of 65, 43 of 65, 28 of 65, and 34 of 65 unrelated HMW1/HMW2-expressing NTHi. As a group, the four sera mediated killing of 51 of 65 HMW1/HMW2-expressing strains. The two Hia-OMV antisera mediated killing, respectively, of 17 of 25 and 14 of 25 unrelated Hia-expressing NTHi. Together, they mediated killing of 20 of 25 Hia-expressing strains. The HMW1/HMW2 antisera did not mediate killing of Hia-expressing strains, but the Hia-OMV antisera mediated killing of 33 of 65 HMW1/HMW2-expressing strains.

Conclusions: Antibodies directed against native HMW1/HMW2 proteins and outer membrane vesicles expressing Hia are capable of mediating broad-based opsonophagocytic killing of homologous and heterologous NTHi. A vaccine formulated with a limited number of HMW1/HMW2 proteins and Hia-OMVs might provide protection against disease caused by most NTHi.

9:20 - 9:35 AM **WEDNESDAY, JUNE 10**

OM2015179

VIRAL VACCINES FOR OTITIS MEDIA

Tasnee Chonmaitree *Presenter*

University Of Texas Medical Branch, Department Of Pediatrics, Galveston, TX, USA

Respiratory viruses play an important role in the pathogenesis of acute otitis media (AOM). Bacterial otopathogens that are colonized in the nasopharynx gain access into the middle ear during or after viral upper respiratory tract infection (URI). Viruses alone can cause AOM in the absence of nasopharyngeal bacterial colonization. Therefore, success in reducing AOM incidence relies on not only prevention of nasopharyngeal bacterial colonization, but also prevention of viral URI. Because a variety of viruses cause URI, prevention of OM using viral vaccines is a major challenge. To date, vaccines against influenza viruses have been the only respiratory virus vaccines available, and the vaccines have been shown for a few decades to reduce OM incidence during influenza season by preventing influenza illness and influenza-associated AOM. The effectiveness of the vaccines on AOM prevention varies from year to year, depending on the efficacy of the vaccine against influenza and the level of influenza activity in the community. Respiratory syncytial virus (RSV), rhinovirus, coronavirus, and adenovirus have also been identified as important AOM-associated viruses. Numerous obstacles have prevented the availability of vaccines against these viruses; for example, high antigenic diversity of rhinovirus and adenovirus has made vaccine development difficult. RSV vaccine development goal has been to prevent lower respiratory tract infection and live-attenuated RSV vaccine has caused URI. Nevertheless, some progress has been made towards the goal of making vaccines against respiratory viruses other than influenza. Success in making vaccines against common OM-associated viruses will have a great potential to prevent AOM.

9:45 - 10:15 AM **WEDNESDAY, JUNE 10**

EXHIBIT HALL A

COFFEE BREAK IN EXHIBIT/POSTER HALL

10:15 - 11:15 AM **WEDNESDAY, JUNE 10**

CHERRY BLOSSOM BALLROOM

MINISYMPOSIUM 5 (C): IMPACT OF OM ON HEARING AND AUDITORY FUNCTION

Moderators:

Joseph Kerschner (US)

Kenny Chan (US)

Speakers:

Joseph Kerschner (US)

Howard Hoffman (US/NIDCD)

Andrés Sibbald (Argentina)

Mark Haggard (UK)

10:15 - 10:27 AM **WEDNESDAY, JUNE 10**

OM2015050

IMPACT OF OTITIS MEDIA ON HEARING AND AUDITORY FUNCTION

Joseph E Kerschner, FACS, FAAP *Presenter*

Medical College Of Wisconsin, Otolaryngology And Communication Sciences, Milwaukee, WI, USA

Introduction: Middle ear effusion (MEE) following an episode of otitis media (OM) is the most common cause of hearing loss in children. Gel forming mucins (GFM) are thought to be the primary components of MEE leading to increased viscosity and hearing loss. However, no previous clinical studies have been conducted to assess these assumptions.

Objective: To describe the inflammatory processes in OM pathophysiology which lead to mucin gene up-regulation and increased secretion of GFM and subsequent hearing loss, and to describe current clinical trials underway examining this pathophysiology.

Method: GFM expression, MEE viscosity, ME mucosal characteristics and audiometric data from patients undergoing routine tympanostomy tube insertion (TTI) for recurrent OM (RecOM) and chronic OM with effusion (COME) were assessed to ascertain correlations between pathophysiologic events in OM and hearing loss.

Results: Increased MUC5B and a sum of all mucins was correspondingly associated with greater hearing loss, $p<0.05$. Ears with effusion demonstrated greater hearing loss than those without ($p<0.05$) and the GFM expression was higher in ears with ≥ 30dB hearing loss; this difference was statistically significant in MUC2 ($p=0.034$). Higher MUC2 ($p=0.032$) was detected in ears with greater MEE viscosity ratings. Intra-patient analysis indicated a trend towards more viscous effusion in the worse–hearing ear.

Conclusion: This clinical trial demonstrates a direct correlation between the expression of specific GFM, MEE viscosity, and hearing levels. Implications of these findings on potential novel treatments and patient care will be discussed.

10:27 - 10:39 AM **WEDNESDAY, JUNE 10**

OM2015107

OTITIS MEDIA AND HEARING LOSS IN EARLY PRIMARY SCHOOL GRADES: THE UNITED STATES EARLY CHILDHOOD LONGITUDINAL STUDY–KINDERGARTEN CLASS OF 2010–11 (ECLS–K:2011)

Howard Jay Hoffman, M.A.[1] *Presenter*

Christa L. Themann, M.A.[2]
Kathleen E. Bainbridge, Ph.D.[1]
Katalin G. Losonczy, M.A.[1]
May S. Chiu, B.S.[1]
Chuan-Ming Li, M.D.,Ph.D. , MSPH[1]

[1]*National Institute On Deafness And Other Communication Disorders (NIDCD), Epidemiology And Statistics Program, Bethesda, MARYLAND, USA*
[2]*National Institute For Occupational Safety And Health (NIOSH), CDC, Hearing Loss Prevention Team, Cincinnati, OHIO, USA*

Objective: To describe associations between reported ear infections/otitis media since birth and hearing loss in kindergarten and first grade.

Methods: ECLS–K:2011 children (n=13,399) were drawn from a national sample of public and private schools, both full- and part-day kindergarten classes in 2010–11. Information on children's health and development, including medically-diagnosed ear infections (EIs) and hearing loss, were reported by parents; additional information was provided by teachers, schools, and daycare providers. Trained examiners administered age-appropriate assessments of intellectual development and hearing exams in school settings. Logistic regression models were statistically-adjusted for covariates using national sampling weights.

Results: Before age 2, 39.6% experienced 1+ EIs and 20.9% had 3+ EIs. By kindergarten entry, 66.1% had experienced 1+ EIs and 8.4% had been treated with surgically-implanted ear tubes (ETs). From kindergarten-to-spring first grade, annual EI prevalence, 19.1%, remained high and 98.2% of EIs were medically-diagnosed. From birth-to-spring first grade, 81.6% had experienced 1+ EIs and 9.9% had been treated with ETs (usually both ears). Hearing loss prevalence was 1.2% if no EIs reported, compared to 2.9% with EIs (without ETs), and 10.9% with ETs. Hearing loss was associated with EIs (without ETs), odds ratio (OR)=2.2, 95% confidence interval (CI): 1.0–4.9, while ETs increased the risk, OR=7.5, 95%CI: 3.4–16.6 in multivariable models adjusted for parents' education, health insurance, children's sex, race, plurality, birth weight, birth complications/NICU, breastfeeding, and general health status.

Conclusion: Hearing loss in early primary school grades is associated with EIs and risk is 3-fold higher for children treated with ETs.

10:39 - 10:51 AM **WEDNESDAY, JUNE 10**

OM2015250

A STRATEGY FOR IMPROVING PEDIATRICIANS DETECTION AND MANAGEMENT OF INFANTS "AT RISK" FOR SEVERE PATTERNS OF OTITIS MEDIA IN A TEACHING HOSPITAL.

Andrés Daniel Sibbald *Presenter*

Lucila Fernie
Natalia Müller

Hospital Brit·nico De Buenos Aires, Departamento De Pediatrìa, Buenos Aires, Argentina

Objective: Recurrent acute otitis media and persitent otitis media with effusion are most prevalent in early infancy,when diagnosis of middle ear disease is fraught with practical classification difficulties and inconsistent management decisions. Evidence based guidelines provide inceasingly rigorous otoscopic criteria that must be brought into primary care practice, and they also support case finding of potentially severe disease forms of otitis media in childhood. These recommendations however are often disregarded in daily practice and our objective is to affirm their relevance and to further their instrumentation.

Method: We describe the initial implementation of a pediatric program that seeks to identify 6 to 36 month old patients with patterns of otitis media that place them "at risk" of advanced disease, and to offer a format for follow up of their middle ear status over the 3 to 6 month recommended observation period. Outpatient pediatric staff and residents, duly trained in pneumatic otoscopy and accoustic reflectometry, are encouraged to share abnomal findings with validated otoscopists at an "Otitis Media Clinic" created with the purpose of doubling as an enhanced care facility and a training center to improve compliance with guideline recommendations.

Results: Preliminay results disclose expected difficulties in fulfilment and recording of otoscopic appraisals and in case finding of infants with persistent bilateral middle ear effusions. The follow up form is shown.

Conclusion: An active search for infants with some important presentations of otitis media in a general pediatric practice is hampered by obstacles that are identified and discussed.

10:51 - 11:03 AM **WEDNESDAY, JUNE 10**

OM2015336

DIFFERING SEASONALITIES OF HEARING MEASURES AND PARENT QUESTION RESPONSES REQUIRE SEASONAL ADJUSTMENT OF ANALYSES AND OF REFERRAL CRITERIA IN OM

Mark Haggard[4] *Presenter*

Snezana Andric Filipovic[1,2]
Paola Marchisio[3]
Helen Spencer[4]

[1]*Clinical Centre Of Serbia, Clinic Of ENT And Maxillofacial Surgery, Belgrade, Serbia*
[2]*Mater Dei Hospital, ENT Department, Msida, Malta*
[3]*University Of Milan, Department Of Pathophysiology And Transplantation, Milan, Italy*
[4]*University Of Cambridge, Multi-Centre Otitis Media Study Group, Cambridge, United Kingdom*

Introduction: We previously showed that tympanometry (modified Jerger, pre-mapped to hearing level as ACET) combines fruitfully with parental responses on hearing difficulty questions (RHD) in predicting HL. This offers screening applications in settings lacking audiometry, but these various hearing measures, even different RHD items, have slightly differing seasonalities.

Objective: To establish whether seasonality adjustment improves mapping between RHD plus ACET-scaled tympanometry and HL.

Methods: In the Eurotitis-2 multi-national secondary care database, 1415 OM cases had complete data on the two objective hearing measures, on parental overall hearing rating (a) and on three questionnaire items reflecting communication impact of poor hearing (b). Multiple regression predicted HL from ACET, RHD measures (a) and average (b), paired sine/cosine functions of 1-year period sampled weekly, and their 1st order interactions.

Results: Interaction of ACET with (b) was significant, but no season interactions were. Overall (main) effects explained 47% of the HL variance with widely differing effect sizes: tympanometry (mapped as ACET: partial eta-squared 0.348); hearing rating (a: 0.039); seasonality (sine/cosine pair: 0.009); communication items (b: 0.001.) However using the interaction term, communication impact items (b) improved prediction among more severe cases.

Conclusions: Under constrained circumstances, hearing questions to parents perform better than their poor reputation suggests, especially if scoring takes season and differences in item type into account. Impact (b)-type items reflect wider impact and can be proliferated to accumulate reliability. Ratings (like VAS scales) have higher predictive validity, but cannot be acceptably repeated, so ways to supplement their reliability are needed.

11:15 AM - 12:00 PM **WEDNESDAY, JUNE 10**

CHERRY BLOSSOM BALLROOM

PODIUM 10: VACCINE 1

Moderator:

Tal Marom (Israel)

Speakers:

Tal Marom (Israel)

Tatsuya Hayashi (Japan)

Amanda Leach (Australia)

Frida Enoksson (Sweden)

Laura Novotny (US)

11:15 - 11:22 AM **WEDNESDAY, JUNE 10**

OM2015005

BACTERIOLOGY OF ACUTE OTITIS MEDIA IN YOUNG CHILDREN IN THE 7- AND 13-PNEUMOCOCCAL CONJUGATE VACCINES ERA IN CENTRAL ISRAEL

Tal Marom, M.D. *Presenter*

Sharon Ovnat Tamir

Edith Wolfson Medical Center, Sackler School Of Medicine, Tel Aviv University, Otolaryngology-Head And Neck Surgery, Holon, Israel

Objective: To describe the changing trends in acute otitis media (AOM) bacteriology in a narrow time frame, when the 7-valent pneumococcal conjugate vaccine (PCV7) and PCV13 were introduced in the Israeli National Immunization Program (NIP).

Method: We retrospectively identified children younger than 6 years of age who presented to our hospital with "severe" AOM episodes, and had middle ear fluid (MEF) cultures obtained during tympanocentesis or from spontaneous otorrhea during 2008-2013, when PCV7 (2009) and PCV13 (2010) were gradually implemneted in the routine childhood vaccination program. Data were extracted for demographics, clinical and microbiological parameters, according to vaccination status.

Results: Of the 295 eligible "severe" AOM episodes reported in 279 children, 224 (76%) had MEF cultures from tympanocentesis and 71 (24%) from spontaneous otorrhea. Boys and children under 2 years of age contributed 178 (60%) and 219 (74%) AOM episodes, respectively. Acute mastoiditis complicated 58 (20%) of these episodes. While none of the children were PCV immunized in 2008, >90% had received ≥1 PCV dose(s) by 2011 or later. Of the 106 (36%) MEF cultures which tested positive for otopathogens in the entire study period, Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis and multiple bacteria grew in 60 (57%), 39 (37%), 2 (2%) and 5 (5%) episodes, respectively. S. pneumoniae positive MEF culture rate in unimmunized children (31, 69%) was significantly higher than in PCV7- (22, 59%) or PCV13- (12, 50%) immunized children.

Conclusion: PCV7 and PCV13 implementations in the Israeli NIP were associated with a rapid reduction of "severe" pneumococcal AOM episodes.

11:22 - 11:29 AM **WEDNESDAY, JUNE 10**

OM2015041

DECREASE IN MYRINGOTOMIES TO THE PEDIATRIC PATIENTS WITH ACUTE OTITIS MEDIA AFTER INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINES IN JAPAN

Tatsuya Hayashi *Presenter*

Haruyuki Ichikawa
Tomohiko Michizuka
Seigo Ueda
Kan Kishibe
Miki Takahara
Akihiro Katada
Yasuaki Harabuchi

Asahikawa Medical University, Otolaryngology-Head And Neck Surgery, Asahikawa, HOKKAIDO, Japan

Backgrounds: Pneumococcal conjugate vaccine (PCV) was introduced to Japan in 2010, 10 years since it became available in the United States and other many countries. Most of otolaryngologists in Japan provide the primary care to the pediatric patients with acute otitis media (AOM). “Clinical practice guidelines for the diagnosis and management of AOM in children in Japan” recommends myringotomy as a treatment option to the patients with moderate diseases with marked bulging of tympanic membranes or severe ones. Therefore, the number of myringotomies could be a good indicator of the overall disease severity of AOM at specific periods.

Objective: The primary objective of this study is to clarify the changes in clinical practice for the pediatric patients with acute otitis media after introduction of PCV in Japan.

Method: The changes in the number of myringotomies performed to the patients under 24 months of age in an isolated local area were investigated between 2009 and 2013. Nasopharyngeal swabs were collected from all patients with AOM under age of 24 months. The number of myringotomies was compared with overall pneumococcal carriage rate.

Results: The rate of the patients who underwent myringotomies declined gradually from 14% (109 myringotomies out of all patients under 24 months old) in 2009 to 5% (21/433) in 2013. The pneumococcal carriage rates of the patients also decreased gradually from 55% (312 positives/ 570 patients) to 35% (149/420).

Conclusion: PCV has had great impact on daily clinical practice of AOM in Japan.

11:29 - 11:36 AM **WEDNESDAY, JUNE 10**

OM2015059

REDUCED MIDDLE EAR INFECTION WITH NON-TYPEABLE H. INFLUENZAE, BUT NOT S. PNEUMONIAE, AFTER TRANSITION TO 10-VALENT PNEUMOCOCCAL NON-TYPEABLE HAEMOPHILUS INFLUENZAE PROTEIN D CONJUGATE VACCINE.

Amanda Jane Leach, Ph.D.[1] *Presenter*

Christine Wigger[1]
Kim Hare[1]
Vanya Hampton[1]
Jemima Beissbarth, BScEd[1]
Ross Andrews[1]
Mark Chatfield[1]
Heidi Smith-Vaughan[1]
Peter Stanley Morris[1,2]

[1]*Menzies School Of Health Research, Child Health Division, Darwin, NORTHERN TERRITORY, Australia*
[2]*Royal Darwin Hospital, Paediatrics, Darwin, NORTHERN TERRITORY, Australia*

Objective: To determine whether the less severe otitis media measured in the PHiD-CV10 era was also associated with changes in the nasopharyngeal (NP) carriage and middle ear discharge (ED) microbiology

Method: Standardised surveillance of NP carriage and ED microbiology in remote Indigenous communities between September 2008 and December 2012. Children less than 3 years of age and having received a primary course of 2 or more doses of one PCV and not more than one dose of an alternative PCV were included in the primary analysis; children with non-mixed PCV schedules were also compared.

Results: The change from PCV7 to PHiD-CV10 was associated with a shift in the prevalence of any suppurative OM (AOM with or without perforation, or chronic suppurative OM) from 52% to 39%, and a concomitant increase in OME from 41% to 51%. NP swabs were obtained from 421 of 444 (95%) children in the PCV7 group and 443 of 451 (98%) children in the PHiD-CV10 group. Non-mixed PCV schedules were received by >=70%. Pneumococcal (Spn) NP carriage was 76% and 82%, and non-typeable Haemophilus influenzae (NTHi) carriage was 68% and 73%, respectively. ED was obtained from 60 children in the PCV7 group and from 47 children in the PHiD-CV10 group. Data from bilateral perforations were combined. Spn was cultured from 25% and 18%, and NTHi from 61% and 34% respectively (p=0.008).

Conclusion: PHiD-CV10 vaccination was associated with lower prevalence rates of suppurative OM and NTHi-infected ED. Randomised controlled trials are needed to answer this question.

11:36 - 11:43 AM **WEDNESDAY, JUNE 10**

OM2015068

SEROTYPES OF STREPTOCOCCUS PNEUMONIA IN 19 CASES OF ACUTE MASTOIDITIS IN SWEDEN IN RELATION TO PNEUMOCOCCAL VACCINATION.

Frida Enoksson, M.D.[1] *Presenter*

Asa Melhus[2]
Ann Hermansson[3]

[1]*Lund University, ENT-dep, Lund, Sweden*
[2]*Uppsala University, Microbiology, Uppsala, Uppsala, Sweden*
[3]*Lund University, ENT-dep, Lund, Sweden*

Objective: Pneumococcal vaccination was introduced in the Swedish paediatric immunization programme in 2009. The heptavalent Prevenar vaccine was used the first years and is now substituted by Prevenar 13 or Synflorix. The number of invasive pneumococcal diseases have declined but the protection against acute otitis media (AOM) is low. However, we so far lack evaluation of the impact on complications to AOM. In this study we compare detected serotypes of pneumococci in the middle ear or mastoid between vaccinated and non-vaccinated patients with acute mastoiditis (AM).

Method: In the Swedish prospective study of AM, bacterial cultures are stored for further analysis, such as serotyping of pneumococci. The samples presented in this study were collected from cases included 2009-2014. Cultures from the middle ear or mastoid area showing pneumococci were serotyped after reculturing of the stored samples. Recorded data on vaccinations were compared to the detected serotypes to evaluate the impact of pneumococcal vaccination on complications to AOM.

Results: In 19 patients out of the 117 included AM cases with stored samples, pneumococci were retrieved in ear cultures. Eleven of them had been vaccinated against pneumococci before the episode of AM. The serotypes most commonly found in both vaccinated and unvaccinated cases were 3 and 19A/F.

Conclusion: The most aggressive serotypes of pneumococci apparently cause AM in even fully vaccinated children in Sweden.

11:43 -11:50 AM **WEDNESDAY, JUNE 10**

OM2015146

TRANSCUTANEOUS IMMUNIZATION WITH A TYPE IV PILUS AND OMP P5-TARGETED IMMUNOGEN BY BANDAID VACCINE PREVENTS THE ONSET OF NONTYPEABLE HAEMOPHILUS INFLUENZAE- INDUCED OTITIS MEDIA IN A POLYMICROBIAL MODEL OF DISEASE

Laura A Novotny, M.S.[1] *Presenter*

John D Clements[2]
Lauren O Bakaletz[1]

[1] *Nationwide Children's Hospital Research Institute And The Ohio State University College Of Medicine, Center For Microbial Pathogenesis, Columbus, OH, USA*
[2]*Tulane University School Of Medicine, Microbiology And Immunology, New Orleans, LA, USA*

Objective: Otitis media (OM) is a polymicrobial disease, wherein upper respiratory tract viral infection predisposes to ascension of nontypeable Haemophilus influenzae (NTHI) from the nasopharynx, the site of colonization, to the sterile middle ear, resulting in disease. Herein, we utilized a clinically-relevant chinchilla model of viral-bacterial superinfection to determine the preventative efficacy afforded by transcutaneous immunization (TCI) with a chimeric antigen that targets the critical NTHI adhesins OMP P5 and the Type IV pilus (called chimV4), admixed with the adjuvant dmLT, a double mutant of E. coli heat-labile enterotoxin.

Method: Chinchillas were immunized by placement of bandaid vaccines containing chimV4+dmLT or dmLT alone onto the skin behind the ears. Two days after receipt of the second weekly dose, chinchillas were inoculated with adenovirus, followed one week later by intranasal challenge with NTHI.

Results: ChimV4-specific antibody-secreting cells were detected in the blood of animals immunized with chimV4+dmLT, and 2-fold more chimV4-specific IgG, compared to -IgM, was shown ($p \leq 0.01$). By otoscopy, OM was observed 5 days after NTHI challenge in the cohort immunized with dmLT; however receipt of chimV4+dmLT induced a significant 9-day delay to onset of OM ($p \leq 0.0001$) and only 25% of middle ears exhibited signs of OM, compared to 83% in the cohort administered dmLT ($p \leq 0.01$).

Conclusion: These data are the first to demonstrate preventative efficacy afforded by TCI with a bandaid vaccine in a clinically-relevant model of viral-bacterial superinfection wherein AV predisposed to NTHI-induced OM. The simplicity and significant efficacy observed by TCI with chimV4+dmLT holds great promise.
NIDCD/NIH R01 003915 to LOB

12:00 - 1:30 PM **WEDNESDAY, JUNE 10**

EXHIBIT HALL A

LUNCH IN EXHIBIT/ POSTER HALL

1:30 - 2:30 PM **WEDNESDAY, JUNE 10**

CHERRY BLOSSOM BALLROOM

PANEL 8 (C): E TUBE AND MIDDLE PHYSIOLOGY & PATHOLOGY

Moderators:

Cuneyt Alper (US)

William Doyle (US)

Speakers:

Cuneyt Alper (US)

William Doyle (US)

Samir Ghadiali (US)

Haruo Takahashi (Japan)

1:30 - 2:30 PM **WEDNESDAY, JUNE 10**

OM2015013

IMAGE ANALYSIS OF VIDEOENDOSCOPY RECORDING DURING SWALLOW ACCURATELY ASSESSES THE EUSTACHIAN TUBE OPENING

Cuneyt M Alper, M.D.[1,2,3] *Presenter*

John Douglas Swarts, Ph.D.[2]
Miriam S Teixeira, M.D.,Ph.D.[2]
Julianne Banks, B.S.[2]
William J Doyle, Ph.D.[2]

[1]*Children's Hospital Of Pittsburgh Of UPMC, Division Of Pediatric ENT, Pittsburgh, PA, USA*
[2]*University Of Pittsburgh School Of Medicine, Otolaryngology, Piitsburgh, PA, USA*
[3]*University Of Pittsburgh School Of Medicine, Clinical And Translational Science Institute, Piitsburgh, PA, USA*

Objective: Describe the relationship between Eustachian tube (ET) openings during swallowing observed on trans-nasal videoendoscopy and detected by sonotubometry.

Methods: Simultaneous trans-nasal videoendoscopic and sonotubometric recordings were done on 30 adults with no middle-ear disease. Briefly, microphones were placed in the ear-canals, a 45º telescope introduced through one side of the nose to visualize ipsilateral ET movements, and the probe from a sound generator place in the opposite nostril. At specified nasopharyngeal (NP) sound-levels, ET movements and ipsilateral microphone signals were continuously recorded while the subject performed a series of swallows. For each swallow, relational measurements among ET structures were made and microphone signal amplitudes were recorded at swallow onset (T1), and at the times of maximum soft-palate elevation (T2) and maximum ET luminal opening (T3).

Results: Data for 81 swallows were analyzed. Average medial-rotations of the ET cartilage and lateral wall for the T1-T2 interval were 33.5±15.7º and 8.7±19º, respectively. The average T1-T3 change in the angle relating the medial and lateral ET walls was 7.4±14.6º. The average microphone signal-envelope amplitude and Width-50% during swallowing were 50±300 mV and 208±160 msec. Correlational analysis demonstrated significant relationships between sonotubometry variables and each of the 3 angular measures made for the T1-T2 interval (all $p<0.05$) and the change in linear width between the medial and lateral ET laminas for the T1-T3 interval ($P<0.01$).

Conclusions: There is a direct relationship between the assigned degree of ET opening during swallowing determined by videoendoscopy and by sonotubometry. Supported in part by: NIH grant DC007667

1:30 - 2:30 PM **WEDNESDAY, JUNE 10**

OM2015129

MIDDLE EAR PRESSURE-REGULATION AS AN INTER-RELATED SYSTEM OF PASSIVE GAS EXCHANGES

William J. Doyle, Ph.D.[1,2] *Presenter*

[1]*University Of Pittsburgh School Of Medicine, Department Of Otolaryngology, Piitsburgh, PA, USA*
[2]*Children's Hospital Of Pittsburgh Of UPMC, Division Of Pediatric Otolaryngology, Pittsburgh, PA, USA*

Introduction: Middle-ear (ME) pressure-regulation (MEPR), the primary ME homeostatic mechanism, maintains the ME-environment pressure-gradient (MEEPG) within a range optimized for "normal" hearing and preservation of a gas-filled ME.

Objective: Describe MEPR using equations applicable to passive, gas-exchange between the ME and adjacent biological compartments and determine if this description predicts the increasing ME pressure observed under certain conditions and interpreted by some as evidencing active gas-production by the ME mucosa.

Methods: MEPR was modeled as 4 passive gas-exchanges: ME and perilymph via the round window membrane, ME and environment via the tympanic membrane, ME and blood via the ME mucosa, and ME and nasopharynx during a Eustachian tube opening. The first 3 were described at the species level using Fick's diffusion equation and the last as a bulk gas-transfer governed by Poiseuille's equation. The model structure is a time-iteration of the basic equation: $PMEg(t=i+x\Delta t)=\sum S(PMEs(t=i+(x-1)\Delta t)+(1/(\beta MEsVME))\sum b(K_bs(PCs(t=i+(x-1)\Delta t)-PMEs(t=i+(x-1)\Delta t))))$, where $PMEg(t=i+x\Delta t)$ and $PMEs(t=i+(x-1)\Delta t)$ are the ME total and species-pressures at the indexed times, $PCs(t=i+(x-1)\Delta t)$ is the species-pressure for each exchange-compartment, $\beta MEsVME$ is the product of the ME species-capacitance and volume, K_bs is the species-conductance for each barrier and $\sum S$ and $\sum P$ indicate summing the expression over all ME species and exchange pathways.

Results: This model robustly predicts the empirically measured and clinically observed ME species-pressures and the time-trajectories for total ME pressure and the MEEPG under physiologic, pathologic and non-physiologic conditions.

Conclusions: This passive model is sole and sufficient to describe MEPR and, by Occam's Razor, discounts gas-production by the ME mucosa. Supported in part by: NIH grant DC007667

1:30 - 2:30 PM **WEDNESDAY, JUNE 10**

OM2015061

CLINICAL PRACTISE GUIDELINES FOR THE DISGNOSIS AND MANAGEMENT OF ACUTE OTITIS MEDIA (AOM) IN CHILDREN IN JAPAN - 2013 UPDATE

Haruo Takahashi, M.D. *Presenter*

Ken Kitamura
Yukiko Iino
Yosuke Kamide
Fumiyo Kudo
Kenji Suzuki
Hidenobu Taiji
Noboru Yamanaka
Yoshifumi Uno

Nagasaki University, Department Of Otolaryngology - Head And Neck Surgery, Nagasaki City, NAGASAKI, Japan

Objective: To 1) indicate methods of diagnosis and testing for childhood (<15 years) acute otitis media (AOM); and 2) recommend methods of treatment in accordance with the evidence-based consensus reached by the Subcommittee of Clinical Practice Guideline for Diagnosis and Management of AOM in Children (Subcommittee of Clinical Practice Guideline), in light of the causative bacteria and their drug sensitivity of AOM in Japan.

Methods: We investigated the most recently detected bacteria causing childhood AOM in Japan as well as antibacterial sensitivity and the worldwide progress of vaccination, produced Clinical Questions concerning the diagnosis, testing methods, and treatment of AOM, searched literature published during 2000–2004, and issued the 2006 Guidelines. In the 2009 and 2013 Guidelines we performed the same investigation with the addition of literature, which were not included in the 2006 Guidelines and published during 2005–2008 and during 2009–2012, respectively.

Results: We categorized AOM as mild, moderate, or severe on the basis of tympanic membrane findings and clinical symptoms, and presented recommended treatment for each degree of severity.

Conclusion: Accurate assessment of tympanic membrane findings is important for judging the degree of severity and selecting a method of treatment. Some of the new antimicrobial agents and pneumococcal vaccination are recommended as new treatment options.

1:30 - 2:30 PM **WEDNESDAY, JUNE 10**

OM2015026

USING ENGINEERING TECHNOLOGIES TO EVALUATE THE EFFECTIVENESS OF SURFACTANT AND MUCOLYTIC THERAPIES FOR EUSTACHIAN TUBE DYSFUNCTION

Samir Ghadiali, Ph.D.[1,2] *Presenter*

Natalia Higuita-Castro[2]
Jennifer Malik, B.S.[1]
Vasudha Shukla[1]

[1]*Ohio State University, Biomedical Engineering, Columbus, OH, USA*
[2]*Ohio State University, Davis Heart & Lung Research Insitute, Columbus, OH, USA*

Objective: Elevated adhesion forces within the Eustachian Tube (ET) play a major role in development of chronic Otitis Media. Although surfactant and mucolytic therapies can reduce mucosal adhesion, the effectiveness of these therapies may be patient-specific due to variations in ET structure/mechanics. In this study, we developed a novel microfluidic device that can measure the adhesion properties of mucosal-like fluids and integrated these measurements into computational models of ET function. Our goal was to investigate the relative effectiveness of surfactant and mucolytic therapies in restoring ET function under different pathological conditions.

Method: Engineering tools were used to manufacture a device that simulates ET opening and can measure the adhesion properties of 1μL samples. The adhesion properties of samples containing 250-2000 μg/mL of porcine type-II/type-III mucin were measured and integrated into computational models of ET function. We also investigated how surfactants and mucolytics alter adhesion properties.

Results: Adhesion forces demonstrated a non-linear dependence with mucin concentration with adhesion values ranging from 0.110 to 0.265 N/m. Computational models indicate that this increase in adhesion would not affect ET function in adults but would dramatically hinder ET function in young children. Models also indicate that mucolytics would be more effective at reducing adhesion as compared to pulmonary surfactants.

Conclusions: Engineering technologies were used to directly measure mucosal adhesion properties and investigate the relative effectiveness of surfactant and mucolytic therapies in different populations. Continued development of this device may lead to a novel diagnostic platform that can guide clinical decisions for treating chronic OM.

2:30 - 3:15 PM **WEDNESDAY, JUNE 10**

CHERRY BLOSSOM BALLROOM

PODIUM 11: VACCINE 2 / DIAGNOSIS 1

Moderator:

Snezana Andric Filipovic (Serbia)

Speakers:

Nikki Mills (New Zealand)

Janet Casey (US)

Carmel Capewell (UK)

Naohiro Yoshida (Japan)

Nora Erkkola-Anttinen (Finland)

2:30 - 2:37 PM **WEDNESDAY, JUNE 10**

OM2015226

OTITIS MEDIA AND VACCINATION IMPACT – COMPARISON OF 7 AND 10 VALENT CONJUGATED PNEUMOCOCCAL VACCINATED COHORTS

Nikki Mills, BHB, MBChB[1] *Presenter*

T Walls[2,4]
D Murdoch[2,3]
M Souter[4]
T Anderson [4]
L Salkeld[1]
Z Ahmad[5]
M Mahadevan [1]
M Neeff[1]
C Barber[1]
C Walker[2]
E J Best[1,2]

[1]*Starship Children's Hospital, Auckland, New Zealand*
[2]*University Of Auckland, Auckland, New Zealand*
[3]*University Of Otago, Christchurch, New Zealand*
[4]*Canterbury District Health, Christchurch, New Zealand*
[5]*Counties Manukau Distric Health Board, Auckland, New Zealand*

Objective: Otitis media (OM) is the commonest reason for antibiotic prescriptions and surgical procedure (ventilation tube VT) in young children. We aim to describe and compare the microbiology of middle ear fluid (MEF) in two cohorts of children, one vaccinated with PCV7 (data collected in 2011) and another vaccinated with PCV10 (2014). We describe nasopharyngeal (NP) carriage rates of otopathogens in these children and compare them with a matched cohort without history of otitis media.

Method: The study was conducted in two phases between May and October in 2011 (Phase 1) and in 2014 (Phase 2). In each Phase MEF and NP samples were collected from over 300 children aged <3 years during ventilation tube insertion. An age-matched non-otitis-prone comparison group of around 150 children had NP samples collected; surgical details and parental-questionnaire was completed by all.

Results: In otitis prone children, non-typeable Haemophilus influenzae (NTHi) was the dominant pathogen present in both NP and MEF in both phases of the study. Moraxella catarrhalis was the most prevalent pathogen in the nasopharynx of children who were non-otitis prone. Streptococcus pneumoniae was the least prevalent of the main otopathogens (in NP and MEF), with dominant serotypes changing over the two Phases. Details of bacterial culture and Polymerase Chain Reaction results of MEF and NP culture results will be presented, with the changes identified between the two Phases.

Conclusion: In the era of conjugated pneumococcal vaccination, NTHi remains the dominant pathogen in both the nasopharynx and MEF in children with established ear disease.

2:37 - 2:44 PM **WEDNESDAY, JUNE 10**

OM2015271

OTOPATHOGENS CAUSING ACUTE OTITIS MEDIA IN THE 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ERA

Janet Casey [1] *Presenter*

Ravinder Kaur[2]
Michael Pichichero[2]

[1]*Legacy Pediatrics, Rochester, NY, USA*
[2]*Rochester General Hospital, Research Institute, Rochester, NY, USA*

Objective: The otopathogen distribution causing acute otitis media (AOM) is in flux following the introduction of PCV7 and PCV13 and will continue to change.

Method: 485 children were followed prospectively from 6 to 36 months of age from October 2010 through 2014; tympanocentesis was performed to obtain middle ear fluid (MEF) during 384 AOM episodes of 190 children. Oxacillin sensitivity was assessed on all S. pneumonia (Spn) isolates and beta-lactamase production was determined for all non-typable H. influenzae (NTHi) and M. catharrhalis (Mcat) isolates. All children received PCV13 for the 3 primary vaccines and booster dose at 2, 4, 6 and 15 months of age.

Results: The overall number AOM episodes declined over the study period, p value <0.009. The frequency of isolation of Spn was 9-23% compared with 16-35% for NTHi and 20-27% for Mcat. The proportion of Spn that were penicillin non-susceptible fell from 33-20%. Beta-lactamase-producing NTHi rose 43-62% and all M. catarrhalis were beta-lactamase producing.

Conclusion: The total number of AOM episodes fell following the introduction of PCV13. The prevalence of Spn from late 2010 through 2014 has started rising but penicillin susceptibility has not changed. Supported by NIDCD RO1 08671

2:44 - 2:51 PM **WEDNESDAY, JUNE 10**

OM2015067

HEARING MAPS: CHILDREN'S PERCEPTIONS OF HEARING FUNCTIONALITY IN DIFFERENT ENVIRONMENTS

Carmel Irene Capewell, Ph.D. *Presenter*

The University Of Northampton, School Of Education, Northampton, NORTHAMPTONSHIRE, United Kingdom

Objective: To produce a tool which engages children (aged 4-7 years) by which they can communicate to healthcare and educational professionals their hearing functionality in their daily environments.

Method: The children had a GP/ENT consultant diagnosis of Otitis Media (OM) and were recruited via social media and word of mouth. Their parents gave permission for participation. The task could only be completed by the child. They were provided with stickers, with faces representing their responses to the environments: Smiling face = Easy to understand what is said; Straight face = I can understand some of what is said; Unhappy face = I can understand very little of what is said. They completed a table giving date, place, used the relevant sticker and made additional comments (sometimes supported by an adult). They also made a 10-20 second video recording of each environment using an i-Pad.

Results: The children engaged with the activity and produced details of which environments enabled/disabled their understanding. The video clips provided visual and auditory information to supplement the children's assessment of each environment. Patterns were constructed for each child of their frequency of functionality environments and comparisons made between children's experience of environments.

Conclusion: This method actively involves children in providing information for professionals about their experience which is in line with patient participation policies. This tool could supplement treatment decisions which are currently largely based on the state of the ear drum and audiogram results. This approach could increase educational professionals understanding of the impact of OM.

2:51 - 2:58 PM **WEDNESDAY, JUNE 10**

OM2015025

OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV): A RETROSPECTIVE MULTI-CENTER STUDY IN JAPAN – 4) AUDIOLOGICAL FINDINGS AND OUTCOME

Naohiro Yoshida[1] *Presenter*

Kan Kishibe[2]
Kaori Tateyama[3]
Yuka Morita[4]
Yukiko Iino[1]
Yasuaki Harabuchi[2]
OMAAV Working Group Of the Japan Otological Society[5]

[1]*Jichi Medical University Saitama Medical Center, Otolaryngology, Saitama, SAITAMA, Japan*
[2]*Asahikawa Medical University, Otolaryngology Head And Neck Surgery, Asahikawa, ASAHIKAWA, Japan* [3]*Oita University Faculty Of Medicine, Otolaryngology Head And Neck Surgery, Yufu, OITA, Japan*
[4]*Niigata University Faculty Of Medicine, Otolaryngology Head And Neck Surgery, Niigata, NIIGATA, Japan*
[5]*Japan Otological Society, Minato, TOKYO, Japan*

Objective: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) presents the otologic symptom as an initial symptom. In most cases, rapid progressive hearing loss is observed as localized AAV. In this study, audiological features and hearing outcome after immunosuppression therapy were evaluated.

Methods: A total 284 cases 480 ears audiologically evaluated at pre- and post-treatment in the nationwide surveys were enrolled in this study. Hearing outcomes were compared among the following factors: 1. hearing loss type (conductive, sensorineural or mixed), 2. otitis media type (secretion or granulation), 3. ANCA subtype, 4. another organ involvements (nose, lung, facial palsy, hypertrophic pachymeningitis), 5. immunosuppressive therapy; prednisolone (PSL) only or / PSL and cyclophosphamide (CPA).

Results: The overall hearing outcome was as follows: complete recovery in 30%, partial recovery (<10dB) in 30%, no change or worse in 40%. The completely deaf could not be recovered. The hearing outcome of ANCA negative group showed worse than that of another group. No significant difference of hearing recovery was observed among nose, lung involvement. On the other hand, the patients combined with facial palsy showed significantly worse hearing outcome compared with no facial palsy patients. Patients treated by the immunosuppressive therapy with both PSL and CPA showed significantly better hearing outcome compared with PSL only (odds ratio 2.30).

Conclusions: This study showed the effectiveness of immunosuppressive therapy for hearing loss at an early stage. The combination of facial palsy influenced on the hearing outcome. OMAAV is a new entity among the causes of intractable and progressive hearing loss.

2:58 - 3:05 PM **WEDNESDAY, JUNE 10**

OM2015047

CAN LAYMAN PARENTS USE SPECTRAL GRADIENT ACOUSTIC REFLECTOMETRY RELIABLY?

Nora Erkkola-Anttinen, M.D.[1,2] *Presenter*

Miia K Laine, M.D.[1]
Paula A Tahtinen, M.D.,Ph.D.[1,3,4]
Aino Ruohola, M.D.,Ph.D.[1,5]

[1]*Turku University Hospital, Department Of Pediatrics And Adolescent Medicine, Turku, Finland*
[2]*City Of Turku Welfare Division, Primary Healthcare Services, Turku, Finland*
[3]*Boston Medical Center, Division Of Pediatric Infectious Diseases, Boston, MA, USA*
[4]*Boston University School Of Medicine, Departement Of Pediatrics, Boston, MA, USA*
[5]*University Of Turku, Turku, Finland*

Objective: Cornerstone in diagnosing otitis media is accurate pneumatic otoscopy performed by physicians. Middle ear effusion (MEE) can also be detected by spectral gradient acoustic reflectometry (SG-AR). Our aim was to define, whether layman parents are able to use SG-AR reliably.

Method: Sufficiently co-operative children (age 6-35 months) were eligible if parents were voluntary and learned to use SG-AR. We included those parental SG-AR examinations which were performed at home on the same day as study physicians´ pneumatic otoscopy. The SG-AR angle values were classified according to the manufacturer's recommendations into five levels (1-5) corresponding to the risk of MEE, and predictive values calculated.

Results: We analyzed 417 SG-AR examinations of 179 children. Success rate was 97%. In symptomatic children with level 1, otoscopic diagnosis was healthy middle ear in 55% (17/31) of SG-AR examinations. The negative predictive value (NPV) for level 1 to exclude MEE was 55% (95%CI: 36% to 73%). With levels 2-5, otoscopic diagnosis was MEE in 74% (98/133) of SG-AR examinations. The positive predictive value (PPV) for levels 2-5 to detect MEE was 74% (95%CI: 65% to 81%). In asymptomatic children with level 1, the otoscopic diagnosis was healthy middle ear in 92% (102/111) of SG-AR examinations. The NPV for parental SG-AR level 1 to exclude MEE was 92% (95%CI: 86% to 96%).

Conclusion: Layman parents are able to use SG-AR reliably. In asymptomatic children, SG-AR level 1 was reliable in excluding MEE. However, the accuracy of SG-AR is inadequate in excluding MEE in symptomatic children.

3:15 - 3:45 PM **WEDNESDAY, JUNE 10**

EXHIBIT HALL A

COFFEE BREAK IN EXHIBIT/POSTER HALL

3:45 - 4:45 PM **WEDNESDAY, JUNE 10**

CHERRY BLOSSOM BALLROOM

PODIUM 13: DIAGNOSIS 2

Moderator:

Paolo Marchisio (Italy)

Speakers:

Paolo Marchisio (Italy)
Kan Kishibe (Japan)
Jeehong Kim (US)
Joseph Kerschner (US)
Allison Cullen Doyle (US)
Guillermo Monroy (US)
Beverly Richert (US)

3:45 - 3:52 PM **WEDNESDAY, JUNE 10**

OM2015110

CERUMEN IN CHILDREN: A NEGLECTED BUT FUNDAMENTAL PROBLEM

Paola MARCHISIO, M.D.[1] *Presenter*

Carlotta Pipolo[2]
Dario Consonni[4]
Alberto Saibene[2]
Nicola Mansi[3]
Giovanni Felisati[2]

[1]*Fondazione IRCCS C‡ Granda Ospedale Maggiore Policlinico, Pediatric Highly Intensive Care Unit, Milan, MILAN, Italy*
[2]*University Of Milan, Otorhinolaryngology Unit, Head And Neck Department, San Paolo Hospital, Milan, MILAN, Italy*
[3]*Santobono Pausilipon, Pediatric Otorhinolaryngology, Naples, NAPLES, Italy*
[4]*Fondazione IRCSS C‡ Granda Ospedale Maggiore Policlinico, Epidemiology Unit, Milan, MILAN, Italy*

Introduction: In order to correctly diagnose otitis media, the external ear canal must be completely free from cerumen and the eardrum fully visible. Limited data are available concerning the prevalence of cerumen in healthy and sick infants and children.

Objective: To assess the prevalence of cerumen in a large population of infants and children and to compare the cerumen removal attitudes by pediatricians (PEDs) and otorhinolaryngologists (ENTs).

Methods: in this cross-sectional survey healthy or sick children seen in hospital or outpatient clinics in Italy were enrolled. The following data were recorded: presence, laterality, type and amount of cerumen; presenting complaints; presence or absence of acute or chronic otitis media; cerumen removal during the visit; type of physician.

Results: Among 819 children aged 1 month to 12 years, cerumen was present in 594 (72.5%), bilateral in 492 (80.5%) and in a relevant amount (visibility < 50% of the eardrum) in 261 (43.9%). The presence of cerumen was significantly higher in younger and in non-caucasians children. PEDs were less prone to remove cerumen than ENTs (28.8% vs 91.0%, p=0.0001), both in healthy children (PEDs 27.7% vs ENTs 80.9%, p=0.0001) and in sick children in whom a diagnosis of AOM was done (PEDs 24.7% vs ENTs 90.0%, p=0.0001).

Conclusion: Cerumen is highly prevalent both in healthy and sick children but is quite neglected by paediatricians. Educational programs to reinforce the importance of cerumen and to improve the techniques for removal in case of suspected AOM should be implemented and rigorously evaluated.

3:52 - 3:59 PM **WEDNESDAY, JUNE 10**

OM2015085

OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV): A RETROSPECTIVE MULTICENTER STUDY IN JAPAN - 1) CLINICAL FINDINGS.

Kan Kishibe, M.D.,Ph.D.[1] *Presenter*

Kaori Tateyama[2]
Yuka Morita[4]
Naohiro Yoshida[3]
Yukiko Iino[3]
Yasuaki Harabichi[3]
OMAAV Working Group Of The Japan Otological Society[5]

[1]*Asahikawa Medical University, Otolaryngology Head And Neck Surgery, Asahikawa, HOKKAIDO, Japan* [2]*Oita University Faculty Of Medicine, Otolaryngology Head And Neck Surgery, Yufu, OOITA, Japan*
[3]*Jichi Medical University Saitama Medical Center, Otolaryngology, Saitama, SAITAMA, Japan*
[4]*Niigata University Faculty Of Medicine, Otolaryngology Head And Neck Surgery, Niigata, NIIGATA, Japan*
[5]*Japan Otological Society, Tokyo, TOKYO, Japan*

Introduction: ANCA - associated vasculitis (AAV) often involves initially middle ear and intractable otitis media is possible to be OMAAV. However, clinical characteristics of OMAAV have not been clarified yet. In this study, we aimed to describe a series of OMAAV patients and underline the difficulties involved in diagnosing and treating this challenging disease.

Method: In this multicenter study, we assigned 297 patients (86 males and 211 females) with OMAAV from 65 departments of otolaryngology in Japan. Their age were ranged from 13 to 89 years.

Results: At the initial visit, ear, nose, other upper respiratory tract, lung, and kidney lesions were involved in 294 (97%), 95 (32%), 24 (6%), 80 (27%), 55 (18%) patients, respectively. Facial nerve palsy and hypertrophic pachymeningitis were observed in 54 (18 %) and 44 (15 %) patients at the initial visit, respectively. Serum PR3-ANCA and MPO-ANCA were detected in 76 (27%) and 169 (59%) patients, respectively. A definitive histological diagnosis of AAV could be done in only 54 (30%) patients. All patients responded to treatments with prednisolone and/or immunosuppression therapy. Three (1%) patients died from subarachnoid hemorrhage due to vasculitis of basiar artery.

Conclusions: It is difficult to make definitive diagnosis of OMAVV. We found that facial nerve palsy, hypertrophic pachymeningitis and MPO-ANCA positivity are characteristic in OMAAV.

3:59 - 4:06 PM **WEDNESDAY, JUNE 10**

OM2015099

LOW PREDICTIVE VALUE OF R-VALUE OF TUBOMANOMETRY IN ASSESSING THE PRESENCE AND THE DEGREE OF MIDDLE EAR PRESSURE CHANGE WITH EUSTACHIAN TUBE OPENING

Jeehong Kim, B.S.[1] *Presenter*

J. Douglas Swarts, Ph.D.[3]
Miriam S. Teixeira, M.D.,Ph.D.[3]
Julianne Banks, B.S.[3]
Cuneyt M. Alper, M.D.[2,3,4]

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[2]*Children's Hospital Of Pittsburgh Of UPMC, Division Of Pediatric ENT, Pittsburgh, PA, USA*
[3]*University Of Pittsburgh School Of Medicine, Otolaryngology, Pittsburgh, PA, USA*
[4]*University Of Pittsburgh School Of Medicine, Clinical And Translational Science Institute, Pittsburgh, PA, USA*

Background: Tubomanometry is an Eustachian tube (ET) function test that detects the tympanic membrane displacement indicating ET opening with the application of controlled nasal positive pressure while the velum is closed.

Objective: Determine the degree of accuracy of Tubomanometry for detecting ET opening.

Method: Patients with or without clinically diagnosed ET dysfunction were enrolled. Tubomanometric criteria for ET opening, i.e., presence of R-value, calculated as per timing of the changes in the nasopharyngeal and middle ear pressure (MEP) during Tubomanometry and the magnitude of R-value were compared to the tympanometric evidence of the change in middle ear pressure (MEP).

Results: The R value was present in 72 (95%) out of 76 measurements from 46 ears of 26 subjects. However, there was 5 and 32daPa increase of MEP in 2 out of 4 measurements without the R-value. Of the 72 measurements that had an R-value, 21 (29%) had undetectable (<5daPa) MEP change. Of the 41 measurements that had an R-value less than 1, 22 (44%) had no change in MEP. The R-values less than 0.2 (n:7), values between 0.21-0.5 (n:16), 0.51-1 (n:18), 1.01-1.5 (n:17), and 1.51-3 (n:14) had MEP differences before and after Tubomanometry, of 9±26daPa, 27±55daPa, 34±48daPa, 93±63daPa, 108±77daPa respectively. False positive results for the R-values less than 0.2, 0.5, 1, and greater than 1 were 57%, 48%, 44% and 10% respectively.

Conclusions: Criteria described in the manuscripts on Tubomanometry are sensitive but not specific to the ET-opening. Supported in part by: NIH grant DC007667

4:06 - 4:13 PM **WEDNESDAY, JUNE 10**

OM2015116

SMARTPHONE-BASED FIELD SCREENING DEVICES ENABLING SCALEABLE AND STANDARDIZED DIAGNOSIS, REFERRAL, AND TREATMENT OF OTITIS MEDIA IN UNDERSERVED PATIENT COMMUNITIES IN INDIA AND BANGLADESH

Joseph Kerschner[2] *Presenter*

Nicole Rani Leeds[1]
Jacob Paul[1]
Ruchika Singhal[1]
Ananth Annaswamy[1]

[1]*Medtronic Surgical Technologies, Jacksonville, FL, USA*
[2]*University Of Wisconsin, Madison, WI, USA*

Objective: The Shruti Program leverages smartphone technology and community health workers to address the critical problem of otitis media in underserved communities in India and Bangladesh. By providing an "ecosystem solution" that tracks patients from the point of screening in their homes and communities through referral, reporting, and treatment in the clinical setting, Shruti provides insight into the prevalence of otitis media and other ear conditions in a population of over 60,000 people in urban slum settings in three cities.

Method: Community health workers screen patients using an Android-phone based otoscope and accompanying screening app which captures, uploads, and stores images of the patient's tympanic membrane as well as demographic information, symptoms, treatment history and other clinical data. Patients are referred for treatment at partner clinical sites.

Results: Over 60,000 patients have been screened, 22,000 referred for treatment and 2,200 reported for clinical treatment since the project's launch in July 2012. After patients have reported to partner clinical sites, otitis media patients are treated using medical and surgical intervention.

Conclusion: The project is an effective means of leveraging community health workers to screen large numbers of patients. Planned product additions over the next six months to one year include a mobile hearing test, field wax syringing tools, and the tympanic membrane patcher. A broader suite of products available in the clinical setting will allow future research on the efficacy of current clinical protocols and products used to treat otitis media in adult populations and in the developing world.

4:13 - 4:20 PM **WEDNESDAY, JUNE 10**

OM2015120

CRANIOFACIAL MORPHOLOGY IN CHILDREN WITH AND WITHOUT OTITIS MEDIA

Allison P. Cullen Doyle, M.S.[1] *Presenter*

Margaretha L. Casselbrant, M.D.,Ph.D.[2,3]
Ellen M Mandel, M.D. [2,3]
Seth M. Weinberg, Ph.D.[4]
J. Douglas Swarts, Ph.D.[2]

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[4]*University Of Pittsburgh School Of Dentistry, Center For Craniofacial And Dental Genetics, Piitsburgh, PA, USA*

Introduction: Past studies identified differences in craniofacial length/angle measures between individuals with and without otitis media (OM). These types of measures are typically quite limited in their ability to describe complex morphology. Geometric morphometrics (GM) offers an alternative, powerful approach to quantifying biological shape based on the relative positions of homologous anatomical landmarks.

Objective: Determine if craniofacial shape quantified by GM differs among children with no past OM (CONTROL), with OM with effusion (OME) and with recurrent acute OM (RAOM).

Methods: Standard lateral cephalometric radiographs were done on 97 children (41 CONTROL, 18 OME, 38 RAOM) at 3 years of age and 63 children (27 CONTROL, 11 OME, 25 RAOM) at 6 years of age. Nineteen standard landmarks were identified on the digital images and analyzed by GM. Variation in overall craniofacial shape and in selected regions (cranial base, maxilla and mandible) was explored using principal components (PC) analysis. PC scatterplots were constructed to modes of shape variation capable of shape separation by disease history.

Results: PC analysis did not document OM-control group separation for overall craniofacial or sub-region shapes at either age. PC1 for maxillary and mandibular shape discriminated children by race at both ages. Combining the 3 and 6 year ages, PC2 and PC6 distinguished older from younger individuals, and PC1 and PC3 distinguished individuals of different races.

Conclusions: The evaluated craniofacial shapes were not different among 3 or 6 year old children with different OM histories, but expected age and racial shape-differences were detected using this methodology. Supported in part by: NIH grant DC007667

4:20 - 4:27 PM **WEDNESDAY, JUNE 10**

OM2015155

NONINVASIVE REAL-TIME OPTICAL MEASUREMENTS OF THE TYMPANIC MEMBRANE AND MIDDLE EAR FOR CHARACTERIZATION AND DIAGNOSIS OF OTITIS MEDIA

Guillermo L Monroy, M.S.[1,3] *Presenter*

Ryan L Shelton[3,5]
Ryan M Nolan, MSe[3,5]
Michael A Novak[1,2]
Malcolm C Hill[1,2]
Zita Hubler, B.S. [1]
Nathan D Shemonski[1,3]
Daniel T McCormick[4]
Stephen A Boppart[1,2,3,5]

[1]*University Of Illinois At Urbana-Champaign, Urbana, IL, USA*
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[4]*Advanced MEMS, San Francisco, CALIFORNIA, USA*
[5]*PhotoniCare, Champaign, IL, USA*

Objective: The precise diagnosis of otitis media relies on the accurate interpretation of often confounding factors that may present during a patient's physical exam. Optical coherence tomography (OCT) has the potential to provide quantitative image-based data in real-time to classify pathological changes in tissue earlier and more accurately in vivo. By supplementing the qualitative cues from physical examinations with quantitative structural and functional information, this technique may improve the ease and accuracy of diagnosing different stages of otitis media.

Method: A recent clinical study, performed under IRB supervision, observed 34 patients with normal, acute, and chronic ear infections. We developed an OCT system and handheld probe that provides a high resolution cross-sectional image encompassing both the tympanic membrane (TM) and if present, any biofilm adhered to the TM within the middle ear cavity. This allowed for noninvasive objective measurements of the thickness of the TM and an ability to identify the presence of a biofilm. Additional algorithms have been developed to improve the ease of use and utility of the device.

Results: Overall, the total thickness of the TM and any associated biofilm were statistically different between the normal, acute, and chronic groups. While previously calculated after manual analysis, one additional algorithm provides an automated measurement and calculation of the thickness of the TM in real-time during a typical exam.

Conclusion: The use of OCT alongside standard otoscopy may help better classify and quantify the physical changes that occur at different stages of infection, and with further prospective study, lead to improved treatment strategies for the many presentations of otitis media.

4:27 - 4:34 PM **WEDNESDAY, JUNE 10**

OM2015130

ASSESSMENT AND MANAGEMENT OF CHILDREN AND ADULTS WITH EUSTACHIAN TUBE DYSFUNCTION IN A SPECIALTY CLINIC SETTING

Beverly C Richert, Ph.D.,RN , CRNP, PNP-BC[1,2] *Presenter*

J. Douglas Swarts, Ph.D.[2]
Miriam S Teixeira, M.D.,Ph.D.[2]
Juliane M Banks, B.S.[2]
Jenna A. El-Wagaa[2]
Cuneyt M Alper, M.D.[1,2,3]

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[2]*University Of Pittsburgh School Of Medicine, Department Of Otolaryngology, Piitsburgh, PA, USA*
[3]*University Of Pittsburgh School Of Medicine, Clinical And Translational Science Institute, Piitsburgh, PA, USA*

Background: The primary function of the ET (ETF) is to maintain near-ambient middle-ear (ME) pressure while limiting ME exposure to nasopharyngeal (NP) pathogens and pressures. ET dysfunction (ETD) is diagnosed when the ET exhibits a closing failure or if volume gas transfer during ET openings is insufficient to preserve near-ambient ME pressure. ETD causes distressing symptoms and participates in the pathogenesis of the most common ME disease, otitis media, as well as other pathologies such as retraction pockets and cholesteatoma. Objective: Report the translational application of the knowledge, experience and test protocols gained from research to the clinical care of patients presenting with ETD.

Methods: Children and adults with suspected ETD referred to the clinic provide a thorough health history, complete a series of targeted questionnaires and have an ENT examination, static/dynamic videoendoscopic recording of ET relational movements at the NP during swallowing and other maneuvers, and a panel of ETF tests including tympanometry, sonotubometry, tubomanometry, manometric testing and pressure-chamber protocols, as applicable.

Results: Findings, test results and interpretations are presented for 20 children and 20 adults evaluated at the ETD clinic. Details regarding referral patterns, reasons for referral, and the distributions of risk factors, otologic histories and testing results are presented and compared between children and adults. Examples of treatment plans initiated to target the suspected/diagnosed cause of ETD and treatment outcomes are reviewed.

Conclusion: This experience emphasizes the broad utility of a specialized clinic for the diagnoses, treatment and continued management of patients with suspected ETD.

4:45 - 5:30 PM **WEDNESDAY, JUNE 10**

CHERRY BLOSSOM BALLROOM

PODIUM 15: DIAGNOSIS 3

Moderator:

Sara Torretta (Italy)

Speakers:

John Swarts (US)

Ellen Mandel (US)

Selma Cetin-Ferra (US)

Christian Heidemann (Denmark)

Makoto Ito (Japan)

4:45 - 4:52 PM **WEDNESDAY, JUNE 10**

OM2015172

MEASURED TRANSMUCOSAL SPECIES EXCHANGE-CONSTANTS FOR THE HUMAN MIDDLE EAR

John Douglas Swarts, Ph.D.[2] *Presenter*

Miriam S. Teixeira, M.D.,Ph.D.[2]
Juliane M Banks, B.S.[2]
Selma Cetin-Ferra, M.D.[2]
Sara M Rogerson, B.S.[2]
Cuneyt M. Alper, M.D.[1,2,3]
William J. Doyle, Ph.D.[2]

[1]*Children's Hospital Of Pittsburgh Of UPMC, Division Of Pediatric Otolaryngology, Pittsburgh, PA, USA*
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[3]*University Of Pittsburgh School Of Medicine, Clinical And Translational Science Institute, Piitsburgh, PA, USA*

Introduction: Between Eustachian tube openings, the middle-ear (ME) pressure-trajectory is governed by the relative rates of passive transmucosal volume O2, N2 and CO2 exchange; rates calculated as the product of the transmucosal species pressure-gradient (measured previously) and exchange-constant (unknown).

Objective: Estimate transmucosal CO2, O2 and N2 exchange-constants for adults.

Methods: Six adults with healthy MEs had a ventilation tube inserted unilaterally and custom acrylic-molds embedded with a valved-line to a Mass Spectrometer (MS) and a central tube coupled via valves to a micropressure-transducer and a microsyringe (probe) were constructed. On 6 separate days, the probe was sealed within the ipsilateral ear-canal, probe and ME volumes measured, and the probe/ME volume pulse-washed for about 15 minutes with a specified test-gas. System-pressure was monitored continuously and gas samples taken and analyzed for composition after the wash and again between 5 and 20 minutes post-wash. The 6 test-gas compositions were: physiologic ME species-pressures, and physiologic species-pressures adjusted to a low N2-pressure, and to high and low O2 and CO2-pressures with reference to blood species-pressures. The between-sample change in species-pressure for the adjusted-gas in each mixture was expressed as a fraction of the established species-pressure gradient and exchange-constants calculated using an exponential function.

Results: Estimated transmucosal exchange-constants (mean, range) for CO2, O2 and N2 were 0.104 (0.052-0.190), 0.038 (0.006-0.160) and 0.003 (0.001-0.006) daPa/min/daPa, respectively. Estimate accuracy and sources of error are discussed.

Conclusions: The best-estimate exchange-constant ratio for CO2:O2:N2 was 46:12:1 documenting that transmucosal exchange-rates are greatest for CO2 and least for N2. Supported by NIH Grant DC007667

4:52 - 4:59 PM **WEDNESDAY, JUNE 10**

OM2015173

EUSTACHIAN TUBE FUNCTION IN 6-YEAR-OLD CHILDREN WITH AND WITHOUT A HISTORY OF MIDDLE-EAR DISEASE

Ellen M Mandel, M.D.[1,2] *Presenter*

Margaretha L. Casselbrant, M.D.,Ph.D. [1,2]
Beverly C. Richert, Ph.D. , CRNP, PNP-BC[1,2]
James T. Seroky, M.S.[2]
Juliane M. Banks, B.S.[2]
Jenna A. El-Wagaa[2]
Miriam S. Teixeira, M.D.,Ph.D.[2]
Sara M. Rogerson, B.S.[2]
J. Douglas Swarts, Ph.D.[2]

[1]*Children's Hospital Of Pittsburgh Of UPMC, Division Of Pediatric Otolaryngology, Pittsburgh, PA, USA*
[2]*University Of Pittsburgh School Of Medicine, Department Of Otolaryngology, Piitsburgh, PA, USA*

Introduction: Previous studies reported that Eustachian tube (ET) opening efficiency is poorer for adults without extant middle-ear (ME) disease but with a history of childhood otitis media (OM) when compared to such with a negative OM history.

Objective: Test the hypothesis that ET efficiency expressed as the fractional gradient equilibrated (FGE) by swallowing is lower in 6-year-old children with no ME disease but well-documented recurrent acute OM (RAOM) by 3 years of age when compared to such children with no history of OM (Control).

Methods: Bilateral ET function was evaluated in 44 healthy 6-year-old children (19 male, 26 white) enrolled in an ongoing longitudinal study. None had ME disease at the time of testing, but 23 had diagnosed RAOM and 21 had no past OM by 3 years of age. ET function was measured using a pressure-chamber protocol that established negative ME-chamber pressure-gradients and recorded those gradients before and after a swallow. FGE was calculated as the change in gradient with a swallow divided by the applied gradient, a measure related to the trans-ET gas conductance. Between-group comparisons of driving-gradients and FGEs for ears were made using a 2-tailed Student's t test.

Results: FGE was independent of driving-gradient. For the 39 and 45 evaluable ears in the control and RAOM groups, the average (+/-std) driving-gradients were -194+/-52 versus -203+/-41 daPa (P=0.38) and FGEs were 0.32+/-0.33 vs 0.16+/-0.26 (P=0.01), respectively.

Conclusions: In children with past RAOM, residual ET inefficiency is maintained after the child had "outgrown" their ME disease. Supported in part by: NIH grants DC007667

4:59 - 5:06 PM **WEDNESDAY, JUNE 10**

OM2015192

A METHOD TO QUANTITATIVELY DESCRIBE RELATIONAL MOVEMENTS OF EUSTACHIAN TUBE COMPONENTS RECORDED DURING TRANS-NASAL VIDEO-ENDOSCOPY

Selma Cetin-Ferra, M.D.[1] *Presenter*

Miriam S. Teixeira, M.D.,Ph.D. [1]
William J. Doyle, Ph.D. [1]
Cuneyt M. Alper, M.D.[1,2,3]

[1]*University Of Pittsburgh School Of Medicine, Department Of Otolaryngology, Pittsburgh, PA, USA*
[2]*Children's Hospital Of Pittsburgh, Department Of Pediatric Otolaryngology, Pittsburgh, PA, USA*
[3]*University Of Pittsburgh School Of Medicine, Clinical And Translational Science Institute, Pittsburgh, PA, USA*

Introduction: Video-endoscopy of the Eustachian tube (ET) at the nasopharynx can visualize ET component translations of importance to ET opening mechanics.

Objective: Describe ET component movements during swallowing using a graphic function that relates component position to time.

Method: This was a pilot study of relational event capture using a polar coordinate system operating on trans-nasal video-endoscopic recordings of the ET during 3 swallows in 5 adults. After topical anesthesia of the nose, a 45º telescope was introduced unilaterally and focused on the ipsilateral ET orifice. For each recording, successive still-frame images were analyzed by identifying 4 fixed-point locators; the luminal apex, lateral and medial luminal walls and the torus. Then, a frame-normal, horizontal line was constructed through the apex and the medial angles defined by the intersection of the horizontal line and the lines from apex to each point locator were measured. The magnitudes of these angles were plotted together as a function of time (i.e. successive frames) for each swallow.

Results: The graph captured the relational movements among the locator points during a swallow. Complex interactions among the ET components were resolvable and these patterns were reproducible for each swallow from an individual and certain pattern aspects were shared across persons. Individual peculiarities observable on review of the visual "movies" such as double-swallows or delayed swallows were easily identified in the graphic representation.

Conclusion: This methodology has potential application for developing quantitative descriptions of ET mechanics in persons with different levels of ET functional efficiency. Supported in part by: NIH grant DC007667

5:06 - 5:13 PM **WEDNESDAY, JUNE 10**

OM2015316

OTITIS MEDIA AND CAREGIVER QUALITY OF LIFE: PSYCHOMETRIC PROPERTIES OF THE DANISH VERSION OF CAREGIVER IMPACT QUESTIONNAIRE

Christian Hamilton Heidemann, M.D.,Ph.D.[1,2] *Presenter*

Christian Godballe, M.D.,Ph.D. [1,2]
Anette Drøhse Kjeldsen, M.D.,Ph.D. [1,2]
Christian Emil Faber, M.D.,Ph.D. [1,2]
Eva Charlotte Jung Johansen, M.D.,Ph.D.[4]
Henrik Hein Lauridsen, Ph.D. , M.Sc.[3]

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[3]*University Of Southern Denmark, Research Unit For Clinical Biomechanics, Odense, 5000, Denmark*
[4]*ENT Private Clinic, Odense, 5000, Denmark*

Objective: The disease specific Caregiver Impact Questionnaire is designed to assess caregiver quality of life in relation to child otitis media. Assessment of the psychometric properties of this instrument is limited. This study assesses the psychometric properties of this instrument including validity, reproducibility, responsiveness and interpretability.

Method: Four-hundred-ninety-one families were enrolled in the study. Validity was assessed using confirmatory factor analysis, internal consistency and hypothesis testing. Test-retest reliability and measures of smallest detectable change were investigated in the assessment of reproducibility. Responsiveness was investigated by means of hypothesis testing and receiver operating characteristic analysis. An anchor based distribution method was applied for determining minimal important change as perceived by the respondent.

Results: Factor analysis confirmed the hypothesized 1-factor structure with an acceptable fit. Chronbach's alpha was 0.90. 88.9% of the hypothesized correlations were correctly predicted in the analysis of construct validity. intra-class correlation coefficient was above 0.8 and smallest detectable change corresponded to approximately one fourth of the scale. Responsiveness was found to be good and a change score of 13.8 represented minimal important change.

Conclusion: Caregiver Impact Questionnaire has proven to be a valid and reproducible measurement tool which is also sensitive to measuring change in the current setting. A change score representing minimal important change as perceived by the respondent is proposed. Results of this study support the use of this instrument.

5:13 - 5:20 PM **WEDNESDAY, JUNE 10**

OM2015210

CLINICAL PRACTICE GUIDLINE FOR THE DIAGNOSIS AND MANAGEMENT OF OTITIS MEDIA WITH EFFUSION (OME) IN CHILDREN IN JAPAN -2015

Makoto Ito, M.D.,Ph.D.[1] *Presenter*

Haruo Takahashi[2]
Yukiko Iino[3]
Yosuke Kamide[4]
Fumiyo Kudo[5]
Hitome Kobayashi[6]
Haruo Kuroki[8]
Atsuko Nakano[9]
Hiroshi Hidaka[10]
Goro Kobayashi[7]
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[9]*Chiba Children's Hospital, Otoryngology, Chiba, CHIBA, Japan*
[10]*Tohoku University Graduate School Of Medicine, Otolaryngology-Head And Neck Surgery, Sendia, Sendai, Japan*

Objective: To 1) indicate methods of diagnosis and testing for otitis media with effusion (OME) in childhood (<12 years); and 2) recommend methods of treatment in accordance with the evidence-based consensus reached by the Subcommittee of Clinical Practice Guideline for Diagnosis and Management of OME in Children (Subcommittee of Clinical Practice Guideline).

Method: We produced Clinical Questions concerning the diagnosis, testing methods, and treatment of OME and searched literature published until 2014 April. The recommendations are based on the results of the literature review and the expert opinion of the Subcommittee.

Results: Because children with Down's syndrome and cleft palate are susceptible to OME, we categorized OME as low-risk group and high-risk group (such as Down's syndrome and cleft palates), and presented recommended treatment for each group.

Conclusion: Accurate assessment of tympanic membrane findings is important for selecting an indication of surgical intervention of OME. Evidence showed that a period of 3 months of "watchful-waiting" would allow resolution of many cases of OME, but Japanese Clinical Practice Guideline recommend to treat complicated infectious or inflammatory diseases of surrounding organs such as sinusitis and upper respiratory infections during this period.

10:15 AM - 12:00 PM **WEDNESDAY, JUNE 10**

BALTIMORE 3-5

MINISYMPOSIUM 6 (B): INNATE IMMUNITY

Moderators:

Allen Ryan (US)

Allan Cripps (Australia)

Keynote Speaker:

Noam Cohen (US)

Speakers:

Allen Ryan (US)

Allan Cripps (Australia)

Jian-Dong Li (US)

Michael Pichichero (US)

10:15 - 10:50 AM **WEDNESDAY, JUNE 10**

OM2015028

THE GENETICS OF BITTER TASTE IN UPPER AIRWAY INFECTIONS

Noam A Cohen, M.D.,Ph.D. *Presenter*

University Of Pennsylvania, Otorhinolaryngology - Head And Neck Surgery, Philadelphia, PA, USA

Innate and adaptive defense mechanisms protect the respiratory system from attack by microbes. Here, we describe our recent studies that demonstrate that the bitter taste receptor T2R38 is expressed in the human upper respiratory epithelium and is activated by acyl-homoserine lactone quorum sensing molecules secreted by Pseudomonas aeruginosa and other gram-negative bacteria. T2R38 regulates human upper airway innate defenses through nitric oxide production, resulting in stimulation of mucociliary clearance and direct antibacterial effects. Moreover, common polymorphisms of the TAS2R38 gene are linked to significant differences in the ability of upper respiratory cells to clear and kill bacteria. Lastly, TAS2R38 genotype correlates with human sinonasal gram-negative bacterial infection. These data suggest that T2R38 is an upper airway sentinel in innate defense, and that genetic variation that contributes to human individual differences in ability to taste phenylcarbamide (PTC) and related molecules also contributes to individual differences in susceptibility to respiratory infection.

10:50 - 11:05 AM **WEDNESDAY, JUNE 10**

OM2015277

CONTRIBUTIONS OF THE NOD-LIKE FAMILY OF INNATE IMMUNE RECEPTORS TO OTITIS MEDIA

Allen F Ryan, Ph.D.[1] *Presenter*

Jasmine Lee, B.S. [1]
Arwa Kurabi[1]
Jeffrey Pan, B.S. [1]
Chelsea Wong, B.S.[1]
Emily Zuckerman, B.S. [1]
Kwang K Pak, B.S. [1]
Hal Hoffman[2]
Nicholas J Webster[2]
Stephen I Wasserman[2]

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[2]*UCSD, Medicine, La Jolla, CA, USA*

Objective: The NLR family of innate immune receptors consists of the NODs and NLRPs. These intracellular receptors bind bacterial lipoproteins and other pathogen molecules to provide responses to infection independent of prior sensitization. The NODs signal through the adaptor RIP2 to elicit pro-inflammatory cytokine and chemokine expression, while the NLRPs activate ASC leading to the formation of the inflammasome and cleavage/activation of IL1beta and IL-18.

Methods: We evaluated the role of NLRs and their downstream effector protein in otitis media (OM) by documenting the expression of their genes during OM and by infecting the middle ears (MEs) of knockout mice with nontypeable Haemophilus influenza (NTHi).

Results: Many genes encoding the NLRs and their downstream adaptor/effector molecules were strongly up-regulated during OM. Deletion of NOD1, NOD2 or especially RIP2 resulted in prolonged OM, with RIP2 showing the most severe effect. However, initial recruitment of leukocytes to the ME was reduced in each of these knockouts. Deletion of NLRP3 or ASC resulted in reduced activation of IL1beta in the ME, but prolonged OM to a lesser extent reflecting perhaps the limited set of cytokines affected by this pathway.

Conclusion: The results demonstrate that the NLR family of receptors, like the Toll-like receptors, plays a critical role in pathogenesis and recovery of OM. All of the NLR pathway genes tested appear to participate in bacterial clearance and OM resolution. In addition, the NOD pathway is critical for the efficient recruitment of leukocytes into the ME. Supported by grants DC000129, DC006279 and DC012595

11:05 - 11:20 AM **WEDNESDAY, JUNE 10**

OM2015188

INNATE IMMUNITY IN THE MIDDLE EAR

Allan W Cripps *Presenter*

Helen M Massa

Griffith University, Griffith Health, Southport, QLD, Australia

Immune protection of the middle ear involves a complex array of interactions between invading pathogens, localised innate immune mechanisms and specific adaptive immune responses. Innate immune mechanisms provide the initial defensive response against infection and are highly important in the middle ear where, in healthy subjects, organised mucosa associated lymphoid tissue is not typically observed. Initial activation of immune mechanisms within the middle ear occurs via microbial pattern recognition receptors (PRRs), which identify infecting pathogens. PRRs such as Toll-like receptors, are located on the surface of epithelial cells and sentinel cells, such as dendritic cells and macrophages, and recognise structurally conserved molecules on microbial surfaces known as pathogen-associated molecular patterns (PAMPS). PRR-PAMP interactions initiate a variety of complex signaling cascades within the cell, which result in activation and regulation of the local innate response within the middle ear and the induction of both mucosal and systemic adaptive immune responses. PRR deficiency, demonstrated using animal models, may enhance otitis media (OM) pathogenesis. Furthermore, increased susceptibility to OM has been reported in children who have gene polymorphisms in PRRs, signal transduction pathways and cytokines. Speculatively, OM disease severity and recovery may be related to the location of the polymorphism in the immune induction cascades and the number of polymorphisms involved. Recent advances in microbial recognition via PAMPs and elucidation of complex signalling cascades has improved understanding of the co-ordination and regulation of the middle ear immune immunity. This knowledge continues to inform new therapeutic approaches and multi-microbial vaccine design.

11:20 - 11:35 AM **WEDNESDAY, JUNE 10**

OM2015001

REGULATION OF INNATE IMMUNITY AND INFLAMMATION AND NOVEL ANTI-INFLAMMATORY STRATEGIES

Jian-Dong Li, M.D., Ph.D. *Presenter*

Georgia State University, Institute For Biomedical Sciences, Atlanta, GA, USA

Inflammation is a hallmark of many important human diseases including otitis media (OM), chronic obstructive pulmonary diseases, asthma, arthritis, inflammatory bowel disease, atherosclerosis and cancer. Although an appropriate inflammation is beneficial, if excessive, it is clearly detrimental to health. Thus, inflammation must be tightly regulated. However, how inflammation is tightly controlled remains largely unknown. Inducible negative feedback regulators play an essential role in controlling overactive inflammation. Our objective is to understand the molecular mechanisms by which inflammation is tightly regulated in OM and identify novel therapeutic targets. We and others have shown that CYLD, a novel deubiquitinase, and IRAK-M, act as key inducible negative feedback regulators for inflammation. Over the past decades, most anti-inflammatory strategies have focused on directly targeting the positive pathways to suppress inflammation. While these agents often showed reasonable efficacy, they exhibited significant adverse effects, e.g., increased susceptibility to infection, which prevented their further clinical use. Thus, there is an urgent need for developing novel therapeutic strategies without serious side effects by up-regulating the negative regulators of inflammation. We recently found that Roflumilast, an existing drug for COPD, suppressed middle ear inflammation by up-regulating CYLD. These studies may lead to the development of new anti-inflammatory strategies for OM.

11:35 - 11:50 AM **WEDNESDAY, JUNE 10**

OM2015272

IMMUNE DYSFUNCTION IN OTITIS PRONE CHILDREN

Michael E Pichichero, M.D. *Presenter*

Rochester General Hospital, Research Institute, Rochester, NY, USA

Objective: Understand immunologic dysfunction in SOP children.

Background: 30% of children experience 3-4 episodes of clinically diagnosed AOM within a 6- to 12- month time span during their first three years of life, termed otitis prone (OP). We have recently defined a subset of OP children, representing 5% of the total population, who meet the above definition, but all cases are confirmed by microbiologic diagnosis using tympanocentesis cultures of middle ear fluid, we term these children stringently defined otitis-prone (sOP).

Methods: ELISA, Luminex, PCR, Flow cytometry

Results: sOP children have recurrent ear infections associated with significantly elevated bacterial burden in the nasopharynx and middle ear, lower adaptive and innate immune responses to RSV infections that progress to AOM, higher pro-inflammatory cytokine levels within the middle ear space, significantly lower serum and mucosal antibody titers to Streptococcus pneumoniae and Haemophilus influenzae proteins after nasopharyngeal colonization and AOM compared to age matched non-OP (NOP) children. We also found that sOP children have a deficiency in functional and memory CD4+ T cell responses and lower percentage of antigen-specific CD19+ CD27+ memory B cells, and significantly dysfunctional professional antigen presenting cells.

Conclusion: In many respects it appears that sOP children have an immune maturational delay resembling a prolonged neonatal immune profile (PNIP) that is eventually outgrown. Our studies rest on a rigorous definition of otitis-prone and speculate that all prior studies relying on the clinical diagnosis of AOM had a mixed population of true OP children and many clinically over-diagnosed children.
Supported by NIDCD RO1 08671

12:00 - 1:30 PM **WEDNESDAY, JUNE 10**

EXHIBIT HALL A

LUNCH IN EXHIBIT/ POSTER HALL

1:30 - 2:30 PM **WEDNESDAY, JUNE 10**

BALTIMORE 3-5

PANEL 9 (B): ANIMAL MODEL

Moderator:

Allan Ryan (US)

Speakers:

Jae Hyang Lim (South Korea)

Stephen Wasserman (US)

Qing Zheng (US)

Alistair Harrison (US)

1:30 - 2:30 PM **WEDNESDAY, JUNE 10**

OM2015223

PAI-1 PREVENTS CHRONIC OTITIS MEDIA AND TYMPANOSCLEROSIS DURING NTHI INFECTION

Jae Hyang Lim, Ph.D. *Presenter*

Ewha Womans University, Department Of Microbiology, School Of Medicine, Seoul, South Korea

Delayed resolution of acute otitis media (OM) significantly contributes to the etiology of conductive hearing loss in children. In this study, the role of PAI-1 in the pathogenesis of OM and subsequent development of tympanosclerosis has been investigated. NTHi OM was induced in PAI-1 KO and C57BL/6 mice, and mRNA expression of PAI-1, tPA and uPA was measured in the bullae of C57BL/6 mice. mRNA expression of IL-1β, TNFα, MIP-2, tPA and uPA between PAI-1 KO and C57BL/6 mice was compared, and OM pathologies were compared too. NTHi up-regulated PAI-1 and tPA expressions in the bullae of C57BL/6 mice, but not uPA. mRNA expressions of IL-1β, TNFα and MIP-2 were low in PAI-1 KO mice at early time points, but significantly higher at later stage of OM. Similarly to the gene expression results, histological changes associated with OM were less at Days 1 and 3 in PAI-1 KO mice. However, unlike gradual resolution of OM pathologies in C57BL/6 mice at Day 7, PAI-1 KO mice showed pathological changes of tympanosclerosis. Taken together, bullae of PAI-1 KO mice showed low inflammatory responses against NTHi at the early stage of OM. However, PAI-1 KO mice fail to terminate inflammation, which may significantly contribute to the development of tympanosclerosis in PAI-1 KO mice.

1:30 - 2:30 PM **WEDNESDAY, JUNE 10**

OM2015276

INFECTION WITH A MURINE PARAINFLUENZA VIRUS ENHANCES OTITIS MEDIA INDUCED BY NONTYPEABLE HAEMOPHILUS INFLUENZAE

Stephen I Wasserman, M.D.[1] *Presenter*

Kwang K Pak, B.S.[2]
Mitchell Grayson[3]
Allen F Ryan [2]

[1]*UCSD, Medicine, La Jolla, CA, USA*
[2]*UCSD, Otolaryngology, La Jolla, CA, USA*
[3]*Medical College Of Wisconsin, Medicine, Milwaukee, WI, USA*

Objective: The fact that prior upper respiratory viral infections enhance the probability of subsequent otitis media (OM) has been well established, both in humans and in animal models. To develop a new mouse model for this interaction, we evaluated the effects of infection with a murine parainfluenza virus (MPaV; Sendai virus) on simultaneous or subsequent middle ear (ME) infection with nontypeable Haemophilus influenzae (NTHi).

Methods: Two co-infection paradigms were employed. In the first, inoculation of the nasopharynx (NP) with MPaV was carried out one week prior to ME injection of NTHi. In the second, the ME was inoculated simultaneously with MPaV and NTHi. MEs were harvested 3 or 7 days after ME infection and analyzed for culture positivity and histopathology. Results were compared to virus or NTHi alone.
Results: Pre-inoculation with MPaV in the NP resulted in prolonged ME culture positivity as well as persistent and greatly enhanced mucosal hyperplasia and leukocyte infiltration of the ME in response to NTHi infection, when compared to NTHi or virus alone. Simultaneous infection with MPaV and NTHI resulted in enhanced mucosal hyperplasia when compared to NTHi or virus alone.

Conclusion: Our results provide a foundation for studies using the mouse to explore molecular mechanisms underlying the viral enhancement of bacterial OM.
Supported by grants DC006279, DC000129 and DC012595.

1:30 - 2:30 PM **WEDNESDAY, JUNE 10**

OM2015159

BLOCKING MACROPHAGE MIGRATION INHIBITORY FACTOR ACTIVITY ALLEVIATES MOUSE OTITIS MEDIA IN VIVO

Qing Yin Zheng, M.D.,Ph.D.[1] *Presenter*

Ping Zhu[1]
Shuyang Xie[1]
Heping Yu[1]
Xiaolin Zhang[1]
Luke Apisa[1]
Pingyu Wang[1]
Michael Roy Jacobs[2]

[1]*Case Western Reserve University School Of Medicine, Department Of Otalaryngology-HNS, Cleveland, OH, USA*
[2]*Case Western Reserve University School Of Medicine, Department Of Pathology, Cleveland, OH, USA*

Introduction: SH3PXD2B (TKS4) is crucial to the formation of podosomes of macrophages and other cell types. This is an essential element in phagocytosis of pathogens. Lipopolysaccharide (LPS), a component of Gram-negative bacterial pathogens, is recognized by toll-like receptor 4 (TLR4) as a danger signal to initiate immune activation.

Methods: Here we investigate the role of SHP3PXD2B in the macrophage chemotaxis and phagocytosis in a previously established murine model of otitis media (OM).

Results: We found that LPS treatment decreased phagocytic function of macrophages through suppressing the expression of SH3PXD2B in LPS-treated peritoneal macrophages. In contrast, the expression of TLR4-related factors (TLR4, NF-?B and TNF-α) was increased in LPS-treated macrophages. LPS treatment yielded the same effects on the expression of SH3PXD2B and TLR4-related factors in cultured macrophages from Sh3pxd2bn/n- mutant mice, but not from Tlr4-/-- mutant mice. This implies the TLR4 pathway takes part in LPS-stimulated down-regulation of SH3PXD2B expression. TNF-α treatment similarly reduced SH3PXD2B expression in cultured macrophages, an effect which was neutralized by TNF-α antibody. Moreover, LPS treatment of macrophage cultures disrupted formation of podosomes and phagocytosis of Chinese ink particles and of bacteria. SH3PXD2B expression in LPS-treated, cultured macrophages was rescued by ibuprofen. Ibuprofen also rescued macrophage function as measured by Chinese ink and bacterial ingestion assays.

Conclusion: Our study reveals a novel pathway in which LPS decreases SH3PXD2B levels by a TLR4-related factor. This previously unappreciated pathogenic mechanism of Gram-negative bacteria may have important ramifications for understanding the pathogenesis of OM and other LPS-mediated infections and their treatment strategies.

1:30 - 2:30 PM **WEDNESDAY, JUNE 10**

OM2015273

COMPREHENSIVE PROTEOMIC AND METABOLOMIC SIGNATURES OF ACUTE OTITIS MEDIA

Alistair Harrison, Ph.D.[1] *Presenter*

Laura G Dubois, B.S.[7]
Lisa St. John Williams, B.S.[7]
M. Arthur Moseley, Ph.D.[7]
Rachael L Hardison, B.S.[1]
Derek R Heimlich, B.S.[1]
Alexander Stoddard, M.S.[4]
Joseph E Kerschner, M.D.[5,6]
Sheryl S Justice, Ph.D.[1,2,3]
J. Will Thompson, Ph.D.[7]
Kevin M Mason, Ph.D.[1,2,3]

[1]*Nationwide Children's Hospital, The Center For Microbial Pathogenesis, Columbus, OH, USA*
[2]*Ohio State University, The Center For MIcrobial Interface Biology, Columbus, OH, USA*
[3]*Ohio State University, Department Of Pediatrics, Columbus, OH, USA*
[4]*Medical College Of Wisconsin, Human And Molecular Genetics Center, Milwaukee, WI, USA*
[5]*Medical College Of Wisconsin, Department Of Otolaryngology And Communication Sciences, Milwaukee, WI, USA*
[6]*Children's Hospital Of Wisconsin, Division Of Pediatric Otolaryngology, Milwaukee, WI, USA*
[7]*Duke University Medical Center, Duke Proteomics And Metabolomics Core Facility, Duke Center For Genomic And Computational Biology, Durham, NC, USA*

Introduction: To ultimately prevent acute otitis media (AOM), the molecular details of the interactions between bacteria and host during disease should be clearly defined. Recent technological advances allow analysis of host and bacterial protein and metabolic profiles from a single small tissue sample to provide a snapshot of the microenvironment of the middle ear during AOM.

Objective: We used the chinchilla model of AOM to determine, for the first time, the most expansive delineation of global changes in host protein and metabolite profiles in response to an experimentally induced disease.

Methods: Chinchillas were transbullarly infected with nontypeable Haemophilus influenzae (NTHI). After 48 hours, tissues lysates were analysed by high-resolution quantitative two-dimensional liquid chromatography-tandem mass spectrometry. Results: We identified dynamic changes in protein and metabolic profiles not previously described during AOM. Peptides representing 742 chinchilla proteins were identified. The levels of 105 were statistically different in response to NTHI

infection. Analyses revealed overrepresentation of proteins and metabolites indicative of suppressed immune responses and cytoskeleton remodeling. We have experimentally demonstrated a role for Arp2/3 in actin remodeling and NTHI invasion.

Conclusion: Quantitative characterization of the molecular signatures of infection will redefine our understanding of host response driven developmental changes during pathogenesis. These data represent the first global study of host protein and metabolite profiles in vivo in response to AOM and show the feasibility of extensive characterization of host protein profiles during disease. Identification of novel protein targets and metabolic biomarkers will advance development of therapeutic options for treatment of disease.

2:30 - 3:15 PM **WEDNESDAY, JUNE 10**

BALTIMORE 3-5

PODIUM 12: IMMUNOLOGY 2

Moderator:

Sung Moon (US)

Speakers:

Sung Moon (US)
Stephanie Val (US)
Kyung Wook Heo (US)
Laura Novotny (US)
Kenneth Brockman (US)

2:30 - 2:37 PM **WEDNESDAY, JUNE 10**

OM2015213

RESPONSE OF COCHLEAR CELLS TO OTITIS MEDIA PATHOGENS

Sung K Moon, M.D.,Ph.D. *Presenter*

David J Lim

University Of California - Los Angeles, Los Angeles, CA, USA

Middle ear infection can induce inner ear inflammation, i.e. tympanogenic labyrinthitis. Excessive inflammation can cause pathologic changes in the organ of Corti and cochlear lateral wall, impairing normal hearing. Pro-inflammatory molecules in the middle ear cavity are known to enter the cochlea via the round window membrane, but how cochlear cells respond to pro-inflammatory signals is not clear. Previously, we have shown that the spiral ligament fibrocytes (SLFs) up-regulate various inflammatory mediators in response to otitis media pathogens such as nontypeable H. influenzae (NTHi) and S. pneumoniae. Based on these findings, we further demonstrated that SLFs are able to recognize NTHi molecules, resulting in up-regulation of a monocyte chemokine, CCL2, via TLR2/NF-kB signaling. We also showed that NTHi-induced SLF-derived molecules are chemoattractive to monocytes via CCR2. Besides CCL2, we found NTHi-induced up-regulation of a neutrophil chemokine, CXCL2, mediated by ERK2/c-Jun signaling. Furthermore, we demonstrated IL-10-mediated negative regulation of NTHi-induced CCL2 up-regulation, which was mediated by heme oxygenase-1 and carbon monoxide (CO). We found that a CO-releasing molecule mimics the inhibitory effect of IL-10 on NTHi-induced CCL2 up-regulation. Taken together, this study is expected to enable us to better understand the molecular pathogenesis of tympanogenic labyrinthitis and provide a scientific basis for potential therapeutic targets. [Supported partly by DC005025 and DC011862]

2:37 - 2:44 PM **WEDNESDAY, JUNE 10**

OM2015267

PROTEOMIC CHARACTERIZATION OF MIDDLE EAR EFFUSION PROTEINS FROM CHILDREN WITH CHRONIC OTITIS MEDIA: IMPORTANCE OF NEUTROPHIL EXTRACELLULAR TRAPS IN THE EAR MUCOSAL IMMUNITY

Stephanie Val, Ph.D.[1] *Presenter*

Marian Poley, BS, BA[1]
Kristy Brown[2]
Yetrib Hathout[2]
Mary Rose[2]
Diego Preciado[1]

[1]*Children's National Medical Center, Sheikh Zayed Institute For Pediatric Surgical Innovation, Washington, DC, USA*
[2]*Children's National Medical Center, Center For Genetic Medicine, Washington, DC, USA*

Objective: This study aims at characterizing the proteome of middle ear effusions (MEEs) from children having chronic OM and to investigate the signaling pathways activated during the disease.

Method: Six MEEs were collected from children undergoing myringotomy at Children's National Medical Center for proteomics analysis using a liquid chromatography tandem mass spectrometry (LC-MS/MS) and 16 other samples were collected for Western Blot and immunofluorescence analysis.

Results: 687 proteins were identified by LC-MS/MS in the 6 samples. 136 were identified as not immunoglobulins. The more abundant proteins were LPLUNC, Lactotransferrin, MUC5B, Actin alpha 2, Histone H4 and the proteins S100-A8 and S100-A9, that were also present in most of the 16 other samples analyzed by Western Blot. The unusual high abundance of Histone H4 and actin as well as neutrophil biomarkers were hypothesized to be due to the presence of a high content in neutrophil extracellular traps (NETs). Immunofluorescence analysis of mucoid and serous effusions were performed to visualize NETs and showed the presence of neutrophils releasing their DNA carrying anti-microbial components and MUC5B mucin, as well as S100 proteins. Mucoid effusions showed a very high concentration of extracellular DNA whereas serous effusions contained few.

Conclusion: This work shows an extensive study of MEEs proteins by mass spectrometry, and confirms the importance of the mucin MUC5B in COM. We show the importance of NET implication in the innate immune response in COM.

2:44 - 2:51 PM **WEDNESDAY, JUNE 10**

OM2015297

LEUKOTRIENE B4 CONTRIBUTES TO NEUTROPHIL RECRUITMENT DURING OTITIS MEDIA

Kyung Wook Heo[1] *Presenter*

Stephen I Wasserman[2]
Allen F Ryan[1,3]

[1]*University Of California, San Diego, Surgery / Otolaryngology, La Jolla, CA, USA*
[2]*UCSD, Medicine / Allergy & Immunology, La Jolla, CA, USA*
[3]*VA San Diego Healthcare System, Research, San Diego, CA, USA*

Objective: The leukotrienes are important mediators of inflammation. Leuktriene B4 (LTB4) plays a critical role in neutrophil chemotaxis. In bacterial otitis media (OM), large numbers of neutrophils are rapidly recruited to the middle ear, potentially exerting bacterial clearance and pro-inflammatory effects.

Method: To assess the role of LTB4 in OM, we measured the expression of genes encoding enzymes involved in its synthesis or its receptors during an NTHi-mediated middle ear (ME) infection in mice. We then applied a receptor antagonist during experimental OM, and assessed leukocyte recruitment and mucosal hyperplasia 48 hours after inoculation.

Results: 5-lipoxygenase activating protein (FLAP) and leukotriene A4 hydrolase (LTA4H) synthesize LTB4 from arachidonic acid. The flap gene was significantly up-regulated (2X-10X) in the ME from 3-72 hours after NTHi inoculation, and the lta4h gene (2X) from 24-72 hours. The ltb4r1 gene was strongly up-regulated (160X) at 24 hours, while the ltb4r2 gene was not regulated. When the LTBR1 receptor antagonist U75302 was applied to the ME during NTHi-induced OM at 1.5 or 15 μM, neutrophil recruitment to the ME was reduced, but mucosal hyperplasia was not.

Conclusion: LTB4 plays a significant role in neutrophil recruitment to the ME during OM, acting via the LTB4R1 receptor. LTB4R1 is also antagonized by resolvin E1, a natural pro-recovery compound also produced during arachidonic acid metabolism. Our U75302 results suggest that resolvin E1 could limit neutrophil recruitment to the ME during OM. (Supported by grants DC006279, DC000129, and DC012595 from the NIH/NIDCD and BX001205 from the VA.)

2:51 - 2:58 PM **WEDNESDAY, JUNE 10**

OM2015152

DEFINING THE FUNCTIONAL EPITOPES OF INTEGRATION HOST FACTOR (IHF) TO DEVELOP A NOVEL BIOFILM-FOCUSED IMMUNOTHERAPEUTIC AGAINST NONTYPEABLE HAEMOPHILUS INFLUENZAE-INDUCED CHRONIC AND RECURRENT OTITIS MEDIA

Laura A. Novotny, M.S. [1,2] *Presenter*

Sankalp Malhotra[1,2]
Steven D. Goodman[1,2]
Lauren O. Bakaletz[1,2]

[1]*Nationwide Children's Hospital, Center For Microbial Pathogenesis, Columbus, OH, USA*
[2]*The Ohio State University College Of Medicine, Columbus, OH, USA*

Introduction: Otitis media (OM) due to nontypeable Haemophilus influenzae (NTHI) is a chronic pediatric disease, attributed to the formation of biofilms within the middle ear. These biofilms contain abundant extracellular DNA (eDNA) arranged in a mesh-like structure with a member of the DNABII family of bacterial DNA-binding proteins localized to the vertices of each crossed eDNA strand. Antibody against one such DNABII member, integration host factor (IHF), induces resolution of pre-formed NTHI biofilms in vivo, due to sequestration of free protein in the bulk media resulting in a subsequent shift in equilibrium away from the eDNA bound state.

Objectives: The objective is to fine-map the DNA-binding tip regions of IHF specific to NTHI in an effort to identify functional epitopes and guide the development of novel immunotherapeutics.

Methods: Using surface plasmon resonance (SPR), we tested the reactivity of polyclonal antiserum against IHF from E. coli (IHFE. coli) to overlapping IHF-derived synthetic peptides.

Results: By SPR, antiserum against IHFE. coli was ten-times more reactive to one α-subunit-specific peptide IhfA-5NTHI, compared to peptides from the flanking regions. This epitope is predicted to possess a proline-containing loop, known to be critical for IHF-dsDNA interaction. Functionally, antibodies against IhfA-5NTHI were equally effective to disrupt established NTHI biofilms as antiserum against the full-length IHFE. coli protein in vitro.

Conclusion: Our ongoing efforts to test antisera and monoclonal antibodies against additional promising IHFNTHI epitopes is the first step towards developing a novel, NTHI-specific and biofilm-focused immunotherapeutic against chronic and recurrent otitis media. Support NIDCD/NIH R01 DC011818

2:58 - 3:05 **WEDNESDAY, JUNE 10**

OM2015153

A PHASE VARIABLE DNA METHYLTRANSFERASE FACILITATES ADAPTATION AND SURVIVAL OF NONTYPEABLE HAEMOPHILUS INFLUENZAE WITHIN THE MIDDLE EAR VIA ALTERED BIOFILM FORMATION

Kenneth L Brockman, Ph.D.[1] *Presenter*

John M Atack[2]
Michael P Jennings[2]
Lauren O Bakaletz[1]

[1]*Nationwide Children's Hospital And The Ohio State University College Of Medicine, Center For Micorbial Pathogenesis, Columbus, OH, USA*
[2]*Griffith University, Institute For Glycomics, Southport, QUEENSLAND, Australia*

Objective: Nontypeable Haemophilus influenzae (NTHI) possesses a novel genetic system, termed the phasevarion (phase variable regulon), which mediates a rapid and reversible change in the expression of numerous genes through phase variation of a single gene (mod) that encodes a DNA methyltransferase. Our objective was to determine the selective pressures within the middle ear environment that impact selection for a particular phasevarion status in this host-site.

Methods: NTHI strain 723, a pediatric middle ear isolate which possesses a phase variable modA2, was evaluated to determine whether phasevarion status impacted virulence in a chinchilla model of experimental OM. Chinchillas challenged with NTHI in the modA2ON state exhibited more severe symptoms of OM than those challenged with NTHI in the modA2OFF state. Additionally, NTHI entering the middle ear modA2OFF had switched to modA2ON by eighteen days post-challenge. Biofilm formation and adherence by NTHI 723 modA2ON or modA2OFF were assessed under alkaline conditions designed to mimic those of the middle ear during chronic OM. RNAseq and proteomic analysis to determine the genes and proteins involved in ModA2-mediated alteration of biofilm formation is currently underway.

Results: Under conditions designed to mimic those of a middle ear with chronic OM (e.g. alkaline pH and 37°C), biofilm formation by 723 modA2ON was significantly greater compared to modA2OFF.

Conclusions: Environmental conditions and phasevarion status played an important role in NTHI biofilm formation in vitro. Greater understanding of the complexities of phasevarion-mediated adaptation will enhance the ability to manage diseases of the human respiratory tract. Support: NHMRC(Australia) 1034401

3:15 - 3:45 PM **WEDNESDAY, JUNE 10**

COFFEE BREAK IN EXHIBIT/POSTER HALL

3:45 - 4:45 PM **WEDNESDAY, JUNE 10**

BALTIMORE 3-5

PODIUM 14: MICROBIOLOGY 1

Moderator:

Stephen Barenkamp (US)

Speakers:

Tal Marom (Israel)
Sabine Schnyder (US)
W. Edward Swords (US)
Christopher Lisi (US)
Paula Tähtien (US)
Elaine Mokrzan (US)
Justin Yan (US)

3:45 - 3:52 PM **WEDNESDAY, JUNE 10**

OM2015007

RESISTANCE PATTERNS OF STREPTOCOCCUS PNEUMONIAE ISOLATED FROM MIDDLE EAR FLUID IN CHILDREN WITH SEVERE ACUTE OTITIS MEDIA

Tal Marom, M.D. *Presenter*

Elad Avraham, B.Sc.
Sharon Ovnat Tamir

Edith Wolfson Medical Center, Tel Aviv University, Otolaryngology-Head And Neck Surgery, Holon, Israel

Introduction: Streptococcus pneumoniae (Sp) is a major acute otitis media (AOM) pathogen. Pneumococcal conjugate vaccines (PCVs) implementation in National Immunization Programs worldwide changed AOM bacteriology. In Israel, PCV7 was introduced in 07/2009, and was replaced by PCV13 in 11/2010. Sp resistance patterns in the post-PCV era have not been well studied, but have implications on current AOM antibiotics treatment. Objective: To determine Sp resistance patterns.

Methods: Children <6 years who presented with "severe" AOM episodes with middle ear fluid cultures during 2008-2013 were identified. These episodes were defined when tympanocentesis was required, or when spontaneous otorrhea was present. Children were considered according to their PCV status as "unimmunized" or "PCV7/PCV13 immunized". Antibiotic susceptibility was determined by standard techniques. Multi-drug resistant (MDR) was considered when Sp was non-susceptible to β-lactam + 2 other antibiotics.

Results: Of 295 eligible AOM episodes, 105 (36%) were culture positive: 65 (61%) grew Sp, and 41 (39%) grew other bacteria. There was a downward trend in the number of positive pneumococcal MEF cultures. Concurrently, there was an increased tendency for penicillin-susceptible strains [8/24 (33%) in 2008 vs. 5/5 (100%) in 2013], in concordance with the percentage of PCV catch-up (0% in 2008 vs. >80% in 2013). PCV7/PCV13 immunized children had significantly less MDR isolates than unimmunized children: 8% vs. 22%, respectively.

Conclusion: The introduction of PCVs resulted in higher rates of penicillin-susceptible Sp isolates, and concomitantly in less MDR Sp strains. The current recommended first-line antibiotic therapy with amoxicillin is adequate, even in "severe" AOM cases.

3:52 - 3:59 PM **WEDNESDAY, JUNE 10**

OM2015056

LACK OF MIDDLE EAR VIRULENCE OF STREPTOCOCCUS PNEUMONIAE 33F ISOLATES IN CHINCHILLAS IS ASSOCIATED WITH ABSENCE OF SPECIFIC TOXIN-ANTITOXIN SYSTEMS AND THE PNEUMOCOCCAL SERINE-RICH PROTEIN (PSRP) PATHOGENICITY ISLAND

Sabine Schnyder, M.D.[1] *Presenter*

Paula A Tahtinen, M.D.,Ph.D.[1,2,3]
Brent A Little, Ph.D.[1]
Stephen I Pelton, M.D.[1]
Vishakha Sabharwal, M.D.[1]

[1]*Boston University, Boston Medical Center, Pediatric Infectious Diseases, Boston, MA, USA*
[2]*Turku University Hospital, Department Of Paediatrics And Adolescent Medicine, Turku, Finland*
[3]*Boston University, Department Of Pediatrics, Boston, MA, USA*

Introduction: S.pneumoniae remains an important cause of acute and chronic otitis media (OM) in US children. Objective: To identify specific virulence genes essential for S.pneumoniae to cause otitis media, which could be targeted for prevention or treatment of OM.

Methods: We screened selected serotypes of S.pneumoniae in our chinchilla model of experimental OM both by nasopharyngeal inoculation and barotrauma, and direct intrabullar challenge. Genomic DNA of bacterial isolates was sequenced on a HiSeq Illumina platform. De novo assembled sequences were annotated with RAST (Rapid Annotation by Subsystem Technology). Functional comparative genomic analysis was performed in SEED, BRIG and BLAST.

Results: Two 33F isolates colonized the nasopharynx well, but failed to produce significant disease, even with intrabullar inoculation. Functional genomic comparison against 16 OM producing strains revealed that our 33F strains lack two toxin/antitoxin systems, pneumococcal Epsilon/Zeta (PezAT) and Phd/DOC, as well as the PsrP pathogenicity island. At least one of these three virulence factors was present in all OM causing strains, with most highly virulent strains possessing all three factors.

Conclusion: The inability to cause EOM in specific 33F S.pneumoniae strains is associated with the absence of genes coding for PezAT, Phd/DOC and PsrP. PezAT and PhD/DOC are thought to play a role in survival under environmental stress, biofilm formation and persistence; PsrP is an adhesin linked to host cell adhesion as well as biofilm formation. Further characterization of the exact function of these genomic regions in S.pneumoniae is necessary to define their role in virulence for OM.

3:59 - 4:06 PM **WEDNESDAY, JUNE 10**

OM2015126

IDENTIFYING DETERMINANTS OF AI-2 QUORUM SIGNAL UPTAKE IN NONTYPEABLE HAEMOPHILUS INFLUENZAE 7P49H1

W. Edward Swords, Ph.D. *Presenter*

Ankita Basu Roy

Wake Forest School Of Medicine, Microbiology And Immunology, Winston-Salem, NC, USA

Objective: Nontypeable Haemophilus influenzae (NTHi) is a major cause of chronic/recurrent otitis media infections. A large body of work from this laboratory and others has shown that NTHi bacteria persist during these infections in multicellular biofilm communities. We have shown that the maturation of NTHi biofilms is coordinated by autoinducer-2 (AI-2) quorum signals, which are an important determinant of NTHi persistence in vivo. Prior work from this laboratory has shown that for the widely-used NTHi model strain 86-028NP, uptake of AI-2 quorum signals is determined by the RbsB transporter. However, genomic analyses have shown that NTHi strains gene content with predicted relevance to quorum sensing. Most strains, like 86-028NP, have homologs to the Rbs system, but some NTHi strains have a separate locus with homology to the Lsr system described in other gram-negative bacterial species.

Method: In this study, we examined a NTHi isolate, 7P49H1, which has loci homologous to the Rbs and Lsr systems. Isogenic lsrB, rbsB, and lsrB rbsB mutant strains were generated in the NTHi 7P49H1 background and compared for AI-2 quorum signal uptake and biofilm maturation.

Results: The results indicate that the primary determinant of AI-2 quorum signals for this strain is RbsB, as only modest defects were observed in 7P49H1 lsrB, while 7P49H1 rbsB and 7P49H1 lsrB rbsB showed significant decreases in signal uptake and biofilm maturation.

Conclusion: While there is definitely a need for further testing in different strain backgrounds, these data are consistent with previous findings relative to the importance of RbsB.

4:06 - 4:13 PM **WEDNESDAY, JUNE 10**

OM2015137

BACTERIAL OPRF EXPRESSION HELPS IN THE SURVIVAL OF OTOPATHOGENIC PSEUDOMONAS AERUGINOSA INSIDE MACROPHAGES

Christopher Vincent Lisi, M.D. *Presenter*

Rahul Mittal
Xue-Zhong Liu

University Of Miami Miller School Of Medicine, Department Of Otolaryngology, Miami, FL, USA

Introduction: Otitis media (OM) is a broad term describing a group of infectious and inflammatory disorders of the middle ear. Despite antibiotic therapy, acute OM can progress to chronic suppurative otitis media (CSOM) characterized by tympanic membrane perforation and purulent drainage. Pseudomonas aeruginosa (PA) is the most common bacteria associated with CSOM.

Objective: Although macrophages play an important role in innate immune responses, their role in the pathogenesis of PA induced OM is not known. The objective of this study is to examine the interaction of PA with macrophages.

Methods: Macrophages were generated from mouse bone marrow or human monocytes and infected with PA for different time periods. The survival of bacteria inside macrophages was assessed by gentamicin protection assay, confocal microscopy, and electron microscopy.

Results: We observed that PA enters and multiplies inside human and mouse macrophages. This bacterial entry in macrophages requires both microtubule and actin dependent processes. Transmission electron microscopy demonstrated that PA was present in membrane bound vesicles inside macrophages. Interestingly, deletion of OprF expression in PA abrogates its ability to survive inside macrophages.

Conclusion: Our results suggest that otopathogenic PA survives and multiplies inside macrophages for which OprF expression is required. This leads to evasion of bacterial killing and ability of PA to cause OM. Further studies are warranted to understand the receptors involved in PA entry into macrophages. Understanding host-pathogen interaction will provide novel avenues to design novel treatments against OM.

4:13 - 4:20 PM **WEDNESDAY, JUNE 10**

OM2015158

RISK FACTORS FOR PERSISTENT NASOPHARYNGEAL CARRIAGE OF STREPTOCOCCUS PNEUMONIAE

Paula A Tahtinen[1,2,3] *Presenter*

Aino Ruohola[3,4]
Miia K Laine[3]
Laura Lindholm, MSc[5]
Brent A Little[1]
Stephen I Pelton[1,2]

[1]*Boston Medical Center, Division Of Pediatric Infectious Diseases, Boston, MA, USA*
[2]*Boston University School Of Medicine, Department Of Pediatrics, Boston, MA, USA*
[3]*Turku University Hospital, Department Of Paediatrics And Adolescent Medicine, Turku, Finland*
[4]*University Of Turku, Department Of Paediatrics And Adolescent Medicine, Turku, Finland*
[5]*National Institute For Health And Welfare, Department Of Infectious Diseases, Turku, Finland*

Introduction: Persistent nasopharyngeal carriage of S. pneumoniae is associated with recurrence of acute otitis media (AOM) symptoms, treatment failure, and prolonged presence of middle ear effusion.

Objective: To identify host, environmental and microbiological risk factors for persistent carriage of S. pneumoniae.

Methods: Children (6–35 months) with AOM enrolled in a study of antimicrobial treatment vs. placebo were followed every 1–2 weeks for at least 2 months; nasopharyngeal cultures were performed at most follow-up visits. Persistent carriage was defined as detection of same serotype of S. pneumoniae from the nasopharynx for ≥45 days. The association between each risk factor and persistent carriage was analyzed in univariable model and all risk factors that showed an association (P<0.15) were included in our multivariable model.

Results: S. pneumoniae was detected in 177/300 (59%) children at enrollment, and 31/177 (18%) had persistence of the same serotype in each nasopharyngeal sample for ≥45 days. Median duration of persistent carriage was 62 days (range 45–205). Older age (≥2 years), home care, serotypes 19F and 35B, detection of respiratory virus, no antimicrobial treatment, and penicillin resistance (MIC≥2 mg/L) were associated with persistent carriage in univariable analysis. In multivariable model, when adjusted for other 6 risk factors, serotype 35B increased (odds ratio 7.75; 95% CI, 1.26–47.52) and antimicrobial treatment decreased the risk (odds ratio 0.25; 95% CI, 0.10–0.63) for persistent carriage.

Conclusion: Persistent carriage of S. pneumoniae is common in young children with AOM. Serotype 35B was associated with persistent carriage after adjusting for antimicrobial treatment and penicillin resistance.

4:20 - 4:27 PM **WEDNESDAY, JUNE 10**

OM2015147

THE TYPE IV PILUS OF NONTYPEABLE HAEMOPHILUS INFLUENZAE IS MORE HIGHLY EXPRESSED IN BIOFILMS FORMED AT THE TEMPERATURE OF THE HUMAN NASOPHARYNX THAN AT 37°C, AND IS REQUIRED FOR BIOFILM TOWER FORMATION

Elaine Marie Mokrzan, Ph.D. *Presenter*

Emily Horne
Lauren O. Bakaletz, Ph.D.

Nationwide Children's Hospital And The Ohio State University College Of Medicine, Center For Microbial Pathogenesis, Columbus, OH, USA

Objective: During otitis media, nontypeable Haemophilus influenzae (NTHI), a commensal of the human nasopharynx (hNP), forms biofilms within the middle ear. Type IV pili (Tfp) are important for NTHI biofilm formation; however the kinetics and regulation of Tfp expression are unclear, especially at the average hNP temperature, 34°C. Our objective was to examine relative biofilm growth, architecture, and expression of PilA, the majority subunit of Tfp at 34°C and 37°C; and to clarify the role of Tfp in NTHI biofilm formation.

Method: Biofilms formed by NTHI 86-028NP, ΔpilA, and/or reporter constructs in which GFP expression was driven by the pilA or ompP2 promoter were visualized by confocal microscopy.

Results: Although biofilm biomass increased more slowly at 34°C vs. 37°C, pilA promoter activity relative to biomass was significantly greater at 34°C. At both temperatures, pilA promoter activity occurred initially at the substratum, but over time regions of intense fluorescence appeared at tower apexes. In biofilms formed from a mixture of parent and ΔpilA, both strains were present at the substratum, whereas towers were formed only by the parent strain which could express Tfp.

Conclusion: As estimated by reporter activity, Tfp expression occurred in a regulated manner at both 37°C and 34°C; however, it was significantly greater at the cooler hNP temperature. Moreover, Tfp expression was essential for biofilm tower formation. These results strongly suggested that the vaccine target PilA is expressed within the hNP, likely in biofilms. Future experiments will characterize NTHI biofilms grown on airway epithelial cells. NIH-R01-DC003915 to LOB

4:27 - 4:34 PM **WEDNESDAY, JUNE 10**

OM2015101

INCREASED MUCIN GENE EXPRESSION IS ASSOCIATED WITH HEARING LOSS IN PEDIATRIC OTITIS MEDIA PATIENTS

Justin C Yan, M.D.[1] *Presenter*

Tina Samuels, M.S. [1]
Mengshuang Guo, B.S. [1]
Pawjai Khampang, M.S. [1]
Wenzhou Hong[1]
Peter Dettmar[4]
Alexander C Mackinnon[2]
Pippa M Simpson[3]
Nikki Johnston[1]
Joseph E Kerschner[1]

[1]*Medical College Of Wisconsin, Department Of Otolaryngology And Communication Sciences, Milwaukee, WI, USA*
[2]*Medical College Of Wisconsin, Department Of Pathology, MILWAUKEE, WI - WISCONSIN, USA*
[3]*Medical College Of Wisconsin, Milwaukee, WI, USA*
[4]*RDBiomed Limited, Hull, UK, United Kingdom*

Objective: To compare mucin gene expression of gel-forming mucins (GFM) in patients with chronic otitis media with effusion (OME) and recurrent otitis media (RecOM) and understand how GFM expression impacts hearing levels, and its correlation with middle ear mucosal (MEM) hypertrophy.

Method: Samples from children undergoing tympanostomy tube insertion (TTI) for OM and control children without history of OM undergoing cochlear implantation (CI) were obtained. RNA was extracted to generate cDNA. Audiologic testing was obtained prior to TTI. Expression levels of each targeted GFM (MUC2, MUC5AC, MUC5B and MUC19) were detected by quantitative PCR. Pathological examinations were performed to assess for MEM thickness.

Results: Patients with OME relative to CI, demonstrated an increased GFM expression (MUC2, MUC5AC, MUC5B) and a trend towards higher mucin expression in OME relative to RecOM patients. Increased GFM expression (MUC5B and a sum of all mucins combined) was associated with greater hearing loss. Patients with higher clinical viscosity ratings demonstrated significantly higher GFM expression (MUC2). Specimens with increased GFM expression demonstrated increased MEM hypertrophy.

Conclusion: Patients with OME have increased GFM expression which is associated with greater hearing loss. Increased MEM hypertrophy is associated with higher mucin gene expression and correlates with greater hearing loss.

4:45 - 5:30 PM **WEDNESDAY, JUNE 10**

BALTIMORE 3-5

PODIUM 16: MICROBIOLOGY 2

Moderator:

Anders P Hakansson (Sweden)

Speakers:

Chinh Ngo (Australia)

Tasnee Chonmaitree (US)

Janak Patel (US)

Rachael Hardison (US)

Robert Osgood (US)

4:45 - 4:52 PM **WEDNESDAY, JUNE 10**

OM2015189

PREDOMINANT BACTERIA AND VIRUSES LOCATED WITHIN THE UPPER RESPIRATORY TRACT AND MIDDLE EARS OF AUSTRALIAN URBAN CHILDREN EXPERIENCING OTITIS MEDIA

Chinh C Ngo[1] *Presenter*

Rebecca J Rockett, BSc[2]
Theo P Sloots[2]
Ruth B Thornton[3]
Helen M Massa[1]
Allan W Cripps[1]

[1]*Griffith University, Griffith Health, Southport, QLD, Australia*
[2]*Queensland Paediatric Infectious Diseases Laboratory, Queensland Children's Medical Research Institute, Queensland Chidlren's Health Service And The University Of Queensland, Brisbane, QLD, Australia*
[3]*School Of Paediatrics And Child Health And Telethon Institute For Child Health Research, Centre For Child Health Research, University Of Western Australia, Perth, WA, Australia*

Introduction: Recent studies suggest that the predominant otopathogens in Australian children experiencing otitis media (OM) may differ from that observed elsewhere and favour non-typeable Haemophilus influenzae (NTHi) over Streptococcus pneumoniae (Pnc).

Objective: To identify predominant bacteria and viruses within the middle ear fluid, nasopharynx and adenoids of Australian urban children undergoing ventilation tube insertion for OM. Method: Middle ear fluid (MEF), nasopharyngeal swabs (NPS) and adenoid samples from 23 children, aged 1-7 years, with a history of OM were examined by Real Time PCR for Pnc, NTHi, Moraxella catarrhalis (Mcr) and a panel of 10 viruses; adenovirus, influenza A/B virus, human metapneumovirus, parainfluenza 1/2/3 viruses, respiratory syncytial virus, rhinovirus and WU polyomavirus.

Results: Otopathogens were identified in NP (78.3%; 18/23), adenoids (82.6%; 19/23) and MEF samples (35.6%; 16/45). NTHi was the most common bacteria detected in adenoid, NP and MEF samples. All Pnc and Mcr identified in MEF were also detected in NP and/or adenoid samples of same subjects compared to only 75% for NTHi. Viruses were detected in NP (69.6%; 16/23), adenoid (78.3%; 18/23) and MEF (42.2%; 19/45) samples. WU polyomavirus was the most commonly detected virus in adenoids (52.2%), compared to rhinovirus within NP (30.4%) and MEF (22.2%) samples. All rhinovirus detections in MEF were also identified in NP and/or adenoid samples.

Conclusion: NTHi is the predominant otopathogen for OM in Australian urban children with a history of OM. Pathogen presence within the MEF is associated with identification with the nasopharynx and adenoids of the same child.

4:52 - 4:59 PM **WEDNESDAY, JUNE 10**

OM2015203

UPPER RESPIRATORY TRACT VIRAL INFECTIONS, NASOPHARYNGEAL BACTERIAL COLONIZATION AND ACUTE OTITIS MEDIA IN THE FIRST YEAR OF LIFE

Tasnee Chonmaitree, M.D. *Presenter*

Kristofer Jennings, Ph.D.
Rocio Trujillo, M.D.
Pedro Alvarez-Fernandez, M.D.
Janak A Patel, M.D.
David P McCormick, M.D.
Michael J Loeffelholz, Ph.D.
Johanna Nokso-Koivisto, M.D.
Richard B Pyles, Ph.D.
Aaron L Miller, M.S.

University Of Texas Medical Branch, Department Of Pediatrics, Galveston, TX, USA

Introduction: Acute otitis media (AOM) is generally caused by pathogenic bacteria that colonized the nasopharynx, and occurs after viral upper respiratory tract infection (URI). There is limited information on the interaction between pathogenic bacteria and viruses, in relation to the occurrence of AOM.

Objective: To determine the rates of nasopharyngeal bacterial colonization and viral URIs, and possible bacterial and viral interactions in infants with and without AOM in the first year of life.

Methods: In a prospective, longitudinal study, infants were enrolled from near birth and followed for up to 12 months of age. Specimens were collected at monthly interval (months 1–6 and month 9) and during viral URI episodes for bacterial culture and viral PCR studies. Subjects were followed closely for AOM development.

Results: A total of 311 infants were followed for 267 child-years; there were 859 URI episodes (in 286 infants) and 180 AOM episodes (143 infants). Infants with AOM had significantly more frequent URIs than those without AOM (4.7 vs 2.3 episodes/ child-year) (P=0.00189) and had higher colonization rate with pathogenic bacteria (P= 0.0046). Moraxella catarrhalis interacted with respiratory syncytial virus (RSV) and rhinovirus; M. catarrhalis colonization reduced the risk for RSV-URI (P= 0.00092), and the risk for rhinovirus-URI (P= 0.0000002) and rhinovirus-associated AOM (P=0.0065).

Conclusions: Infants with AOM in the first year of life were colonized with more pathogenic bacteria and had more frequent viral URIs than those without AOM. Colonization with M. catarrhalis reduced the risks for RSV-and rhinovirus- URIs and rhinovirus-associated AOM.

4:59 - 5:06 PM **WEDNESDAY, JUNE 10**

OM2015257

EFFECT OF TNFA-308 AND IL-6-174 GENE POLYMORPHISMS ON NASOPHARYNGEAL COLONIZATION WITH OTOPATHOGENIC BACTERIA IN THE FIRST MONTHS OF LIFE

Janak A Patel *Presenter*

Kristopher Jennings
Pedro Alvarez-Fernandez
Rocio Trujillo
David P McCormick
Michael J Loeffelholz
Reuben Matalon
Tasnee Chonmaitree

University Of Texas Medical Branch, Pediatric Infectious Disease, Galveston, TEXAS, USA

Objectives: Determine the impact of TNFa-308 and IL-6-174 gene polymorphisms on colonization of the nasopharyngx (NP) with otogenic bacteria in first months of life.

Methods: In 311 infants, NP specimens were collected monthly (months 1–6) and at month 9, and during upper respiratory infection (URI) for bacterial and viral studies. After URI, subjects were followed for AOM development. The infants' gene polymorphisms were determined by gene sequencing of the DNA.

Results: NP colonization with Streptococcus pneumoniae (SP), nontypeable Haemophilus influenzae (HI) and Moraxella catarrhalis (MC) progressively increased over time; MC was the highest colonizing pathogen, followed by NTHI and SP. The frequencies of positive NP cultures for SP and NTHI over time per each child were not associated with TNFa-308 and IL-6-174 polymorphic genotypes. However, the frequency of positive MC cultures was significantly lower with IL-6-174 polymorphic genotype than the wild ('normal') genotype (P = 0.0066). While TNFa-308 polymorphic genotype alone had no effect on frequency of positive MC cultures, when TNFa-308 was combined with IL-6-174 polymorphic genotype, there was a significant additional interaction for MC positivity (P = 0.0021). There was no effect of the genotypes on URI episodes or AOM.

Conclusion: In the first months of life, TNFa-308 and IL-6-174 gene polymorphisms protect against colonization with MC but not other otopathogens. However, there was no effect of these genes on AOM development. Additional studies are needed to elucidate the interactions between the host, pathogen and environment in the first months of life.

5:06 - 5:13 PM **WEDNESDAY, JUNE 10**

OM2015261

INTRACELLULAR BACTERIAL COMMUNITY DEVELOPMENT IN NONTYPEABLE HAEMOPHILUS INFLUENZAE (NTHI) SURVIVAL AND PATHOGENESIS

Rachael Hardison, B.S.[1,2] *Presenter*

Sheryl Justice[1,2]
Kevin Mason[1,2]

[1]*Nationwide Children's Hospital, Center For Microbial Pathogenesis, Columbus, OH, USA*
[2]*Ohio State University, College Of Medicine, Columbus, OH, USA*

Introduction: The nasopharynx and middle ear microenvironments differ in nutrient availability. Host sequestration of essential nutrients at privileged sites (e.g. middle ear) limits microbial outgrowth. Fluctuations in heme-iron availability, however, influence disease severity, biofilm formation, and invasion of NTHI.

Objective: We observed intracellular NTHI communities in the middle ear in response to heme-iron restriction. Concurrent with this observation, heme-iron restricted NTHI suppress host pro-inflammatory responses. The objective of this study is to delineate the intracellular trafficking and immunosuppression that promotes NTHI survival.

Methods: Normal human bronchial epithelial (NHBE) cells were infected with either heme-iron replete or heme-iron restricted NTHI. The mechanism of intracellular trafficking was visualized through the co-localization of GFP-labeled NTHI with endolysosomal pathway markers, anti-EEA1 and anti-LAMP1. In addition, supernatants of NHBEs and chinchilla middle ear fluids were collected following infection with nutritionally conditioned NTHI to determine changes in inflammatory cytokine production.

Results: Consistent with intracellular community development, co-localization with endolysosomal pathway markers was not observed when NTHI were restricted for heme-iron but was observed when NTHI were replete for heme-iron. In vitro cytokine profiles demonstrated significantly decreased levels of GM-CSF in response to only heme-iron restricted NTHI. Further, heme-iron restricted NTHI suppress pro-inflammatory mediators in vivo.

Conclusion: Our findings illuminate a paradox that host sequestration of nutrients may promote NTHI pathogenesis through differential trafficking of NTHI coupled with changes in pro-inflammatory cytokine production. We predict that inhibition of intracellular community development will augment current approaches to enhance the therapeutic outcome of otitis media.

5:13 - 5:20 PM **WEDNESDAY, JUNE 10**

OM2015240

BIOFILM FORMATION BY NONTYPEABLE HAEMOPHILUS INFLUENZAE (NTHI) GROWING ON HUMAN NASOPHARYNGEAL CELLS

Robert C Osgood[1] *Presenter*

Michael E Pichichero[2]

[1]*Rochester Institute Of Technology, Department Of Biomedical Sciences, Rochester, NY, USA*
[2]*Rochester General Hospital, Research Institute, Rochester, NY, USA*

Objective: Biofilms occur in animal models of acute otitis media (AOM) and in children with recurrent AOM (rAOM) and chronic otitis media with effusion (OME). We therefore studied the ability of Nontypeable Haemophilus influenzae (NTHi) strains from children to form biofilms in vitro under various physiologic conditions that might occur in the nasopharynx. We recently found that not all clinical NTHi strains form biofilms (75% do); (2) the pH of MEF collected from AOM (n=170, age 4-36 months), rAOM (n=54, age range 7-36 months),and OME (n=30, age range 9-60 months) subjects, tested immediately after withdrawal was similar; mean= 8.0 (range 7.0-9.0) [Osgood et al Laryngoscope 2015, in press]

Design: Evaluate NTHi isolates for biofilm formation while growing on human nasopharyngeal epithelial cells (Detroit 562 cells) across a pH range of 6-8 and under aerobic,microaerophilic and anaerobic conditions.

Method: Using a crystal violet biofilm assay we studied 12 NTHi pediatric clinical isolates.

Results: When NTHi grow on the surface of nasopharyngeal cells, our findings include: (1) biofilms form optimally at pH 8.0 and (2) Biofilms do not form under aerobic conditions whereas under microaerophilic and anaerobic conditions biofilm formation was observed.

Conclusion: We conclude that biofilm formation by NTHi when the bacteria are attached and growing on human nasopharyngeal cells occurs best under conditions of pH=8.0 and in a microaerophilic or anaerobic environment but is limited or absent under aerobic conditions. This study was supported in part by NIDCD RO1 08671.

THURSDAY SCIENTIFIC PRESENTATIONS

8:00 - 9:45 AM **THURSDAY, JUNE 11**

CHERRY BLOSSOM BALLROOM

MINISYMPOSIUM 7 (C): DEVELOPMENTAL AND LEARNING SEQUELAE OF OM AND EPIDEMIOLOGY

Moderators:

Mark Haggard (UK)

Jørgen Lous (Denmark)

Speakers:

Mark Haggard (UK)

Jørgen Lous (Denmark)

Robert Ruben (US)

Chuan-Ming Li (US)

Yan Zhang (China)

8:00 - 8:18 AM **THURSDAY, JUNE 11**

OM2015094

COMPREHENSIVE EVIDENCE-BASED MODEL FOR DEVELOPMENTAL IMPACT FROM SPECIFIC DISEASE FACETS IN OTITIS MEDIA

Mark Pergrine Haggard, Ph.D.[1] *Presenter*

Snezana Andric Filipovic[2,3]
Krzysztof Trzpis, MB, BS[4]

[1]*University Of Cambrigge, Psychology, Cambridge, United Kingdom*
[2]*Clinical Center Of Serbia, ENT And Maxilllofacial Surgery, Belgrade, Serbia*
[3]*Mater Dei Hospital, ENT, Valetta, VALETTA, Malta*
[4]*Medical University Of Bialystok, Pediatric ENT, Bialystok, BIALYSTOK, Poland*

Objective: Many studies of OM cognitive/behavioural sequelae have been underpowered, included insufficiently severe OM cases, inadequate prior constraint on model links or hypotheses tested and neglected specific causal paths plus the ultimate outcome Quality of Life (QoL).

Method: The Eurotitis-2 questionnaire standardisation study (N with sufficient data 2262) and its subset, the TARGET RCT (594 with 2 baseline assessment visits), permits strengthened causal inference within structural equation modelling (SEM), by examining entire cascaded and/or parallel networks of up to 11 facets of disease and development. We tested international generality via 5 large sub-samples: UK, Serbia, Poland, and other countries in two bands: high/low ENT access.

Results: Models all had good absolute fit (RMSEA~0.06). We addressed two main contrasts quasi-experimentally: (1) Does the theoretically desired split of URTI into primary infection and secondary obstruction items lead to more causally coherence and similarly good fit, as when aggregated,? (2) Does a single aggregate ('development') of speech/language, balance and behaviour fit the pattern of intercorrelations better than having these variables separated, with distinct regression links (from disease facets and mediators and onwards to QoL)?

Conclusion: Clear answers were obtained: (1) YES; (2) NO, and speech/language was not a specially privileged mediator. Two semi-independent channels to QoL were consistently obtained: (A) infection à obstruction à hearing à speech/languageà developmentà QoL: (B) infection à RAOM à sleep à development à QoL. The slight sub-sample differences in resulting model were consistent with the internationally differing presentation profiles largely resulting from differing referral systems.

8:18 - 8:36 AM **THURSDAY, JUNE 11**

OM2015180

DEVELOPMENTAL AND LEARNING SEQUELAE OF OTITIS MEDIA; REVIEW OF RESULTS FROM DANISH COHORT STUDIES

Jørgen Lous, M.D., DMSc[1] *Presenter*

Maj-Britt Glenn Lauritsen, [2]

[1]*University Of Southern Denmark, Research Unit For General Practice/department Of Public Health, DK-5000 Odense C, Denmark*
[2]*Copenhagen University, Research Unit For General Practice/department Of Public Healtha, DK-1014 Copenhagen K, Denmark*

Introduction: Developmental and learning sequelae of otitis media have been discussed since Holm & Kunze in 1969 published their paper on 32 children, where they found a significant difference in articulation in favour of the otitis-free children. Subsequently many retrospective studies, cohort studies and even some randomized studies have been published. Some studies found significant relations, other studies did not.

Objective: In this review we will concentrate on studies carried out in Denmark, because most of you do not know them.

Methods: All the studies were performed by professions other than ENT or audiologists. Two long-term studies from the Danish Conscription Board included young men aged 18-25 years before entering the military. They had different tests and questionnaires, including hearing screening and a Danish written IQ test (BPP) with four elements: Letter matrices, verbal analogies, number series, and geometric figures.

Results: The first study with 22 162 participants was published in 2007 by a psychologist and a conscription board office. They found a significant relation between mild and severe hearing loss and attending high school and a relation between hearing loss and IQ. The other Conscription Board study on 18 412 participants published in 2013 found that the 5% who had been hospitalized with acute otitis media before the age of 8 years had a significantly higher adjusted prevalence ratio (1.20, 95%ci 1.09 to 1.33) of being in the bottom quartiles in IQ compared to the rest. Results from short-term studies and conclusion will be presented at the symposium.

8:36 - 8:54 AM **THURSDAY, JUNE 11**

OM2015310

A REPORT CARD: ANALYSIS OF PUBLICATIONS CONCERNING OTITIS MEDIA 1875 TO 2015, AND CONSIDERATION OF THEIR EFFECTIVENESS

Robert Joel Ruben, M.D. *Presenter*

Albert Einstein College Of Medicine, Otolarygology Head And Neck Surgery, Bronx, NY, USA

Objective: During the past four decades there has been an international effort to the study of the many facets of otitis media. These have included basic biological mechanism, epidemiology, interventions and ascertainment of sequelae. This report will quantify the types of reports published on otitis media and their origins over time and explore the outcome of these efforts.

Method: A PubMed and a Scopus search were conducted for articles classified as otitis media, acute otitis media, serous otitis media, otitis media with effusion, middle ear effusion, chronic otitis media, with note made of incidence, prevalence, morbidity and mortality within these published studies. These data were analyzed for the type of publication: randomized clinical trial, clinical trial phases I–IV, guideline, conference, meta-analysis, and country of origin.

Results: PubMed listed 25,000 and Scopus 30,600 OM articles from 1875 through 02/02/2015 of which 22,000 (PubMed) to 30,000 (Scopus) are from 1974 - 2014. In this cohort, the percentage of increase in publications from the previous year for OM was in all years less than that for all indexed medical articles for the same years. Each form of OM was analyzed for type of publication. The epidemiological data were analyzed to document the changes in incidence, prevalence and sequelae over the 40 years from 1974 – 2014 and from 1875. There was little change in incidence and prevalence of OM. Some of the sequelae were reduced in the post industrial world but OM remains a critical healthcare burden in most developing nations.

Conclusion: OM articles increased at a lesser rate when compared with all medical publications. There was little or no diminution in incidence or prevalence, with continuing disparities for serious sequelae between developed and developing nations. These data mandate a focus on resource use for prevention to reduce the OM burden worldwide.

8:54 - 9:12 AM **THURSDAY, JUNE 11**

OM2015244

EAR INFECTION PREVALENCE AND RISK FACTORS IN PRE-SCHOOL AGED CHILDREN: THE UNITED STATES EARLY CHILDHOOD LONGITUDINAL STUDY–BIRTH COHORT: 2001 (ECLS–B:2001)

Chuan-Ming Li, Ph.D. *Presenter*

Howard J Hoffman, M.A.

National Institute On Deafness And Other Communication Disorders, Epidemiology And Statistics Program, Bethesda, MD, USA

Objective: To analyze ear infection (EI) prevalence and risk factors using mothers' report of medically-diagnosed EIs in a nationally-representative study.

Methods: ECLS–B is a longitudinal study of 2001 United States live births. Parent interviews and brief exams were conducted at 9 months (N=10,688 infants), 2 years, 4 years, and kindergarten entry.

Results: Among 5,548 singletons, 41.7% had one or more medically-diagnosed EIs by 9 months; 61.7% by 2 years; 70.1% by 4 years; 72.7% by kindergarten entry. Multivariable logistic models for 'ever' EI showed increased risk for center-based program care (CBPC; odds ratio=2.9, 95% confidence interval: 1.3-6.5), child's health rated "good" (3.1, 1.2-8.0) vs. "excellent", Midwest (1.5, 1.1-2.0) and South (1.4, 1.1-1.9) vs. Northeast region; risk decreased for non-Hispanic (NH) Black, Asian and Chinese versus NH white children. Risk of highly frequent EIs (≥3 EIs at each age interval, or ≥10 EI any age interval, or ≥12 EIs across the four age intervals) was increased for very low birth weight (2.6, 1.3-5.3), CBPC (14.9, 6.0-36.9), Midwest (2.5, 1.3-4.7), South (2.5, 1.4-4.7) and West (2.5, 1.3-4.7), but decreased for Hispanic, NH Black, Asian and Chinese. After limiting analysis to NH white children, CBPC (3.1, 1.2-8.4) and South (1.6, 1.2-2.3) showed increased 'ever' EI risk. For highly frequent EIs, CBPC (14.6, 5.7-37.2), Midwest (2.5, 1.1-5.8) and South (2.5, 1.1-5.6) showed increased risk. EIs were not associated with language delay.

Conclusion: The relative strength of risk factors for EIs in childhood, geographic/regional burden, and lack of association with language delay are demonstrated.

9:12 - 9:30 AM **THURSDAY, JUNE 11**

OM2015054

RISK FACTORS FOR CHRONIC AND RECURRENT OTITIS MEDIA—A META-ANALYSIS?

Yan Zhang, M.D.,Ph.D.[1] *Presenter*

Qingyin Zheng [1,2]
Min Xu[1]

[1]*Second Hospital, Xi'an Jiaotong University School Of Medicine, Otolaryngology HNS, Xi'an, SHAANXI, China*
[2]*Case Western Reserve University School Of Medicine, Otolaryngology HNS, Cleveland, OH, USA*

Objective: Risk factors associated with chronic otitis media (COM) and recurrent otitis media (ROM) have been investigated in previous studies. Our study was to integrate the findings and determine the possible risk factors for COM/ROM based on our meta-analysis.

Method: A comprehensive search of electronic bibliographic databases from 1964 to Dec 2012, and a manual search of references of articles, was performed.

Results: A total of 2971 articles were searched, and 198 full-text articles were assessed for eligibility; 24 studies were eligible for this meta-analysis. Regarding risk factors for COM/ROM, there were two to nine different studies from which the odds ratios (ORs) could be pooled. The presence of allergy or atopy increased the risk of COM/ROM (OR, 1.36; 95% CI, 1.13-1.64; P = 0.001). An upper respiratory tract infection (URTI) significantly increased the risk of COM/ROM (OR, 6.59; 95% CI, 3.13-13.89; P < 0.00001). Snoring appeared to be a significant risk factor for COM/ROM (OR, 1.96; 95% CI, 1.78-2.16; P < 0.00001). A patient history of acute otitis media (AOM)/ROM increased the risk of COM/ROM (OR, 11.13; 95% CI, 1.06-116.44; P =0.04). Passive smoke significantly increased the risk of COM/ROM (OR, 1.39; 95% CI, 1.02-1.89 P =0.04). Low social status appeared to be a risk factor for COM/ROM (OR, 3.82; 95% CI, 1.11-13.15; P =0.03).

Conclusion: Our meta-analysis identified that allergy/atopy, URTI, snoring, previous history of AOM/ROM, Second-hand smoke and low social status are important risk factors for COM/ROM. Other unidentified risk factors need to be identified in further studies with critical criteria.

8:00 - 9:45 AM **THURSDAY, JUNE 11**

BALTIMORE 3-5

MINISYMPOSIUM 8 (B): DRUG DELIVERY TO MIDDLE EAR AND INNOVATIVE THERAPIES

Moderators:

Steve Brown (UK)

Anthony Campagnari (US)

Keynote Speaker:

Daniel Kohane (US)

Speakers:

Steve Brown (UK)

Anthony Campagnari (US)

Sung Moon (US)

Qing Zheng (US)

8:00 - 8:35 AM **THURSDAY, JUNE 11**

OM2015038

TRANS-TYMPANIC DELIVERY OF ANTIBIOTICS

Daniel S Kohane, M.D.,Ph.D. *Presenter*

Children's Hospital Boston, Anesthesia, Boston, MA, USA

Otitis media (OM) is a major burden in terms of child health care in the United States and elsewhere. AOM is the most common reason for antimicrobial prescribing in US children and due to the high prevalence of disease and frequent recurrences is believed to be partially responsible for the ongoing increase in antibiotic resistance among pathogenic bacteria. On a practical level, the treatment of otitis media can be quite challenging for parents who may have to convince toddlers to take oral medications for many days. To address these issues, we developed a formulation that would be applied directly to the tympanic membrane by the pediatrician at the time of diagnosis and was intended to provide extended release of antibiotics into the middle ear. The formulation was designed so that it would flow on easily then readily gel on the surface of the TM, providing for sustained release. Drug flux of ciprofloxacin across the chinchilla tympanic membrane was enhanced ex vivo by co-incorporation of chemical permeation enhancers.

8:35 - 8:50 AM **THURSDAY, JUNE 11**

OM2015288

NOVEL MOUSE MODELS OF CHRONIC OTITIS MEDIA (COME) IDENTIFY VEGF PATHWAYS AS A CRITICAL TARGET: TOWARDS NEW THERAPIES FOR OM

Steve D.M. Brown, Ph.D.[1] *Presenter*

Mike Crompton[1]
Hayley Tyrer[1]
Hilda Tateossian[1]
Debbie Williams[1]
Mahmood F Bhutta[3]
Paul K Potter[1]
Michael Cheeseman[1,2]

[1]*Mammalian Genetics Unit, MRC Harwell, Harwell, OXON, United Kingdom*
[2]*Roslin Institute, Edinburgh, SCOTLAND, United Kingdom*
[3]*UCL Ear Institute, London, LONDON, United Kingdom*

Mouse models of COME, such as Junbo, Jeff and Tgif mutants, have uncovered the role of TGF-b signalling in OM. Hypoxia is a feature of inflamed microenvironments and there is cross-talk between TGF-b and HIF-1a signalling pathways. We investigated the occurrence of hypoxia and HIF mediated responses in Junbo and Jeff mutants. Mutant mice showed cellular hypoxia in middle ear mucosa and middle ear lumen WBC. Inflammatory gene networks were upregulated in the middle ear WBC including cytokines IL-1b and TNF-a that modulate HIF. HIF-1a gene expression was elevated in ear fluid WBC along with the target genes VEGF, its receptor KDR and VEGF protein. Administration of VEGFR inhibitors PTK787, SU-11248, BAY 43-9006 significantly reduced hearing loss and modulated inflammatory changes in middle ear mucosa. The effectiveness of VEGFR signalling inhibitors in suppressing OM implicates HIF mediated VEGF as playing a pivotal role in OM pathogenesis via its actions in angiogenesis, vascular leakiness and inflammatory cell chemotaxis. Additional efficacy studies of a broader range of VEGFR inhibitors will be merited. New mouse models will elaborate further the underlying pathways for COME and identify new targets. A novel mouse mutant, edison, displays COME with features similar to Junbo and Jeff. edison carries a mutation in the gene Nischarin (NISCH) that interacts with integrin a5, thought to modulate VEGF-induced angiogenesis. NISCH also interacts with PAK1, LIMK1 and RAC1, and analysis of the edison mutant implicates RAC1 signalling in the development of COME and further underscores the importance of TGF-b signalling.

8:50 - 9:05 AM **THURSDAY, JUNE 11**

OM2015292

PHOTODYNAMIC THERAPY AND OTITIS MEDIA

Anthony Campagnari, Ph.D.[1] *Presenter*

Nicole Luke-Marshall, Ph.D. [1]
Lisa Hansen, M.S. [1]
Brian Wrazen, B.S.[2]
David Bellnier, Ph.D.[2]
Wolfgang Baumler, Ph.D.[3]
Gal Shafirstein, D.Sc.[2]

[1]*State University Of New York At Buffalo, Microbiology/Immunology, Buffalo, NY, USA*
[2]*Roswell Park Cancer Institute, Cell Stress Biology/Photodynamic Therapy Center, Buffalo, NY, USA*
[3]*University Medical Center Regensburg, Dermatology, Regensburg, , Germany*

Introduction: Treatment of bacterial otitis media (OM) has become increasingly more difficult due to antibiotic resistance, polymicrobial infections and the presence of biofilms. Standard antibiotic therapy often fails leading to recurrent OM and OM-prone children receive multiple courses of antibiotics, further perpetuating antimicrobial resistance and potentially disrupting the microbiome. There is clearly a need for new antimicrobial treatments that do not rely on the development of antibiotics. Antimicrobial photodynamic therapy (aPDT) represents one possible novel approach for the treatment of OM as it combines non-toxic photosensitizers (PS) and low intensity visible light to produce cytotoxic singlet oxygen species, which exhibit significant bactericidal activity.

Objective: These studies were performed to determine if aPDT using multiple PS induces bactericidal activity versus planktonic and biofilm-associated isolates of Streptococcus pneumoniae, nontypable Haemophilus influenzae and Moraxella catarrhalis.

Methodology: The bactericidal activity of aPDT using different PS was assessed against clinical isolates of the OM-associated pathogens grown planktonically as well as in biofilms. The bactericidal activity was quantified by enumeration of colony forming units post-treatment.

Results: Significant bactericidal activity was achieved versus all three species evaluated under all experimental conditions. aPDT generated an average of 5-6 logs decrease in viable planktonic bacteria and an approximate decrease of 4-5 logs in biofilm-associated organisms compared to the controls ($P < 0.01$).

Conclusion: aPDT elicits significant bactericidal activity against planktonic and biofilm-associated isolates of S. pneumoniae, nontypable H. influenzae and M. catarrhalis suggesting this technology warrants further analysis as a potential antimicrobial treatment for acute or recurrent OM.

9:05 - 9:20 AM **THURSDAY, JUNE 11**

OM2015222

THERAPEUTIC POTENTIAL OF ADENOVIRUS-MEDIATED DELIVERY OF B-DEFENSIN 2 FOR EXPERIMENTAL OTITIS MEDIA

Sung K Moon, M.D.,Ph.D. *Presenter*

David J Lim, M.D.

University Of California - Los Angeles, Los Angeles, CA, USA

Otitis media (OM), one of the most prevalent diseases in young children, is clinically important owing to its high incidence in children and its potential impact on language development and motor coordination. OM is the most common reason for the prescription of antibiotics (accounting for 25% of prescriptions) due to its extremely high incidence. A recent increase in antibiotic resistance among OM pathogens is emerging as a major public health concern globally, which led us to consider non-antibiotic approaches for the management of OM. In this study, we evaluated gene transfer of an antimicrobial peptide, human β-defensin 2 (DEFB4), using an adenoviral vector (Ad5 with deletions of E1/E3/E4) as a potential therapeutic approach. We demonstrated that the transduction of human β-defensin 2 induces the production of human β-defensin 2 and suppresses non-typeable Haemophilus influenzae (NTHi) adhesion to human middle ear epithelial cells. Moreover, intratympanic inoculation of Ad-DEFB4 was found to attenuate NTHi-induced middle ear effusions without eliciting a significant immune response. Most importantly, intratympanic inoculation of Ad-DEFB4 appeared to significantly augment clearance of NTHi from middle ear cavity. Collectively, our results suggest that intratympanic gene delivery of antimicrobial molecules may serve as an alternative/adjuvant approach for the management of OM. [Supported partly by DC005025 and DC011862]

9:20 - 9:35 AM **THURSDAY, JUNE 11**

OM2015280

A NEW THERAPY ALLEVIATES STREPTOCOCCAL PEPTIDOGLYCAN POLYSACCHARIDE (PGPS)-INDUCED OTITIS MEDIA IN TLR2-DEFICIENT HOSTS

Qing Yin Zheng, M.D [1,2] *Presenter*

Xiao-lin Zhang[1,2]
Yan-Fei Wang[1]
Ti-Hua Zheng[1]
Luke Apisa[2]
Hong-Chun Zhao[1]
Qing-zhu Wang[1]

[1]*Binzhou Medical University, Yantai, SHANDONG, China*
[2]*Case Western Reserve University School Of Medicine, Cleveland, OH, USA*

A recent study showed the Toll-like receptor 2 (TLR2) expression level in middle-ear mucosa was significantly lower in patients with chronic suppurative otitis media (CSOM) (Si et al 2014). Residual streptococcal peptidoglycan-polysaccharide (PGPS) persistent in middle ears (MEs) could cause chronic otitis media (COM) (Fulghum et al 1998). Here, to mimic the reduced TLR2 condition, we established an otitis media (OM) model in Tlr2-/- mice by PGPS challenge. Intriguingly, despite right-ear-only PGPS inoculation, induced otitis media was observed in middle ears bilaterally. In comparison to wide-type (WT) mice, the Tlr2-/- mice were more susceptible to PGPS-induced OM with the following novel characteristics: 1) at day 3 after middle ear inoculation with PGPS, a much larger number of neutrophils appeared and were sustained in the middle ear cavity through day 15; 2) higher expression levels of oxidative-stress genes were noted with concurrent goblet cell absence; 3) lower expression levels of certain cytokines and mucin genes were observed. Previous studies suggested that sodium aescinate (SA) could improve local inflammation and block oxidative-stress and reduce apoptosis via the glucocorticoid pathway (Xin et al). Thus we hypothesized that treatment with SA could mitigate OM, decrease the expression of oxidative-stress genes, and improve ear function in Tlr2-/- mice. Our data demonstrated the above unique pathophysiological features and most significantly, indicated for the first time that SA could improve pathological outcomes of OM.

9:45 - 10:15 AM **THURSDAY, JUNE 11**

CHERRY BLOSSOM FOYER

COFFEE BREAK IN CHERRY BLOSSOM FOYER

10:15 AM - 12:00 PM **THURSDAY, JUNE 11**

CHERRY BLOSSOM BALLROOM

PLENARY 4 (B): OMICS

Moderators:

Garth Ehrlich (US)

Melinda Pettigrew (US)

Speakers:

Garth Ehrlich (US)

Melinda Pettigrew (US)

Diego Preciado (US)

Michele Sale (US)

Keynote Speaker:

Axel Visel (US)

10:15 - 10:30 AM **THURSDAY, JUNE 11**

OM2015104

A MULTI-NEXT-GENERATION DNA SEQUENCING PLATFORM APPROACH TO STUDY BACTERIAL POPULATION EVOLUTION IN SITU

Garth David Ehrlich, Ph.D. , F.A.A.A.S[1] *Presenter*

Joshua Earl, M.S. [1]
Joshua Chang Mell[1]
Benjamin Janto[1]
Sergey Balashov[1]
Jaroslaw E Krol[1]
Bhaswati Sen[1]
Jocelyn Hammond, B.S.[1]
Janet R Gilsdorf, FPIDS[2]
Fen Z Hu, M.S. [1]

[1]*Drexel University College Of Medicine, Microbiology And Immunology, And Otolaryngology-Head And Neck Surgery, Philadelphia, Pa, USA*
[2]*University Of Michigan, Infectious Diseases/Pediatrics/Medicine, Ann Arbor, MI, USA*

Objective: Test the prediction of the distributed genome hypothesis that moderately virulent nontypeable Haemophilus influenzae (NTHi) strains and populations (compared to nonvirulent carriage strains) will evolve to be more virulent as they spend time in an environmental niche where they are under host pressures.

Methods: Employ a combination of ultra-long read (Pacbio) and ultra-deep (Illumina) sequencing technologies that respectively provide closed genomes, and gene frequencies for bacterial populations. Apply these technologies to examine how strains evolve in situ via horizontal gene transfer and determine changes in virulence gene frequencies over the two year study period.

Results: Two pediatric populations have been identified and followed longitudinally: OM-prone; and healthy. From within each clinical grouping we have identified cohorts of children who are polyclonally colonized with NTHi and obtained both individual nasal isolates for whole genome sequending (WGS), and swabs for ultra-deep sequencing to determine relative gene copy numbers at the population level. Pacbio sequencing has demonstrated that we can routinely close a genome to a single circular contig using data from at single SMRT cell by using only the reads of greater than 6 Kb that have been partially error-corrected with the shorter reads. The entire closed contig is then error-corrected again with all of the shorter reads to obtain a genome with Q-scores of >40.

Conclusion: Through the use of clinically defined populations and a combination of cutting edge WGS technologies it will be possible to visualize and compare the evolution of bacterial populations over time.

10:30 - 10:45 AM **THURSDAY, JUNE 11**

OM2015114

TRANSCRIPTIONAL PROFILING OF OTITIS MEDIA PATHOGENS: THE TRANSITION FROM COLONIZATION TO DISEASE

Melinda M Pettigrew, Ph.D.[1] *Presenter*

Anders P Hakansson[2]

[1]*Yale School Of Public Health, Epidemiology Of Microbial Diseases, New Haven, CT, USA*
[2]*Lund University, Department Of Laboratory Medicine, Malmo, SKANE COUNTY, Sweden*

Otitis media pathogens asymptomatically colonize the nasopharynx. The transition from colonization in biofilms to invasion of the middle ear may be induced by respiratory virus infection, competitive interactions amongst bacteria, or other environmental factors. Understanding of mechanisms underlying the transition from colonization to otitis media is limited. Whole-transcriptome shotgun sequencing (RNA-seq) of bacterial otitis media pathogens allows for comparisons of transcriptional profiles under experimental conditions. We use Streptococcus pneumoniae and influenza as a model bacteria-virus system to explore transcriptional changes as pneumococci are actively dispersed from biofilms and transition from avirulent colonizers to planktonic pathogens. S. pneumoniae transcriptional profiles change in response to influenza virus and environmental stimuli (e.g., increased temperature and extracellular ATP). When comparing avirulent biofilm pneumococci to actively dispersed and virulent planktonic pneumococci, we observed up-regulation of genes associated with carbohydrate metabolism (e.g., transporters for mannose/fructose and glucose), competition (e.g., genes involved in bacteriocin production), and virulence factors (e.g., neuraminidases). Genes involved in the induction of competence and amino acid metabolism were down-regulated in virulent pneumococci compared to pneumococci in biofilms. The transcriptional profiles of otitis media pathogens during co-colonization will also be discussed. These data help explain the link between respiratory virus infection and otitis media and suggest that disease is caused by pneumococci primed to move to tissue sites with altered nutrient availability and to protect themselves from competitors and host immune responses. Moreover, our data reveal how transcriptomics can be used to gain greater insight into the pathogenesis of otitis media.

10:45 - 11:00 AM **THURSDAY, JUNE 11**

OM2015287

A PROTEOMIC CHARACTERIZATION OF CHRONIC OTITIS MEDIA: IS MUC5B FRIEND OR FOE?

Diego Preciado, M.D.,Ph.D. *Presenter*

Children's National Medical Center, Otolaryngology, Washington, DC, USA

Objective: This study aims to characterize the proteome of middle ear effusions (MEEs), both mucoid and serous. Furthermore, in order to investigate the evolution of OM from acute bacterial infection to a chronic mucoid response, we aimed to quantify the time course conditional secretome of bacterially challenged middle ear epithelium in vitro.

Methods: 40 MEEs were collected from children undergoing tympanostomy tube placement at Children's National Medical Center for proteomics analysis using a liquid chromatography tandem mass spectrometry (LC-MS/MS), immunofluorescence (IF), Western Blots, cytokine multiplex assays, and Next Generation DNA sequencing. Human middle ear epithelial cells (HMEEC) were used in vitro to measure the effects of bacterial challenge on mucogenic, pro-inflammatory and remodeling responses using stable isotope labeling of amino-acids in culture.

Results: LC-MS/MS identified important innate immune response mediators including MUC5B, as well as abundant NET proteins in mucoid middle ear effusions, confirmed by IF and western blots. Copious extracellular human DNA was also identified in mucoid effusions. The secretome of HMEEC after bacterial challenge revealed an up-regulation of extracellular remodeling proteins, likely implicating exosomes, and inflammatory response cytokines, mostly IL8.

Conclusion: Our work characterizes essential innate immune components in middle ear secretions both in vivo and in vitro, including the mucin MUC5B and NETs. Further work will explore the hypothesis that bacteria strongly induce the formation of NETS, pro-inflammation, and eventual epithelial secretion of MUC5B which in turn plays an important role in helping clear middle ear bacteria, protecting middle ear epithelium, and modulating initial inflammatory responses.

11:00 - 11:15 AM **THURSDAY, JUNE 11**

OM2015078

DEFINING GENETIC RISK OF CHRONIC OTITIS MEDIA WITH EFFUSION AND/OR RECURRENT OTITIS MEDIA: A GENOME-WIDE ASSOCIATION FOLLOW-UP STUDY

Michele M Sale, Ph.D.[1] *Presenter*

E Kaitlynn Allen, Ph.D. [1]
A. Manichaikul[1]
Stephen R Williams, Ph.D. [1]
Keith L Keene, Ph.D.[2]
Josyf C Mychaleckyj, Ph.D.[1]
Aaron Quinlan, Ph.D.[1]
Wei-Min Chen, Ph.D.[1]
Mazhar Adli, Ph.D.[1]
Stephen S Rich, Ph.D.[1]
Kathleen A Daly, Ph.D.[3]

[1]*University Of Virginia, Charlottesville, VA, USA*
[2]*East Carolina University, Greenville, NC, USA*
[3]*University Of Minnesota, Minneapolis, MN, USA*

Objective: We previously performed a genome-wide association study (GWAS) of chronic otitis media with effusion and recurrent OM (COME/ROM). The current study reports on fine-mapping of two high priority loci.

Method: In 100 individuals from 45 families, sequencing was performed on a region of chromosome 2 containing the replicated single nucleotide polymorphism (SNP) rs10497394, and the chromosome 15 region containing the most significantly associated SNP, rs1110060. Common and infrequent variants (minor allele frequency >0.01) were genotyped in 596 participants using the Fluidigm platform. Chromatin immunoprecipitation sequencing (ChIP-seq) and Quantitative reverse transcription PCR (RT-qPCR) assays were conducted using the human middle ear epithelial cell line HMEEC-1 and adenoid tissues.

Results: A total of 303 SNPs were detected in the two regions, and 240 were genotyped in all families. Two SNPs on chromosome 2 and four SNPs on chromosome 15 were significantly associated with COME/ROM ($P<2.6x10-4$). ChIP-seq supported enhancer activity in HMEEC-1 cells in the intergenic chromosome 2 region. SNP rs1110060 on chromosome 15 remained the most associated ($P=4.3x10-6$), and is an eQTL for IQGAP1 in lymphocytes. Using RT qPCR, rs1110060 genotype significantly influenced IQGAP1 expression in adenoids ($P=0.026$). Four-hour lipopolysaccharide treatment of HMEEC-1 cells up-regulated expression of IQGAP1 ($P=0.028$).

Conclusion: We fine-mapped two GWAS loci and identified key variants. Enhancer activity in the 537.5kb intergenic region of chromosome 2 containing associated SNPs may impact regulation of a distant gene(s). The impact of chromosome 15 SNP rs1110060 on IQGAP1 adenoid expression is consistent with a function of this variant in COME/ROM risk.

11:30 AM - 12:00 PM **THURSDAY, JUNE 11**

OM2015105

EXPLORING THE DARK MATTER OF THE HUMAN GENOME

Axel Visel *Presenter*

Lawrence Berkeley National Laboratory, Genomics Division, Berkeley, CA, USA

The complete 3.2 billion base-pair sequence of the human genome has been known for more than a decade, yet our understanding of how linear DNA provides the blueprint for building a complex organism remains far from complete. In biomedical studies, most attention has focused on protein-coding genes within the genome – however, genes collectively account for less than 2% of the human genome. The remaining 98% remains largely unexplored territory, with limited information about its function beyond the raw DNA sequence. Initially widely considered to be "junk DNA", there is now strong evidence that important functions are embedded in this vast amount of non-coding DNA. In particular, it harbors hundreds of thousands of transcriptional "enhancers", a class of sequences that activate gene expression and play important roles in the development and function of the human body. Using illustrative examples from our own work and ongoing large-scale consortium efforts such as the ENCODE project, I will describe current strategies for studying the non-coding genome in general, and enhancers in particular, using sequencing-based methods in conjunction with mouse models. I will highlight how distant-acting transcriptional enhancers regulate morphogenetic processes, such as craniofacial and limb development, and describe how disruptions of enhancers can cause disease phenotypes in human patients. Finally, I will discuss how the functional annotation of enhancer sequences in the human genome achieved through genome-scale studies is expected to facilitate the interpretation of human genetic data to elucidate the genetic causes of common diseases.

12:00 PM **THURSDAY, JUNE 11**

CHERRY BLOSSOM BALLROOM

CLOSING REMARKS & SYMPOSIUM ADJOURNMENT

SCIENTIFIC POSTERS

POSTER PRESENTATIONS

#	CATEGORY	TITLE	AUTHOR	ABSTRACT #
1	Diagnosis	MODIFIED FURLOW PALATOPLASTY TO ENHANCE THE EUSTACHIAN TUBE FUNCTION	Cuneyt Alper	OM2015175
2	Diagnosis	CRITICAL ANALYSIS OF THE TUBOMANOMETRY IN THEORY AND APPLICATION	Cuneyt Alper	OM2015181
3	Diagnosis	DEPTH-RESOLVED OPTICAL IMAGING OF THE MIDDLE EAR IN OTITIS MEDIA USING OPTICAL COHERENCE TOMOGRAPHY	Stephen Boppart	OM2015136
4	Diagnosis	ISOLATION OF ALLOIOCOCCUS OTITIDIS FROM ROUTINE OUTER EAR SWABS	Sharron Hall	OM2015138
5	Diagnosis	NEW DANISH GUIDELINES ON THE DIAGNOSIS OF ACUTE OTITIS MEDIA AND THE SURGICAL MANAGEMENT OF RECURRENT ACUTE OTITIS MEDIA AND CHRONIC OTITIS MEDIA WITH EFFUSION	Christian Heidemann	OM2015241
6	Diagnosis	FIVE CASES OF OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV) WITH HYPERTROPHIC PACHYMENINGITIS	Haruyuki Ichikawa	OM2015111
7	Diagnosis	EUSTACHIAN TUBE FUNCTION TEST RESULTS IN ADULTS WITH VENTILATION TUBES INSERTED FOR OTITIS MEDIA WITH EFFUSION	Jeehong Kim	OM2015098
8	Diagnosis	PRESSURE DIFFERENCE RECORDED BY TUBOMANOMETRY EAR PIECE WITH EUSTACHIAN TUBE OPENING DOES NOT PREDICT THE MIDDLE EAR PRESSURE CHANGE.	Jeehong Kim	OM2015207
9	Diagnosis	CLINICAL EFFICACY OF INSERTION OF MIDDLE EAR VENTILATION TUBE AGAINST INTRACTABLE ACUTE OTITIS MEDIA	Hiroshi KONO	OM2015228
10	Diagnosis	CAN TRAINED NURSES EXCLUDE MIDDLE EAR EFFUSION WITH TYMPANOMETRY IN YOUNG ASYMPTOMATIC OUTPATIENTS?	Miia Laine	OM2015076
11	Diagnosis	ATYPICAL DURAL ENHANCEMENT AND THICKENING IN ACUTE MASTOIDITIS	Tal Marom	OM2015003

#	CATEGORY	TITLE	AUTHOR	ABSTRACT #
12	Diagnosis	ACUTE MASTOIDITIS IN CHILDREN: NECESSITY AND TIMING OF IMAGING	Tal Marom	OM2015029
13	Diagnosis	THE BRAIN'S RESPONSE TO EAC PRESSURE VARIATIONS: AN FMRI STUDY	Peter Mortensen	OM2015219
14	Diagnosis	CAN EUSTACHIAN TUBE FUNCTION TESTS PREDICT BAROTRAUMA RISK IN DIVERS?	Sameera Nadimpalli	OM2015135
15	Diagnosis	EUSTACHIAN TUBE MORPHOMETRY: COMPARISON BETWEEN A 3D DIGITIZER AND A CT SCAN	Sara Rogerson	OM2015187
16	Diagnosis	NASOPHARYNGEAL SWAB ENHANCES PCR-BASED DETECTION OF OTITIS MEDIA PATHOGENS IN THE ADENOID	Tina Samuels	OM2015115
17	Diagnosis	CHANGES IN THE EUSTACHIAN TUBE FUNCTION WITH GROWTH AND DEVELOPMENT IN CHILDREN WITH REPAIRED CLEFT PALATE	John Swarts	OM2015200
18	Diagnosis	INTRA-OPERATIVE EUSTACHIAN TUBE FUNCTION TESTING DURING FURLOW PALATOPLASTY SHOWS VARIABLE RESULTS	John Swarts	OM2015174
19	Diagnosis	A FUNCTIONAL EXPLANATION OF THE RELATIONSHIP BETWEEN MASTOID SIZE AND OTITIS MEDIA WITH EFFUSION RISK	John Swarts	OM2015193
20	Diagnosis	ET MORPHOLOGICAL MEASUREMENTS FROM MRI IMAGES OF CHILDREN	John Swarts	OM2015234
21	Diagnosis	CT SCAN RESOLUTION IS INADEQUATE TO VISUALIZE THE EUSTACHIAN TUBE LUMEN	Miriam Teixeira	OM2015209
22	Diagnosis	MULTI-WAVELENGTH DUAL MODALITY OTOSCOPE FOR OTITIS MEDIA DIAGNOSIS	Tulio Valdez	OM2015325
23	Diagnosis	DETERMINANTS OF CHRONIC OTITIS MEDIA WITH EFFUSION IN PRESCHOOL CHILDREN	Rebecca Walker	OM2015327
24	Epidemiology	PARENT-REPORTED SYMPTOMS OF ACUTE OTITIS MEDIA DURING THE FIRST YEAR OF LIFE: WHAT IS BENEATH THE SURFACE?	Alexandre Fortanier	OM2015060
25	Epidemiology	RISK FACTORS ASSOCIATED WITH A INTRACTABLE ACUTE OTITIS MEDIA	Yukari INOUE	OM2015237
26	Epidemiology	TRENDS IN AMBULATORY CARE VISITS FOR OTITIS MEDIA: 1990-2010	Susan Schappert	OM2015106

#	CATEGORY	TITLE	AUTHOR	ABSTRACT #
27	Epidemiology	OME PREVALENCE FROM 6 MONTHS THROUGH 5 YEARS IN CLEFT PALATE CHILDREN	James Seroky	OM2015132
28	Epidemiology	A SYSTEMATIC REVIEW OF RISK FACTORS ASSOCIATED WITH CHRONIC SUPPURATIVE OTITIS MEDIA	Anna Stephen	OM2015333
29	Immunology	POOR MEMORY B-CELL GENERATION CONTRIBUTES TO REDUCED ANTIGEN-SPECIFIC IGG RESPONSES IN OTITIS-PRONE CHILDREN	Saleem Basha	OM2015253
30	Immunology	OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV): A RETROSPECTIVE MULTI-CENTER STUDY IN JAPAN?3) CLINICAL DIFFERENCES ACCORDING TO INITIAL AND SEQUENTIAL INVOLVEMENTS	Yuka Morita	OM2015033
31	Immunology	FUNCTION OF FOLLICULAR T HELPER CELLS (TFH) IN THE TONSILS AND ADENOIDS OF OTITIS-PRONE (OP) AND NON-OP	Matthew Morris	OM2015260
32	Immunology	IMMUNOPROTEASOMES MAY PLAY A SIGNIFICANT ROLE IN CHOLESTEATOMA RELATED TISSUE DAMAGE	Ewa Olszewska	OM2015100
33	Immunology	C-REACTIVE PROTEIN AND LEUKOCYTOSIS AS CRITERIA FOR SEVERITY OF PNEUMOCOCCAL VS. NON-PNEUMOCOCCAL ACUTE OTITIS MEDIA IN CHILDREN	Sharon Ovant Tamir	OM2015006
34	Immunology	SEROUS AND MUCOID MIDDLE EAR EFFUSION CHARACTERIZATION FOR MUC5B, MUC5AC AND PRO-INFLAMMATORY CYTOKINES	Marian Poley	OM2015263
35	Immunology	NTHI LYSATE PROTEIN CHARACTERIZATION FOR THE USE IN IN VIVO AND IN VITRO EXPERIMENTS	Diego Preciado	OM2015269
36	Immunology	COMPARISON OF THE PHENOTYPE AND FUNCTION OF HUMAN PERIPHERAL BLOOD MONOCYTES AND DENDRITIC CELLS IN OTITIS-PRONE AND NON-OTITIS PRONE INFANTS	Naveen Surendran	OM2015242

#	CATEGORY	TITLE	AUTHOR	ABSTRACT #
37	Immunology	COMPARISON OF INNATE IMMUNITY RELATED TRANSCRIPTIONAL PATTERNS AND CYTOKINE PROFILE OF PERIPHERAL BLOOD MONONUCLEAR CELLS IN OTITIS-PRONE AND NON-OTITIS PRONE INFANTS	Naveen Surendran	OM2015252
38	Immunology	MONOPHOSPHORYL LIPID A ENHANCES NONTYPEABLE HAEMOPHILUS INFLUENZAE-SPECIFIC MUCOSAL IMMUNE RESPONSES IN THE NASAL MUCOSA	Masashi Suzuki	OM2015036
39	Immunology	NASAL NITRIC OXIDE IN CHILDREN WITH CHRONIC RHINOSINUSITIS AND RECURRENT ACUTE OTITIS MEDIA	Sara Torretta	OM2015278
40	Microbiology	INCREASED INCIDENCE OF RESPIRATORY ILLNESSES IN OTITIS PRONE CHILDREN	Janet Casey	OM2015270
41	Microbiology	BACTERIAL FLORA OF TONSILLS IN OTITIS MEDIA EVOLUTION	Svetlana Diacova	OM2015322
42	Microbiology	PERSISTENCE OF NONTYPEABLE HAEMOPHILUS INFLUENZAE IS DEPENDENT UPON SELECTIVE IMPORT OF NUTRIENTS AND HOST ANTIMICROBIAL PEPTIDES	Derek Heimlich	OM2015311
43	Microbiology	POPULATION ANALYSIS OF NASOPHARYNGEAL MICROBIOTA AMONG CHILDREN WITH ACUTE OTITIS MEDIA.	Masanobu Hiraoka	OM2015206
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POSTER SESSION AND WELCOME RECEPTION

Join your colleagues and friends on Monday, June 8 from 5:30 – 8:00 pm for the opportunity to network and view over 80 posters in the following categories:

- Diagnosis
- Epidemiology
- Immunology
- Microbiology
- Pathogenesis
- Treatment
- Vaccine

The posters will be located in Prince George's Exhibit Hall A.

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OM2015175

MODIFIED FURLOW PALATOPLASTY TO ENHANCE THE EUSTACHIAN TUBE FUNCTION

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Introduction: Furlow palatoplasty (FP) is a surgical technique for palatal closure that reorients the Levator Veli Palatini muscles (mLVPs) to establish better VP competence and improved speech. However, in order to push the palatal flaps back for better closure of velum, this technique disrupts the fixed insertions of the Tensor Veli Palatini muscles (mTVPs). Eustachian tube (ET) opening is primarily related to TVPm constriction, therefore this specific release is expected to decrease the effectiveness of the muscle constriction and suboptimal improvement in ET function.

Objective: To test the effectiveness of modification of FP to improve the ET function, reduce risk of persistent effusion and need for tubes.

Methods: A randomized clinical trial is being conducted to determine if FP with tendon tenopexy improves ETF and resolves OME post-palatoplasty. During the FP surgery, on each side, TVP aponeurosis and its attachments to the bony palate, hamulus and TVP tendon turning around the hamulus was identified. As per randomization, blinded to the subject families and clinicians that follow the otologic status, routine FP was completed with or without the placement of a slow absorbing stitch to fix the tendon to the hamulus. To date 39 subjects were enrolled and the surgeries were completed. Follow-up is continued periodically to assess the ear status and test the ET function.

Conclusions: Close follow up of the ear status and repeated ET function testing will allow insight in role of palatoplasty in ET function, and may provide a method to improve the otologic outcomes. Supported in part by NIH Grant DC011524

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OM2015181

CRITICAL ANALYSIS OF THE TUBOMANOMETRY IN THEORY AND APPLICATION

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Introduction: A number of recent studies focused on diagnosing Eustachian tube (ET) dysfunction used Tubomanometry as the sole assessment method. However, the proposed theory underlying Tubomanometry and results interpretation is difficult to reconcile with known ET physiology.

Objective: Describe the theory, test methods and results interpretation for Tubomanometry and identify any deficiencies.

Methods: Describe Tubomanometry within the context of extractable features of ET physiology.

Results: Tubomanometry creates a known positive nasopharyngeal (NP) pressure while continuously monitoring middle-ear (ME) pressure directly or indirectly. The test-subject swallows during the test and results are parameterized as the "R-value" and calculated based on the relationship between the onsets and termination of ME and NP pressure changes. Identified weaknesses in this test method include: 1) Inability to standardize the timing of NP pressure increase with respect to timing and duration of closure of velum; 2) Inability to selectively test or differentiate passive and active ET opening, 3) Disproportionately large pressure scale relative to monitored ME pressure for the intact ear drum, limiting the ability to identify the specific points; 4) Subjective assignment of the points on the pressure curves that give the R-value, and 5) Lack of a threshold for true ME pressure change, an essential input for the R-value.

Conclusion: While Tubomanometry has the potential to quantify passive and active ET functions, there is insufficient evidence that existing protocols provide unbiased, consistent and reproducible output. A focused program of study is needed before Tubomanometry can be accepted as a valid ET function test.

3

OM2015136

DEPTH-RESOLVED OPTICAL IMAGING OF THE MIDDLE EAR IN OTITIS MEDIA USING OPTICAL COHERENCE TOMOGRAPHY

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Objective: Challenges associated with accurately diagnosing otitis media (OM) are often based on subjective interpretation during physical exam and the experience of the healthcare provider. New methods to visualize pathological processes within the middle ear may offer more information to better understand disease etiology and enable more informed decision-making by otolaryngologists, primary care physicians, and other healthcare providers.

Method: Optical coherence tomography (OCT) is a label-free bioimaging technology that is analogous to ultrasound imaging except reflections of light, rather than sound, are detected and assembled into depth-resolved images of tissue microstructure. Using a handheld scanner similar to an otoscope, cross-sectional OCT images of the tympanic membrane (TM), and if present, optically scattering biofilms and effusions in the middle ear, can be acquired noninvasively in real-time with micron-scale resolution. Dynamic TM displacements during pneumatic insufflation can also be tracked and quantified with micron-scale precision.

Results: Following a series of imaging studies of in-vitro and in-vivo biofilms, ongoing clinical studies involving over 75 pediatric and adult subjects with OM have demonstrated the potential of OCT for quantifying TM thickness, the optical properties and thickness of biofilm adherent to the TM, and the optical and biomechanical properties of middle-ear effusions. Real-time algorithms have been developed to provide new quantitative metrics that may correlate with disease severity.

Conclusion: The integration of this depth-resolved optical image-based data for medical decision making in OM has the potential to provide new quantitative and automated information for improved diagnostic accuracy, appropriate referral to specialists, and effective disease management.

4

OM2015138

ISOLATION OF ALLOIOCOCCUS OTITIDIS FROM ROUTINE OUTER EAR SWABS

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Objective: Most reports on detection of Alloiococcus otitidis in ear infections have been studies of children with chronic otitis media with effusion (OME); there are few reports investigating its role in acute otitis media (AOM) (Harimaya et al., 2009; Kaur et al., 2010; Leskinan et al., 2004; Tano et al., 2008). A. otitidis is usually detected in clinical material by polymerase chain reaction (PCR) as current culture methods and standard incubation times for routine cultures are not sufficient for its detection. Our improved culture method obtained A. otitidis from nearly 50% of 78 children with OME (Ashhurst-Smith et al., 2007). Using the improved culture method, we analysed a collection of routine swab specimens from patients attending outpatient clinics, emergency rooms or general practitioners for suspected ear infections to determine if A. otitidis could be cultured with the classical external otopathogens such as Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pyogenes and Aspergillus spp.

Method: All swabs were from the outer ear canal and collected at the time of presentation. Special transport media or priority transport of the specimens was not used. A. otitidis was identified as previously described (Ashhurst-Smith et al., 2007) with the additional confirmation by the Vitek 2 automated microbial testing system (Biomerieux, USA) and Matrix Assisted Laser Desorption Ionization - Time of Flight Mass Spectrometry.

Results: A. otitidis was grown from 50 samples (aged 1- 82 years), which were notable for not producing significant growth of other common otopathogens. A.otitidis was the sole isolate in 10/50 (20%) of these cases. Preliminary assessment of antibiotic susceptibilities indicate that these isolates obtained from the outer ear had a similar pattern of resistance and sensitivity as A. otitidis isolates obtained from the inner ear of children with documented chronic infections.

Conclusion: Our results indicate that A.otitidis is a likely isolate from outer ear specimens if improved bacterial culture procedures are in place. The significant presence of A.otitidis in our clinical specimens suggests a role in outer ear disorders. Investigations are in progress to identify possible bacteriocin activity by some strains of A. otitidis.

5

OM2015241

NEW DANISH GUIDELINES ON THE DIAGNOSIS OF ACUTE OTITIS MEDIA AND THE SURGICAL MANAGEMENT OF RECURRENT ACUTE OTITIS MEDIA AND CHRONIC OTITIS MEDIA WITH EFFUSION

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Objective: Otitis media is one of the most common diseases in small children. This underlines the importance of optimizing diagnostics and treatment of these children. Recent literature points toward a stricter approach to diagnosing acute otitis media (AOM). Moreover, tympanostomy tube treatment for recurrent AOM

(rAOM) and chronic otitis media with effusion (COME) has become the most frequently performed surgical procedure in pre-school children. There is a need for an updated Danish guideline on the diagnostic criteria for acute otitis media and surgical treatment of rAOM and COME.

Method: The GRADE system (The Grading of Recommendations Assessment, Development and Evaluation) was used in order to comply with current standards of evidence assessment in formulation of recommendations. The GRADE approach, assessing both the quality of evidence and strength of recommendations, provides a comprehensive and transparent approach for developing clinical guidelines. An extensive literature search was conducted in October 2013 and will be updated before publication. The quality of the existing literature was assessed using AGREE II (Appraisal of Guidelines for Research & Evaluation), AMSTAR (assessing the Methodological Quality of Systematic Reviews), QUADAS-2 (Quality of Diagnostic Accuracy Studies), Cochrane Risk of Bias Tool for randomized trials and ACROBAT-NRSI (A Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies). The working group consisted of otolaryngologists, general practitioners, pediatricians, microbiologists and epidemiologists.

Conclusion: Recommendations are proposed regarding diagnostic criteria for AOM, surgical management for rAOM and COME including the role of adenoidectomy and treatment of tympanostomy tube otorrhea.

6

OM2015111

FIVE CASES OF OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV) WITH HYPERTROPHIC PACHYMENINGITIS

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Introduction: Recently, refractory otitis media with progressive sensorineural hearing loss or facial palsy with ANCA-associated vasculitis has been reported. Otitis media with ANCA-associated vasculitis (OMAAV) can be complicated with hypertrophic pachymeningitis. We report 5 cases of OMAAV with hypertrophic pachymeningitis.

Method: We accumulated the OMAAV patients with hypertrophic pachymeningitis by retrospective chart review of the patients who were diagnosed and treated in our clinic between 2000 and 2013.

Results: OMAAV with hypertrophic pachymeningitis was 5 cases. There were 2 males and 3 females. Their ages at the time of the initial visit ranged from 28 to 83 years. All patients had ear symptom and sever headache. Two patients were positive PR3-ANCA at initial visit. One case was positive MPO-ANCA at initial visit. The pathological findings that were characteristic of ANCA-associated vasculitis were obtained in only one patient. The probable cases of the Japanese diagnostic criteria for Granulomatosis with polyangitis (GPA) were 2 patients at initial visit, and inapplicable cases were 3 patients. The hypertrophic pachymeningitis complicated in 3 patients at initial visit, and remaining 2 patients were complicated all over the course. Also, 2 patients had facial paralysis all over the course. All patients were treated with prednisolone (PSL) and cyclophosphamide (CY), 4 patients methylprednisolone pulse therapy followed by oral PSL and CY. After treatment, the symptoms disappeared from 1.5 to 2 months.

Conclusion: In OMAAV case, we have to note that the hypertrophic pachymeningitis could be complicated and also it could induce intracranial complications.

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OM2015098

EUSTACHIAN TUBE FUNCTION TEST RESULTS IN ADULTS WITH VENTILATION TUBES INSERTED FOR OTITIS MEDIA WITH EFFUSION

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Background: Adults with ventilation tubes (VT) inserted for previous middle ear (ME) effusion are suspected to have Eustachian tube (ET) dysfunction.

Objective: Investigate the ET function test results in adults with VT.

Methods: Adults with a history of suspected ET dysfunction due to needing VT for ME effusion are evaluated for possible eligibility for balloon dilation of the ET (BDET). Subjects underwent detailed history, examination and ET function testing with forced response test (FRT). During the FRT testing, a constant air flow is delivered with a pump, through the ear canal of the ear with VT, which increases ME pressure to a level that passively opens the ET lumen (PO). After ET opening, pressure drops to steady pressure (PS) while the air flow (QS) keeps the ET open. Swallowing during this steady state changes the ET lumen diameter resulting in an increased or decreased flow (QA) with active function. The pump is then turned off decreasing the pressure to a level that stops the flow with closing of the ET (PC). A high PO and PC and/or low dilatory efficiency (DE=QA/QS) indicate ET dysfunction with potential to benefit from BDET.

Results: Subjects who have undergone FRT to date revealed median (and interquartile range) values for PO: 455dapa(287,637), PC: 39dapa (21,66) and DE: 1.09 (1.04, 1.7) with the flow of 11ml/min, and PO: 409dapa(278,181), PC: 88.5dapa(18,195) and DE 1.02 (.29, 1.2) with the flow of 23ml/min.

Conclusions: Adults with VT with verified ET dysfunction may benefit from BDET.
Supported in part by: NIH grant DC013167

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OM2015207

PRESSURE DIFFERENCE RECORDED BY TUBOMANOMETRY EAR PIECE WITH EUSTACHIAN TUBE OPENING DOES NOT PREDICT THE MIDDLE EAR PRESSURE CHANGE.

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Background: In the presence of a pressure gradient between the middle ear (ME) and ambient pressure, the Eustachian tube (ET) opening results in a bolus transfer of gas, causing a difference in middle ear pressure (MEP) pre (P1) and post (P2) test. Tubomanometry is an ET function test that detects the tympanic membrane displacement, measuring the pressure difference (P2-P1) when the ET opens with the application of controlled nasal positive pressure while the velum is closed.

Objective: Determine predictive value of Tubomanometric P2-P1 output, using the MEP change measured by tympanometry.

Method: Subjects with or without a history of ET dysfunction were enrolled. The Tubomanometric output of P2-P1 and tympanometric output of MEP2-MEP1 (pre- and post- test difference) for the 84 tests on 51 ears of 29 subjects were analyzed for correlation and the thresholds of P2-P1 that are more sensitive and specific for detecting the tympanometric MEP change were tested.

Results: The P2-P1 was present in 78 out of 84 tests, indicating a detectable change in the MEP recorded by Tubomanometry. However, the correlation between P2-P1 and MEP2-MEP1 was not statistically significant (p:0.423). Presence of P2-P1 was false positive in 24% of the tests with MEP2-MEP1, when threshold was set as: <5daPa. P2-P1thresholds of >0.49mbar, >0.99mbar, >1.19mbar and >1.49mbar had 48%, 40%, 36%, and 31% false positives respectively.

Conclusions: Change in the MEP during the test for ET opening measured by Tubomanometry is not accurate when compared to the MEP change measured by tympanometry. Support: in part by NIH grant DC013167 and CSTP and CTSI programs.

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OM2015228

CLINICAL EFFICACY OF INSERTION OF MIDDLE EAR VENTILATION TUBE AGAINST INTRACTABLE ACUTE OTITIS MEDIA

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Introduction: Myringotomy is widely accepted for one of the effective treatment modalities against AOM. Insertion of ventilation tube is an effective alternative treatment modality against intractable AOM. In this study, we studied the clinical efficacy of ventilation tubes against intractable AOM. The improvement of middle ear and mastoid cavity findings were evaluated by 3D-computed tomography (3D-CT).

Methods: Pediatric patients with intractable case of AOM were enrolled into this study. Intractable case of AOM was defined without improvement even after the first treatment with amoxicillin and the second treatment with alternative antibiotics with/without myringotomy. We evaluated middle ear and mastoid findings before and after the insertion of ventilation tubes by 3D-CT.

Results: All pediatric patients with intractable AOM showed strong bulging of tympanic membrane, fluid occupying middle ear cavity, and mastoid air cells evaluated by 3D-CT. The typical intractable AOM cases showed highly edematous and/or granulomatous changes of middle ear mucosa by trans-tympanic membrane microscopy. After insertion of ventilation tubes, the middle ear and mastoid findings of all the patients were improved within 3 months.

Conclusion: The current 3D-CT and trans-tympanic membrane microscopic study suggested that extension of inflammation and exudative fluids in the middle ear and mastoid cavities likely would cause intractability of AOM. The insertion of ventilation tube rapidly improved both middle ear and mastoid pathology and prevented the prolongation of AOM. Insertion of ventilation tube would be one of the effective treatment modality against intractable AOM.

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OM2015076

CAN TRAINED NURSES EXCLUDE MIDDLE EAR EFFUSION WITH TYMPANOMETRY IN YOUNG ASYMPTOMATIC OUTPATIENTS?

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Introduction: Tympanometry is an adjunctive diagnostic tool for pneumatic otoscopy to detect the presence or absence of middle ear effusion (MEE). In Finland, the resolution of MEE is routinely controlled by a physician after an episode of acute otitis media because MEE is thought to affect hearing and the development of speech.

Objective: The aim was to study whether nurses without otoscopic experience can reliably exclude MEE in young asymptomatic outpatients.

Methods: We trained 3 nurses, who performed examinations on 156 outpatients aged 6-35 months. Pneumatic otoscopy by the study physician served as the diagnostic standard. We calculated predictive values for type A and C1 tympanograms (peak pressure >-200 daPa) vs. type C2 (pressure ≤-200 daPa), Cs (width >300 daPa), and B (flat) tympanograms, and the clinical usefulness, i.e. the proportion of visits where nurses obtained type A or C1 tympanogram from both ears of the child.

Results: At 196 visits, nurses performed 272/373 (73%) successful tympanograms. For type A and C1 tympanograms to exclude MEE, sensitivity was 84% (95% CI 73-91%); specificity 87% (82-91%); positive predictive value 66% (55-75%); and negative predictive value 95% (91-97%). Based on type A and C1 tympanograms, the nurse could exclude MEE at 81/196 (41%) visits.

Conclusion: Due to the high negative predictive value, tympanograms with peak pressure >-200 daPa (types A and C1) obtained by nurses are reliable test results in excluding MEE. However, these test results were obtained from both ears of the child at less than half of the asymptomatic visits.

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OM2015003

ATYPICAL DURAL ENHANCEMENT AND THICKENING IN ACUTE MASTOIDITIS

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Dural enhancement and thickening in imaging studies observed in acute mastoiditis pediatric patients is an uncommon phenomenon. It is rarely seen in dural sinus thrombosis, and may be caused by infiltration of inflammatory cells. We present a 3 year-old boy with acute mastoiditis, which was complicated by a subperiosteal abscess. A computerized tomography (CT) scan was performed, and demonstrated a subperiosteal abscess, which required surgical drainage. Despite adequate antibiotic treatment, symptoms worsened and neurological sequelae became evident. A second CT scan and magnetic resonance imaging (MRI) studies demonstrated an atypical dural enhancement at the sigmoid perisinus area and a suboccipital abscess. The child underwent revision surgery and drainage of the deep abscess. Following the second procedure, resolution of symptoms was noted. Follow-up MRI did not demonstrate any dural pathologies.

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OM2015029

ACUTE MASTOIDITIS IN CHILDREN: NECESSITY AND TIMING OF IMAGING

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Introduction: Acute mastoiditis (AM) can be clinically diagnosed, and be supplemented by imaging modalities, such as computerized tomography (CT) scan and magnetic resonance imaging (MRI). Debate exists whether clinical diagnosis alone does not jeopardize patients from undetected complications which are observed only in imaging studies. We sought to study the multitude of reasons leading to perform or defer an imaging study during AM course.

Methods: Medical records of children <8 years who were admitted with AM during 10-years period (2005-2014) were retrospectively reviewed. Data collected included medical history, signs and symptoms, laboratory results, imaging studies, treatment methods and final outcomes.

Results: 86 children were diagnosed with 88 AM episodes. Of AM episodes, 55 (63%) were boys and 46 (52%) were <2 years of age. All children were treated with parenteral antibiotics, and 82 (95%) underwent myringotomy upon admission. Only 20 (23%) of children underwent imaging studies. Of them, 20 (100%) children underwent CT scans, and 3 (15%) underwent complementary MRI studies, on the 6th median day (range 0-15) of AM course. Reasons for imaging studies included evolvement of subperiosteal abscess (9/20, 65%), persistence of fever despite adequate medical therapy (7, 35%) and focal neurological signs (4, 20%). Fourteen (16%) children underwent surgery. Our rates of imaging studies were significantly lower than in other reports, yet the outcome in our study children were favorable.

Conclusion: Children presenting with AM can be diagnosed clinically without necessitating imaging studies, and can be safely treated with intravenous antibiotics, combined with myringotomy with minimum peril.

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OM2015219

THE BRAIN'S RESPONSE TO EAC PRESSURE VARIATIONS: AN FMRI STUDY

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Introduction: Eustachian tube function (ETF) may be conditioned by middle ear (ME) and nasopharyngeal (NP) stimuli. The response is initiated by chemo or baroreceptors acting via central neural pathways that modulate blood vessel and muscle tonus. Histologic tracer studies documented central nervous processing pathways in primates. Using fMRI it should be possible to simultaneously assess in vivo ETF and the central neural pathway activation during the application of specific stimuli.

Objective: Evaluate an fMRI method (Job etal. 2010) to define the central pathways acting between ME stimuli and ETF.

Methods: Right-handed adult subjects with normal middle ears by history and clinical exam were enrolled. Three to four 10 minute BOLD fMRI runs were performed. Each run consisted of 10, 1-minute blocks (30 seconds of no stimulus followed by 30 seconds of stimulus). The unilateral stimulus (right) was pressure cycles (60/min) varying between 0 and 40 daPa applied to the external auditory canal. The resulting fMRI images were corrected for motion, spatially normalized, and smoothed (SPM8). Voxel-based BOLD hemispheric differences between the stimulus conditions were compared to determine the brain regions in which significant changes in signal intensity occurred.

Results: Five subjects were screened and underwent fMRI. Significant decreases in activation were evident (165 voxel threshold), but activation increases were not. These changes were not robust: that is, they were sensitive to the analytical parameters.

Conclusions: Although changes in neural activity could be demonstrated, they did not correspond to those found by Job. Supported in part by NIH grant DC007667

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OM2015135

CAN EUSTACHIAN TUBE FUNCTION TESTS PREDICT BAROTRAUMA RISK IN DIVERS?

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Introduction: Some individuals only experience symptoms/signs of middle ear (ME) barotrauma when exposed to rapid environmental pressure-changes as occur during diving and flying. While often attributed to situational unveiling of a subtle form of Eustachian tube (ET) dysfunction, recent reports suggest that simple ET function (ETF) tests can accurately assign group-membership.

Objective: Determine the sensitivity/specificity of 3 standard ETF tests and of a simulated-dive protocol for assigning a mixed-population of recreational divers to the group that typically experiences mild-moderate barotrauma while scuba-diving.

Methods: Approximately 80 subjects aged 10-50 years, 40 without and 40 with a history of barotrauma during scuba-diving are being enrolled. On presentation, they report their diving experience and provide a medical history with a focus on ME diseases and post-dive episodes of barotrauma. ETF is evaluated by the 9-step test, sonotubometry and barotubometry and then by a simulated-dive in a pressure-chamber. Simple contingency tests are used to estimate the sensitivity/specificity for each test and for the simulated-dive with respect to identifying individuals with diving-related barotrauma.

Results: To date, the simulated-dive protocol was developed, field-tested and modified to better reproduce the diving experience. Subject enrollment and testing is ongoing with study completion anticipated by August 2016. This presentation details the dive-simulation protocol, the experiences of subjects tested under that protocol and the correspondences between ear-problems occurring during the protocol and scuba-diving for individual subjects.

Conclusions: This study promises to identify tests that accurately assign persons to groups that will and will not experience barotrauma during scuba-diving.
Supported in part by: NIH grant DC007667

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OM2015187

EUSTACHIAN TUBE MORPHOMETRY: COMPARISON BETWEEN A 3D DIGITIZER AND A CT SCAN

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Introduction: Eustachian tube (ET) anatomy is the substrate upon which its function depends. Although quantitative methods for assessing ET function are available, characterizing the in vivo morphology is qualitative and rudimentary. Doyle showed quantitative ET morphologic differences in skeletal populations with a range of OM prevalence. Application of this method to living populations requires CT or MRI scanning with accurate placement of the relevant landmarks.

Objective: ET morphometry derived from ET osseous landmarks identified on CT scans accurately reflect the measurements obtained from a 3D Digitizer in a sample of human skulls.

Methods: Thirteen points reflecting ET and cranial base morphology, such as the hamulus, orifice of the osseous ET, and medial pterygoid point, were marked with metal beads on seven skulls from the tertiary care institution research laboratory. The 3 dimensional coordinates for each point were obtained using a Microscribe G2L 3D Digitizer and from CT images using ImageJ. For each method the distances between the points were calculated and used as input for the ET morphometric model (Doyle and Swarts, 2010).

Results: Plots of the CT results against those of the 3D digitizer yielded regression slopes varying from 1.07 to 0.6 with R2 between 0.95 and 0.49. Coefficients of variation averaged 10%.

Conclusions: Estimates of ET morphometric variables from CT images accurately reflect their values obtained from a 3D digitizer. Thus CT based quantitative assessment of ET structure becomes possible, opening an avenue for evaluating the relationship of function to structure in vivo. Supported in part by: NIH grant DC007667

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OM2015115

NASOPHARYNGEAL SWAB ENHANCES PCR-BASED DETECTION OF OTITIS MEDIA PATHOGENS IN THE ADENOID

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Objective: Biofilm forming bacteria (BPB) have been shown to be important in the pathogenesis of otitis media (OM) and the adenoid has been shown to be an important reservoir for BPB. Many previous investigations have utilized adenoid biopsy to assess for BPB. The objective of this investigation was to determine the diagnostic accuracy of a novel nasopharyngeal sampling swab as a sensitive, inexpensive and less invasive technique to study BPB in the nasopharynx.

Method: Transoral NP swabs and adenoids were collected from infants and children aged 1 to 10 years undergoing tympanostomy tube placement and adenoidectomy for chronic or recurrent otitis media. DNA was extracted directly from swabs or adenoids and PCR of 16s RNA genetic sequences unique and universal to Haemophilus influenza, Streptococcus pneumonia and Moraxella catarrhalis was performed.

Results: Use of NP swabs significantly increased signal strength of PCR-based BPB detection and reduced the probability of false negative results relative to whole adenoid tissue.

Conclusion: Nasopharyngeal swab is superior to adenoid biopsy for use in PCR-based detection of BPB. NP swabs are a reliable, inexpensive, noninvasive specimen collection method for PCR-based detection of BPB.

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OM2015200

CHANGES IN THE EUSTACHIAN TUBE FUNCTION WITH GROWTH AND DEVELOPMENT IN CHILDREN WITH REPAIRED CLEFT PALATE

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Objective: Otitis media (OM) persists after the palatoplasty in children with cleft palate (CP). As in the general population a gradual decrease in OM between ages 2-5 could be ascribed to better Eustachian tube function (ETF) due to growth and development. A study was conducted to assess the change in ETF in children with repaired CP.

Method: Infants with non-syndromic cleft palate were enrolled. The protocol included otoscopy to verify the presence and patency of the tympanostomy tubes (TT), or if absent, the status of the middle ear (ME) behind the intact tympanic membrane (TM) and tympanometry. For the ears with patent TTs, the force response test (FRT) was performed. Children with an intact TM and no OM underwent an inflation and deflation test (IDT) in a pressure chamber using sonotubometry. Testing occurred at yearly intervals up to 6 years after the CP repair.

Results: Eighty-two subjects were enrolled in the study. Thirty-two subjects are still active and 37 have completed the study. ET function testing was performed using FRT, IDT, Pressure Chamber, as applicable a total of 52, 30, 41, 46, 28, 19, and 4 subjects immediately after palatoplasty, and at 1, 2, 3, 4, 5, and 6 year follow-ups respectively. The analysis of these ETF test demonstrate gradual improvement over years.

Conclusion: The prevalence of OM after CP repair continues to decrease with growth and development as a result of improvement of ETF with growth and development. Supported in part by NIH Grant DC007667

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OM2015174

INTRA-OPERATIVE EUSTACHIAN TUBE FUNCTION TESTING DURING FURLOW PALATOPLASTY SHOWS VARIABLE RESULTS

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Introduction: A modification of the cleft palate repair technique Furlow palatoplasty (FP), tendon tenopexy that re-attaches the Tensor Veli Palatini muscles (mTVPs) tendons to the ipsilateral hamular processes was described as a way to promote more "normal" mTVP tonus and ET function and resolve OME. A randomized clinical trial is being conducted to determine if FP with tendon tenopexy improves ET function (ETF) and resolves OME post-palatoplasty. However, the impact of surgical maneuvers and the tensor tenopexy on the muscle tone and constriction during the ETF tests is not known.

Objective: To test the mechanism of a modification in FP technique that is proposed to improve ETF.

Methods: Six subjects have undergone intra-operative ETF assessed with the Forced-Response test while the mTVP and mLVP are stimulated before and after the various surgical steps of FP. Opening (OP), steady state (SP) and closing pressures (PC) and steady state resistance (RS), and muscle stimulation thresholds at each surgical step were recorded.

Results: There were significant amplitude and directional changes in the test results over the first 4 surgical steps prior to the randomized 5th step. The change in the test results between the 3rd and 4th step were -52.2±28.9daPA (range:-86,-11), 26.4±22.7daPA (range:-56,2), 6.2±46.7daPA(range:-48.5,+74), and -2.5±4.3 (range:-10,2.3) for OP, SP, CP, and RS respectively.

Conclusions: Current results fail to demonstrate a consistent ET dilation during the muscle stimulations. Significant variability in the results dampen the enthusiasm for pursuing this novel method. Supported in part by NIH Grant DC011524

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OM2015193

A FUNCTIONAL EXPLANATION OF THE RELATIONSHIP BETWEEN MASTOID SIZE AND OTITIS MEDIA WITH EFFUSION RISK

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Introduction: Well accepted is the inverse relationship between the size/volume of the aerated mastoid and that middle-ear's (ME) risk for otitis media with effusion (OME). Past studies suggested that this relationship is mediated by a buffering effect of large mastoids on the trans-ME mucosal (transMEM) gas-exchange rate.

Objective: Test the hypotheses that the rate of diffusive transMEM gas-exchange is inversely related to mastoid size and is greater for adults with a history of OME.

Method: A total of approximately 60 adults, 30 without and 30 with an OME history are being enrolled in a study that measures that area of the aerated mastoid from Schuller projection x-rays and the rate of transMEM gas-exchange from the slope of the ME pressure-time curve captured while subjects breath a 50%N2O:50%O2 gas-mixture. Under conditions applicable to this experiment, that slope is directly proportional to the N2O diffusion conductance, K, for the ME mucosa as given by the Fick diffusion equation.

Results: To date, 17 (8,9) subjects completed the study. The average+std mastoid-area was 4341+1048 vs. 2874+958 mm2 ($p<0.01$) and average+std pressure-time slope was 5.24+2.24 versus 6.78+4.65 /min. ($p<0.11$) for ears without and with a history of OME. The regression equation for all ears was: Slope=-0.001xArea+9.66, r=0.33, p=0.03.

Conclusion: These results reproduce the previously reported smaller mastoid size in ears with a history of OME and provide support for the 2 tested hypotheses. Results for all subjects will be presented and the significance of this Volume-Rate relationship to ME pressure-regulation and OME risk discussed. Supported in part by: NIH grant DC007667

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OM2015234

ET MORPHOLOGICAL MEASUREMENTS FROM MRI IMAGES OF CHILDREN

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Introduction: Cross-sectional studies report a lower prevalence of otitis media (OM) and better Eustachian tube function (ETF) in older compared to younger children. ETF is constrained by its anatomy. Although there are quantitative methods for assessing ETF, methods to characterize in vivo ET morphology are qualitative and rudimentary. While boney landmarks defining the course of the ET and paratubal muscles can be identified on CT images, the size and morphologic relationships of ET soft tissue components, e.g. the cartilage (C) and the tensor (mTVP) and levator veli palatini (mLVP) muscles cannot. Objective: Assess the feasibility of quantifying the ET soft tissue morphology using MRI.

Methods: A subgroup of children enrolled in a longitudinal study of the effects of growth and development on ETF had double oblique coronal MRI. Using ImageJ the cartilage, mTVP and mLVP were traced and characteristics of their morphometric features such as area, perimeter, circularity, feret lengths, and angular relationships were determined from images perpendicular to the long axis of the ET.

Results: Twenty-three children (10 recurrent acute OM, 3 OM with effusion, 10 controls) 6-7 years of age underwent unsedated MRI. An average of 7 images per subject contained identifiable ET structures. The first 9 subjects analyzed showed area (C>mLVP>mTVP), perimeter (C>mTVP>mLVP) and circularity (mLVP>mTVP) relationships consistent with those found in studies of histologic specimens.

Conclusions: The soft tissue components of the ET can be identified and their characteristics measured on appropriately obtained MR images. Supported in part by NIH grant DC007667.

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OM2015209

CT SCAN RESOLUTION IS INADEQUATE TO VISUALIZE THE EUSTACHIAN TUBE LUMEN

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Objective: 1) Image the in vivo Eustachian tube (ET) lumen with CT during ET function (ETF) testing and 2) Establish a methodology to concurrently assess ET structure and function for use in research projects.

Method: In 5 adults with a tympanic membrane perforation, ETF testing was done using the air forced response test (FRT) to measure the opening (OP), steady state (PS) and flow resistance (FR) pressures during an induced airflow from the middle ear through the ET to the nasopharynx. At baseline and during the PS phase of the FRT, a low dose temporal-bone CT scan with continuous 0.625 mm thickness was obtained. Image analysis was performed using commercially available software to view the ET in standard and oblique planes.

Results: The average OP, PS and FR for the five subjects were 299±105, 263±118 and 7.5±2.6 daPa, respectively. The baseline CT scan demonstrated normal temporal bone and peri-tubal anatomy, as did re-constructed images parallel to the ET lumen. CT scans obtained during the FRT PS phase did not delineate a distinct air filled ET lumen. Small foci of air in the ET lumen were suspected, but not measureable, due to partial volume averaging.

Conclusion: Functional CT scanning while the ET lumen is dilated by a constant flow of air is a novel technique for assessing ET anatomy and function. While the current imaging parameters failed to resolve the air-soft tissue interface throughout the open ET, further advances in imaging may obviate this limitation. Supported in part by: NIH grant DC007667

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OM2015325

MULTI-WAVELENGTH DUAL MODALITY OTOSCOPE FOR OTITIS MEDIA DIAGNOSIS

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Objective: To describe the development and implementation of a video- otoscope using multiwavelength auto fluorescence and reflectance to characterize optical features in otitis media

Method: Images of 20 patients undergoing tympanostomy tube placement were obtained using both fluorescence and reflectance images with multiple excitation wavelengths on the visible spectrum. Different fluorescence filters were employed to select for various tissue fluorophores. Contrast-limited adaptative histogram equalization (CLAHE) was performed to evaluate for contrast differences between wavelengths.

Results: Wavelengths have different tissue interactions enhancing certain characteristic both in fluorescence and reflectance imaging. There is strong autofluorescence fro the malleus and promontory. The tympanic membrane on the other hand has no autofluorescence signal.In the prescence of middle ear effusion the autofluorescence from the promontory is absent. Vascularity is signifficantly enhanced in the blue and green excitation wavelengths .CLAHE maps can provide a method to calculate contrast.

Conclusion: A dual modality fluorescence /reflectance otoscope can provide valuable information by enhancing contrast of vasculature and providing changes in the pattern of autofluorescence in the presence of middle ear efusion.

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OM2015327

DETERMINANTS OF CHRONIC OTITIS MEDIA WITH EFFUSION IN PRESCHOOL CHILDREN

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Objective: To determine risk factors for chronic otitis media with effusion (COME) in New Zealand preschool children.

Methods: A case-control design was used to compare children aged 3 and 4 years referred for tympanostomy tube insertion due to a diagnosis of COME (n = 178) to healthy children selected at random from primary care practices (n = 209). The children's guardians completed a questionnaire that covered topics including socio-demographic information, pregnancy and birth, infant feeding practices, and respiratory health. In addition skin prick tests for atopy were performed.

Results: Children with COME frequently had nasal obstruction (OR: 4.38 [95% CI: 2.37–8.28]), always snored (OR: 3.64 [95% CI: 1.51–9.15]) or often snored (OR: 2.45 [95% CI: 1.04–5.96]), spent longer in daycare (OR per hour: 1.03 [95% CI: 1.00–1.05]), had frequent colds (OR: 2.67 [95% CI: 1.59–4.53]), had siblings who had undergone tympanostomy tube insertion (OR: 2.68 [95% CI: 1.22–6.02]), underwent long labor (OR: 2.59 [95% CI: 1.03–6.79]), and had early introduction of cow's milk (OR: 1.76 [95% CI: 1.05–2.97]). Asian ethnicity (OR: 0.20 [95% CI: 0.07–0.53]) and having older siblings (OR: 0.54 [95% CI: 0.31–0.93]) had a protective effect.

Conclusion: New Zealand preschool children displayed several risk factors for COME that may reflect exposure to infection. Early perinatal events and infant feeding practices may also be determinants. Maori and Pacific Island preschool children were not at increased risk of COME as has previously been reported, however Asian ethnicity appeared to be protective.

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OM2015060

PARENT-REPORTED SYMPTOMS OF ACUTE OTITIS MEDIA DURING THE FIRST YEAR OF LIFE: WHAT IS BENEATH THE SURFACE?

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Objective: To determine the incidence of acute otitis media (AOM) symptoms in the community and to assess how often parents consulted a general practitioner (GP) when their children experienced AOM symptoms.

Method: We measured parent-reported AOM symptoms daily for 12 consecutive months in 1,260 children participating in a prospective birth cohort in the Netherlands. A parent-reported AOM symptom episode was defined as fever (temperature 38?C or above) plus at least one of the following symptoms: ear pain and ear discharge. These symptom episodes were linked to GP-consultations and diagnoses in the GP electronic health records.

Results: Of the 1,260 included children (total duration of follow-up 1,029 child-years), 397 children (32%) experienced at least one parent-reported AOM symptom episode in their first year of life. The incidence of AOM symptoms during the first year of life was 624 episodes per 1,000 child-years (95% CI: 577 to 674). The GP was consulted in 326 of the 642 episodes (51%) and AOM was diagnosed in 49% of these consultations.

Conclusion: The incidence of AOM symptoms in the first year of life is high in Dutch children and leads to a GP-consultation in only half of the cases. This suggests that AOM symptomatology in the community is considerably underestimated when focussing on GP-diagnosed AOM episodes only. Having data on community AOM symptomatology available for each country is important when the potential impact of preventive and therapeutic interventions for AOM are studied.

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OM2015237

RISK FACTORS ASSOCIATED WITH A INTRACTABLE ACUTE OTITIS MEDIA

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Objectives: Acute otitis media (AOM) is the most common disease in childhood. The vast majority of children improve rapidly. Symptoms disappear early while the middle ear returns to normal more slowly. Although the spontaneous cure rate of AOM is known to be high, almost every child with AOM in the United States and other developed nations receive antibiotics. If predictors of outcome were known, it would be possible to individualize therapy. Our aim was to identify risk factors for intractable AOM.

Methods: We enrolled 103 cases of pediatric AOM. Ages, sex, concurrence with acute rhinosinusitis, prevalence of antimicrobial resistant pathogens and day care attendance were compared between simple AOM and intractable AOM. The intractable AOM was defined as the cases with AOM more than 3 episodes in 6 months or 4 episodes in 12 months and persistent tympanic membrane findings over 3 weeks.

Results: The ratio of cases younger than 2 years old (p=0.027), day care attendance (p=0.018) and concurrence with acute rhinosinusitis (p=0.032) were significant higher in intractable AOM than in simple AOM.

Conclusion: Younger age, day care attendance and concurrence with acute rhinosinusitis proved to be important determinants of outcome in AOM and should be considered in the selection of the most appropriate therapy.

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OM2015106

TRENDS IN AMBULATORY CARE VISITS FOR OTITIS MEDIA: 1990-2010

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Objective: To track ambulatory health care utilization for otitis media from 1990 to 2010. Otitis media (OM) is a common disorder, primarily affecting young children. The number of office visits for OM increased steadily between 1975-1990, and the annual visit rate more than doubled. What has happened since?

Method: Data from the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey (which began in 1992) were used to analyze trends in OM visits to physician offices and hospital emergency (EDs) and outpatient departments (OPDs).

Results: There were an estimated 25 million visits with an OM diagnosis to physician offices, hospital OPDs and EDs in 2010; office visits accounted for 79% of the total. The number and rate of office visits decreased between 1990-2010, with the largest change occurring between 1995-2000. The office visit rate was highest for children under 2 years, but their rate fell from 122.8 visits per 100 in 1990 to 67.1 per 100 in 2010. Black children under age 15 had higher rates of OM visits to EDs than white children did in each year except 2010 when rates did not differ; black rates declined in EDs between 1995-2010 but not in physician offices.

Conclusion: After steadily increasing from 1975-1990, visit rates for otitis media declined in physician offices from 1990-2010. From 1995-2010, ED rates declined significantly but OPD rates showed no change. Nevertheless, otitis media remains one of the most frequent illness-related diagnoses at ambulatory care visits for children under 15 years.

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OM2015132

OME PREVALENCE FROM 6 MONTHS THROUGH 5 YEARS IN CLEFT PALATE CHILDREN

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Introduction: Chronic OME is nearly universal in cleft palate (CP) infants. Previous studies reported OME child-prevalences of 90 to100% between birth and 3, 70% at 4, and, then, a decrease to approximately 30% by 6 years of age. Not known are the factors that influence the time to disease-resolution.

Objective: Describe the temporal pattern of COME-resolution for a cohort of CP children.

Methods: 73 non-syndromic CP children, enrolled between 4 and 24 months of age, are being prospectively followed through age 5 years for the presence/absence of COME by otoscopy and tympanometry at 6 month intervals to age 2 and then at yearly intervals to age 6, with observations supplemented by diagnoses made at their more frequent visits to the CP center. At each visit, middle-ear (ME) status was assigned bilaterally as: perforation, tube, acute OM, otorrhea, OME, or disease-free. Age in years of the first in a sequence of disease-free diagnoses not interrupted by any other diagnosis was defined as the COME resolution-age.

Results: To date, 48 children (27 Male, 41White, Veau 1-4 distribution 2, 11, 24, 11) are >5 years of age. All had a Furlow-type palatoplasty between 12 and 24 months of age done by 1 of 6 surgeons. For ears, the distribution of COME resolution-ages was 2, 9, 17, 11, 12, 11 and 31/3 for age-groups <1, 1, 2, 3, 4, 5 years and un-resolved/not-evaluable.

Conclusions: The COME-resolution curve for this cohort was shifted to earlier ages than previously reported. Possible influential factors will be discussed.
Supported in part by: NIH grants DC007667 and DC011524

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OM2015333

A SYSTEMATIC REVIEW OF RISK FACTORS ASSOCIATED WITH CHRONIC SUPPURATIVE OTITIS MEDIA

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Aim: To systematically review the literature on risk factors associated with chronic suppurative otitis media (CSOM) in children.

Methods: We systematically searched for literature in Pubmed. The inclusion criteria were: 1) cohort, case control or cross-sectional design; 2) participants ≤ 18 years; 3) cases had clinically defined CSOM; 4) diagnosis confirmed by otoscopy, 5) concurrent control group; and 6) ear examination and risk factor assessments were conducted at the same time. Studies were evaluated for risk of bias using the Newcastle Ottawa Scale. Important risk factors were assessed using multivariate estimates from studies at low risk of bias.

Results: 12 studies were evaluated. 21 risk factors were assessed. In three studies at low risk of bias, the strongest risk factors associated with CSOM were: tympanostomy tube surgery (odds ratio, OR >100); recurrent URI (OR 1.2 and 12); daycare attendance (OR ~6); older sibling (OR ~4); maternal history of CSOM (OR ~3); and Inuit ethnicity (OR ~3). There is insufficient evidence to confirm the effects of passive smoking, breastfeeding, preterm birth, low birth weight, family size, crowding (people per house and per room), poor sanitation, certain dietary deficiencies, socio economic status, parental education and maternal employment.

Conclusion: In a developed setting, tympanostomy tube surgery was an exceptionally strong risk factor for CSOM. Across a range of settings, we found recurrent URI, daycare attendance, older sibling and maternal history of CSOM were consistently associated with CSOM. Intervention studies are needed to address these risk factors.

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OM2015253

POOR MEMORY B-CELL GENERATION CONTRIBUTES TO REDUCED ANTIGEN-SPECIFIC IGG RESPONSES IN OTITIS-PRONE CHILDREN

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Objective: We recently identified a subset of young children who experience recurrent otitis media despite individualized care including tympanocentesis (stringently-defined otitis prone [sOP]) and do not develop protective antibody response to several vaccine candidate protein antigens. Our group seeks a more precise explanation for immunologic dysfunction that causes the otitis prone condition. Because exposure to Streptococcus pneumonia and Haemophilus influenza occurs at different ages, for different durations and by different mechanisms (nasopharyngeal colonization and acute otitis media), variability in exposure complicates immunologic analysis. Therefore we sought to analyze circulating antigen secreting memory B cell populations induced by routine vaccinations that occur at fixed time points in identical doses. We sought a correlation between memory B cell responses and the IgG responses to DTaP vaccine antigens in age-matched sOP and non-sOP (NOP) children.

Method: Peripheral blood mononuclear cells (PBMC) were stimulated with a TLR9 agonist CpG-ODN 2006 or with DTaP vaccine antigens, diphtheria toxoid (DT) tetanus toxoid (TT) and acellular pertussis toxoid (PT). The B cell subsets were identified using anti CD19 and anti CD27 and analyzed by flow cytometry.

Results: sOP children had a significant lower percentage of antigen-specific memory B cells (CD19+ CD27+) compared to NOP children. We also found a significant correlation between the frequencies of memory B cells and IgG antibodies to DT, TT and PT.

Conclusion: Lower antigen-specific memory B cell responses in sOP children correlates with reduced IgG responses. This immune dysfunction may cause susceptibility to recurrent infections. Supported by NIAID RO1 08671.

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OM2015033

OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS (OMAAV): A RETROSPECTIVE MULTI-CENTER STUDY IN JAPAN 3) CLINICAL DIFFERENCES ACCORDING TO INITIAL AND SEQUENTIAL INVOLVEMENTS

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Introduction: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is characterized by systemic necrotizing vasculitis. Throughout the course of these diseases, almost all patients exhibit otolaryngological symptoms such as sinusitis, septal perforation, otitis media and subglottic stenosis. Recently, reports of otitis media with AAV (OMAAV) with bone-conduction hearing loss have increased and there is increasing recognition of OMAAV. Facial nerve palsy and hypertrophic pachymeningitis are symptoms that are frequently associated with OMAAV.

Objective: The purpose of this study was to investigate the clinical features of OMAAV, particularly facial nerve palsy and hypertrophic pachymeningitis. Additionally, we examined the characteristics of relapse cases.

Methods: We carried out a nationwide questionnaire survey of OMAAV at major hospitals in Japan. The collected data were used in this study.

Results: Of 297 cases, patients with facial nerve palsy numbered 94 (32%) and patients with hypertrophic pachymeningitis numbered 70 (25%). There were 125 cases (43%) with relapse in their clinical course. Concerning treatment, patients treated with steroid therapy without immunosuppressive drugs relapsed more than patients treated with steroid and immunosuppressive drugs (p=0.04).

Conclusion: Facial nerve palsy and hypertrophic pachymeningitis were relatively common symptoms in OMAAV. These findings might be key for the diagnosis. Furthermore, it was revealed that OMAAV can easily relapse. Initial immunosuppression therapy that includes corticosteroid, cyclophosphamide or methotrexate is therefore essential for achieving long-term remission for OMAAV.

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OM2015260

FUNCTION OF FOLLICULAR T HELPER CELLS (TFH) IN THE TONSILS AND ADENOIDS OF OTITIS-PRONE (OP) AND NON-OP

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Objective: Our group seeks a more precise immunological explanation for the otitis prone condition. In the course of an ongoing NIDCD-supported study, we have identified a subset of otitis-prone (OP) young children who experience frequent episodes of otitis media. These OP children fail to develop protective antibody responses to several Streptococcus pneumonia and Haemophilus influenza candidate protein vaccine protein antigens. Otitis media pathogenesis begins in the nasopharynx, and the tonsils and adenoids are the key regional lymph nodes protecting against colonization and infection of the upper respiratory tract. We sought to identify differences in the functioning of follicular T helper cells (TFH) in the tonsils and adenoids of OP and NOP children by studying the differentiation and activity of TFH and B cells in response to bacterial antigens.

Method: Mononuclear cells from whole tonsils and adenoids removed from children (median age 3.3 years) were stimulated for varying durations of time with vaccine antigens from bacteria commonly encountered in the upper respiratory tract. Responses were measured by flow cytometry and multiplex ELISA.

Results: Among children with a history of otitis proneness we found no significant differences in the expansion or differentiation of TFH and B cell compartments from tonsils and adenoids compared to NOP children age 3-5 years old. Cytokine secretion by the immune cells studied was not significantly different between groups.

Conclusion: We found no significant differences in the functioning of TFH in the tonsils and adenoids OP and NOP children, but the age at which the samples were collected may contribute to this finding since the OP condition is largely outgrown by 3 years of age. Supported by NIDCD R01 08671.

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OM2015100

IMMUNOPROTEASOMES MAY PLAY A SIGNIFICANT ROLE IN CHOLESTEATOMA RELATED TISSUE DAMAGE

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Objective: Middle ear cholesteatoma (MEC), accompanied by chronic inflammatory response is characterized by invasive growth and osteolytic activity. The cellular processes including the importance of proteasome in MEC are not completely established. Proteasomal degradation pathway may affect the proteolytic cleavage of the extracellular bone matrix adjacent to cholesteatoma. Immunoproteasomes can promote cytokine production and progression inflammatory reaction.

Objective: to investigate the biological activity of acquired cholesteatoma by analysis of the expression of low-molecular mass polypeptide-7 subunit of the immunoproteasome (LMP7).

Method: Acquired cholesteatoma (n=12) and normal auditory meatal skin (n=12) specimens taken from patients who underwent surgery for cholesteatoma were stained with anti-LMP7 antibody, using immunohistochemistry techniques based on bounding of biotinylated secondary antibody with the enzyme-labeled streptavidin and the Envision FLEX system. Negative and positive controls were performed. Statistical analyses were performed.

Results: Significantly more intense expression of immunoproteasome subunit LMP7 was present in cholesteatoma compared to meatal skin. The LMP7(+) cells were observed in matrix and perimatrix of cholesteatoma tissue. Angiogenesis intensity in cholesteatoma was higher compared than in the skin. It may be possible that keratinocyte migration within layers of cholesteatoma matrix as well as inflammation within its perimatrix is related to the expression of LMP7 subunit of immunoproteasome.

Conclusion: Inflammation and osteolytic activity are critical aspects of progressive damage in chronic suppurative otitis media with cholesteatoma. Detection of immunoproteasome subunit LMP7 gene transcription in cholesteatoma may help developing selective inhibitors in order to block cytokine production and progression inflammatory reaction.

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OM2015006

C-REACTIVE PROTEIN AND LEUKOCYTOSIS AS CRITERIA FOR SEVERITY OF PNEUMOCOCCAL VS. NON-PNEUMOCOCCAL ACUTE OTITIS MEDIA IN CHILDREN

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Objective: To study whether pneumococcal acute otitis media (AOM) is still considered a more severe disease than that caused by other otopathogens, following the implementation of pneumococcal conjugate vaccines (PCVs).

Methods: Children <6 years of age presenting with "severe" AOM episodes and middle ear fluid (MEF) cultures during 2008-2013 were retrospectively identified. Cultures were collected during tympanocentesis or from spontaneous otorrhea. Data were extracted for demographics, clinical and laboratory tests, and analyzed according to their pneumococcal conjugate vaccine (PCV) immunization status. Children were categorized as "unimmunized" or "PCV7/PCV13 immunized", and according to their MEF culture result, into the "pneumococcal" or the "non-pneumococcal" group, respectively. Leukocytosis was defined as white blood cells (WBC) >15,000/μL, and elevated C-reactive protein (CRP) level was considered as >50 mg/L.

Results: Of 295 eligible AOM episodes, 106 (36%) were culture positive. Children in the pneumococcal group (65, 61%) had a significantly higher WBC counts and higher CRP levels, tended to be younger <2 years and were more prone to complicate with acute mastoiditis (AM), when compared to children in the non-pneumococcal group, p=0.03, p=0.02, p=0.04 and p=0.03, respectively. In the pneumococcal group, "unimmunized" children had higher WBC counts when compared with "PCV13 immunized" children (p=0.04), but there were no appreciable differences in CRP levels between "unimmunized" and "PCV7/PCV13 immunized" children.

Conclusion: Pneumococcal AOM is associated with higher WBC counts and CRP levels than non-pneumococcal AOM. Circulating Streptococcus pneumoniae strains causing "severe" AOM in "PCV13 immunized" children yielded lower inflammatory responses when compared with "unimmunized" children.

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OM2015263

SEROUS AND MUCOID MIDDLE EAR EFFUSION CHARACTERIZATION FOR MUC5B, MUC5AC AND PRO-INFLAMMATORY CYTOKINES

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Otitis Media (OM) is one of the most common conditions characterized by middle ear infectious inflammation that leads to persistent effusions that can be serous or mucoid, characteristic of chronic OM. This study aims at evaluating the presence of MUC5B and MUC5AC in a large number of MEE samples as well as pro-inflammatory cytokines. 40 MEEs were collected during myringotomy at Children's National Health System. They were characterized as serous or mucoid by the surgeon and the lab manager. Mucin western blot was performed for human MUC5B and MUC5AC and a Luminex multiplex assay was used to evaluate a panel of inflammatory cytokines. MEEs mainly showed the presence of MUC5B mucin protein whereas MUC5AC was less expressed. The samples characterized as very mucoid showed the higher presence of MUC5B, the serous samples not showing any mucin. The Luminex multiplex assay permitted to evaluate the concentration of different pro-inflammatory cytokines in the MEEs. IL-8 was showed to be in very high concentrations (until 60ng/ml) whereas other cytokines were detected in lower concentrations (IL-1beta, TNF-alpha, IL-10, IL-12 and CCL22). A higher MUC5B signal characterized by the western Blot analysis seemed to be associated to higher cytokine content. In conclusion, we confirm that MUC5B is the predominant mucin expressed during chronic OM. The high presence of inflammatory cytokines in effusions showed the crucial role of inflammation in this disease and the lack of resolution of it, likely sustaining the production of mucoid effusions.

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OM2015269

NTHI LYSATE PROTEIN CHARACTERIZATION FOR THE USE IN IN VIVO AND IN VITRO EXPERIMENTS

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Otitis Media (OM) is one of the most common conditions characterized by middle ear infectious inflammation. Non-typeable Hemophilus influenza (NTHi) is the most common pathogen cultured in middle ear disease progression and is used in laboratories to study OM in vivo and in vitro. This study aims at characterizing the proteins present in NTHi lysates and better understands their biological effects. We generated 3 NTHi lysate batches using the same technical conditions and separated the proteins by SDS-PAGE. The peptides generated where analyzed by Liquid chromatography MS/MS. An NF-kB reporter plasmid assay was performed to compare the effect of the 3 batches on mouse middle ear epithelial cells (mMEEC). The MS identified 793 unique NTHi proteins, 113 were present in all 3 NTHi lysate preparations, showing variability in protein profile. Most common and abundant proteins found were described to either contribute to biofilm formation (i.e. Adhesins), elude the innate immune system (i.e. IgA protease), or activate epithelial pro-inflammatory pathways such as Toll Like Receptor 2 (TLR-2) signaling and NF-kB transcription factor (Outer membrane proteins). Strong positive signal for OMP-6 was found in all the NTHi lysate preparations. Significant NF-kB promoter response activation was also noted with each NTHi lysate preparation, without showing any difference despite the protein variability in the different batches. In conclusion, NTHi lysates generated in laboratories exhibit different protein profiles but seem to all contain the main proteins identified as biologically responsive. Despite this variability, they were able to induce a similar NF-kB promoter activation.

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OM2015242

COMPARISON OF THE PHENOTYPE AND FUNCTION OF HUMAN PERIPHERAL BLOOD MONOCYTES AND DENDRITIC CELLS IN OTITIS-PRONE AND NON-OTITIS PRONE INFANTS

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Objective: Our group seeks a more precise explanation for immunologic dysfunction that causes the otitis prone condition. We recently identified a subset of young children who experience recurrent otitis media despite individualized care including tympanocentesis (stringently-defined otitis prone [sOP]). We have previously determined that sOP children generate lower antibody levels, fewer memory B and T cells in response to most common otopathogens. In this study, we sought to determine whether there are defects in the phenotype and function of professional Antigen Presenting Cells (APCs), at the single cell level, in sOP compared to age-matched non-otitis prone (NOP) infants.

Method: Peripheral blood mononuclear cells were obtained from OP and NOP infants. APC phenotypic counts, MHC II expression, activation and intracellular cytokine levels were determined with or without TLR 7/8 (R848) stimulation by flow cytometry.

Results: A significant ($p<0.05$) increase in the phenotypic counts of monocytes and classical DCs (cDC) but not plasmacytoid DCs (pDC) was observed in sOP compared to NOP infants. There were no significant differences in baseline MHC II between sOP and NOP infants. R848 induced IL-12p40/70 and TNF-α secreted by monocytes and cDCs or IFN-α secreted by pDCS were not significantly different between sOP vs. NOP infants.

Conclusion: Higher number of APCs in sOP infants might suggest the existence of an elevated inflammatory status. However, in this study APCs did not show maturational or functional defects in sOP compared to NOP infants. Supported by NIDCD R01 08671.

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OM2015252

COMPARISON OF INNATE IMMUNITY RELATED TRANSCRIPTIONAL PATTERNS AND CYTOKINE PROFILE OF PERIPHERAL BLOOD MONONUCLEAR CELLS IN OTITIS-PRONE AND NON-OTITIS PRONE INFANTS

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Objective: Otitis proneness characterized by frequent episodes of middle ear infection despite individualized care including tympanocentesis, was recently identified by our group as stringently-defined otitis prone (sOP). We had previously reported that sOP children during acute otitis media (AOM) had lower innate mucosal and systemic responses characterized by lower expression of TLR7 and proinflammatory cytokines and chemokines whereas an upregulation of TLR2, 4, 5. In this study, we sought to investigate whether there were differences in the innate immune transcriptional pattern or cytokine levels from peripheral blood mononuclear cells (PBMCs) between sOP and non-otitis prone (NOP) infants during health visits.

Method: PBMCs were obtained from sOP and NOP infants at 6-9 months. Innate immune gene expression was measured using RT-PCR and cytokines were measured from the PBMC supernatant with or without TLR 7/8 agonist stimulation using Luminex technology.

Results: Expression of TLR2, 4, 7, 8, intracellular signaling molecules such as MyD88, TRIF, IRAK4, IRF3, IRF7 as well as IL-12p35 and IL-10 were not significantly different in sOP compared to NOP infants. IL-1β, IL-6, IL-8, IL-10,TNF-α, IFN-γ, CCL2, CCL3, CCL4, CCL5 and CXCL10 levels from R848 stimulated supernatants were also not significantly different between sOP vs. NOP infants.

Conclusion: Transcriptional and cytokine profiles of sOP infants during health visits suggest their innate responses are not different compared to NOP infants. From an immunologic perspective, lower antibody levels to otopathogens leading to higher nasopharyngeal bacterial colonization and low B and T cell responses appears to account for recurrent infections in sOP infants. Supported by NIDCD RO1 08671.

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OM2015036

MONOPHOSPHORYL LIPID A ENHANCES NONTYPEABLE HAEMOPHILUS INFLUENZAE-SPECIFIC MUCOSAL IMMUNE RESPONSES IN THE NASAL MUCOSA

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Objective: Acute otitis media (AOM) is one of the most common infectious diseases in children. Nontypeable Haemophilus influenzae (NTHi) , Moraxella catarrhalis and Streptococcous pneumoniae are considered major pathogens of AOM and respiratory tract infections. In this study, we investigated the adjuvant effect of monophosphoryl lipid A (MPL) which is a toll-like receptor (TLR) 4 agonist to induce mucosal immune responses against NTHi.

Method: Mice were intranasally administered 10μg outer membrane protein (OMP) from NTHi plus 0, 10 or 20μg of MPL once in a week for 3 times. Control mice were administered phosphate buffered saline only. Three weeks after the initial immunization, mice were challenged with NTHi intranasally. At 6 and 12 hours after the bacterial challenge, the mice were killed to collect nasal washes and sera. The number of NTHi was counted in nasal wash, and OMP-specific antibody titers in nasal wash and sera were quantitated by ELISA.

Results: MPL(20μ g) group showd a significant reduction in the number of bacteria recovered from the nasal washes at 12 hours after the bacterial challenge when compared to control and OMP groups. MPL groups also augmented OMP-specific IgA titers in nasal washes and OMP-specific IgG titers in sera when compared to control and OMP groups.

Conclusion: MPL is one of the suitable adjuvant for eliciting effective mucosal immune responses against NTHi. As MPL has been evaluated as a systemic vaccine adjuvant in published human clinical trials, our results indicate MPL such as TLR4 agonist may be effective for mucosal vaccine adjuvant.

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OM2015278

NASAL NITRIC OXIDE IN CHILDREN WITH CHRONIC RHINOSINUSITIS AND RECURRENT ACUTE OTITIS MEDIA

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Objective: Nasal nitric oxide (nNO) is a highly reactive mediator involved in eosinophilic upper airway inflammation which is spontaneously released by ciliated epithelium, especially the paranasal sinusal mucosa. It is impaired in allergic rhinitis and rhinosinusitis, and recently reduced nNO levels have been reported also in children with adenoidal hypertrophy predisposing to chronic nasosinusal inflammation. Given the strict anatomic and physio-pathologic link between the nasosinusal and middle ear compartments, and considering the high prevalence of otitis prone children among those affected with chronic rhinosinusitis (CRS), we designed a study aimed to test any possible difference in nNO levels between non allergic children with and without recurrent acute otitis media (RAOM) associated with CRS.

Method: A prospective cross-sectional study with planned data collection was performed on consecutive non-allergic 3-12 years old children with CRS confirmed by nasal fiberendoscopy were included. They underwent nNO on-line tidal measurement by means of a dedicated chemiluminescence analyser (CDL 88 sp, Ecomedics, Switzerland). Nasal cytology was also performed in order to evaluate the possible difference in inflammatory cells between groups.

Results: The study involved 54 children with RAOM (44.4% males; mean age= 7.5 ± 3.5 years) and 51 children without RAOM (47.4% males; mean age= 7.0 ± 3.8 years). Demographic characteristics were comparable among two groups. nNO levels were significantly reduced in children with RAOM compared to children without RAOM (676.9 ± 250.7 ppb vs. 831.8 ± 320.4 ppb respectively; p= 0.02). Nasal cytotype characterized by neutrophils and becteria was the most common in both groups (37.0% in RAOM vs. 35.3% in non-RAOM, p= ns), followed by the eosinophilic cytotype (22.2% in RAOM vs. 19.6% in non-RAOM, p= ns).

Conclusion: This is the first study evaluating nNO levels in children with CRS associated with RAOM. We found that nasosinusal NO levels were significantly reduced in children with RAOM compared to those without; likewise decreased nNO levels have been previously reported in patients with acute nasosinusal inflammations compared to healthy controls, and in children with large obstructive adenoids compared to children with non-obstructive adenoids. These data could be related to reduced NO production by the ciliated paranasal, nasopharyngeal

and middle ear epithelium and the impaired sinusal ostial and Eustachian tube patency due to chronic inflammation, and seem to confirm the involvement of NO pathway in recurrent upper airway infections related to impaired ciliated respiratory mucosa.

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OM2015270

INCREASED INCIDENCE OF RESPIRATORY ILLNESSES IN OTITIS PRONE CHILDREN

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Background: We have identified a population of otitis prone (OP) children who suffer from recurrent episodes of acute otitis media (AOM) in their first three years of life. A subset of these children, representing 5% of the total population, experience especially frequent microbiologically confirmed AOM episodes. We term these children stringently defined otitis-prone (sOP).

Objective: We sought to determine if sOP children have more illnesses than non-otitis prone (NOP) children.

Method: 558 children (39 sOP and 519 NOP) were prospectively followed from 6 months to 5 years of age. All illness visits were recorded. For the purposes of this analysis, illness visits for acute otitis media (AOM) were excluded from the visit numbers and the analysis. Lobar pneumonia was diagnosed when the child had fever, tachypnea, rales on exam and an elevated white blood cell count (WBC). Influenza was diagnosed clinically and with a rapid influenza test. Sinusitis was diagnosed when purulent rhinorrhea persisted for more than 10-14 days.

Results: sOP children had more frequent illness visits and more visits per child during the first 4 years of life, $p=0.0001$. There was a trend, $p = 0.07$, in the 5th year of life. Lobar pneumonia, influenza and sinusitis occurred more frequently in sOP children, $p<0.0001$, $p=0.0019$ and $p=0.0001$ respectively. There was no difference in the illness visits for urinary tract infection, skin infections and acute gastroenteritis.

Conclusion: sOP children under 5 years of age experience a higher rate of both viral and bacterial illnesses than NOP children. Supported by NIDCDR0108671.

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OM2015322

BACTERIAL FLORA OF TONSILLS IN OTITIS MEDIA EVOLUTION

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Objective: We analyzed the correlations between pharyngeal bacterial flora and otitis media (OM) recurrence and chronicity.

Method: A total of 148 children at the age of 3 – 4 years with OM were involved in our prospective study which included microbiological test from nasopharynx, standard treatment (medical and surgical) and otomicroscopical, functional examinations of ears and charts analysis in 5 years after surgery. All children were divided on 4 groups according to the OM outcome.

Results: The most complicated outcome of OM with the formation of chronic suppurative and adhesive forms was registered in children with Str. beta-hemolytic pyogenes presented in pharynx in early childhood. Majority of these patients (90%) underwent ear surgery for more than 3 times due to chronicity and adenotonsillectomy due of chronic tonsillitis. Relatively benign OM evolution was registered in children with Str. pneumoniae and Staph. aureus in pharynx, usually it was necessary one surgical treatment. Children with Moraxella catarrhalis and Haemophilus influenzae in pharynx in the majority of cases were successfully treated by medical methods. Only in 15% of cases we made surgical treatment in that group.

Conclusion: The pharyngeal microbial flora in children with OM influences on further evolution of the middle ear pathology. Children with Str. beta-hemolytic pyogenes and OM have to be on close observation, need early comprehensive treatment including surgical one.

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OM2015311

PERSISTENCE OF NONTYPEABLE HAEMOPHILUS INFLUENZAE IS DEPENDENT UPON SELECTIVE IMPORT OF NUTRIENTS AND HOST ANTIMICROBIAL PEPTIDES

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Introduction: Nontypeable Haemophilus influenzae (NTHI) responds to host microenvironmental cues, including host-derived antimicrobial peptides (AMPs) and the essential nutrient heme-iron, to mediate pathogenesis of diseases, which include otitis media. We identified multifunctional roles for the Sap ABC transporter, critical to import of heme-iron for nutrition and AMPs for intracellular degradation. The Sap transporter shares a common five subunit architecture with other ABC transporters, a periplasmic substrate binding protein, two membrane associated permease proteins and two cytoplasmic ATPase proteins. Yet, we hypothesize that transporter assembly dictates substrate utilization, and thereby pathogenesis, in NTHI. Objective: The objective of this study was to determine whether coordination of protein assembly of the Sap transporter complex dictates selectivity of substrate import.

Methods: NTHI mutants deficient in ATPase and permease proteins were assessed for roles in heme-iron utilization and neutralization of AMPs.

Results: One ATPase was required for heme-iron utilization but was dispensible for AMP resistance. In contrast, the second ATPase was required for AMP resistance. NTHI strains engineered to produce select permease-ATPase complexes demonstrated differential growth and susceptibility to AMPs, supporting our hypothesis that selective coupling of permease-ATPase proteins dictates substrate import.

Conclusion: Functional studies suggest that assembly and architecture of the Sap transporter does not fit the canonical description of other ABC transporter systems. Instead, the constituent proteins of the Sap transporter may vary, and so dictate selectivity of substrate import. These studies provide potential for the development of novel therapeutic alternatives to neutralize essential import functions and thereby reduce NTHI persistence during disease.

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OM2015206

POPULATION ANALYSIS OF NASOPHARYNGEAL MICROBIOTA AMONG CHILDREN WITH ACUTE OTITIS MEDIA

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Objective: Nasopharyngeal bacterial colonization evolves rapidly during the first year of life. Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis colonize the nasopharynx early in life and are responsible for the vast majority of acute otitis media (AOM) and acute rhinosinusitis (ARS). These leading pathogens of S. pneumoniae and H. influenzae are normal and transient residents of the nasopharyngeal niche, where they are embedded in a complex microbiota of generally presumed harmless commensals.

Method: Children between 0 to 4 years of ages with AOM and healthy children were enrolled in this study. A total of 53 nasal washes, 19 middle ear effusions and 12 nasal washes from healthy infants were used for evaluating microbita by popuation analysis based on Sanger method.

Results: Children between 0 to 4 years of ages with AOM and healthy children were enrolled in this study. A total of 53 nasal washes, 19 middle ear effusions and 12 nasal washes from healthy infants were used for evaluating microbita by popuation analysis based on Sanger method.

Conclusion: Our previous study revealed the dramatic changes in the nasopharyngeal pneumococcal density during the course of upper respiratory infections. In this study, despite an abundance of data on incidence, prevalence and density of potential pathogens in NP microbiota of children and adults, the detailed composition of the NP microbial community, both during health and disease have not been studied. We, therefore, will discuss microbita in the nasopharynx for better understanding the change of nasopharyngeal bacterial flora during various infectious situations.

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OM2015313

SIMULTANEOUS DEFINITION OF HOST AND BACTERIAL TRANSCRIPTOMES FROM A SINGLE SAMPLE: A SYSTEM APPLICABLE TO MANY DISEASE STATES INCLUDING OTITIS MEDIA

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Background: Changes in gene expression contribute to bacterial and host responses to infections including otitis media. The low percentage of bacterial RNA present during infection has made it challenging to accurately define the bacterial transcriptome without enrichment; however, enrichment of bacterial RNA can introduce bias. RNA-Seq provides the potential to accurately define the host-bacterial transcriptome from a single sample, but there are still challenges to be overcome. Definition of the host-bacterial transcriptome will increase our understanding of the dynamic interplay that occurs during infection.

Objective: The objective of this study is to develop methodologies to accurately define the host-bacterial transcriptome.

Method: We have developed methodology to: 1) efficiently extract host and bacterial RNA from a single sample, 2) simultaneously reduce host and bacterial ribosomal RNA, and 3) use RNA-Seq to accurately define host-bacterial transcriptional profiles.

Results: As a proof of principle we used these methodologies to define the host-bacterial transcriptome following adherence of the major otitis media pathogen Streptococcus pneumoniae to a human cell line. We obtained sufficient host and bacterial RNA sequences to ensure a highly accurate host-bacterial transcriptional profile. Using biological replicates and relevant controls we identified and validated significant host and bacterial transcriptional changes during infection.

Conclusion: Our methodologies allow efficient and accurate definition of the host-bacterial transcriptome. Further refinement of this methodology will enable transcriptomics of specific bacteria in a polymicrobial environment. This technology will be adapted to study the interactions of different bacterial species and hosts, including the chinchilla model of pneumococcal otitis media.

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OM2015162

OTOPATHOGENIC PSEUDOMONAS AERUGINOSA ACTIVATES PKC-ALPHA TO INVADE MIDDLE EAR EPITHELIAL CELLS

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Introduction: Otitis media is a group of complex inflammatory disorders affecting the middle ear which can be acute or chronic. Chronic suppurative otitis media (CSOM) is a form of chronic OM characterized by tympanic membrane perforation and discharge. Pseudomonas aeruginosa (PA) is the most common pathogen associated with CSOM.

Objective: Our previous studies have demonstrated that PA invades middle ear epithelial cells (MEECs). However, molecular mechanisms leading to invasion of MEECs by PA are not known. The aim of this study is to characterize the role of PKC pathway in ability of PA to colonize MEECs.

Methods: MEECS were infected with PA and activation of PKC pathway was examined by Western blotting and PepTag assay. Immunocytochemistry was performed on PA infected MECCs to determine PKC activation and actin condensation. PKC signaling was disrupted by transfecting MEECs with dominant-negative form of PKC or inhibitors.

Results: We observed that PA activates PKC pathway specifically phosphorylation of PKC-alpha as compared to other isoforms in vitro and in vivo for which bacterial OprF expression is required. This activation of PKC-alpha was associated with actin condensation. Blocking PKC pathway attenuated ability of PA to invade MECCs and subsequent actin condensation. The overexpression of PKC-alpha led to enhanced invasion of MECCs by PA.

Conclusion: This study suggests that host PKC-alpha pathway is involved in invasion of MECCs by PA and subsequently to cause OM. Characterizing the role of host signaling pathway in the pathogenesis of CSOM will help in designing effective treatment modalities against the disease.

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OM2015312

REPLICATION OF GROUP C ADENOVIRUS TYPES 1 AND TYPE 5 AND MIDDLE EAR INFECTION BY STREPTOCOCCUS PNEUMONIAE IN THE CHINCHILLA MODEL OF OTITIS MEDIA

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Introduction: Adenoviral infections are associated with chronic or recurrent otitis media in children. Intranasal infection of the chinchilla with adenovirus type 1 promoted middle ear infection by Haemophilus influenzae (Suzuki and Bakaletz, 1994, Infect Immun 62:1710) whereas infection with the closely related adenovirus type 5 did not (Tong et al., 2000, Ann Otol Rhinol Laryngol 109:1021).

Objective: This study evaluates the ability of adenovirus type 5 to promote middle ear infection by Streptococcus pneumoniae in the chinchilla and the replication of adenovirus type 1 and type 5 in primary cells of the chinchilla.

Method: Seven days after intranasal inoculation with adenovirus, chinchillas were again inoculated with S. pneumoniae. Bacterial and viral loads were enumerated in nasal tissue, Eustachian tubes, and middle ear bullae. Proximal kidney tubule epithelial cells were infected in vitro with adenovirus to study virus replication.

Results: Precedent infection with adenovirus type 5 resulted in greater incidence of middle ear disease by Streptococcus pneumoniae than non-adenovirus infected animals. Infection with the hyperinflammatory adenovirus mutant dl327 induced a comparable degree of bacterial ascension into the middle ear as the wild-type adenovirus. Infection with the non-replicating adenovirus mutant H5wt300?pTP resulted in less extensive middle ear infection compared to the wild-type adenovirus. Adenovirus type 1 and type 5 transduced primary chinchilla cells with comparable efficiency. Ongoing studies seek to elucidate different cellular responses to these two closely related adenoviruses.

Conclusion: Viral replication is necessary for adenoviral-induced pneumococcal middle ear disease, possibly independent of its ability to induce inflammation.

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OM2015168

FIBRIN AND HISTONE (H4) EXPRESSION IN MIDDLE AND INNER EARS OF CHINCHILLAS WITH PNEUMOCOCCAL INFECTION

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Objective: The pathogenesis of otitis media involves bacterial factors and host defense. The middle and inner ears present a challenge to the host defense system for containment of bacteria in a large air and/or fluid filled spaces. Neutrophils are the first line of innate immune defense, they localize activation of coagulation to small vessels, and prevent tissue dissemination of pathogens through increased fibrin formation. Neutrophil extracellular traps (NETs) and biofilms have been described in middle ear effusions in experimental animals models and in humans with otitis media. We investigated the middle and inner ear cavities using histopathology and immunohistochemistry, in an effort to determine some of the host factors involved in pneumococcal infection of the ear.

Methods: Middle ears of 7 chinchillas were inoculated with 0.5 ml of 106 CFU of D39 Streptococcus pneumoniae. They were killed 2 days following inoculation and middle ear effusion harvested for CFU counts. Bullae were fixed in 10% buffered formalin. Samples were embedded in paraffin, sectioned, stained with hematoxylin and eosin and examined by histology. Adjacent sections were stained with propidium iodide, anti-histone H4, and anti-fibrin.

Results: Two days after inoculation, we observed bacteria and inflammatory cells within an extensive fibrous network in 7/7 middle ears and 3/7 inner ears. 6/7 middle ears and 1/7 inner ears stained positively with histone H4 and 7/7 middle ears and 3/7 inner ears were positive for fibrin.

Conclusion: Both fibrin and neutrophil extracellular traps are involved in the host response to pneumococcal infection in the middle and inner eas of chinchillas.

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OM2015334

GENOMIC ANALYSIS OF CARRIAGE- AND DISEASE-ASSOCIATED NONTYPEABLE HAEMOPHILUS AND H. HAEMOLYTICUS ISOLATES

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Introduction: Nontypeable Haemophilus influenzae (NTHi) associated disease, including otitis media, represents a major health burden globally. Reports suggest correlation of NTHi clades with certain virulence determinants, but no clear clinical or phylogeographic signal. There is also no clear method to distinguish between NTHi and the primarily commensal H. haemolyticus (Hh). Our aims were to determine the relatedness of common carriage NTHi genotypes and those associated with disease, and to define core genomic differences between NTHi and Hh.

Methods: Whole genome sequence data were generated from 106 Australian NTHi and Hh isolates associated with asymptomatic carriage, otitis media, bronchiectasis, or neonatal sepsis, and analysed with 124 publicly available Haemophilus spp. genomes.

Results: Phylogenetic analysis based on core orthologous SNPs showed a clear delineation between NTHi and Hh isolates, allowing us to design a specific fucP-targeted diagnostic PCR for H. influenzae. A separate cluster was also identified that may represent a new species, with an apparent tropism for the lung. Australian NTHi isolates were not distinct from non-Australian isolates. Further, we found that while 976kb of the NTHi genome was shared amongst these global strains, only 17kb (0.9%) was common to NTHi and not present in the Hh sequenced. Preliminary comparison of NTHi isolates from asymptomatic carriage and disease did not identify significant genome-level differences.

Conclusions: The clear delineation between NTHi and Hh allows for unambiguous discrimination between these species for diagnostic purposes. Genomic approaches to investigating NTHi infection will require larger GWAS studies interrogating the accessory genome.

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OM2015205

ACTINOMYCOSIS OF THE MIDDLE EAR

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Introduction: Actinomycosis of the middle ear is an exceedingly rare granulomatous anaerobic infection with an atypical and relentless course. The aim is to present the first report of such an infection in Portugal.

Case Report: Seven year-old girl with persistent pain on the right ear, conductive hearing loss and headache was referred to a tertiary university hospital with a suspected complication of congenital cholesteatoma. Otoscopic findings included a thickened, intact and bulging tympanic membrane. CT imaging showed soft tissue density filling the middle ear and mastoid with areas of bone erosion. Surgical exploration of the mastoid and middle ear showed abundant granulation tissue with sticky secretions and yellowish granules plus caseous-like material. Cultures were negative for mycobacteria and fungi but pathology reported infection by an Actinomyces species. Intravenous penicillin G was prescribed for five weeks followed by oral amoxicillin for seven weeks. Recovery was uneventful and at a six months follow-up no recurrence or complications were registered.

Conclusions: Due to its unspecific character and rarity middle ear actinomycosis may lead to a late diagnosis with increased risk of morbidity or even mortality. Microbiological studies are often negative and histopathology analysis of the middle ear contents is mandatory. Appropriate treatment must comprise surgery and a prolonged penicillin course.

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OM2015243

ANTIBODIES AGAINST THE MAJORITY SUBUNIT OF THE TYPE IV PILUS MEDIATES DISPERSAL OF NONTYPEABLE HAEMOPHILUS INFLUENZAE BIOFILMS IN A LUXS-DEPENDENT QUORUM SIGNALING MANNER

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Objective: Nontypeable Haemophilus influenzae (NTHI) is a commensal, yet also a primary causative agent of bacterial otitis media (OM). OM is persistent and difficult to treat due to the ability of NTHI to form a recalcitrant biofilm in the middle ear. Herein, we investigated the formation, maturation and dependence of NTHI biofilms on co-regulated expression of Type IV pili (Tfp) and density-dependent quorum signaling as mediated by LuxS.

Method: Using NTHI strain 86-028NP, along with isogenic, non-polar pilA and luxS mutants and their complemented variants, we assessed twitching motility, directionality of twitching motility and biofilm formation in vitro. Further, we examined the role of quorum signaling in biofilm dispersal as mediated by antibodies directed against PilA, the majority subunit of Tfp.

Results: Upon exposure of Tfp-expressing NTHI strains to antibodies against PilA, twitching motility was significantly inhibited and biomass of pre-formed biofilms was significantly reduced in vitro. We determined that this dispersal of NTHI biofilms was dependent upon expression of both PilA and quorum signaling via LuxS.

Conclusion: These data support continued PilA-targeted vaccine development and begin to uncover the mechanisms by which this therapeutic immunogen effectively resolves experimental otitis media caused by NTHI. Support: NIDCD/ NIH R01 003915

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OM2015194

THE CAVALIER KING CHARLES SPANIEL: BRACHYCEPHALY, EUSTACHIAN TUBE MORPHOLOGY AND OTITIS MEDIA PREVALENCE

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Introduction: Previously we suggested that reduction of the mid-face during the evolution of Homo sapiens underlies the high prevalence of OM in modern populations. The veterinary literature documents the high prevalence of primary secretory otitis media (OME) in brachycephalic dogs (eg. Cavalier King Charles Spaniel, CKS). Charles Darwin's Origin of Species analogized evolution through natural selection to the outcomes of artificial selection. Perhaps the prevalence of OM in CKS is analogous to that produced by evolution in humans.

Objective: Differences in Eustachian tube (ET) morphology correlate with the cranial morphology and OM prevalence in dogs.

Method: The formalin fixed ETs of 3 CKS and 3 same sized mesocephalic specimens were blocked, sectioned at 7 μm and stained with hematoxylin-eosin (H&E). Sections were imaged in Metamorph then measured using Image-J. Morphometric variables characterizing the shape and size of the cartilage, lumen, and the Tensor Veli Palatini (TVP) and Levator Veli Palatini (LVP) muscles were measured.

Results: The ET lengths were not different. The CKS TVP and LVP areas were smaller (especially nasopharyngeally) and the cartilage size was reduced (mid-portion) compared to the mesocephalic dogs. Although the TVP attachment length varied, posteriorly it is shorter in the CKS.

Conclusion: Morphometric differences in the CKS ET are consistent with cranio-facial structure (brachycephalic CKS vs mesocephalic) and the prevalence of OME. The morphologic configuration of the brachycephalic CKS dog and the mechanism of artificial selection recapitulate Darwin's explanatory paradigm, thus might be invoked in explanations of the consequences human cranio-facial evolution for OM prevalence.

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OM2015122

PALEOPATHOLOGY: MIDDLE EAR DISEASE AT MOUNT NEBO, JORDAN

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Introduction: The temporal bone is often well preserved within the archaeological context and is an important source of information on the presence/absence of middle-ear (ME) diseases in the individual and their prevalence in the population.

Objective: Evaluate the temporal bones of comingled monastic remains from Robebus Crypt, Mount Nebo, Jordan, a site dated at 530CE, for evidence of ME diseases.

Methods: A total of 56 right and 51 left temporal bones were examined by gross examination, endoscopy and microscopy to assess external and internal temporal bone pathology. All identifiable remains were classified as male and only adults were included in this analysis.

Results: The analysis documented evidence of poor mastoid air cell pneumatization (46%), ossicle erosion (62.5%), stapedial footplate fixation (3%), and mastoid lesions (33%). One case of stapedial footplate fixation was in a skull with possible Paget's disease and supports that diagnosis. The mastoid lesions resulted from incomplete fusion of the squamo-mastoid suture, known as Korner's septum. Although etiology is unknown, the clinical literature suggests a link with ME disease.

Conclusion: There is a high prevalence of abnormal mastoid development, ossicular erosion and stapedial footplate fixation in this population. These pathologies are considered to be expressions of chronic ME disease with episodes often accompanied by pain and fever, and with complications that include hearing-loss, balance disturbance and depressed speech/language proficiency. Focused evaluation of temporal bone paleopathology can provide key diagnostic features for reconstructing the impact of ME disease and complications on morbidity and mortality of past populations. Supported in part by Wenner-Gren Foundation Grant #8029

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OM2015318

INFANTS CARE IN PATHOGENESIS OF OTITIS MEDIA

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Objective: Bottle feeding and night feeding of infants are very common trends in contemporary care of infants. We analyzed the influence of the feeding factor on otitis media development in children of the first year of life.

Method: A total number of 193 children at the age 3 – 12 months were included in the study and divided in 4 groups according to type of feeding (combination of position and formula). The results of anamnesis, pneumatic otoscopy, impedance audiometry, audiometry and surgical findings (when it was necessary) were used for diagnosis.

Results: The horizontal position and night feeding correlated with the presence of middle ear fluid. Some pathogenic features of OM in infants in function of feeding position were established using data of impedance audiometry in dynamics and analysis of electro-acoustic compliance. Children from the groups with horizontal position and night feeding had OM with silent course in 79% of cases, comparing to 28 % from the groups with vertical position. Elaborated preventive measurers of middle ear reflux were effective in OM treatment.

Conclusion: The horizontal position of a child in time of feeding, night alimentation and presence of regurgitation influences on otitis media development in infants. Diagnostics of OM in infants is based on analysis of the electroacoustic compliance. Otoscopy changes in this age group are minimal and not significant for the evaluation by pediatrician. Treatment of otitis media in infants has to include changes of a child position.

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OM2015320

OTITIS MEDIA IN CHILDREN WITH RECURRENT SOMATIC PATHOLOGY

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Objective: Sub-clinical course of the middle ear pathology provokes late diagnostics, inadequate treatment and unfavorable outcome of otitis media (OM) in children. We analyzed dependence of OM clinical evolution in children from presence of recurrent somatic pathology.

Method: Three groups of children at the age between 1 and 7 years were examined: Group R consisting with 238 children with recurrent respiratory pathology, Group G – with 54 children with recurrent gastrointestinal pathology and Group H – with 142 healthy children. Monitoring of middle ear status by tympanometry and otoscopy was performed every three months during 1 year. Complete audiological assessment and otomicroscopy were carried out in children who failed the screening tests during 6 months. Treatment approaches included medical and surgical methods of OM treatment in combination with treatment of somatic pathology.

Results: We diagnosed OM with effusion in 57 % of ears from Group R, in 18 % of ears from Group G and in 15 % of ears from group H. It became chronic in 33 % of OM ears from group R, in 16 % of OM ears from group G and in 2 % of OM ears from group H. Recurrent acute OM was registered in 22 % of ears from group R, in 25 % from group G and in 2 % from group H. Chronic and recurrent forms of OM correlated to respiratory tract infection-prone children, aged younger than 5 years of life.

Conclusion: Children with recurrent somatic pathology have to be included in the middle ear monitoring. High rate of OM chronicity is predetermined by recurrent somatic pathology. These groups of patients need comprehensive diagnostics and intensive treatment, including the surgical one. In healthy children OM is a relatively rare, temporary and benign condition.

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OM2015125

DENTAL ARCH LENGTH, PALATAL VAULT HEIGHT AND TOOTH MORPHOMETRY IN CHILDREN 4-7 YEARS OF AGE WITH AND WITHOUT A HISTORY OF RECURRENT ACUTE OTITIS MEDIA

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Introduction: Eustachian tube dysfunction (ETD) is associated with an increased risk for the various expressions of otitis media (OM), including chronic OM with effusion (COME) and recurrent acute OM (RAOM). Past studies reported that children and adults with abnormal mid-face morphologies have constitutively poor ET function and evidence a higher than normal OM risk level.

Objective: Determine if those aspects of mid-face morphology reflected in the dentition of children aged 4-7 years are different between children without past OM and with a strong history of rAOM.

Results: Palate-length (17.01 + 0.06mm vs. 16.18 + 0.10mm; $p<0.01$) and palate-height (11.71 + 0.18mm vs. 12.00 + 0.15mm; $p<0.04$) were significant predictors of group assignment.

Conclusions: Subtle differences in mid-face dimensions may affect RAOM risk by constraining ET functional efficiency. Supported in part by: NIH grant DC007667

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OM2015289

DEVELOPMENT OF COMPUTATIONAL MODELS OF EUSTACHIAN TUBE FUNCTION USING MAGNETIC RESONANCE IMAGES

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Objective: Previous computational models of Eustachian Tube (ET) function were developed using high-contrast histological images. Although patient-specific information about the ET anatomy can be obtained via Magnetic Resonance Imaging (MRI), the lower contrast of these MRI images makes model construction using previous histology-based algorithms difficult. Our objective is to develop new model construction algorithms that can generate computational models of ET function using MRI images.

Methods: In this study our previous histology-based algorithm and our new MRI-applicable algorithm were applied to cross-sectional histological data obtained from n=5 adults subjects with no history of chronic OM. Briefly, high-quality outlines of ET cartilage, mucosal tissue, lumen surface and tensor (mTVP) and levator (mLVP) veli palatini muscles were used to generate histology-based models while only the cartilage and mTVP and mLVP outlines were used to generate MRI-applicable models. Results from both the histology-based and MRI-applicable models were compared and the MRI-applicable algorithm was then applied to MRI images obtained in 6-year old subjects.

Results: Preliminary results indicate that both the histology-based and MRI-applicable models were able to simulate ET opening. Ongoing simulations are being used to compare the degree of opening in these two models and to develop models of ET function based on MRI images in 6-year old subjects.

Conclusions: We have developed a new computational algorithm that can create computational models of ET function using the limited anatomical information available via MRI. Application of this technique in the future may lead to patient-specific models of ET function. Supported by NIH-DC007667.

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OM2015285

HYPOXIA INACTIVATED NA+-K+-ATP PUMP IN OTITIS MEDIA WITH EFFUSION: IN VIVO AND VITRO STUDY

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Objective: This study was designed to investigate the possible involvement of the hypoxia on the activity of Na+-K+-ATP pump in otitis media with effusion (OME) induced by dysfunction of the Eustachian tube.

Method: We adopted a soft palate approach to obstruct orifice of the eustachian tube to establish otitis media in a rat model. Then using RT-PCR , Western blot and ELISA to detect the expression of HIF-1α and activity of Na+-K+-ATPase. We also adopted BEAS-2B epithelial cell to study how hypoxia inactivated Na+-K+-ATPase . Culture media was pre-perfusion with 95% O2/5% CO2 (normal condition) and 95%N2/5% CO2 (hypoxia condition), Sodium pump current and membrane current of cells were measured by patch-clamp technique in the whole cell mode.Changes of Na+ pump current induced by hypoxia were also examined 4 min, 10min after hypoxia with Ouabain in the cells.

Result: Obstruct orifice of the eustachian tube successfully established OME rat model, the success rate was 92.3%. The expression of HIF-1α as up-regulated in middle ear mucosa in OME rat model and the activity of Na+-K+-ATPase was decreased. Vitro study showed that total sodium pump current were significantly decreased 4 min and 10min after hypoxia compared to the normal.

Conclusion: The effect of hypoxia due to obstruction of Eustachian tube on the activity of Na+-K+-ATPase and Na+ pump resulting in exudation maybe one of mechanisum of OME.

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OM2015220

INHIBITION OF PDE4B SUPPRESSES MIDDLE EAR INFLAMMATION BY UP-REGULATING CYLD

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Objective: To investigate how inflammation is tightly regulated in the pathogenesis of otitis media and identify potential therapeutic targets.

Method: Multiple experimental approaches including human middle ear cell culture in vitro and mouse otitis media model in vivo were used. The mRNA expression of CYLD and pro-inflammatory mediators was measured by real-time quantitative PCR (Q-PCR). Western blot analysis and immunofluorescence (IF) staining were used to assess the protein level of CYLD and PDE4B, and activation of c-jun N-terminal kinase (JNK). Hematoxylin and eosin (H&E) staining and otoscopic examination were used to assess the middle ear inflammation in a mouse otitis media model.

Results: The inhibition of phosphodiesterase 4B (PDE4B) significantly enhanced up-regulation of CYLD expression in response to bacteria. Interestingly, in Cyld-deficient mice, inhibition of PDE4B no longer suppressed middle ear inflammation. Importantly, ototopical post-inoculation administration of PDE4 inhibitor suppressed inflammation in a mouse otitis media model, thus demonstrating the therapeutic potential of targeting PDE4. Our results demonstrate that CYLD is a key negative regulator for tightly controlling overactive inflammatory responses in the pathogenesis of otitis media.

Conclusion: Upregulating the expression of CYLD using pharmacologic agents may represent a novel therapeutic strategy for controlling inflammation in otitis media.

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OM2015293

PDE4B MEDIATES STREPTOCOCCUS PNEUMONIAE-INDUCED UP-REGULATION OF MUCIN MUC5AC VIA ERK AND MKP-1 DEPENDENT PATHWAYS IN EXPERIMENTAL OTITIS MEDIA

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Objective: Mucus overproduction is a clinical hallmark of otitis media (OM), and mucin MUC5AC has been found to be greatly up-regulated in the middle ear mucosa of human patients with OM. Here, we investigated how phosphodiesterase (PDE) act as a positive regulator for Streptococcus pneumoniae (S. pneumoniae)-induced MUC5AC expression through in experimental otitis media.

Method: The mRNA expression of MUC5AC, PDE4B, and MKP-1 induced by S. pneumoniae was measured by real-time quantitative PCR (Q-PCR), and their protein levels were determined by Western blot analysis and immunofluorescence (IF) staining both in the human middle ear epithelial cells in vitro and in the middle ear of mice in vivo. Pathological changes of OM in eardrums of the inoculated mice were assessed under the otoscope, and pathohistological analysis was performed using H&E-stained mouse middle ear tissue.

Results: We found that PDE4B mediates up-regulation of S. pneumoniae-induced MUC5AC by inhibiting the expression of a negative regulator MKP-1, which in turn leads to enhanced MAPK ERK activation and subsequent up-regulation of MUC5AC in a cAMP-PKA-dependent manner. Moreover, we showed that topical post-infection administration of PDE4-specific inhibitor rolipram into the mouse middle ear potently inhibits S. pneumoniae-induced up-regulation of MUC5AC.

Conclusion: Identifying the novel role of PDE4B as a molecular target for inhibiting up-regulation of bacteria-induced MUC5AC via up-regulation of MKP-1 may lead to the development of new therapeutics for treating OM.

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OM2015236

MULTI-SCALE MODELS OF ADHESION DYNAMICS AND EUSTACHIAN TUBE FUNCTION IN OTITIS MEDIA PRONE POPULATIONS

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Objective: Previous studies indicate that increased mucosal adhesion, as occurs during middle ear infections, can alter the biomechanical mechanisms of ET function. However, the relative importance of mucosal adhesion on ET function in Otitis Media prone populations is not known. In this study, we used multi-scale computational models of ET opening during swallowing to investigate how mucosal adhesion alters ET function in adults, young children and cleft palate subjects.

Method: 3D finite element models of the ET were created using histological images obtained from adults (age 19-76, n=6), young children (age 4-10, n=3) and cleft palate subjects (age 1mo-2.5yrs, n=3). Non-linear springs were used to simulate adhesion within the ET lumen and tensor veli palatini (TVP) forces were applied to simulate ET opening. Variations in the degree of ET opening as a function of adhesion energy were used to identify a critical value of adhesion (Ac) above which the ET did not open (i.e. complete dysfunction).

Results: Adults demonstrated a statistically higher critical adhesion value (Ac=1.07e-2 N/m) than the value observed in young children (Ac=1.67e-4 N/m) and cleft palate subjects (Ac=2.26e-3 N/m). This data indicates that although adults can overcome relatively high values of adhesion, modest/minor increases in adhesion can result in complete ET dysfunction for young children and cleft palate subjects.

Conclusions: Multi-scale computational models of ET opening and adhesion dynamics indicates that the pathological anatomy of the ET in young children and cleft palates makes these populations very sensitive to changes in mucosal adhesion. Supported by NIH-DC007667.

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OM2015258

DOES THE OTITIS PRONE CONDITION SHOW FAMILIAL PREDISPOSITION?

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Objective: We have identified a population of otitis prone (OP) children who suffer from recurrent episodes of acute otitis media (AOM) in their first three years of life. A subset of these children, representing 5% of the total population, experience especially frequent microbiologically confirmed AOM episodes. We term these children stringently defined otitis-prone (sOP). Previously, we have shown that this condition is associated with underlying immunological defects, resulting in a failure to generate protective antibody titers against common otopathogens. We sought to determine whether the sOP condition showed a familial association.

Method: From a total population of 705 children enrolled in an ongoing NIDCD-supported study of the OP condition, we identified 92 families where 2 or more siblings were included in the study population, including 11 pairs of fraternal twins, 1 pair of identical twins and 1 set of triplets. Permutation analysis was performed to identify any familial association with the OP condition.

Results: We found significant statistical evidence that an sOP child predisposed additional siblings to become OP themselves ($p = 0.024$).

Conclusion: The sOP condition displays a familial predispostion. However, our study cannot disentangle heritability from the influence of shared environment.
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OM2015217

CHANGES IN THE EUSTACHIAN TUBE FUNCTION WITH CLEFT PALATE REPAIR

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Objective: Eustachian tube (ET) dysfunction is thought to underlie the high prevalence of otitis media (OM) in infants with cleft palate (CP). The prevalence of OM decreases after palatoplasty. It is not clear if this improvement is due to the changes in ET function due to the closure of the cleft palate and/or to the realignment of peri-tubal muscles. A study was conducted to assess the change in ET function with the cleft palate repair.

Method: Infants with non-syndromic cleft palate being followed in the cleft palate center were enrolled in the research study. Routine medical and surgical management of the children conducted as per cleft palate center and otolaryngology management protocols. The ET function testing protocol for the ears with patent ventilation tubes included force response test (FRT), to measure opening pressure (OP), steady state pressure (SP), passive resistance (PR) active resistance (AR), and dilatory efficiency (DE), measurement of increased or decreased air flow with swallowing, latter indicating constriction.

Results: Pre-operative FRT was possible in 58 of the 82 subjects enrolled. Evaluable pre-operative and post-operative FRT pairs were available in 46 ears of 24 subjects. The OP, CP, PR, and AR were measured on pre- and post-repair FRTs on 28, 11, 22, and 27 ears respectively. Of the 18 ears that DE could be calculated, constriction rate during the active function decreased from 61%, to 44% after the repair.

Conclusion: Decreased ET constriction rate may be a factor in reduced prevalence of OM after the CP repair. Supported in part by NIH Grant DC007667

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OM2015218

EFFECTS OF MIDDLE EAR GAS COMPOSITION ON EUSTACHIAN TUBE FUNCTION IN HUMANS

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Introduction: An unanswered question is whether or not Eustachian tube (ET) function (ETF) is modulated by middle ear (ME) status? Experiments in animals documented changes in ETF in response to changes in ME gas composition and also demonstrated the existence of central neural pathways connecting potential ME receptors to ET effectors.

Objective: Determine if differences in ME gas composition condition ETF.

Methods: Eight subjects (> 18 y.o., 4 females) without a significant history of otitis media were enrolled in the study. Six gas mixtures of varying CO2, O2, N2 concentrations were administered through a tympanostomy tube the recumbent subject. ETF was assessed before, during and after ME exposure to these gas compositions during test sessions at least 3 days apart. Forced response test opening and closing pressures, steady-state and active resistances, and dilatory efficiencies were recorded.

Results: For 3 of the 6 gas mixtures, opening pressure and steady-state resistance were increased significantly after exposing the ME to the gas mixture. In contrast, closing pressure and dilatory efficiency were not affected by exposure to any gas mixture and ETF was unchanged when argon was substituted for nitrogen.

Conclusions: As in animal experiments, human ETF is affected by changes in ME gas composition. Whether or not this physiological response differs between subjects with and without a history of OM remains an open question. Supported in part by NIH grant DC007667.

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OM2015144

CHANGES OF STRUCTURE OF THE TYMPANIC MEMBRANE DURING ITS TRANSFORMATION TO RETRACTION POCKET IN CHILDREN

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Objective: To study the histological and proliferation characteristics of the pars tensa retraction pocket in child. To identify of morphological signs of its transformation into cholesteatoma in child.

Methods: We examined tympanic membranes taken during operations at Pediatric ENT Department Brno with the diagnosis of retraction pocket of pars tensa in stadium III or IV by Sadde cassification.. We prepared paraffin sections stained with hematoxylin and eosin. Evaluation of continuity of basement membrane, evaluation of cellular proliferation and evaluation of collagen stroma of middle layer of tympanic membrane by immunohistochemistry.

Results: Following are findings noted as frequent in pars tensa retraction pockets: (1) acanthosis, spongiosis and intraepithelial infiltration in the external layer (squamous epithelium), (2) changes in continuity of the basement membrane, (3) regressive changes in collagen stroma, (4) atypical hypervascularisation, (5) presence of fragmentation of elestic fibres and (6) presence of inflammatory infiltrate with a high concentration of T-lymfocytes. A trend was noted along progressive grades of retraction (III-IV) for an increasing incidence of these morphological changes and abnormalities.

Conclusion: The morphological and functional changes of the retraction pocket show that there is an active process in the tympanic membrane, which probably leads to the development of cholesteatoma. A continuum of progressive histological features akin to cholesteatoma is noted with increasing grades of retraction (III-IV). We believe that our results may help otolaryngologists in decision about surgery treatment of the retraction pocket in child.

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OM2015118

BALLOON DILATION OF THE EUSTACHIAN TUBE: A SYSTEMATIC REVIEW

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Introduction: Balloon dilation (BD) of the Eustachian tube (ET) has recently emerged as a treatment for ET dysfunction (ETD).

Objective: Perform a systematic review of English publications with a focus on the indications, methods and outcomes of BDET.

Methods: Medline search.

Results: A total of 23 references were found on the use of BDET from infancy to adults. Six were in German and there was 2 presentation abstracts, 1 commentary, 2 reviews and 4 cadaver studies (not included in the review). Two retrospective studies reported on 531 ears of 305 patients and 5 prospective studies reported on 166 ears of 115 patients. None was a randomized clinical trial or included a control group. In the cohort studies, diagnosis of ETD was by history, physical exam, audiometry, tympanometry, "tube score", ETD questionnaire, ability to perform Valsalva and tubomanometry. Tubomanometry was the only objective test presumably specific to ETD but was used only in 2 studies.

Discussion: Randomized-controlled clinical trials of BDET efficacy need to be conducted on adults with well-defined disease conditions, such as: chronic effusion, retraction pockets or atelectasis without effusion or with tubes/perforations and documented ETD by objective testing. In addition to subjective assessments, repeated post-BDET testing needs to be performed to document the true risk/benefits of that procedure.

Conclusion: From the literature, there is no evidence supporting the use of BDET for treating ETD. Until controlled trials that include objective test methods to document benefit, BDET should not be done to treat ETD in adults or children.
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OM2015212

ORAL DECONGESTANT DOES NOT IMPROVE EUSTACHIAN TUBE FUNCTION

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Objective: Determine if systemic decongestant improves Eustachian tube (ET) function. Study Design: Randomized, double blind, crossover study

Methods: Twelve healthy adults with normal ear exam underwent two test sessions at least 2 weeks apart in which they breathed room air for 20 minutes, 50% N2O:50% O2 for 20 minutes (experimental period) and 100% O2 for 10 minutes (recovery period). In each of the sessions the subjects received either an immediate release pseudoephedrine HCl tablet or a placebo tablet. Swallows were continuously recorded with sub-mental surface EMG electrodes and a tympanometer measured the change in middle ear pressure (MEP) every minute. Pre-swallow MEP that were ≥10 daPa, and the decreases that were ≥5 daPa were included in the analysis.

Results: During N2O inhalation period, MEP increased on average 90±55daPa in all subjects. A total of 164 and 162 swallows were recorded at MEP values of 43±33 and 37±32daPa in the pseudoephedrine and placebo sessions respectively. In the pseudoephedrine session, 15 swallows elicited ET opening at 70±44 daPa with decrease of 19±29daPa in MEP, while in the placebo session, 17 swallows at 56±45daPa resulted in decrease of 17±19daPa in MEP.

Conclusion: Systemic decongestant does not appear to have an effect in improving the ET function by increasing the ability to open and correct the MEP difference from ambient in subjects that do not have any apparent illness or congestion. Further studies in affected subjects may demonstrate a benefit of systemic pseudoephedrine use in reducing the risk for negative MEP or otitis media. Supported in part by: NIH grant DC007667

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OM2015323

PREVENTION OF OTITIS MEDIA RECURRENCE

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Objective: Recurrence rate of otitis media (OM) after classical myringotomy with tympanostomy tube insertion (T) is relatively high. We elaborated the modified technique of surgery. The aim of our study was to compare the results of the modified and classical types of surgery.

Method:A total of 146 children with chronic otitis media with effusion (COME) and recurrent otitis media (RAOM) were treated by surgery: T and adenoidectomy. The ears were divided into two groups according to technique of T: classical (Group C) versus modified (Group M). Clinical and audiological examinations were performed every 3 months during 1 year after T. Quality of life (QL) and General health (GH) dynamics were analyzed before and in 1 year after surgery. Otomicroscopical evaluation of ears was done under general anesthesia in 12 months after the T, at the time of tube removal. Presence of retractions, adhesions, granulation tissue and effusion was noted.

Results: Recurrence of OM was characteristic for 18 % of ears from Group C and 2 % of ears form Group M. Undulating hearing loss was recorded in Group C in 31 % of cases, comparing to 6 % of Group M. Significant improvement of QL and GH after modified T in comparison to the same data after classical T was registered. Presence of attic retraction and adhesions in 1 year after T in Group C was recorded in 18 % of cases, in Group M – in 3 %.

Conclusion: Modified technique of Myringotomy with Tympanostomy tube insertion is more effective than classical one in preventing of recurrence, chronicity, hearing loss, attic retraction, adhesions, and granulation tissue in children with COME and RAOM with mucous effusion in time of surgery.

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OM2015109

INDIVIDUAL-LEVEL EFFECTS OF ANTIBIOTICS ON COLONIZING BACTERIA IN THE NASOPHARYNX

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Antimicrobial resistance is a growing problem worldwide, and though a correlation between high antibiotic prescription rates and high resistance rates has been noted on the population level, a causal relationship has yet to be confirmed. To do this, it is desirable to investigate the association between antibiotic use and resistance in the individual, something few studies have done. To evaluate the effect of heptavalent pneumococcal conjugate vaccine on acute otitis media (AOM), we performed a randomised, single-blinded trial in young children at risk of developing recurrent AOM. A total of 109 children with an onset of AOM before six months of age were included and followed for three years with clinical evaluations and repeated nasopharyngeal cultures. During the first year after inclusion, the children came for scheduled visits every other month, and during the entire three-year period, they paid a visit every time the parents suspected a new episode of AOM. In order to measure acquisition and loss rates in this cohort, where the subjects were serially cultured before, during, and after antibiotic therapy, data on antibiotic treatment and nasopharyngeal growth were entered into a Cox proportional hazards model to estimate the time-to-event for resistant AOM pathogens (pneumococci with decreased susceptibility to penicillin, beta-lactamase producing Haemophilus influenzae and beta-lactamase negative ampicillin-resistant Haemophilus influenzae or BLNAR). This design allows us to distinguish between the effects of different antimicrobials on the risk for acquisition and the risk for clinical infection once a patient was actually colonized with a resistant organism.

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OM2015283

FREE-POSTAURICULAR MUSCULO-PERIOSTEAL FLAP COMBINE WITH CARTILAGE FOR MASTOID OBLITERATION AND RECONSTRUCTION IN CANAL WALL DOWN MASTOIDECTOMY

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Objective: The primary objective of this study was to explore the clinical effects observed in the extensive middle ear cholesteatoma receiving canal wall down mastoidectomy with mastoid obliteration and reconstruction using free-postauricular musculo-periosteal flap.

Method: This was an observational case series with the extensive middle ear cholesteatoma who received canal wall down mastoidectomy with mastoid obliteration and reconstruction using free-postauricular musculo-periosteal flap at Sun Yat-set Memorial hospital. We observed the flap survival, dry-up period, hearing level and the morphological result at the different timepoint after operation(3week ,6week, 3month and 12month postoperation). For comparision, we also observed the patient without mastoid obliteration and reconstruction.

Results: Fifty-two patients were included. we performed endootoscopy to observe the recovery of surgical cavity from 3 weeks after operation, regularly 2 week-interval. 2 patients experienced the flap necrosis and the flaps were removed at 5-6 weeks after operation, the flap survival was 96.1%. The average dry-up time was 4-5 weeks after operation, we observed that the musculo-periosteal flap was much more edema at the early stage and was gradually epithelized 4 weeks later. The morphological result showed the epitympanic lateral wall was flat to the level of facial nerve ridge, which remain enough space of cavity for tympanoplasty.The hearing levels were increased recheckedat 6 months after operation.

Conclusion: mastoid obliteration and reconstuction is necessary clinical application in canal wall down mastoidectomy, free-postauricular musculo-periosteal flap is a useful material for mastoid obliteration.

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OM2015117

DEXAMETHASONE INHIBITS CYTOKINES INDUCED GEL FORMING MUCIN EXPRESSION IN HUMAN MIDDLE EAR EPITHELIUM CULTURE

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Objective: Mucins, a family of high molecular weight glycoproteins, are responsible for the rheologic properties of mucus secretions. Hypersecretion of mucins lead to muco-stasis and important pathology such as otitis media with effusion (OME) and associated hearing loss with OME. Secreted gel forming mucins (GFM) are particularly important as major contributors to the viscoelastic properties of fluid found in the middle ear during and after the inflammatory events associated with OM. Resolution of mucin hypersecretion is an important aspect for OME resolution. This study assessed the ability of an anti-inflammatory agent to modulate the cytokine induced GFM gene expression.

Method: In vitro human middle ear epithelium cultured cells (HMEEC) were treated with proinflammatory cytokines, TNFα or IL-1β in time and dose-dependent exposures. Conditions providing the highest response of targeted GFM transcripts, MUC2, MUC5AC, were used to study the impact of anti-inflammatory agent, dexamethasone, on mucin regulation. The expression of GFM genes was determined by quantitative PCR.

Results: Transcripts of the two major secreted GFM produced by HMEEC, MUC2 and MUC5AC were both significantly increased when exposed to either TNFα or IL-1β. Among the two, MUC5AC showed the most significant change. Dexamethasone significantly inhibited basal expression of MUC5AC in a time and dose dependent manner. Cytokine induced MUC2 and MUC5AC transcript expression in HMEEC was reversed to normal levels in the presence of dexamethasone.

Conclusion: The cytokine induced mucin modulation, observed in the otitis media culture model, is reversed in the presence of an anti-inflammatory agent.

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OM2015097

ROLE OF MEDICAL TREATMENT OF RISK FACTORS IN IMPROVING EUSTACHIAN TUBE DYSFUNCTION

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Introduction: Adult Eustachian tube (ET) dysfunction is associated with concurrent diseases such as nasal allergies, rhinosinusitis and/or gastroesophageal reflux disease (GERD), causing ET dysfunction (ETD) via inflammation in or around the ET.

Objective: Investigate the role of medical treatment of risk factors in improving ETD.

Method: Subjects ages 18 to 50 years with a ventilation tube inserted for previous middle ear effusion and the diagnosis of ETD as per abnormal ETF test results were enrolled. Subjects underwent a thorough history including completion of validated questionnaires for ETD (ETDQ-7), allergic rhinitis (Allergy-Control-SCORE), sinusitis (SNOT-20) and GERD (ReQuest). Subjects underwent a panel of ETF tests including: force response test, tests for effectiveness of nasopharyngeal maneuvers that enhance ETF, inflation and deflation test, static/dynamic video-endoscopy during swallowing and specific maneuvers. Subjects were then treated for a minimum of 4 weeks with topical nasal steroids, and also, if indicated, with antihistamines, antibiotics, proton pump inhibitors, H-2 blockers and/or antibiotics. After the treatment, subjects underwent a second visit consisting of the same history, examination and testing protocol.

Results: Subjects enrolled to date showed clinical improvement in the conditions they were treated for. However, improvement of symptoms and signs of the risk factors did not lead to resolution of ETD as determined by ETF test results.

Conclusion: Preliminary results suggest that medical treatment of the risk factors for ETD does not improve ETF significantly. Further studies with more subjects are needed to support this conclusion. Support: in part by NIH grant DC013167 and CSTP and CTSI programs.

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OM2015202

TYMPANOPLASTY IN PATIENTS WITH CLEFT-PALATE

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Background: Cleft-palate (CP) is a known risk factor for Eustachian tube dysfunction (ETD) and otitis media with effusion. Children with CP usually need ventilation tube(s) (VT) and receive close follow-up due to the potential sequalae or complications.

Objective: To describe surgical treatment for patients with CP that underwent tympanoplasty at a tertiary center.

Method: Retrospective chart review was conducted for patients with CP who received tympanoplasty with/without mastoidectomy between 2003-2013. Data on demographics, comorbidities, CP and otologic history, surgical treatment methods and findings, and need for multiple surgeries were recorded.

Results: A total of 21 ears from 17 patients (8 males and 9 females) met the inclusion criteria. Mean age at first surgery was 10.7 years . 12 out of 17 patients had congenital malformations, associated syndromes or other developmental delays at the time of presentation. Out of 21 ears, 11 presented with chronic suppurative otitis media (CSOM) with cholesteatoma (52%). Four ears (3 were syndromic) had conductive hearing loss related to ossicular fixation. A total of 12 mastoidectomy procedures were performed. 6 cases were canal wall up (CWU) and 1 case was converted to canal wall down (CWD) at the second surgery. Ossicular chain reconstruction was performed In 16 ears. Multiple surgeries were needed in 15 cases.

Conclusion: Despite early VT placement and regular follow-up, children with CP may develop significant otologic problems including cholesteatoma requiring tympanoplasty. High rate of CWD mastoidectomy implies advanced or recurrent disease and/or persistence of the risk factors. Supported in part by NIH grants DC007667, DC013167 and CSTP/CTSI programs.

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OM2015238

WHEN AND HOW SHOULD WE SWITCH ANTIMICROBIAL AGENTS IN THE MANAGEMENTS IN THE MANAGEMENT OF PEDIATRIC ACUTE OTITIS MEDIA?

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Objective: The decision making for selecting antimicrobial switch is sometimes difficult when we treat intractable pediatric acute otitis media (AOM). We evaluated whether an outcome could be predicted using a scoring system 3 days after initiating drug administration in the treatment of AOM.

Method: On the post-marketing clinical research of tebipenem pivoxil, we evaluated the associations among the scores at the initiation of drug administration, the variation of the scores from the baseline on 2-4 days, and the judgment of the attending physician within 3 days after completion or cancellation of the treatment.

Results: Compared to cured patients with simple AOM , redness scores of the eardrum were significantly higher (p=0.003) at the first visit, a smaller change of severity scores (p=0.049) and a larger increase of otorrhea scores were noted (p=0.049) in non-cured patients with simple AOM. In patients with recurrent/ persistent AOM, a tendency similar to those found in simple AOM was observed. According to variations of the scores for severity or for tympanic membranes, patients were classified as having Effectiveness Index (EI) A (decrease of scores >50%) and EI-B (decrease of scores <=50%); thus, all patients in the failure group were classified as EI-B.

Conclusion: The current findings suggest that the clinical response to antibiotic therapy for AOM can be predicted to some extent based on whether the patient is EI-A or EI-B at 2-4 days after initiating drug administration. The decision of effectiveness based on the variations of the scores was useful to determine the treatment strategy for patients with AOM.

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OM2015123

TARGETING THE TYMPANIC MEMBRANE IDENTIFIES NOVEL PEPTIDES THAT TRANSPORT TO THE MIDDLE EAR

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Objective: Otitis media (OM) is a common pediatric disease that leads to a substantial medical burden and may result in developmental complications and hearing loss. Systemic antibiotics are often used to treat OM; however, recently this has been challenged due to the potential for side-effects including antibiotic resistance and gastrointestinal disorders. While local treatment would avoid these issues, the tympanic membrane (TM) prevents drug penetration unless the eardrum is surgically breached. We hypothesized that the TM might harbor innate biological mechanisms that could mediate trans-TM transport.

Method: We used M13 bacteriophage display biopanning to search for mediators of trans-TM transport. A phage library displaying 1010th 12mer peptides was applied onto the rat TM in vivo. The middle ear (ME) contents were then harvested and amplified for additional rounds.

Results: Several unique but related peptides were discovered from TM screens. Each phage isolate was applied to the TM, and transport with varying kinetics was verified. These peptide-bearing phage exhibited ME recovery significantly greater than that of wild-type (WT) phage, with transport of the best being 106th above that of WT phage. Temperature and oxygen dependence suggest an active transport mechanism. A chamber assay has been developed for in vitro testing of human TM.

Conclusion: Historically, the TM has been viewed as an impermeable barrier. However, our studies reveal that it is possible to translocate small particles across the TM. The identified mechanism offers a new platform for drug design and delivery into the ME. Future aims include enhancing the transport rate, testing peptides on human TM, and identifying the transporter.

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OM2015139

SUCCESSFUL COCHLEAR IMPLANTATION IN A CASE OF OTITIS MEDIA WITH ANCA-ASSOCIATED VASCULITIS.

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Introduction: Otitis media developing to the patients with ANCA (antineutrophil cytoplasmic antibody)-associated vasculitis, such as granulomatosis with polyangitis (GPA), has attracted a lot of interest of many researchers and clinicians. Otitis media with ANCA-associated vasculitis (OMAAV) is important not only because otitis media with effusion (OME) could be the initial manifestation of GPA, but also it could follow sever sensorineural hearing loss, sometimes progressing to deafness.

Case report: We report a deaf patient diagnosed with OMAAV who underwent cochlear implantation with satisfied hearing outcome. A 49-old woman visited our clinic complaining bilateral hearing impairment and otalgia. These symptoms showed a significant improvement after the treatment with predonisolone (PSL) temporarily. Two months later the recurrence of these symptoms and newly developed left facial palsy had appeared. Head and neck CT and MRI did not show any abnormal findings. OMAAV diagnosis was made based on intractable otitis media, facial palsy, and positive PR3-ANCA. A significant improvement of her clinical manifestations with normalization of PR3-ANCA level was observed after the concurrent use of PSL and cyclophosphamide (Cy). However, her hearing loss had been gradually progressed bilaterally to the level of 100dB or over in spite of the continuous use of the drugs. She underwent unilateral cochlear implantation to her right ear. It has been very effective with almost no problem in her speech recognition.

Conclusions: OMAAV can lead to severe cochlear dysfunction. Cochlear implantation could play an important role in the treatment of the patients with sever hearing impairment caused by OMAAV.

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OM2015020

THE EFFECT OF THE LEUKOTRIENE ANTAGONIST PRANLUKAST ON PEDIATRIC ACUTE OTITIS MEDIA

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Objective: Conventional treatment for acute otitis media mainly targets bacteria with antibiotics, neglecting to control for mediators of inflammation. Mediators of inflammation, such as leukotrienes, have been identified in patients with acute otitis media (AOM) or subsequent secretory otitis media (SOM). They can damage the eustachian tube or increase mucous in the middle ear, causing persistent SOM following AOM. The objective of the present study was to evaluate whether or not administration of pranlukast, a widely used leukotriene C4, D4, and E4 antagonist, together with antibiotics could inhibit the progression to SOM.

Method: Children with AOM, who were from two to 12 years old, were randomly divided into two groups as follows: a control group in which 52 patients received antibiotic-based conventional treatment according to guidelines for treating AOM proposed by the Japan Otological Society (version 2006); and a pranlukast group, in which 54 patients were administered pranlukast for up to 28 days as well as given conventional treatment. Cases were regarded as persistent SOM when a tympanogram was type B four weeks after treatment was initiated.

Results: Two patients in the pranlukast group and 3 patients in the control group were excluded because they relapsed AOM within 28 days after initial treatment. Therefore, the analysis included 52 and 49 subjects in the pranlukast and control groups, respectively. Findings on tympanometry four weeks after initial treatment improved significantly in the pranlukast group compared with the control group ($p=0.024$, Mann-Whitney test). The percentage of patients diagnosed with persistent SOM (17.3%) was significantly smaller in the pranlukast group compared with the control group (38.8%) ($p=0.016$, chi-squared test).

Conclusion: The results indicate that combined treatment of AOM with antibiotics and a leukotriene antagonist to control inflammation is useful for preventing progression to persistent SOM.

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OM2015069

ANTROMASTOIDECTOMY IN CHILDHOOD – PAST, PRESENT AND FUTURE

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Objective: The aim of this study was to analyze and evaluate a group of pediatric patients with performed antromastoidectomy (AMT) in Department of pediatric ENT, Brno, Czech Republic (CR), in the years 1997-2013.

Method: A retrospective study.

Results: While in 1997, 35 operations were performed, and in 2002 it was 19 and in 2013 only 3 AMT. This is a decrease of 82%. The number of operations was 187, of which 90 acute and 97 chronic diseases. Until 2008, acute operation dominated, since 2008 shows conversion ratio in favor of the planned operations for chronic ear disease. Finding of microbial cause of the disease has been achieved in 58%. By 2009, the most common pathogen was S. pneumoniae (31%) since 2009, is a major pathogen of both S. pyogenes (13%) and S. peumoniae (13%), followed by H. influenzae (11%).

Conclusion: The number of AMT in child in CR has been falling rapidly. There are changes of the microbial pathogen causing the acute mastoiditis. This fact is related to the introduction of pneumococcal vaccination in CR. The decrease of acute AMT is caused also timely and racional antibiotics therapy. The decrease of planned AMT for chronic ear disease is caused by improving of diagnostic methods, early detection of the disease and introducing the use of ventilation tubes. It can be assumed that the number of AMT in child will continue to decrease. It is necessary to concentrate these patients on specialized ENT department with skilled ear surgeon.

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OM2015086

EVALUATION OF PROTECTIVE EFFECT OF BOTULINUM TOXIN TYPE A INJECTION ON SEROUS OTITIS MEDIA IN RATS

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Objective: Serous otitis media is a specific type of otitis media with effusion secreted by middle ear tissue without infection. Botulinum toxin type A (BTA) is known to inhibit the release of Acetylcholine from cholinergic nerve endings. BTA has been used for reduction of rhinorrhea in experimentally induced nasal hypersecretion in dogs after nasal application, also used to decrease allergic rhinitis symptoms. To investigate any therapeutic effect of BTA on serous otitis media in rats

Method: Twenty-four rats were included 3 groups of 8 rats in each group with BTA, Saline or Histamine administration by transtympanic route. BTA was administered (0.2 ml=20 unit) to Group 1 on day 1. Histamine (0.2 ml) was administered to all Groups on day 5. Distortion-product otoacoustic emissions (DPOAE) and auditory brainstem response (ABR) tests were conducted on all rats as baseline, on days 5, 10, 15 and, 20.

Results: The baseline evaluation of the study, revealed no statistically significant differences among the Groups. The DPOAE levels of the BTA and Saline groups significantly decreased on days 5 and 10, but not on days 15 and 20. The ABR thresholds of the groups were insignificant for all days.

Conclusion: In this study preventive effect of BTA was assessed for the formation of serous otitis media by DPOAE and ABR measurements. There was no inhibiting effect of BTA to the serous otitis media over the middle ear glands. This is the first study in the literature investigating the effect of BTA on serous otitis media.

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OM2015143

IMPACT OF PROTEIN D-CONTAINING PNEUMOCOCCAL CONJUGATE VACCINES ON NON-TYPEABLE HAEMOPHILUS INFLUENZAE ACUTE OTITIS MEDIA AND NASOPHARYNGEAL CARRIAGE

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Objective: Inclusion of protein D (PD) in the pneumococcal non-typeable Haemophilus influenzae (NTHi) PD-containing vaccine, PHiD-CV, offered potential to extend protection against acute otitis media (AOM) to include NTHi disease.

Method: We reviewed evidence from pre-clinical, clinical and post-marketing studies of PD-containing pneumococcal conjugate vaccine (PCV) to better describe the clinical utility of PD in preventing NTHi AOM.

Results: Proof-of-concept for prevention of NTHi AOM by PD-containing formulations was demonstrated in pre-clinical studies and a clinical trial (POET study in children1). A phase III trial of PHiD-CV suggested effects on NTHi AOM but did not provide conclusive evidence on efficacy (COMPAS2). Positive point estimates of efficacy against NTHi AOM observed in COMPAS and POET contrast with negative point estimates observed in a study of non-PD-containing PCV formulations (FinOM3,4). Implementation of PHiD-CV in routine clinical practice worldwide has shown encouraging reductions in OM for <2-year-olds, in some cases greater than predicted assuming efficacy against pneumococcal vaccine-types alone. Pathogen-specific data remain limited but in one study where available5, a trend towards a reduction in NTHi OM was observed. Trends for transient reductions in NTHi nasopharyngeal carriage (NPC) were observed in some randomized controlled trials (e.g. COMPAS) and post-marketing surveillance studies. Clinical significance of these findings is unclear as NTHi NPC may not be tightly linked to disease.

Conclusion: Available data suggest that PHiD-CV may decrease NTHi AOM. More evidence including pathogen-specific outcomes is warranted. PHiD-CV is not licensed in the US.

1Prymula, Lancet-2006; 2Tregnaghi, PLosMed-2014; 3Eskola, NEJM-2001; 4Kilpi, CID-2003; 5Leach, ISPPD-2014.

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OM2015049

PNEUMOCOCCAL SURFACE PROTEIN A (PSPA) -BASED SUBLINGUAL VACCINE PROVIDES PROTECTIVE IMMUNITY TO NASOPHALYNGEAL CARRIAGE OF STREPTOCOCCUS PNEUMONIAE

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Objective: Pneumococcal infection is a major upper respiratory tract disease which causes severe illness and mortality. It is important to induce safe and effective immune responses against this pathogen to prevent pnuemococcal infections. Sublingual (SL) antigen delivery, as opposed to nasal immunization, is a non-invasive route which avoids possible entry into olfactory region and the central nervous system. In this regard, we examined the potential of polyinosinic-polycytidylic acid [Poly (I:C)] as a SL adjuvant for the induction of specific immune responses against pneumococcal infection.

Method: C57BL/6 mice were SL immunized with 1 μg of recombinant pneumococcal surface protein A (PspA) and 10 μg Poly (I:C) four times at weekly intervals. One week after the last immunization, nasal washes (NWs), saliva and sera samples were collected and subjected to PspA-specific ELISA. Further, mice were challenged with S. pneumonia strain EF3030, and the numbers of CFU in NWs and nasal passage (NP) were determined.

Results: Significantly increased levels of PspA-specific secretory IgA antibody (Ab) responses were seen in NWs of mice given SL PspA plus Poly (I:C) when compared with controls. Further, higher level of PspA-specific IgG and IgA Abs were noted in sera of mice given Poly (I:C) as sublingual adjuvant. Importantly, mice given SL PspA plus Poly (I:C) showed significantly lower numbers of bacteria in the NP and NWs when compared with controls.

Conclusion: These results show that SL immunization is effective as a mucosal immunization strategy for the induction of protective pnuemococcal-specific Ab responses in both mucosal and systemic compartments.

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OM2015259

RESULTS FROM THE NATIONAL SWEDISH QUALITY REGISTER ON VENTILATING TUBE TREATMENT (1997-2012)

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Objective: To increase the knowledge and efficacy related to the two main indications for ventilation tube treatment the Swedish quality register on ventilating tube treatment was established in1997. The aim was to register, in a standardized manner, all ventilating tube procedures due to recurrent acute (rAOM) and secretory otitis media (SOM) The objective was to increase knowledge about ventilation tube practice in a large homogenous population based on information about gender, age, indications and procedure outcome.

Results: 32893 registrations were included throughout 1997 to 2012. Mean age were 4.9 years for boys and 5.3 for girls. Forty percent were girls irrespective of indication. In the youngest age group rAOM dominated as indication, but declined from age two by the rise of SOM. At 6 months follow up more than 60% of the tubes were still in place, more commonly in rAOM children and the younger ones. More than 80% of the children had a socially acceptable hearing at follow up.

Discussion and conclusion: In general the major indication for ventilating tube treatment was SOM related to hearing impairment, but rAOM played a major role in the children up to 2 years of age. This correlates well to SOM as the most common reason for hearing impairment in children and its connection with language skills impairment. The data strongly support the excellent results related to hearing improvement after ventilating tube treatment and shows that although the procedure is most commonly used in the younger ages it is frequently practiced even for older children.

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OM2015230

PNEUMOLYSIN IS ESSENTIAL FOR EARLY PHASE OF ESTABLISHING PNEUMOCOCCAL COLONIZATION IN THE NASOPHARYNX.PNEUMOLYSIN IS ESSENTIAL FOR EARLY PHASE OF ESTABLISHING PNEUMOCOCCAL COLONIZATION IN THE NASOPHARYNX.

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Objectives: Streptococcus pneumoniae is responsible for a significant proportion of the acute otitis media (AOM). The acquisition of S. pneumoniae as asymptomatic nasal colonization and transmission to others is thought to be a primary event of infection from carriers. Pneumococcal infections invariably begin with nasopharyngeal colonization on mucosal surfaces. In this study, we investigated the role of pneumolysin (PLN) in nasopharyngeal carriage with S. pneumoniae in an established mouse colonization model.

Methods: 6-week-old CBA/N mice were inoculated intranasally with different numbers of variable pneumococcal cells in 10 µl PBS in the absence of anesthesia. The nasal cavity of each mouse was washed by flushing 1 ml of PBS into the trachea and out through nostrils. And washed nasal tissues were excised to evaluate CFUs of pneumococci.

Results: PLN of wild type strains were higher identified in both nasal washes and washed nasal tissues than PLN knockout transformants at early phase for establishing nasal colonization (at day 1 to 3).

Conclusions: In the current studies, we focus on the effects of PLN on developing nasal carriage with S. pneumoniae in mice model to address the question why pneumococci have virulent factors that allow them to invade local tissue and causes severe lethal infections. PLN will have important roles at the onset of nasal colonization and subsequent development of nasal carriage.

SCHEDULE AT A GLANCE

SUNDAY, JUNE 7		
03:45 PM	**05:00 PM**	Newcomer's gathering and orientation session
06:00 PM	**08:00 PM**	Welcome Reception
MONDAY, JUNE 8		
8:00 AM	**8:30 AM**	Welcome & Special Remarks
8:30 AM	**9:45 AM**	Plenary 1: CSOM
9:45 AM	**10:15 AM**	Coffee Break
10:15 AM	**11:15 AM**	Parallel Sessions: Minsymposium 1 & 2
11:15 AM	**12:00 PM**	Parallel Sessions: Podium 1 & 2
12:00 PM	**01:30 PM**	Lunch
01:30 PM	**02:30 PM**	Parallel Sessions: Panel 1 & NIH Workshop
02:30 PM	**03:15 PM**	Parallel Sessions: Podium 3 & 4
03:15 PM	**03:45 PM**	Coffee Break
03:45 PM	**05:00 PM**	Parallel Sessions: Panel 2 & Workshop 1
05:00 PM	**05:30 PM**	Parallel Sessions: Podium 5 & Workshop 1 (continued)
05:30 PM	**08:00 PM**	Poster Reception
TUESDAY, JUNE 9		
8:00 AM	**9:45 AM**	Plenary 2: Current clinical practice guidelines for OM
9:45 AM	**10:15 AM**	Coffee Break
10:15 AM	**11:15 AM**	Parallel Sessions: Minsymposium 3 & 4
11:15 AM	**12:00 PM**	Parallel Sessions: Podium 6 & 7
12:00 PM	**01:30 PM**	Lunch
01:30 PM	**02:30 PM**	Parallel Sessions: Panel 3 & 4
02:30 PM	**03:15 PM**	Parallel Sessions: Podium 8 & 9
03:15 PM	**03:45 PM**	Coffee Break
03:45 PM	**04:45 PM**	Parallel Sessions: Workshop 2 & Panel 5
04:45 PM	**05:30 PM**	Parallel Sessions: Panel 6 & 7
05:30 PM	**06:30 PM**	ISOM General Assembly (members only)
WEDNESDAY, JUNE 10		
8:00 AM	**9:45 AM**	Plenary 3: Vaccine
9:45 AM	**10:15 AM**	Coffee Break
10:15 AM	**11:15 AM**	Parallel Sessions: Minsymposium 5 & 6
11:15 AM	**12:00 PM**	Parallel Sessions: Podium 10 & Minisymposium 6 (continued)
12:00 PM	**01:30 PM**	Lunch
01:30 PM	**02:30 PM**	Parallel Sessions: Panel 8 & 9
02:30 PM	**03:15 PM**	Parallel Sessions: Podium 11 &12
03:15 PM	**03:45 PM**	Coffee Break
03:45 PM	**04:45 PM**	Parallel Sessions: Podium 13 & 14
04:45 PM	**05:30 PM**	Parallel Sessions: Podium 15 & 16
07:00 PM	**10:00 PM**	ISOM Banquet
THURSDAY, JUNE 11		
8:00 AM	**9:45 AM**	Parallel Sessions: Minisymposium 7 & 8
9:45 AM	**10:15 AM**	Coffee Break
10:15 AM	**12:00 PM**	Plenary 4: OMICS
12:00 PM		Closing Remarks and Symposium Adjournment