

PROGRAM and ABSTRACTS

of the

One Hundred Forty-Fifth Annual Meeting

AMERICAN OTOLOGICAL SOCIETY, INC.

April 21-22, 2012

Elizabeth Ballroom DE

Manchester Grand Hyatt San Diego, CA

OFFICERS JULY 1, 2011—JUNE 30, 2012

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Accreditation Statement: The American Otological Society is accredited under the entity *the AOS/ANS Joint Council* as a provider for continuing medical education for physicians by the Accreditation Council for Continuing Medical Education (ACCME).

Credit Statement:

The AOS/ANS Joint Council designates this educational activity for a maximum of 8 AMA PRA Category 1 Credit $(s)^{\text{TM}}$. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Certificate of Attendance will be issued at the close of the meeting upon completion of the questionnaire required by us for the certifying organizations.

The AOS/ANS JOINT COUNCIL MISSION

Organizational Structure: The AOS/ANS Joint Council is the organizational entity that oversees the Continuing Medical Education activities of two sister societies, the American Neurotology Society and the American Otological Society. The AOS/ANS Joint Council reflects the complementary and collaborative missions of these two societies in their commitment to improving the science, knowledge and care of patients with otologic, neurotologic and skull base disorders.

The AOS/ANS Joint Council provides strategic direction and oversight for the Otology & Neurotology Journal and fosters collaboration and cross-pollination of research, advances and approaches to care that reflect the ACGME/ABMS competencies. The formalization of the long-standing collaboration between the AOS and ANS reflects our commitment to the challenges identified in recent Institute of Medicine recommendations focused on a commitment to collaborative and team based care.

Purpose: The AOS/ANS Joint Council provides strategic direction and oversight for the common interests, values and priorities in otology and neurotology. This Council is designed to maximize the expertise from both sister societies, create opportunities for educational cross-pollination, enhanced dialogue and advancement in the science and standards of care for patients with otology and neurotology conditions and move this field toward collaborative and seamless team based education and care. The AOS/ANS Joint Council oversees the Corporation named Otology & Neurotology, Inc. The objective of this Corporation is to publish scientific advancements in the field of medicine with the purpose of promoting and advancing the profession through this educational endeavor. The primary vehicle for this objective is a publication entitled "Otology & Neurotology".

The AOS/ANS Joint Council is dedicated to improving public health care through the development, dialogue and dissemination of advances in evidence-based diagnosis and management of otologic, neurotologic and related skull base disorders. The focus on the scientific advances in these combined fields is translated into approaches to quality care that are consistent with ACGME/ABMS general competency areas and the Institute of Medicine recommendations.

Target Audience: The primary target audience that are served through *the AOS/ ANS Joint Council* include members of both the American Otological Society and the American Neurotology Society as well as healthcare professionals in the fields of otology, otolaryngology neurotology and skull base research and healthcare. The members served include physicians, otologists, neurotologists, residents, fellows, researchers, nurses, occupational and speech therapists and other healthcare professionals who are involved in the care of patients with otologic and neurotologic conditions.

Activities: The educational activities under the auspices of *the AOS/ANS Joint Council* will continue to utilize the existing and well-respected live conference/ annual meeting formats that are currently provided through the ANS and AOS. Since many of the members of these societies are members of both groups, *the AOS/ANS Joint Council* plans to explore new strategies to develop educational activities that can maximize the benefits of this collaboration and leverage the science, evidence and standards of care in both otology and neurotology to the benefit of the patients with these conditions. The Otology & Neurotology Journal provides an additional vehicle for further collaboration and dissemination of new information, science and standards of care.

Content: The content areas of otology and neurotology will continue to serve as the primary educational focus for the CME program under the auspices of *the ANS/AOS Joint Council*. The educational efforts will also highlight the ACGME/ABMS general competencies within the context of this field and relate the significance of communication, professionalism, patient safety and systems-based practice within these workplace environments.

Expected Results: The expected outcomes from these live educational activities are received through multiple sources including immediate post conference evaluations, AOS/ANS leadership and membership feedback, and commitment to change reporting. The other expected outcome from this CME program is continued development of new evidence-based science, dissemination of ongoing research in the clinical areas of otology and neurotology.

2012 AOS Spring Meeting CME Activity Planning

Each Attendee of the AOS 2011 Spring Meeting was asked to complete an evaluation at the close of the scientific program. Respondents provided extensive feedback on what they learned from the Program as well as what they would like to see addressed at an upcoming AOS CME activity. Responses were collected and summarized from 204 attendees.

Based on the response, the following data regarding professional practice gap among attendees was noted:

- Inconsistent diagnosis and treatment of vestibular disorders, specifically, tinnitus and Meniere's disease.
- Under-utilization of improved diagnostic strategies for patients with vestibular dysfunction.
- Inconsistent awareness or ability to implement strategies for improving conductive hearing loss with the long term goal of expanding opportunities for research, diagnosis, and treatment options.
- The lack of awareness/knowledge as to expected results and limitations of cochlear implants.

IDENTIFICATION OF PROFESSIONAL PRACTICE GAPS

Professional practice gaps are the variations or differences in the practice patterns when compared to current evidence, standards of care or clinical guidelines that are designed to provide quality of care to patients. Authors were asked to describe how to translate identified professional practice gaps into educational needs; how the need is expressed in terms of knowledge, competence, performance and patient outcome; what should the learners be able to apply to their profession after they participate in the educational activity; list the desired results in terms of changes in physician knowledge, competence, performance and/or patient outcome.

The following competency areas will be addressed through this CME activity/scientific session.

- 1. **Patient Care** that is compassionate, appropriate, and effective for the treatment of health problems and the promotion of health.
- 2. Medical Knowledge about established and evolving biomedical, clinical, and cognate (e.g. epidemiological and social-behavioral) sciences and the application of this knowledge to patient care.
- 3. **Practice-Based Learning and Improvement** that involves investigation and evaluation of their own patient care, appraisal and assimilation of scientific evidence, and improvements in patient care.
- 4. Interpersonal and Communication Skills that result in effective information exchange and teaming with patients, their families, and other health professionals.
- 5. **Professionalism** as manifested through a commitment to carrying out professional responsibilities, adherence to ethical principles, and sensitivity to a diverse patient population.
- 6. **Systems-Based Practice** as manifested by actions that demonstrate an awareness of and responsiveness to the larger context and system of health care and the ability to effectively call on system resources to provide care that is of optimal value.

Goals & Objectives

The overall goal of this course is to provide up-to-date information that focuses on the advancement of the scientific and clinical evidence that supports advances in otologic and neurotologic care to patients. The **target audiences** are physicians, otologists, residents, fellows, and researchers in the fields of otology and neurotology, as well as nurses, occupational and speech therapists, audiologists, and other healthcare professionals with specific interests in otologic and neurotologic disorders.

Learning Objectives:

1) A complete overview of the development of vestibular testing and our future needs by an expert that developed many of the tests.

2) A complete overview of the pathophysiological basis of tinnitus and various rationales for treatment by an international tinnitus expert.

3) A view into the future with cochlear implantation in at risk populations by a panel of implant experts.

4) A complete overview of the long-term outcomes of semicircular canal dehiscence surgery from a well established expert's experience.

Desired Results:

1) The attendees will be able to utilize the significant clinical and research experience in vestibular testing presented by the Guest of Honor. This will allow a physician to determine the current indications, procedures and expected results in vestibular testing.

2) The attendees will be able to utilize the significant clinical and research experience in the pathophysiology of tinnitus, presented by the basic sciences lecturer. This will allow a physician to develop a rationale for appropriate treatment in patients with tinnitus.

3) The attendees will gain insight into future expansion of cochlear implants in at risk populations. This will allow a physician to discuss implantation with patients and family in such groups as Alzheimer's disease and autism.

4) The attendees will gain more extensive knowledge in the outcomes of surgery for superior semicircular canal dehiscence, improving their selection of appropriate candidates.

*** American Otological Society, Inc.***

All authors, presenters, panelists, guest lecturers, AOS Council members, and Program Advisory Committee members, administrative staff and any other contributing individuals who may be in a position to control content of a CME activity were required to complete a Disclosure/Conflict of Interest/Attestation declaration prior to consideration for presentation or appointment to a CME planning committee. All potential conflicts of interest were resolved by members of the AOS Council prior to this CME activity taking place.

(See page 4 for complete AOS Disclosure Statement and Resolution of Conflict process)

Position Statement: Any presentations, conversations, exhibits, or other meeting communications, including description of the use of drugs or devices, does not imply nor constitute endorsement of any company, product, application or use by the American Otological Society.

All Authors/Presenters are required to comply with the following Disclosure Statement prior to submitting their paper to the American Otological Society. All authors/presenters were advised that the submitted paper becomes the property of *Otology & Neurotology* and cannot be reprinted without permission of the Journal.

FULL DISCLOSURE POLICY STATEMENT

In accordance with the ACCME Essential Areas and Policies, it is the policy of the American Otological Society and The AOS/ANS Joint Council, as the ACCME Accredited CME provider, to ensure balance, independence, objectivity and scientific rigor in all of its educational activities. All authors, panelists, guest lecturers, CME and Program committee members, moderators, administrative staff and any other contributing individuals who may be in a position to control content of a CME activity are responsible for disclosing any potential conflict of interest or any significant financial or other relationships with the manufacturer(s) of any commercial product(s) or provider (s) of any commercial service(s) discussed in an educational presentation. The purpose of this form is to identify and resolve all potential conflicts of interests that arise from financial relationships with any commercial or proprietary entity that produces healthcare-related products and/or services relevant to the content you are planning, developing, or presenting for this activity. This includes any financial relationships within the last twelve months, as well as known financial relationships of your spouse or partner.

To further ensure there is no relevant conflict of interest, members of the AOS Council, the Program Advisory Committee, The AOS/ANS Joint Council and/or Program moderators will review manuscripts three weeks prior to the CME activity to identify, address, and resolve any potential conflict of interest. In the event a relevant conflict of interest is noted, one or more of the following actions will be initiated. The presenter will be contacted and asked for clarification or additional information; the presenter will refrain from making recommendations regarding products or services and limit presentation to current evidence/science/research; or an alternate speaker will be chosen in which no conflict of interest is disclosed. The intent of this policy is not to discourage speakers who have relationships with commercial entities from presenting, but to identify these relationships to the listeners so that they may form their own judgments. Failure to disclose this information on submission forms, or failure to return this disclosure form will result in exclusion from this activity and from future CME activities for up to two years. The American Otological Society is committed to the non-promotional advancement of knowledge and science and to a free exchange of medical education in otology and neurotology.

PUBLICATION STATEMENT

The material in this abstract, <u>(Name of Abstract)</u>, has not been submitted for publication, published, nor presented previously at another national or international meeting and is not under any consideration for presentation at another national or international meeting including another COSM society. The penalty for duplicate presentation/ publication is prohibition of the author and co-authors from presenting at a COSM society meeting for a period of three years.

Submitting Author's Signature (required)

FACULTY DISCLOSURES

American Otological Society Council

- Herman A. Jenkins, MD Advanced Bionics Advisory Panel—Middle Ear Devices
- Paul R. Lambert, MD Otonomy Clinical Trial; Investigator and Consultant - Meniere's Disease
- Steven A. Telian, MD Cochlear Americas (no activity in over 2 yrs) Cochlear Implants
- Debara L. Tucci, MD No Disclosures
- Bruce J. Gantz, MD Advanced Bionics Consultant, Cochlear Implants; Cochlear Corp - Consultant, Cochlear Implants
- C. Phillip Daspit, MD No Disclosures
- John W. House, MD No Disclosures

D. Bradley Welling, MD, PhD - No Disclosures

Administrators:

Shirley Gossard –No Disclosures Kristen Bordignon –No Disclosures

2012 Program Advisory Committee

- Paul R. Lambert, MD Otonomy Clinical Trial; Investigator and Consultant - Meniere's Disease
 Herman A. Jenkins, MD - Advanced Bionics Corp—Middle Ear
- Herman A. Jenkins, MD Advanced Bionics Corp—Middle Ear Active Devices
- D. Bradley Welling, MD No Disclosures
- Cliff A. Megerian, MD Cochlear Corp Surgeon's Advisory Board, Cochlear Implants; Grace Corp Surgeon's Advisory Board Middle Ear Implants; Quark Pharmaceuticals Consultant -Inner Ear Drugs
- Charles C. Della Santina, MD Cochlear Corp Surgical Advisory Committee, Cochlear Implants; Med El Codrp Surgical Advisory Committee, Cochlear Implants; Labyrinth Dences UC Ownership Interest, Vestibular Prosthesis; Novartis; Glaxo Consultant, Pharmaceuticals

Brenda Lonsbury-Martin, PhD - No Discisoures

- P. Ashley Wackym, MD No Disclosures
- Jay T. Rubinstein, MD Advanced Bionics Corp Consultant, Research Funding; Cochlear, Ltd. - Consultant, Resarch Funding
- Lawrence R. Lustig, MD Advanced Bionics Corp Medical Advisory Board, Cochlear Implants; Med El Surgical Advisory Board, Cochlear Implants
- Carol A. Bauer, MD No Disclosures
- Craig A. Buchman, MD Advanced Bionics Advisory Board; Med El Corp. Advisory Board; Cochlear Corp. Advisory Board

Primary Authors/Contributing Authors were informed and required to comply with the following prior to submitting their abstract:

1. Disclose financial relationships with a commercial entity producing health-care related products and/or services.

2. Authors were informed a member of the AOS Program Advisory Committee and *The AOS/ANS Joint Council*, as the ACCME Accredited CME provider, would review the content of the presentation prior to the CME activity taking place; Primary author would provide educational content and resources in advance as requested. (if applicable)

3. If Author/Presenter has been trained or utilized by a commercial entity or its agent as a speaker (e.g., speaker's bureau) for any commercial interest, the promotional aspects of that presentation will not be included in any way with this activity. 4. If discussing any product use that is off label, Author/Presenter required to disclose that the use or indication in question is not currently approved by the FDA for labeling or advertising.

5. If discussing specific healthcare products or services, will use generic names to the extent possible. If need to use trade names, will use trade names from several companies when available, not just trade names from any single company.

6. If providing recommendations involving clinical medicine, they will be based on evidence that is accepted within the profession of medicine as adequate justification for their indications and contraindications in the care of patients. All scientific research referred to, reported or used in CME in support of justification of a patient care recommendation will conform to the generally accepted standards of experimental design, data collection and analysis.

7. If presenting research funded by a commercial company, the information presented will be based on generally accepted scientific principles and methods, and will not promote the commercial interest of the funding company.

***Disclosures—Oral Presentations *** Saturday April 21, 2012, Scientific Session Oral Presentations: Authors/Presenters & Panel Participants (listed in order of presentation)

1:10

Guest of Honor

The following individual has nothing to disclose Vicente Honrubia, MD

1:25

The following individuals have nothing to disclose Guangwei Zhou, MD, ScD Dennis Poe, MD Quinton Gopen, MD

1:34

The following individuals have nothing to disclose M. Geraldine Zuniga, MD Roni E. Dinkes, AuD John P. Carey, MD Michael C. Schubert, PT, PhD Jeremy Walston, MD Yuri Agrawal, MD

1:43

The following individuals have nothing to disclose Bryan K. Ward, MD Yuri Agrawal, MD Charles C. Della Santina, MD, PhD Charles J. Limb, MD Lloyd B. Minor, MD John P. Carey, MD ***Disclosures—Oral Presentations*** Saturday April 21, 2012, Scientific Session (Cont)

1:52

The following individuals have nothing to disclose Audrey P. Calzada, MD Ivan A. Lopez, PhD David Elashoff, PhD Gail Ishiyama, MD Akira Ishiyama, MD

2:01

The following individuals have nothing to disclose Clarice S. Clemmens, MD Michael J. Ruckenstein, MD, MS

2:15

Basic Science Lecture The following individual has nothing to disclose Carol A. Bauer, MD

3:15

The following individual disclose Richard A. Chole, MD, PhD - Ownership CheckSite Medical, Inc. Surgical safety systems The following individuals have nothing to disclose Joseph Zenga, MD Patricia M. Gagnon, MS Joseph Vogel, PhD

3:24

The following individuals have nothing to disclose Saad A. Alsaleh, MD Brian W. Blakley, MD, PhD Zameel A. Dewji, MD Kaiser A. Qureshy, MD Sylvie T. Berard, AuD Ling Xie, RA

3:33

The following individuals have nothing to disclose Yukiko Iino, MD, PhD Hiromi Kanazawa, MD Akihiro Shinnabe, MD Naohiro Yoshida, MD, PhD

3:42

The following individual disclose Adrien A. Eshraghi, MD - MedEl Corp - Research Support The following individuals have nothing to disclose Guyan A. Channer, MD Esperanza Bas, PhD Fred F. Telischi, MEE, MD Chhavi Gupta, PhD John T. Dihn, BS Ly Vu, BS Thomas R. Van De Water, PhD

Disclosures—Oral Presentations Saturday April 21, 2012, Scientific Session (Cont)

3:51

The following individual disclose

M. Jennifer Derebery, MD - Sonitus Medical Corp. Consultant Board of Directors; Science Advisory Board -Stockholder

The following individuals have nothing to disclose Andrew Vermiglio, PhD Maria Vargas, AuD Marilee Potthoff

4:05

The following individuals have nothing to disclose Georgios Stamatiou, MD Konstantina M. Stankovic, MD, PhD

4:14

The following individuals have nothing to disclose Theodore R. McRackan, MD Fitsum A. Reda, MS Jack H. Noble, PhD Alejandro Rivas, MD Benoit M. Davant, PhD Robert F. Labadie, MD, PhD

4:23

The following individuals have nothing to disclose C. Eduardo Corrales, MD Richard K. Gurgel, MD Robert K. Jackler, MD

4:32

The following individuals have nothing to disclose Charles A. Mangham Jr., MD, MS A. Davis Mangham

4:41

The following individuals have nothing to disclose Maggie A. Kuhn, MD David R. Friedmann, MD Leon S. Winata, BS Jan Eubig, MD Bidyut K. Pramanik, MD John Kveton, MD Darius Kohan, MD Saumil N. Merchant, MD Anil K. Lalwani, MD

Disclosures—Oral Presentations Sunday, April 22, 2012, Scientific Session

7:30

The following individuals have nothing to disclose Michael B. Gluth, MD John L. Dornhoffer, MD

7:39

The following individuals disclose

Erdem Yavuz - Intelligent Hearing Systems - Employee Rafael E. Delgado - Intelligent Hearing Systems - Director and Stock Owner and Co Owner & Employee **The following individuals have nothing to disclose** Krzysztof Morawski Kazimierz Niemczyk Aleksandra Hryciuk Fred F. Telischi, MD

7:48

The following individuals have nothing to disclose Lauren A. Kilpatrick, MD Fu-Shing Lee, PhD Paul R. Lambert, MD

7:57

The following individuals have nothing to disclose Michael B. Gluth, MD John L. Dornhoffer, MD Aaron M. Metraile, MD

8:06

The following individual disclose

Bradley W. Kesser, MD - Nasco, Inc. Dr Kesser receives royalties for a simulator he patented. This is unrelated to the content of this abstract/presentation.

The following individuals have nothing to disclose

Brian D. Nicholas, MD Kaelyn Krook, BS Lincoln Gray, PhD

8:15

The following individual disclose Michael Hoa, MD- One-time consultant to Cochlear Corporation The following individuals have nothing to disclose John W. House, MD Fred H. Linthicum, Jr., MD

Disclosures—Oral Presentations Sunday, April 22, 2012, Scientific Session (Cont)

8:29

The following individuals have nothing to disclose Ashkan Monfared, MD Gerald Mitteramskogler, MS Simon Gruber, Ms Kenneth Salisbury, PhD Juergen Stampfl, PhD Nikolas H. Blevins, MD

8:38

The following individuals have nothing to disclose Hossein Mahboubi, MD MPH Peyton Paulick, MS Saman Kiumehr, MD Mark Merlo, PhD Mark Bachman, PhD Hamid R. Djalilian, MD

8:47

The following individuals disclose

J. Thomas Roland, Jr., MD - Member of surgical advisory board for Cochlear Corp. and Advanced Bionics **The following individuals have nothing to disclose** Maura K. Cosetti, MD David R. Friedmann, MD Selena E. Heman-Ackah, MD, MBA David Drimmer, BS Susan B. Waltzman, PhD

8:56

The following individuals have nothing to disclose David A. Gudis, MD Douglas C. Bigelow, MD Michael J. Ruckenstein, MD

9:05

The following individual disclose

Clough Shelton, MD - Cochlear Corp- Research Grant for percutaneous implants to study speech processing strategies

The following individual has nothing to disclose Frank M. Warren, MD

Disclosures—Oral Presentations Sunday, April 22, 2012, Scientific Session (Cont)

9:14

The following individuals disclose

 Peter S. Roland, MD - Alcon Labs (speaker, consultant, honorarium), MedEl Corporation (advisory board, consultant, honorarium), Advanced Bionics (advisory board, consultant, honorarium), Cochlear Corporation (advisory board, consultant, honorarium), and GlaxoSmithKline (speaker, honorarium)
Brandon Isaacson, MD - Corresponding Author Medtronic

Midas Rex Institute (consultant, course instructor) The following individuals have nothing to disclose

Evan Walgama, MD

J. Walter Kutz, Jr., MD

9:58

The following individuals disclose

Oliver F. Adunka, MD - Receive research support from: Advanced Bionics Corp, Med-EL Corp Cochlear Inc. Douglas C. Fitzpatrick, PhD - Receive research support from: Advanced Bionics Corp, Med-EL Corp Cochlear Inc. **The following individuals have nothing to disclose** John M. Pike, BS Baishakhi Choudhury, MD Omar Awan, BS Kristine Faulk, BS

10:07

The following individuals have nothing to disclose David Bakhos, MD S. Roux E. Lescanne, MD, PhD F. Bonnet-Brilhaut, MD, PhD N. Bruneau, PhD

10:16

The following individuals have nothing to disclose Stanley Pelosi, MD Alejandro Rivas, MD David Haynes, MD Marc L. Bennett, MD Robert F. Labadie, MD, PhD Linda Hood, PhD Andrea Hedley-Williams, AuD George B. Wanna, MD

10:25

The following individuals have nothing to disclose Ricardo F. Bento, MD, PhD Maria Valeria S.G. Gomez, PhD Rubens V.B. Neto, MD, PhD Robinson Koji Tsuji, MD, PhD Anna Carolina O. Fonseca, MD Liliane S. Ikari, MD ***Disclosures—Oral Presentations*** Sunday, April 22, 2012, Scientific Session (Cont)

10:34

The following individuals have nothing to disclose Jack H. Noble, PhD Benoit M. Dawant, PhD Rene H. Gifford, PhD, Robert F. Labadie, MD, PhD

10:43

The following individuals disclose: Hold intellectual property rights to the device being studied.

Leo Ling, PhD

Steven M. Bierer, PhD

Kaibao Nie, PhD

James O. Phillips, PhD

Jay T. Rubinstein, MD, PhD - A paid consultant and has received research funding from Cochlear, Ltd, the manufacturer of the device and holds intellectual property rights to the device being studied.

The following individual have nothing to disclose Justin S. Golub, MD

11:00

The following individuals disclose

J. Thomas Roland, Jr., MD - Member of the surgical advisory board for Cochlear Corporation and Advanced Bionics

Mario Svirsky, PhD - Cochlear Americas, Research Support; Advanced Bionics, Research Support

Nancy Young, MD - Cochlear Americas, Medical Advisory Board; Advanced Bionics, Medical Advisory Board

The following individuals have nothing to disclose Daniel M. Zeitler, MD

Larry Humes, PhD

The Accreditation Council for Continuing Medical Education (ACCME)

requires that all presenters, contributing authors, guest speakers, Program committee members, & Council members involved in planning and implementing CME activities disclose all financial relationships with commercial interests. All authors have complied with the above. Any potential conflicts of interest were resolved to the satisfaction of the AOS Council, the AOS Program Advisory Committee, the AOS/ANS Joint Council and a select group of non-conflicted peers prior to this CME activity taking place.

2012 Program Advisory Committee Carol A. Bauer, MD Craig A. Buchman, MD Charles Della Santina, MD, PhD Paul R. Lambert, MD Brenda Lonsbury-Martin, PhD Lawrence R. Lustig, MD Cliff A. Megerian, MD Jay T. Rubinstein, MD P. Ashley Wackym, MD D. Bradley Welling, MD, PhD

146th AOS Annual Spring Meeting April 13-14, 2013 J. W. Marriott Grande Lakes Orlando, FL

Abstract Deadline: October 15, 2012 Abstract Instructions and submission form will be available on website after July 1, 2012

Website-www.americanotologicalsociety.org

All primary and contributing authors are required to sign a disclosure/conflict of interest document at time of abstract submission in order for the abstract to be considered by the Program Advisory Committee

Journal Requirements/Instructions to Authors/Presenters

The journal of **OTOLOGY & NEUROTOLOGY** no longer accepts paper manuscripts. All manuscripts must be submitted online **three weeks** prior to the annual meeting, via the journal's website: https://www.editorialmanager.com/on/ Instructions for registering, submitting a manuscript, and the author guidelines can all be found on the Editorial Manager site: https:// www.editorialmanager.com/on/.

One copy of the manuscript (.pdf format) is to be submitted electronically to the AOS Administrative Office a minimum of three weeks prior to the Annual Meeting for content and conflict of interest review and resolution.

Administrative Office Address

American Otological Society, Inc. Shirley Gossard, Administrator 3096 Riverdale Road The Villages, Florida 32162 Ph: 352-751-0932 Fax: 352-751-0696 Email: segossard@aol.com Website: www.americanotologicalsociety.org

AOS CHANGE OF ADDRESS

American Otological Society, Inc. Kristen Bordignon, Administrator 1980 Warson Road Springfield, IL 62704 Ph: 217-638-0801 Fax: 217-679-1677 Email: otosociety@yahoo.com Important-please-noiethe following change-Effective July 1,2012

NAMES AND ADDRESSES OF PRIMARY AUTHORS

Saad A. Alsaleh, MD

Otolaryngology Resident Dept of Otolaryngology - HNS Health Sciences Centre, GB421 - 820 Sherbrook Street Winnipeg, Manitoba, R3A 1R9, Canada

David Bakhos, MD

ENT department CHU de Tours INSERM U930 3700 Tours France

Richardo F. Bento, MD, PhD Rua Dr. Enéas de Carvalho Aguiar 255 sala 6167 05403-000 Sao Paulo - SP Brazil

Audrey P. Calzada, MD 1234 Sixth Street, Apt 210 Santa Monica, CA 90401

Guyan A. Channer, MD Otolaryngology Department University of Miami Miller School of Medicine 1120 NW 14th Street (5th Fl) Miami, FL 33136

Richard A. Chole, MD, PhD Campus Box 8115 660 South Euclid Avenue St. Louis, MO 63131

Clarice S. Clemmens, MD Dept of Otorhinolaryngology 3400 Spruce St. 5 Silverstein Building Philadelphia, PA 19104

C. Eduardo Corrales, MD 801 Welch Road Stanford, CA 94305

Maura K. Cosetti, MD

Department of Otolaryngology New York University SOM 550 First Ave, Suite 7Q New York, NY 10016 Jennifer Derebery, MD House Research Institute 2100 W 3rd St Los Angeles, CA 90057

Michael B. Gluth, MD

4301 W. Markham St., #543 Little Rock, AR 72205

Justin S. Golub, MD

Dept of Oto-HNS Univ of Washington 1959 NE Pacific St Box 356515 Seattle, WA 98195-6515

David A. Gudis, MD

Hospital of the University of Pennsylvania 3400 Spruce Street, 5 Silverstein Building Philadelphia, PA 19104

Lauren A. Kilpatrick, MD

135 Rutledge Ave, MSC 550 Charleston, SC 29425

Maggie A. Kuhn, MD

310 E. 44th St. Apt 1221 New York, NY 10017

Michael Hoa, MD

2100 W 3rd St Los Angeles, CA 90057

Yukiko Iino, MD, PhD

Department of Otolaryngology Jichi Medical University Saitama Medical Center 1-847 Amanuma-cho, Omiya-ku Saitama 330-8503, Japan

Theodore R. McRackan, MD

Vanderbilt University Medical Center 10265 Medical Center East, South Tower Nashville, TN 37232-8606

NAMES AND ADDRESSES OF PRIMARY AUTHORS

Hossein Mahboubi, MD, MPH Dept of Otolaryngology - HNS University of CA, Irvine 101 The City Drive South Bldg. 56, Suite 500 Orange, CA 92868

Charles Mangham, Jr., MD Seattle Ear Clinic 801 Broadway Ste 830 Seattle, WA 98122-4328

Ashkan Monfared, MD 2021 K ST, NW, Suite 206 Washington, DC 20006

Krzysztof Morawski Dept of Otolaryngology, WUM Banacha 1a Street 02-097 Warsaw, Poland

Brian D. Nicholas, MD UVa Dept of Oto HNS PO Box 800713 Charlottesville VA 22908

Jack H. Noble, PhD 2301 Vanderbilt Pl. Box 1662B Nashville, TN 37235

Stanley Pelosi, MD Dept of Otolaryngology-HNS Vanderbilt University Medical Center 7209 Medical Center East-South Tower 1215 21st Avenue South Nashville, TN 37232

John M. Pike, BS 142 Glaxo Building 103 Mason Farm Rd Chapel Hill, NC, 27599

Konstantina M. Stankovic, MD, PhD 243 Charles Street Boston, MA 02114

Clough Shelton, MD 50 N Medical Dr Salt Lake City, UT 84132 Evan Walgama, MD Dept of Otolaryngology-HNS University of Texas SW Medical Center at Dallas 5323 Harry Hines Blvd Dallas, TX 75390-9035

Bryan K. Ward, MD Johns Hopkins Outpatient Ctr, 6th floor Dept of Otolaryngology-HNS 601 North Caroline Street Baltimore, MD 21287

Guangwei Zhou, MD, ScD Dept of Otolaryngology & Communication Enhancement Children's Hospital Boston 300 Longwood Ave. LO-367 Boston, MA 02115

M. Geraldine Zuniga, MD Johns Hopkins University School of Medicine Otolaryngology-HNS Dept. 601 N Caroline St 6th Floor Baltimore, MD 21287-0910

Saturday, April 21, 2012

12:30 Business Meeting (Restricted to Members) Room: Elizabeth Ballroom DE

Minutes of the Annual Meeting 2011

Introduction of New Members

Election of Nominating Committee

Report of the Secretary-Treasurer

Report of the Editor-Librarian

- 1:00 Scientific Program (Open to Registered Members & Non-Members-Badge required for admission) Room: Elizabeth Ballroom DE
- **1:00** Remarks by the President Herman A. Jenkins, MD

Presidential Citations -

Carol A. Bauer, MD Rinaldo F. Canalis, MD Newton J. Coker, MD Brenda Lonsbury-Martin, PhD Shirley Gossard

Guest of Honor Vicente Honrubia, MD

1:10 Vestibular Testing, after 50 Years Still a Challenge Vicente Honrubia, MD

Moderators: Herman A Jenkins, MD Paul R. Lambert, MD

1:25 Clinical Utility of Vestibular Evoked Myogenic Potentials in the Evaluation of Patients with Air-Bone Gaps Guangwei Zhou, MD, ScD Dennis Poe, MD Quinton Gopen, MD

1:34 Association between Hearing Loss and Saccular Dysfunction in Older Individuals M. Geraldine Zuniga, MD Roni E. Dinkes, AuD John P. Carey, MD Michael C. Schubert, PT, PhD Jeremy Walston, MD Yuri Agrawal, MD 1:43 Long-term Hearing Outcomes Following Surgical Plugging of the Superior Semicircular Canal by Middle Fossa Approach Bryan K. Ward, MD Yuri Agrawal, MD Charles C. Della Santina, MD, PhD Charles J. Limb, MD Lloyd B. Minor, MD John P. Carey, MD

1:52 Otolithic Membrane Damage in Patients with Endolymphatic Hydrops and Drop Attacks

Audrey P. Calzada, MD Ivan A. Lopez, PhD David Elashoff, PhD Gail Ishiyama, MD Akira Ishiyama, MD

2:01 Characteristics of Patients with Unilateral and Bilateral Meniere's Disease: Implications as to Etiology

Clarice S. Clemmens, MD Michael J. Ruckenstein, MD, MS

- 2:10 DISCUSSION
- 2:15 Basic Science Lecture: Neuroscience of Tinnitus -Implications for Treatment Carol A. Bauer, MD
- 2:40 DISCUSSION
- 2:45 BREAK WITH EXHIBITORS
- 3:15 Biofilm Formation by Otopathogenic Strains of Ps. aeurginosa is not Consistently Inhibited by EDTA Richard A. Chole, MD, PhD Joseph Zenga, MD Patricia M. Gagnon, MS Joseph Vogel, PhD

3:24 Steroids in Aminoglycoside-Containing Ear Drops: Do they Reduce Cochlear Toxicity? Saad A. Alsaleh, MD Brian W. Blakley, MD, PhD

Zameel A. Dewji, MD Kaiser A. Qureshy, MD Sylvie T. Berard, AuD Ling Xie, RA 3:33 Anti-Ige Therapy for Eosinophilic Otitis Media Yukiko Iino, MD, PhD Hiromi Kanazawa, MD Akihiro Shinnabe, MD Naohiro Yoshida, MD, PhD

3:42 Mannitol Protects Auditory Hair Cells against Tumour Necrosis Factor Alpha (TNF α) -Induced Loss

Guyan A. Channer, MD Esperanza Bas, PhD Fred F. Telischi, MEE, MD Chhavi Gupta, PhD John T. Dihn, BS Ly Vu, BS Adrien A. Eshraghi, MD Thomas R. Van De Water, PhD

3:51 Pre and Post-concert Assessment of Hearing Loss in Teenagers M. Jennifer Derebery, MD Andrew Vermiglio, PhD Maria Vargas, AuD Marilee Potthoff

4:00 DISCUSSION

4:05 Molecular Pathway Analysis of Genetic Hearing Loss Georgios Stamatiou, MD Konstantina M. Stankovic, MD, PhD

4:14 Intratemporal Facial Nerve Variability: Implications for Otologic Surgery

Theodore R. McRackan, MD Fitsum A. Reda, MS Jack H. Noble, PhD Alejandro Rivas, MD Benoit M. Davant, PhD Robert F. Labadie, MD, PhD

4:23 Rehabilitation of Central Facial Paralysis with Hypoglossal-Facial Anastomosis C. Eduardo Corrales, MD Richard K. Gurgel, MD Robert K. Jackler, MD

4:32 Zinc and Ginkgo Biloba as Placebo Interventions Reduce Tinnitus in Selected Patients Charles A. Mangham Jr., MD, MS A. Davis Mangham

4:41 Large Jugular Bulb Abnormalities Involving the Middle Ear Maggie A. Kuhn, MD David R. Friedmann, MD Leon S. Winata, BS Jan Eubig, MD Bidyut K. Pramanik, MD John Kveton, MD Darius Kohan, MD Saumil N. Merchant, MD

Anil K. Lalwani. MD

- 4:50 DISCUSSION
- 5:00 ADJOURN
- 5:10 Group Photograph (AOS Members) Location to be announced
- 6:30 AOS President's Reception and Banquet Randle Ballroom DE (Members and Invited Guests Only)

Sunday, April 22, 2012

7:00 Business Meeting (Restricted to Members) Room: Elizabeth Ballroom DE

Report of the

- A. Board of Trustees of the Research Fund
- B. American Board of Otolaryngology
- C. Award of Merit Committee
- D. American College of Surgeons
- E. American Academy of Otolaryngology-HNS
- F. AAO-HNS Board of Governors

Report of Audit Committee

Report of the AOS Education Committee

Report of the Membership Development Committee

Report of the Nominating Committee

Unfinished Business

New Business

7:30 Scientific Program

(Open to Registered Members & Non-Members -Badge Required for admittance) Room: Elizabeth Ballroom DE

Moderators: Herman A. Jenkins, MD Paul R. Lambert, MD

7:30 Method and Reproducibility of a Standardized Technique for Ossiculoplasty Michael B. Gluth, MD John L. Dornhoffer, MD

7:39 Intraoperative Monitoring of Ossiculoplasty Efficacy by RW-ECochG Krzysztof Morawski Kazimierz Niemczyk Erdem Yavuz Rafael E. Delgado

Aleksandra Hryciuk Fred F. Telischi, MD

7:48 Long-term Results of Titanium Prostheses in Ossiculoplasty Lauren A. Kilpatrick, MD Fu-Shing Lee, PhD Paul R. Lambert, MD

7:57 Patterns of Failure in Canal Wall Down Tympanomastoid Cavity Instability Michael B. Gluth, MD John L. Dornhoffer, MD Aaron M. Metraile, MD

8:06 Does Preoperative Hearing Predict Postoperative Hearing in Patients Undergoing Primary Aural Atresia Repair?

Brian D. Nicholas, MD Kaelyn Krook, BS Lincoln Gray, PhD Bradley W. Kesser, MD

8:15 Petrous Apex Cholesterol Granuloma Histopathology: An Analysis of the Histopathology of Surgical Management and Histopathologic Evidence for the Exposed Marrow Theory Michael Hoa, MD John W. House, MD Fred H. Linthicum, Jr., MD

8:24 DISCUSSION

8:29 High Fidelity, Inexpensive Surgical Middle Ear Simulator Ashkan Monfared, MD

Ashkan Monfared, MD Gerald Mitteramskogler, MS Simon Gruber, Ms Kenneth Salisbury, PhD Juergen Stampfl, PhD Nikolas H. Blevins, MD

8:38 Direct Drive Micro Hearing Aid: Investigation of a Novel Completely-in-the-Canal Hearing Aid

Hossein Mahboubi, MD MPH Peyton Paulick, MS Saman Kiumehr, MD Mark Merlo, PhD Mark Bachman, PhD Hamid R. Djalilian, MD

8:47 Radiographic Findings, Surgical Techniques, and Outcomes of Cochlear Implantation in Patients with X-Linked Deafness

Maura K. Cosetti, MD David R. Friedmann, MD Selena E. Heman-Ackah, MD, MBA David Drimmer, BS Susan B. Waltzman, PhD J. Thomas Roland, Jr., MD

8:56 The Round Window: Is It the 'Cochleostomy' of Choice? Experience in 120 Consecutive Cochlear Implant Patients David A. Gudis, MD

Douglas C. Bigelow, MD Michael J. Ruckenstein, MD

- 9:05 Minimal Access Cochlear Implant Fixation: Tight Pocket with a Plate Clough Shelton, MD Frank M. Warren, MD
- 9:14 Management of Electrode Exposure after Cochlear Implantation Evan Walgama, MD J. Walter Kutz, Jr., MD Peter S. Roland, MD Brandon Isaacson, MD
- 9:23 DISCUSSION
- 9:28 INTERMISSION

9:58 Effects of Intracochlear Trauma on Long-Term Hearing Outcomes in Normal Hearing Gerbils

John M. Pike, BS Oliver F. Adunka, MD Baishakhi Choudhury, MD Omar Awan, BS Kristine Faulk, BS Douglas C. Fitzpatrick, PhD

10:07 Minimization of Cochlear Implant Artifact in Cortical Auditory Evoked Potentials in Children David Bakhos, MD S. Roux E. Lescanne, MD, PhD

- F. Bonnet-Brilhaut, MD, PhD
- N. Bruneau, PhD

10:16 Programming Strategy and Outcomes in Cochlear Implant Patients with Auditory Neuropathy Spectrum Disorder

Stanley Pelosi, MD Alejandro Rivas, MD David Haynes, MD Marc L. Bennett, MD Robert F. Labadie, MD, PhD Linda Hood, PhD Andrea Hedley-Williams, AuD George B. Wanna, MD

10:25 Speech Perception Performance of Double Array Nucleus Multichannel Cochlear Implant Users With Standard and Duplicated Maps in Each of the Arrays

> Ricardo F. Bento, MD, PhD Maria Valeria S.G. Gomez, PhD Rubens V.B. Neto, MD, PhD Robinson Koji Tsuji, MD, PhD Anna Carolina O. Fonseca, MD Liliane S. Ikari, MD

10:34 Automatic, Image-based Cochlear Implant Electrode-to-Spiral Ganglion Position Analysis: Implications for Programming Jack H. Noble, PhD Benoit M. Dawant, PhD Rene H. Gifford, PhD, Robert F. Labadie, MD, PhD

10:43 Implantation of the Vestibular System: Monkey and Man Justin S. Golub, MD

Leo Ling, PhD Steven M. Bierer, PhD Kaibao Nie, PhD James O. Phillips, PhD Jay T. Rubinstein, MD, PhD

- 10:52 DISCUSSION
- 11:00 Panel Discussion Challenges and New Frontiers in Cochlear Implantation Moderator: J. Thomas Roland, Jr., MD

Panel Presentations: Cochlear Implantation in the Prelingually Deafened Adolescent/Young Adult Issues and Outcomes Daniel M. Zeitler, MD

Research Opportunities and Single Sided Deafness Cochlear Implantation *Mario A. Svirsky, PhD*

Auditory Neuropathy/Dys-synchrony and Cochlear Implantation Linda J. Hood, PhD

Hearing Loss, Aging and Dementia and Cochlear Implantation Larry E. Humes, PhD

Cochlear Implantation and the Severely Challenged Child *Nancy M. Young, MD*

11:55 DISCUSSION

- 12:00 Introduction of Incoming AOS President Paul R. Lambert, MD
- 12:02 Adjourn

IDENTIFICATION OF PROFESSIONAL PRACTICE GAPS

When submitting the abstract, the authors were asked to identify the professional practice gap (s), i.e., educational needs, learning objectives, and desired results; as well as competency areas to be addressed. These practice gaps and competency areas are stated at the end of each abstract listed in the order of presentation.

Clinical Utility of Vestibular Evoked Myogenic Potentials in the Evaluation of Patients with Air-Bone Gaps

Guangwei Zhou, MD, ScD, Dennis Poe, MD Quinton Gopen, MD

Objective: To determine the value of vestibular evoked myogenic potential (VEMP)

test in clinical evaluation of air-bone gaps.

Study design: retrospective case review

Setting: tertiary referral center

Patients: A total of 120 patients underwent VEMP testing during clinical investigation of significant air-bone gaps in their audiograms.

Intervention(s): Otologic examination and surgeries, high-resolution computerized tomography (CT), air and bone audiometry, tympanometry, acoustic reflex and VEMP test.

Main outcome measure(s): Imaging studies demonstrating structural anomalies in the temporal bone. Audiologic outcomes of air-bone gaps and VEMP thresholds. Surgical findings confirming imaging results.

Results: Middle ear pathologies, such as otosclerosis and chronic otitis media, were identified in 50 patients and all of them had absent VEMP responses elicited by air-conduction stimuli. Moreover, 13 of them had successful middle ear surgeries with closures of the air-bone gaps. Abnormally low VEMP thresholds were found in 71 out of 73 patients with inner ear anomalies, such as semicircular canal dehiscence and enlarged vestibular aqueduct. Seven patients with superior semicircular canal dehiscence underwent plugging procedure via middle fossa approach and VEMP thresholds became normalized after the surgery in three of them. VEMP test failed to provide accurate diagnosis in only three cases.

Conclusions: Air-bone gaps may be a result of various otologic pathologies and VEMP test is very useful during clinical evaluation, better than tympanometry and acoustic reflexes. To avoid unnecessary middle ear surgery for air-bone gaps with unknown or unsure etiology, VEMP test should be used in the deferential diagnosis before expensive imaging study.

Define Professional Practice Gap & Educational Need: Regular audiometry and tympanometry often fail to provide definitive diagnosis information for the underlying etiology of air-bone gaps.

Learning Objective: Demonstrate the clinical value of VEMP testing in differential diagnosis of air-bone gaps.

Desired Result: Use VEMP testing as a routine tool for evaluation of air-bone gaps.

Patient Care Practice-Based Learning

IRB Approval: Children's Hospital Boston

Association between Hearing Loss and Saccular Dysfunction in Older Individuals

M. Geraldine Zuniga, MD, Roni E. Dinkes, AuD John P. Carey, MD, Michael C. Schubert, PT, PhD Jeremy Walston, MD, Yuri Agrawal, MD

Objective: To describe the association between hearing loss and deficits in each

of the five vestibular end-organs - the horizontal, superior and posterior semicircular canals, saccule and utricle - in older individuals.

Study design: Cross-sectional study.

Setting: Tertiary care academic medical center.

Patients: Fifty individuals age 70 and above.

Interventions: Audiometry, head thrust dynamic visual acuity testing (htDVA), and sound-evoked cervical vestibular-evoked myogenic potential (cVEMP) and tap-evoked ocular VEMP (oVEMP) testing.

Main Outcome Measures: Audiometric pure-tone averages (PTA), htDVA LogMAR scores in each of the three semicircular canal planes as a measure of semicircular canal function, and cVEMP and oVEMP amplitudes as a measure of saccular and utricular function, respectively. Right and left sides were considered individually for a total of 100 ears.

Results: We observed a significant correlation between hearing loss (PTA of 2, 4, 6, 8kHz) and reduced cVEMP amplitudes (or reduced saccular function; r = -0.541, p < 0.001) in subjects age 70 and above. In contrast, hearing loss was not associated with low oVEMP amplitudes (or utricular dysfunction), or poor htDVA LogMAR scores (or semicircular canal dysfunction) in any of the semicircular canal planes.

Conclusion: The concomitant decline in cochlear and saccular function associated with aging may reflect the common embryologic origin of both structures, which comprise the pars inferior of the labyrinth. These findings suggest a potential benefit of screening individuals with presbycusis for saccular dysfunction, which may contribute to fall risk in the elderly.

Define Professional Practice Gap & Educational Need:

The age-related decline in function of specific vestibular end-organs -including the semicircular canals and the otoliths -- is not well characterized, and associations between specific vestibular deficits and hearing loss in older individuals is poorly understood.

Learning Objective: Clinicians will learn that older individuals with presbycusis are also likely to have associated saccular dysfunction, which places them at increased risk of imbalance and falls.

Desired Result: Clinicians will understand that older individuals with presbycusis are also likely to have concomitant saccular dysfunction; these patients may benefit from a thorough balance and fall risk evaluation and referral to vestibular rehabilitation.

Patient Care Medical Knowledge Practice-Based Learning System-Based Practice

IRB Approval: NA_00035749

List outside funding: This work was supported by the American Neurotological Society's Silverstein Award and the Older Americans Independence Center Pilot Award.

Long-term Hearing Outcomes Following Surgical Plugging of the Superior Semicircular Canal by Middle Fossa Approach

Bryan K. Ward MD, Yuri Agrawal MD Charles C. Della Santina, MD, PhD Charles J. Limb, MD, Lloyd B. Minor, MD, John P. Carey, MD

Objective: To determine long-term post-operative hearing outcomes following surgical plugging via middle fossa approach for superior semicircular canal dehiscence syndrome (SCDS).

Study Design: Clinical Review

Setting: Tertiary Care Medical Center

Patients: 42 patients with SCDS based on history, physical examination, vestibular function testing, and computed tomography imaging confirming the presence of a dehiscence. All patients underwent surgical plugging of the superior semicircular canal via middle fossa approach.

Intervention: Pure tone audiometry was performed pre-operatively, and at 7 days and between 3 and 15 months post-operatively.

Main Outcome Measures: Change in air-bone gap (ABG) and pure tone average (PTA).

Results: Pre-operative average ABG across 0.25, 0.5, 1, and 2 kHz was 16.0 dB (SD 7.6). At 7 days post-operatively, average ABG was 16.5 dB (SD 11.1, p=0.42), and at 3-15 months was 8.1 dB (SD 8.4, p<0.001). 52% (95% CI, 33-69) of affected ears had greater than 10 dB decline in their four frequency (0.5, 1, 2, 4 kHz) PTA measured by bone-conduction (BC) threshold 7 days post-operatively and 25% (95% CI 8-39) at 3-15 months post-operatively. Mean BC PTA of affected ears was 8.4 dB (SD 10.4) hearing loss (HL) pre-operatively, 19.2 dB HL (SD 12.6, p<0.001) at 7 days post-operatively and 16.4 dB HL (SD 18.9, p=0.01) at 3-15 months. No significant differences in speech discrimination score were noted (F=0.17).

Conclusions: Low-frequency air-bone gap corrects following surgical plugging. Middle fossa approach to surgical plugging of SCDS is associated with mild high-frequency sensorineural hearing loss that persists in 25%, but no change in speech discrimination.

Educational Need: Improved understanding of post-operative outcomes in superior canal dehiscence.

Learning Objectives: Understand the potential risk of canal plugging and the effect of surgical plugging on the air-bone gap.

Desired Result: Appreciate the effects of middle fossa surgical plugging on post-operative hearing outcomes in patients with superior semicircular canal dehiscence.

Patient Care Medical Knowledge Practice-Based Learning Interpersonal and Communication Skills

IRB # - NA_00035749

Otolithic Membrane Damage in Patients with Endolymphatic Hydrops and Drop Attacks

Audrey P. Calzada, MD, Ivan A. Lopez, PhD David Elashoff, PhD, Gail Ishiyama, MD Akira Ishivama, MD

Objectives: 1. Evaluate the otolithic membrane in patients with endolymphatic hydrops (EH) and vestibular drop attacks (VDA) undergoing ablative labyrinthectomy. 2. Correlate intraoperative findings to archival temporal bone specimens of patients with EH. **Study Design:** Retrospective case review

Study Design: Renospective case re Setting: Tertiary referral center

Patients: 1. Patients undergoing labyrinthectomy for incapacitating Meniere's disease (MD), delayed EH, VDA, or acoustic neuroma (AN) between 2004 and 2011. 2. Archived temporal bone specimens of patients with MD.

Interventions: Ablative labyrinthectomy

Main outcome measures: Examination of the utricular otolithic membrane.

Results: The otolithic membrane of the utricle was evaluated intraoperatively in 28 patients undergoing labyrinthectomy. 7 (25%) had a history of VDA's, 6 (21%) had delayed EH, 9 (32%) had MD, and 6 (21%) had AN's. All patients with VDA's had floating otoconia and a disrupted utricular otolithic membrane, whereas only 50% and 56% of patients with delayed EH and MD respectively, had floating otoconia (p = 0.051). None of the patients with AN's demonstrated a disrupted otolithic membrane (p = 0.004). The mean thickness of the otolithic membrane in 5 archival temporal bone MD specimens was 11.45 micrometers versus 38 micrometers in normal specimens (p = 0.001).

Conclusions: The otolithic membrane appears to be consistently damaged in patients with VDA's. In addition, there is a significantly higher incidence of otolithic membrane injury in patients with MD and delayed EH compared to patients without hydrops, suggesting that the underlying pathophysiology in VDA's results from injury to the otolithic membrane of the saccule and utricle, resulting in free-floating otoliths.

Define Professional Practice Gap & Educational Need:

1. Lack of understanding of the underlying pathophysiology of vestibular drop attacks, or Tumarkin's crisis. 2. Lack of knowledge of optimal treatments for patients suffering from vestibular drop attacks and endolymphatic hydrops.

Learning Objective: 1. Present evidence suggesting otolithic membrane injury as part of the underlying pathophysiology of vestibular drop attacks and endolymphatic hydrops. 2. Discuss otolithic membrane injury and identify potential causes to enable future innovative treatments.

Desired Result: 1. Attendees will understand the clinical presentation of vestibular drop attacks and its relation to endolymphatic hydrops. 2. Listeners will better diagnose and treat this disease based on information gleaned from the presentation. 3. Attendees will pursue their own further research based on our data presented, examining their patients with vestibular drop attacks to enhance our understanding and treatment of this disease.

IRB or IACUC Approval: IRB approval was obtained through the University of California, Los Angeles institutional review committee; appropriate informed consent for inclusion in the study was obtained from each temporal bone donor as part of a National Institute of Health (NIH) funded Human Temporal Bone Consortium for Research Resource Enhancement through the National Institute on Deafness and Other Communication Disorders (NIDCD).

List outside funding: Supported by National Institutes of Health Grant 5U24 DC 008635 (NIDCD).

Characteristics of Patients with Unilateral and Bilateral Meniere's Disease: Implications as to Etiology

Clarice S. Clemmens, MD Michael J. Ruckenstein, MD, MS

Objective: To evaluate epidemiologic differences between patients with unilateral and bilateral Meniere's disease (MD). To evaluate these differences for insights into the possible etiologies of bilateral Meniere's disease.

Background: The diagnosis of MD is based on clinical criteria and its etiology is unknown. Differences in characteristics of patients with unilateral and bilateral MD have been noted but these studies' diagnostic criteria have been variable. In order to delineate findings that might have implications as to the etiology of MD, we have studied rigidly selected patient populations with unilateral and bilateral MD.

Study design: prospective cohort

Materials and Methods: Patients with a potential diagnosis of MD underwent extensive evaluations (audiometric, radiologic, immunologic) and only patients with idiopathic MD were included in this study. Bilaterality of disease was based on clinical and audiometric criteria. Variables identified as part of the evaluation were subjected to statistical analyses to determine if significant differences in the unilateral and bilateral groups.

Results: Patients with bilateral disease presented at a significantly younger age and had a significantly higher incidence of personal history of migraines and a family history of MD. None of the other identified variables were found to be significantly different.

Conclusions: Patients with bilateral MD have a higher incidence of migraines and of a family history of Meniere's disease. Implications as the potential etiologies are discussed.

Define Professional Practice Gap & Educational Need: There is a lack of knowledge and understanding concerning the different characteristics of patients with bilateral and unilateral Meniere's disease.

Learning Objective: To understand the different characteristics of patients with bilateral and unilateral Meniere's Disease and the implications of these characteristics.

Desired Result: Attendees will learn the differences identified in patients with bilateral and unilateral Meniere's disease, understand the implications of these characteristics on etiology, and apply this new knowledge in the diagnosis and treatment of Meniere's disease in their practice.

Medical Knowledge

IRB or IACUC Approval: 806918

Biofilm Formation by Otopathogenic Strains of Ps. aeurginosa is not Consistently Inhibited by EDTA

Richard A. Chole, MD, PhD, Joseph Zenga, MD Patricia M. Gagnon, MS, Joseph Vogel, PhD

Hypothesis: Biofilm formation in otopathogenic strains of

Ps. aeruginosa (PA) is significantly inhibited, in vitro, by EDTA.

Background: EDTA has been shown to inhibit biofilm formation in a number of bacteria including PA. Since EDTA may be a well-tolerated reagent to inhibit biofim formation in patients, we asked if EDTA might be effective in all PA strains isolated from chronically infected cholesteatomas.

Methods: PA was isolated from 15 infected cholesteatomas and grown into log phase. At a standard concentration, they were grown with varying concentrations of EDTA in 96-well culture plates for varying periods. At the end of the incubation period biofilm formation was measured with crystal violet.

Results: Most otopathogenic PA exhibited variable biofilm formation and dissolution with peak production at 12-18 hours. At 10mM EDTA, some strains were completed inhibited and most demonstrated decreased biofilm formation, however, several isolates demonstrated significantly increased biofilm production over baseline.

Conclusion: The dynamic nature of biofilm growth over a short timecourse, along with the demonstrated delay in peak time caused by EDTA treatment, may help to clarify prior conflicting reports since most authors have evaluated biofilm formation at only a single time-point. In addition, since EDTA treatment does not cause suppression of biofilm production in all isolates of otopathogenic PA, it may not be as efficacious an antimicrobial as previously thought. Although decreased planktonic growth was seen at high concentrations of EDTA, biofilm formation is not necessarily inhibited and may serve as a nidus for bacterial seeding in chronic otolaryngologic infections.

Define Professional Practice Gap & Educational Need: Lack of strategies to inhibit chronic biofilm infections of the ear.

Learning Objective: Understand some developing strategies to inhibit biofilm infections in chronic otitis media.

Desired Result: Understand that, although EDTA may inhibit most biofilm infections, many are resistent and will require alternative strategies.

Patient Care Medical Knowledge

IRB or IACUC Approval: #201104239 List outside funding: NIDCD R01 DC000263-24(RAC) and P30 DC004665-11(RAC)

Steroids in Aminoglycoside-Containing Ear Drops: Do They Reduce Cochlear Toxicity?

Saad A. Alsaleh, MD, Brian W. Blakley, MD, PhD Zameel A. Dewji, MD, Kaiser A. Qureshy, MD Sylvie T. Berard, AuD, Ling Xie, RA

Hypothesis: Betamethasone will reduce the cochlear toxicity of otic gentamicin if given together.

Background: Otic drops containing aminoglycosides (AMGs) are valuable in treating gram-negative bacterial infections of the middle & external ear. Their usage, however, is discouraged in an open middle ear due to their ototoxic effects. Nevertheless, AMG/glucocorticoid drops have been used for many years with a rare incidence of hearing loss. Could it be that glucocorticoids are protective against the cochleotoxic effects of AMGs?

Methods: Thirty-four mice were assigned at random to receive intratympanic injections of either 0.1 % betamethasone (BM) (11 mice), 0.3% gentamicin (GM) (10 mice) or a combination of both (GM/BM) (13 mice) in the left ear (treated) and saline on the right (untreated). Six injections were given on alternate days. Hearing thresholds were assessed with auditory brainstem response (ABR) using tone bursts at one, two months and greater than two months.

Results: There was a significantly greater degree of hearing loss in the BM treated ears compared to the untreated ears of 6.48 dB (p=0.007) and in the GM treated ears compared to untreated ears (p=0.010, 6.59 dB hearing loss). However, otic GM/BM did not cause significant additional hearing loss compared with the untreated ears (p=0.242, 3.56 dB hearing loss).

Conclusion: Our data suggests that hearing loss caused by gentamicin otic drops may be reduced by the inclusion of betamethasone. In addition, betamethasone alone in otic drops may be associated with hearing loss.

Define Professional Practice Gap & Educational Need: 1. There is a lack of awareness between some otolaryngologists on the hazards of aminoglycoside use in the middle ear to treat a draining ear. 2. This lack of awareness might be related to the usual packaging of glucocorticoides with aminoglycosides in otic drops which decreases in our animal model the cochlear toxicity of these agents. 3. This topic is very controversial in otology and further evidence such as our study is still needed to prove or disprove these theories. 4. Also, our study shows that steroids alone might be cochleotoxic. This has been found in only one study prior to ours and we will discuss possible etiologies and evidence surrounding that.

Learning Objective: 1. To acknowledge that aminglycosides are cochleotoxic and steroids might possibly decrease that effect. 2. Not to use aminoglycoside otic drops in an open middle ear unless other options are not existent, with steroids and after patient informed consent of possible toxicities. 3. To further study the possible cochlear toxicity of steroids if given alone in the middle ear.

Desired Result: 1. To show that the possible cause of rare incidence of hearing loss with

aminoglycoside drops is the effect of the combination with steroids and not the benign nature of the drug (at least in our animal model). 2. To readdress the issue of not using aminoglycosides in an open middle ear and to remind clinicians about their possible toxicities.

Patient Care Medical Knowledge Practice-Based Learning Interpersonal and Commun Professionalism System-Based Practice

IRB or IACUC Approval: Protocol 09-002/1

List outside funding: None. Funded by the Department of Otolaryngology, University of Manitoba

Anti-Ige Therapy for Eosinophilic Otitis Media

Yukiko Iino, MD, PhD, Hiromi Kanazawa, MD Akihiro Shinnabe, MD, Naohiro Yoshida, MD, PhD

Objective: Eosinophilic otitis media (EOM) is an intractable otitis media characterized by the presence of a highly viscous yellow effusion containing eosinophils and high levels of IgE. The presence of high-level IgE may exacerbate eosinophilic inflammation in the middle ear. We carried out a pilot study to determine whether anti-IgE therapy is efficacious in the treatment of EOM.

Study design: Prospective study.

Setting: Tertiary referral center.

Patients: Seven patients with severe EOM received the anti-IgE agent, omalizumab, for at least 3 months, in addition to ordinary treatments for EOM such as intratympanic instillation of a corticosteroid. For controls, seven patients with EOM without anti-IgE therapy were also included in this study.

Main outcome measures: They were evaluated by a questionnaire for ear, nose and respiratory symptoms, otomicroscopy, a temporal bone CT scan, audiometry, and measurement of surrogate markers in MEE before and after the anti-IgE therapy.

Results: At 3 months, only two of seven patients showed improvement of EOM and hearing acuity. However, eosinophilic cationic protein (ECP) concentrations in the MEE were decreased in most of the patients. Four patients continued the anti-IgE treatment for more than 9 months and all showed improvement of subjective symptoms and the frequency of MEE.

Conclusion: This pilot study provides new evidence establishing that long term anti-IgE therapy reduces the frequency of MEE and ECP concentrations in the MEE. Therefore, long term anti-IgE therapy can be effective in the treatment of EOM to inhibit eosinophilic inflammation in the middle ear.

Define Professional Practice Gap & Educational Need: The goal of the treatment of eosinophilic otitis media has been shown to control the middle ear inflammation and to preserve hearing. However, anti-IgE therapy is new and targeted medication, and resolution of EOM will be expected.

Learning Objective: Although the effectiveness of anti-IgE therapy for bronchial asthma has been established, there have been no trials for anti-IgE therapy for EOM.

Desired Result: Anti-IgE therapy can be effective not only for bronchial asthma but eosinopilic otitis media.

Patient Care

IRB or IACUC Approval: Study Number: 10-11

List outside funding: #12288;Grant-in-Aid for Scientific Research of the Ministry of Education, Culture, Sports, Science and Technology in Japan.

Mannitol Protects Auditory Hair Cells against Tumour Necrosis Factor Alpha (TNF α)-Induced Loss

Guyan A. Channer, MD, Esperanza Bas, PhD Fred F. Telischi, MEE, MD, Chhavi Gupta, PhD John T. Dihn, BS, Ly Vu, BS Adrien A. Eshraghi, MD, Thomas R, Van De Water, PhD

Hypothesis: Mannitol has otoprotective effects against TNF α induced auditory hair cell (HC) loss.

Background: Mannitol has been demonstrated to possess cytoprotective effects in several organ systems. Its protective effect on post-ischemic hearing loss has also been shown. Mannitol's otoprotective mechanism and site of action are at present unknown.

Material and Methods: Organ of Corti (OC) explants were dissected from 3 day-old rat pups. The safety (non-ototoxicity) of mannitol was assessed at several concentrations (1-100mM). Three experimental arms were designed including: a control group; TNF α group; and TNF α + mannitol group. Cell viability was determined by counts of fluorescein isothiocyanate (FITC) phalloidin stained HC. Immunofluorescence assays of phospho-c-Jun and the pro-apoptotic mediators, cleavedcaspase-3, apoptosis inducing factor (AIF) and endonuclease G (EndoG), were performed.

Results: Analysis of HC density confirmed the safety of mannitol at concentrations ranges of 1-100mM. The ototoxic effect of TNF α was demonstrated (p<0.05). The otoprotective effect of 100mM mannitol in TNF α -challenged OC explants was also demonstrated (p<0.001). Mannitol treatment reduced the high levels of phospho-c-Jun observed in the TNF α -challenged group. EndoG cluster formation and its translocation into the nuclei of HCs were also reduced by mannitol treatment.

Conclusion: Mannitol significantly reduces the ototoxic effects of TNF α against auditory HCs potentially by inhibiting EndoG and c-Jun N-terminal kinase (JNK) activation pathway. This local otoprotective effect may have therapeutic implications in inner ear surgery, e.g. cochlear implants, for protection of residual hearing, as well as implications for post-ischaemic inner ear insults.

Define Professional Practice Gap & Educational Need: Although mannitol has demonstrated cytoprotective effects on various organ systems, its effects at a cellular level within the auditory system has never been demonstrated which may have implication for hearing protection.

Learning Objective: The learning objective is to demonstrate the otoprotective capacity of mannitol at the cellular level.

Desired Result: Upon completion of this discussion, otolarygologists should be able to

1). Recognize that mannitol has otoprotective properties 2). Utilize this knowledge in their daily practice

Medical Knowledge Practice-Based Learning

IRB or IACUC Approval: ACUC Protocol # is 11-086

Pre and Post-concert Assessment of Hearing Loss in Teenagers

M. Jennifer Derebery, MD, Andrew Vermiglio, PhD Maria Vargas, AuD, Marilee Potthoff

One in five adolescents has some hearing loss, mostly high frequencies. The study assesses whether attendance at a typical rock concert could contribute to the marked decrease in pure tone sensitivity in this age group.

Objectives: To determine the proportion of teen attendees of a typical rock concert experiencing a change in Distortion Product Otoacoustic Emission (DPOAE) amplitude and to determine the average change in air conduction pure tone thresholds after attendance at a single rock concert.

Study design: Non-randomized, prospective

Setting: Tertiary referral center

Patients: Thirty children and adults between ages 12 and 20 years recruited from the general population, with bilateral air conduction thresholds < 25dB HL.

Interventions: Pre and Post concert air conduction thresholds binaurally and measured DPOAE levels in one ear.

Main outcome measures: Average pure tone threshold (PTA) change and number of subjects experiencing decreased DP amplitudes

Results: T-test results revealed significant PTA shifts on the right at 2 through 6 kHz and in the left ear at 2 through 4 kHz (alpha = .004). The number of subjects experiencing a reduction in DP amplitude (n=17) from pre to post-concert evaluation just reached significance (two-tailed Sign test for n=25). These results suggest that the concert-goers experienced an immediate PTA shift and reduced DP amplitude after attending the concert.

Conclusions: The majority of teen and young adult attendees of a typical rock concert showed significant changes in PTA and a decreased functionality of outer hair cells.

Define Professional Practice Gap & Educational Need: Need to illustrate dangers to hearing from even a single exposure to a very common recreational activity. Lack of knowledge of changes in DPOAE measurements from attendance at a typical concert.

Learning Objective: Illustrate the changes to normal hearing thresholds and measured DPOAE measurements from a single exposure to a typical rock concert in teenage subjects.

Desired Result: Encourage (strongly) the use of noise protection for teen attendees for typical rock concerts. Long term: mandate more stringent limits on sound exposure from a recreational concert

Patient Care Medical Knowledge Practice-Based Learning

IRB or IACUC Approval: Yes
Molecular Pathway Analysis of Genetic Hearing Loss

Georgios Stamatiou, MD Konstantina M. Stankovic, MD, PhD

Hypothesis: Deafness genes are interconnected through common molecular pathways.

Background: There are many genes implicated in genetic hearing loss, and many more to be identified. This daunting complexity can be simplified by analyzing molecular pathways that these genes belong to.

Methods: Genes relevant for hearing and deafness were identified through PubMed literature searches, and assembled into 3 groups: (1) 74 genes that cause non-syndromic deafness, (2) 125 genes that cause non-syndromic and syndromic deafness, and (3) 122 genes associated with otic capsule development and malformations. Each group was analyzed using Ingenuity Pathway Analysis to discover the most interconnected, i.e. 'nodal' molecules, within the most statistically significant networks (p<10-45).

Results: The number of networks that met our criterion for significance was 1 (group 1) or 2 (groups 2 and 3). Nodal molecules of these networks were: Transforming Growth Factor Beta1 (TGFB1) for group 1, p42/p44 MAP Kinase (ERK 1/2) and the G Protein Coupled Receptors (GPCR) for group 2, and TGFB1 and Hepatocyte Nuclear Factor 4 alpha (HNF4a) for group 3. The nodal molecules included not only those known to be associated with deafness (GPCR), or with predisposition to otosclerosis (TGFB1), but also novel genes that have not been described in the cochlea (HNF4a), and signaling kinases (ERK 1/2).

Conclusions: A number of molecules that are likely to be key mediators of genetic hearing loss were identified through three different molecular pathway analyses. The molecules included new candidate genes for deafness. Therapies targeting these molecules may be useful to treat deafness.

Define Professional Practice Gap & Educational Need: There are many genes implicated in genetic hearing loss.

Learning Objective: Genes relevant for hearing and deafness were identified through PubMed.

Desired Result: A number of molecules that are likely to be key mediators of genetic hearing loss were identified through three different molecular pathway analyses. The molecules included new candidate genes for deafness. Therapies targeting these molecules may be useful to treat deafness.

Medical Knowledge

IRB or IACUC Approval: N/A

Intratemporal Facial Nerve Variability: Implications for Otologic Surgery

Theodore R. McRackan, MD, Fitsum A. Reda, MS Jack H. Noble, PhD, Alejandro Rivas, MD Benoit M. Davant, PhD, Robert F. Labadie, MD, PhD

Hypothesis: To determine which portion of the facial nerve (FN) has the highest degree of variability and to determine if differences exist between children and adults.

Background: While anecdotal reports exist regarding the highest degree of FN anatomic variation, there is minimal data on this subject. Herein we describe the location of highest variation of the FN as well as anatomic difference in pediatric patients compared to adult patients.

Method: High resolution CT scans of 20 pediatric patients and 20 adult patients were evaluated using software consisting of a model-based segmentation algorithm that automatically localizes and segments the FN. Aligned centerline variations, mean centerline, and standard deviation at each centerline point were computed. One side of each patient was randomly selected for inclusion in this study. (40 more patients will ultimately be added to this study before presentation)

Results:In children, the FN was on average more lateral at the distal vertical segment (1.55mm, p<0.01), more posterior at the distal tympanic segment (0.85mm, p<0.001), and more inferior at the proximal tympanic segment (2.95mm, p<0.001) when compared to adults. The greatest degree of variation in the FN was at the distal most portion of the tympanic segment in adults (SD 0.42mm) and at the mid portion of the second genu in children (SD 0.52mm).

Conclusion: Differences in the course of the FN between adults and children are quantified in the hopes of improving surgical efficiency and safety. Areas of maximal variation, which should be carefully assessed during surgery, are the tympanic segment in adults and the second genu in children.

Define Professional Practice Gap & Educational Need: 1) Lack of awareness of areas of facial nerve with the highest degree of variability 2) Lack of contemporary knowledge of differences in facial nerve location in children compared to adults

Learning Objective: 1) Understand which areas of the facial nerve have the highest degree of variability 2) Understand differences in facial nerve location in children compared to adults.

Desired Result: 1) Apply new knowledge of facial nerve anatomy and differences in location that exist to otologic operations 2) Improve surgical efficiency and safety with this new understanding

Patient Care Medical Knowledge Practice-Based Learning

IRB Approval No. 101433

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Rehabilitation of Central Facial Paralysis with Hypoglossal-Facial Anastomosis

C. Eduardo Corrales, MD, Richard K. Gurgel, MD Robert K. Jackler, MD

Objective: To evaluate the ability of hypoglossal-facial nerve anastomosis to reanimate the face in patients with nuclear (central) facial nerve palsy.

Study Design: Retrospective case series.

Setting: Tertiary academic medical center

Patients: Four patients with facial nerve paralysis due to a lesion of the brainstem facial nucleus caused by arteriovenous malformations, hemorrhage secondarily to pontine-cavernous lesions (vascular malformations), and brainstem compression due to a petroclival meningioma.

Intervention: All patients underwent end-to-end hypoglossal-facial nerve anastomosis.

Main Outcome Measures: Facial nerve function using the House-Brackmann (HB) scale and physical and social/well-being function using the Facial Disability Index (FDI).

Results: The mean age of the patients was 53.3 years (range 32-73). There were 3 female and 1 male patients. All patients had preoperative facial function HB VI/VI. With a minimum of 12 months follow-up after end-to-end hypoglossal-facial anastomosis, two patients regained function to HB grade III/VI. One patient attained a HB grade IV/VI, although subsequently developed a bulbar palsy with deteriorating facial nerve function bilaterally. One patient had a HB grade V/VI 12 months after surgery. Facial Disability Index scores showed comparable results to complete peripheral facial nerve palsy scores after acoustic neuroma resection followed by hypoglossal-facial anastomosis.

Conclusions: Patients with nuclear facial palsy who undergo end-to-end hypoglossal-facial nerve anastomosis achieve similar degrees of reanimation compared to those with peripheral facial nerve palsies.

Define Professional Practice Gap & Educational Need: Lack of contemporary knowledge regarding rehabilitation of central (nuclear) facial nerve(FN) paralysis with the end-to-end hypoglossal-facial anastomosis reanimation technique. More data is necessary to compare outcomes of patients with peripheral vs central(nuclear) complete facial nerve paralysis.

Learning Objective: To demonstrate facial nerve (FN) rehabilitation outcomes in patients with nuclear facial nerve paralysis who underwent hypoglossal-facial nerve anastomosis through House-Brackmann scores and by the Facial Disability Index.

Desired Result: 1) Clinicians will better inform patients regarding outcomes with the hypoglossal-facial reanimation technique in nuclear FN paralysis. 2) Surgeons can expect same House-Brackmann and Facial Disability Index scores in patients with nuclear FN who undergo hypoglossal-facial reanimation technique.

Patient Care Medical Knowledge Practice-Based Learning

IRB or IACUC Approval: Not required **List outside funding:** No

Zinc and Ginkgo Biloba as Placebo Interventions Reduce Tinnitus in Selected Patients

Charles A. Mangham Jr., MD, MS, A. Davis Mangham

Objective: We examined two drugs with anecdotal effectiveness, few side effects, but little proven benefit in a supportive clinical setting to evaluate the potential placebo effect of these candidates for first-line treatment of tinnitus.

Study design: A prospectively-designed sequential placebo intervention drug trial approved by the chairman of the IRB.

Setting: Subspecialty private practice

Patients: Patients over the age of 18 years with a primary complaint of tinnitus between 2006 and 2010. Those with disorders that may affect hearing acuity during the study were excluded.

Intervention: The first 110 patients were given zinc 50 mg daily and the second 107 patients were given Ginkgo biloba 240 mg twice daily for two months.

Main outcome measures: Previously validated questionnaires for selfrating of tinnitus loudness (11 point ordinal scale from 0-10), severity (44 point ordinal scale from 12-56), and benefit of treatment (5 point categorical scale).

Results: About 55% of patients thought that the drugs were effective in reducing their tinnitus; however, neither drug significantly reduced tinnitus loudness or severity. In a secondary analysis, we used the baseline questionnaire to select patients for treatment, those with either 1) baseline loudness of at least 4, or 2) severity score of at least 35, or 3) current depression. With both drugs, these selected groups had significant reductions of loudness or severity after two months (paired-samples T-test, p<0.05).

Conclusions: In a supportive clinical setting, zinc and Ginkgo significantly reduced tinnitus loudness or severity in selected patients.

Define Professional Practice Gap & Educational Need: 1. Lack of awareness of the design and outcome of placebo drug trials and how they may be appropriate for the treatment of tinnitus

Learning Objective: 1. Awareness of the nature of placebo effects and how they can be used to

improve the outcome of the treatment of tinnitus.

Desired Result: 1. attendees may consider using drugs with few side effects and low cost as

first-line treatment of tinnitus in a supportive clinical environment realizing that in order to get a placebo effect, the patient has to take the placebo treatment.

Patient Care Medical Knowledge Practice-Based Learning Interpersonal and Commun

IRB or IACUC Approval: The study had an expedited review by the chairman of the IRB of Swedish Hospital Medical Center in Seattle and was approved. It was not assigned a number.

Large Jugular Bulb Abnormalities Involving the Middle Ear

Maggie A. Kuhn, MD, David R. Friedmann, MD Leon S. Winata, BS, Jan Eubig, MD Bidyut K. Pramanik, MD, John Kveton, MD Darius Kohan, MD, Saumil N. Merchant, MD Anil K. Lalwani, MD

Objective: Jugular bulb abnormalities (JBA), such as jugular bulb diverticula (JBD) or large jugular bulbs, rarely present in the middle ear. We review a large series of temporal bone histopathologic specimens to determine their prevalence and present a series of cases of JB abnormalities involving the middle ear (JBME) that shed light on the probable mechanism for their development.

Methods: We reviewed 1579 temporal bone specimens to determine the prevalence and presentation of JBME. In addition, the clinical and radiologic findings of a series of individuals with JBME were reviewed.

Results: There were 17 cases of JBME in 1579 temporal bones (1.1%) of which 15 involved the inferior mesotympanum below the level of round window membrane (RWM), while two encroached upon the RWM or ossicles. In addition, four clinical cases of large JBME extending above RWM were encountered; these occurred in both genders with ages spanning from young to old (7 to 66 years). They presented with conductive hearing loss (N=3), ear canal mass (N=1), and intraoperative bleeding (N=1). Radiographically, patients had multiple diverticula of the JB on the side with JBME with one demonstrating growth on serial imaging studies. All

patients who underwent additional imaging had marked stricture of the contralateral transverse sinus.

Conclusions: JBME abnormalities are rare, present across age groups, and may demonstrate serial growth over time. They are usually associated with multiple diverticula within the same JB. Our clinical series suggests that JBME's development and uniquely aggressive behavior results from contralateral transverse sinus outflow obstruction.

Define Professional Practice Gap & Educational Need:

1. Incomplete description of the spectrum of jugular bulb abnormalities involving the middle ear. 2. Lack understanding of the etiologic factors responsible for the development and progression of jugular bulb abnormalities affecting the middle ear.

Learning Objective: 1. Appreciate the prevalence as well as the histologic, radiographic and clinical spectrum of jugular bulb abnormalities involving the middle ear. 2. Consider a possible mechanism for the development and behavior of middle ear jugular bulb abnormalities.

Desired Result: 1. Incorporate enhanced knowledge of jugular abnormalities involving the tympanic cavity when evaluating and treating patients with middle ear disorders. 2. Improve counseling to patients found to have (incidental or symptomatic) jugular bulb abnormalities of the middle ear.

Medical Knowledge

IRB or IACUC Approval: N/A

Method and Reproducibility of a Standardized Technique for Ossiculoplasty

Michael B. Gluth, MD, John L. Dornhoffer, MD

Objective: To evaluate the reproducibility of a standardized surgical technique for ossiculoplasty

Study Design: Retrospective review

Setting: Academic tertiary referral center

Patients: The first 35 consecutive patients undergoing a standardized ossiculoplasty technique performed by an experienced otologist after receiving only verbal and audiovisual media instruction from another senior otologist regarding technique specifics and mode of execution.

Intervention: Standardized technique was comprised of: 1) reconstruction from the stapes to the malleus neck 2) usage of the same length hydroxylapatite head/titanium shaft prosthesis for every case (2 mm PORP, 4 mm TORP) 3) bending the head of the prosthesis 30 degrees to fit the contour of the malleus manubrium 4) creation of a freestanding reconstruction without packing 5) placement of a large cartilage graft over the prosthesis head 6) usage of a footplate shoe for cases involving a TORP. The predicted postoperative air-bone (A-B) gap was calculated according to subjects' risk factors based on a previously published ossiculoplasty outcome scoring system (derived from outcomes at this institution), and then was compared to the actual average postoperative A-B gap achieved.

Main Outcome Measure: Predicted versus actual average postoperative air-bone gap

Results: Of the first 35 consecutive ossiculoplasty procedures with this technique, audiometric results were available for 30. Among these, the average postoperative A-B gap was 16 dB (range 1 dB-31 dB), which was within the predicted range based on underlying risk factors.

Conclusions: Short-term outcomes suggest that this technique appears to be a reproducible means of achieving excellent outcomes in ossiculoplasty.

Define Professional Practice Gap & Educational Need: 1. Lack of knowledge as to the reproducibility of ossiculoplasty outcomes associated with specific techniques. 2. Lack of awareness of the importance of considering the nature of technique specifics as opposed prosthesis type in ossiculoplasty.

Learning Objective: To illustrate the reproducibility of a standardized ossiculoplasty technique in achieving excellent short-term outcomes.

Desired Result: Attendees will understand the components of a standardized technique of ossiculoplasty and will be able to apply these principles to their own surgical practice. They will also be aware of the need to consider the concept of predicted versus actual achieved hearing results based on underlying severity when interpreting ossiculoplasty outcomes.

Patient Care Medical Knowledge

IRB or IACUC Approval: Yes

Intraoperative Monitoring of Ossiculoplasty Efficacy by RW-ECochG

Krzysztof Morawski, Kazimierz Niemczyk Erdem Yavuz, Rafael E. Delgado Aleksandra Hryciuk, Fred F. Telischi, MD

Objective: To assess intraoperative air-bone gap reduction during ossiculoplasty using round window electrocochleography (RW-ECochG).

Study Design: A prospective, feasibility study.

Setting: Academic, tertiary referral center.

Patients: Individuals with history of cholesteatoma undergoing second stage ossicular reconstruction surgery.

Intervention: RW-ECochG recordings during manipulations of ossicular prostheses.

Main Outcome Measure: Correlation of intraoperative RW-ECochG click and tone-burst stimulation threshold reductions to postoperative conductive hearing improvement as measured by audiometry.

Results: Thirty five adult patients underwent two-stage canal wall-up tympanoplasty. During the second look procedure, a needle electrode for RW-ECochG was placed at the RW niche via posterior tympanostomy (transmastoid facial recess). Prosthesis placement efficacy was evaluated by intraoperatively measured RW-ECochG stimulus thresholds. Auditory thresholds for click and frequency specific stimulation (tone-burst: 0.5-, 1.0-, 2.0-kHz), defined as the

last intensity for which RW-ECochG N1 peak was present, were tested for various configurations of ossicular placement. Postoperative

air-bone gap closure ranged between 10 to 45 dB. Hearing improvement measured intraoperatively correlated with 6 months or greater postoperative hearing thresholds (Spearman test - R>0.5; p<0.05). Adjustments in prosthesis configuration and placement resulted in measurable changes in the RW-ECochG thresholds. This technique appeared particularly sensitive to changes in position of total ossicular replacement prostheses (TORPs).

Conclusions: RW-ECochG was found to be an effective tool for evaluation of intraoperative hearing threshold improvement and showed good correlation with postoperative hearing status in cases of second stage ossiculoplasty.

Define Professional Practice Gap & Educational Need: Otologists do not monitor intraoperatively hearing during ossiculoplasty. Application of intraoperative hearing measurements could improve postoperative hearing results improving quality of life of patients

Learning Objective: 1. Presentation of audiological technique of intraoperative monitoring of hearing during ossiculoplasty;

2. Presentation of follow-up data showing utility of a new strategy of intraoperative monitoring of hearing during ossiculoplasty.

Desired Result: 1. Improvement of knowledge about a technique of intraoperative monitoring of hearing during ossiculoplasty;

2. Postoperative hearing results improvement; 3. Patient quality of life improvement.

Patient Care

Medical Knowledge Practice-Based Learning

IRB or IACUC Approval: #KB/34/2009

List outside funding: The National Centre for Research and Development (NCBiR) Grant N R13 0040 06/2009

Patterns of Failure in Canal Wall Down Tympanomastoid Cavity Instability

Michael B. Gluth, MD, John L. Dornhoffer, MD Aaron M. Metraile, MD

Objective: To evaluate and to classify patterns of various factors that may lead to the need for surgical revision of a chronically unstable canal wall down tympanomastoid cavity

Study Design: Retrospective review and statistical analysis

Setting: Academic tertiary referral center

Patients: Subjects were patients that underwent surgical revision of a canal wall down tympanomastoid cavity due to chronic instability and discharge.

Intervention: Factors presumably contributing to chronic open tympanomastoid cavity instability were reviewed and statistical analysis was undertaken to correlate and classify patterns of failure. Medical records and radiologic images were reviewed to evaluate factors such as: persistent diseased mastoid air cells, non-saucerized mastoidectomy, recurrent cholesteatoma, neo-tympanic membrane perforation or retraction, high facial ridge, hourglass-shaped external auditory meatus, high volume cavity, large open mastoid tip, unfavorable microbiology, and patient constitutional risk factors.

Main Outcome Measure: Risk factor correlation according to multivariate statistical analysis.

Results: 151 patients that underwent revision of an unstable open tympanomastoid cavity were reviewed. We found that factors driving the need for revision surgery can be classified class A) constitutional factors, class B) mastoid cavity shape/size, or class C) primary tympanomastoid disease recurrence/persistence.

Conclusion: Although causation is difficult to definitively establish, distinct patterns of failure do appear to exist that may lead towards the need for surgical revision of an unstable canal wall down tympanomastoid cavity.

Define Professional Practice Gap & Educational Need: Lack of contemporary knowledge showing definitive factors that may contribute to the need for surgical revision of an unstable canal wall down tympanomastoid cavity.

Learning Objective: To evaluate and to classify patterns of various factors that may lead to the need for surgical revision of a chronically unstable canal wall down tympanomastoid cavity

Desired Result: To define distinct patterns of failure and contributing factors of canal wall down tympanomastoid cavities.

Medical Knowledge Practice-Based Learning

System-Based Practice

IRB or IACUC Approval: 131220

Does Preoperative Hearing Predict Postoperative Hearing in Patients Undergoing Primary Aural Atresia Repair?

Brian D. Nicholas, MD, Kaelyn Krook, BS Lincoln Gray, PhD, Bradley W. Kesser, MD

Objective: The purpose of this study is to explore the correlation between preoperative hearing and early postoperative hearing results in patients undergoing primary aural atresia repair.

Study design: Retrospective review of 140 patients.

Setting: Academic tertiary referral center.

Patients: One hundred, thirty-three patients (5 to 67 years old)

undergoing primary atresia surgery were included.

Main outcome measure(s): Spearman correlation coefficients were calculated between preoperative and postoperative hearing outcome measures (mean 7.5 weeks; range, 3-40 weeks after surgery) including 3-tone pure-tone average (PTA), speech reception threshold (SRT), speech discrimination scores (SDS), air-bone gap (ABG), change in ABG (Δ ABG), and between preoperative SRT and Jahrsdoerfer score.

Results: Preoperative PTA, SRT, SDS, and ABG correlated strongly with their respective postoperative values (Correlation coefficients [rho] of .356 (p<.01), .199 (p<.05), .480 (p<.01), and .223 (p<.05), respectively). Preoperative PTA (.407; p<.01), SRT (.348; p<.01), SDS (-.247; p<.01), and ABG (.514; p<.01) were also correlated with \triangle ABG. When postoperative results were dichotomized to either normal (SRT < 30dB HL) or abnormal (SRT \ge 30dB HL), preoperative SRT was found to be a positive predictor of normal postoperative hearing (p=.05). Probability of normal postoperative hearing was 66% when preoperative SRT was \le 50 dB HL and 40% when \ge 70 dB HL. Preoperative hearing (SRT) also correlated with Jahrsdoerfer score (-.168 [p<.05]).

Conclusions: Among patients undergoing primary atresia repair, better preoperative hearing correlates with ear anatomy and strongly predicts better postoperative hearing. Preoperative hearing status should be factored when counseling atresia patients on hearing rehabilitation options.

Define Professional Practice Gap & Educational Need: Surgery to repair congenital aural atresia has traditionally met with inconsistent results. Choosing the best candidates preoperatively may ensure better hearing results. The gap is to define what factors are predictive of success in atresia surgery.

Learning Objective: Anatomy of the atretic ear has been a well-studied and well-recognized factor to aid the surgeon in determining a patient's surgical candidacy. Here we evaluate whether preoperative hearing status can be an adjuvant consideration in the evaluation of patients for atresia surgery. We also correlate preoperative hearing with anatomy of the atretic ear - does poorer anatomy truly correlate with poorer preoperative hearing - a "form and function" analysis.

Desired Result: Attendees will use the knowledge from this presentation to better counsel those patients with aural atresia with regard to hearing rehabilitation and the possibility of successful surgical outcomes.

Patient Care Medical Knowledge Practice-Based Learning

IRB or IACUC Approval: IRB number 15874; Approval pending

Petrous Apex Cholesterol Granuloma Histopathology: An Analysis of the Histopathology of Surgical Management and Histopathologic Evidence for the Exposed Marrow Theory

Michael Hoa, MD, John W. House, MD Fred H. Linthicum, Jr., MD

Objectives: 1) To review the histopathologic and radiologic changes associated with surgical drainage of petrous apex (PA) cholesterol granulomas. 2) To provide histopathologic evidence for the exposed marrow theory of petrous apex cholesterol granulomas. 3) To assess the maintenance of drainage pathway patency in patients who undergo surgical management of cholesterol granulomas Study design: Retrospective case review

Setting: Tertiary referral center

Patients: Patients with surgically managed petrous apex cholesterol granulomas at the House Clinic with available followup radiologic imaging. Histopathologic analysis was performed on temporal bones of patients with petrous apex cholesterol granulomas from the Temporal Bone repository at the House Research Institute.

Interventions: Surgical drainage of PA cholesterol granulomas. Followup radiologic imaging (CT or MRI).

Main Outcome Measures: Primary outcome is demonstrated maintenance of a PA outflow drainage pathway following the surgical drainage procedure as assessed by radiologic imaging, available histopathology, and/or recurrence of symptoms indicating failure of maintenance. Recurrence of symptoms is correlated with surgical findings at time of revision surgery.

Results: Histopathologic evidence for the exposed marrow theory of petrous apex cholesterol granulomas is reviewed. A majority of the patients exhibited maintenance of their PA drainage pathway. Histopathologic evidence suggests that the PA drainage pathway can be maintained for many years after surgical drainage. Recurrence of symptoms was correlated to obstruction of the drainage pathway by fibrous tissue and/or granulomatous tissue. Placement of a stent improved the patient's chance of remaining symptom-free.

Conclusions: The majority of patients who undergo surgical drainage of PA cholesterol granulomas remain symptom-free after surgical drainage. Histopathologic analysis of temporal bone specimens provides evidence supporting the exposed marrow theory of PA cholesterol granuloma formation. Loss of patency of the PA drainage pathway may be an important predictor for symptomatic recurrence of petrous apex cholesterol granulomas. Placement of a stent may decrease the likelihood of symptomatic recurrence.

Define Professional Practice Gap & Educational Need: 1) The efficacy of stent placement in surgical drainage of petrous apex cholesterol granulomas is undetermined. 2) While theories for formation of petrous apex cholesterol granulomas have been proposed, little histopathologic evidence has been presented to support these theories.

Learning Objective: 1) To understand the efficacy of stent placement in surgical drainage of petrous apex cholesterol granulomas. 2) To understand the histopathologic evidence that supports the exposed marrow theory of petrous apex cholesterol granulomas.

Desired Result: 1) To contribute to rational surgical decision-making by elucidating the efficacy of surgical drainage of petrous apex cholesterol granulomas in the absence or presence of stent placement. 2) To improve the body of knowledge as it relates to petrous apex cholesterol granuloma formation and the histopathologic and radiologic changes that occur with surgical drainage.

Medical Knowledge Practice-Based Learning

IRB Approval #: 11-014

High Fidelity, Inexpensive Surgical Middle Ear Simulator

Ashkan Monfared, MD, Gerald Mitteramskogler, MS Simon Gruber, MS, Kenneth Salisbury, PhD Juergen Stampfl, PhD, Nikolas H. Blevins, MD

Objective: Development and validation of a high fidelity, inexpensive middle ear surgical simulator.

Study design: Descriptive study

Setting: Academic center

Patients: None.

Intervention: Evaluation of the fidelity of face validity of a novel surgical simulator for middle ear surgery (SMS).

Main outcome measure: Fidelity and face validity of the simulator scores given by academic otologists using a questionnaire

Results: SMS is created using additive manufacturing technology (AMT), which allows for submilimeter resolution rapid prototyping. Using high resolution computer tomography (CT) of normal human ears, we created a physical three-dimensional middle ear model, including the tympanic cavity, ossicles, tendons, ligaments and nerves. Two different resins are used for bone and soft tissue to simulate their tactile and material characteristics. The middle ear model is placed within an outer construct to simulate the normal adult external auditory canal. The current SMS has a fixed stapes to facilitate training in stapedotomy, but it could be made to replicate a variety of normal and pathologic conditions. We will report experts' opinion of the face validity and fidelity of the simulator along with our experience using this system with trainees of various levels.

Conclusions: The SMS is a high fidelity, inexpensive, and reusable middle ear simulator that could be used for introductory training of novice surgeons and potentially serve as measurement tool to assess surgical capacity of otologic surgeons with any level of experience.

Define Professional Practice Gap & Educational Need: 1- Lack of a surgical simulator of middle ear surgery that has high fidelity and is inexpensive, reusable, and readily available.

Learning Objective: 1- Learn about the new Surgical Middle Ear simulator and how it could help with training and assessment of novice surgeons

Desired Result: 1- Audience would learn about a novel method of training novice surgeons in the art of middle ear surgery

Medical Knowledge Practice-Based Learning

IRB or IACUC Approval: yes

Direct Drive Micro Hearing Aid: Investigation of a Novel Completely-in-the-Canal Hearing Aid

Hossein Mahboubi, MD, MPH, Peyton Paulick, MS Saman Kiumehr, MD, Mark Merlo, PhD Mark Bachman, PhD, Hamid R. Djalilian, MD

Objectives/Hypothesis: To describe a novel direct-drive micro hearing aid (DMHA) and to test in temporal bones and evaluate the effectiveness and optimal positioning to prepare the device for clinical testing.

Background: Patient satisfaction with air conduction hearing aids has been low due to sound distortion, occlusion effect, and feedback. Implantable hearing aids provide a higher quality sound but require surgery for placement. The DMHA was developed to combine the ability of driving the ossicular chain with placement in the external auditory canal.

Methods: DMHA is a 3.5 mm wide device that fits entirely into the bony ear canal and directly drives the tympanic membrane (TM) rather than use a speaker. A cadaveric temporal bone was prepared for laser doppler vibrometry (LDV) of the stapes. The device developed in our laboratory was placed on the external surface of the TM and against the malleus. Frequency sweeps between 300Hz to 12kHz were performed at 104 and 120 dB. The DMHA was driven with various levels of current.

Results: The DMHA showed frequency response from 300Hz to 12kHz. Placement against the malleus showed higher amplitudes and lower power requirements than when the device was placed on the TM.

Conclusions: DMHA is a small completely-in-the-canal hearing aid that mechanically drives the TM. This novel device has the frequency output which is wider than air conduction devices. The device's ability to directly drive the TM enables it to potentially sound more naturally and similar to an implantable device. Clinical testing of the device is underway.

Define Professional Practice Gap & Educational Need: Inconsistencies within approaches for selection of different hearing aids and their advantages and disadvantages.

Learning Objective: To better learn the differences between air conduction and implantable hearing aids, and the possibility of combining advantages of both into one device.

Desired Result: Develop a better understanding of the novel approach to design a completely-in-the-canal hearing aid.

Medical Knowledge

IRB: HS# 2011-8482 Funded by a grant from the Center for Hearing Research at UC Irvine.

Radiographic Findings, Surgical Techniques, and Outcomes of Cochlear Implantation in Patients with X-Linked Deafness

Maura K. Cosetti, MD, David R. Friedmann, MD Selena E. Heman-Ackah, MD, MBA David Drimmer, BS, Susan B. Waltzman, PhD J. Thomas Roland, Jr., MD

Objectives: X-linked deafness is a potential etiology of sensorineural hearing loss characterized by bulbous dilatation of the fundus of the internal auditory canal (IAC) and the absence of the bony plates separating the basal turn of the cochlea and IAC. These malformations predispose patients with X-linked deafness to IAC insertion during CI. The objective of this presentation is to describe associated audiometric presentation, surgical techniques, and CI performance in patients with X-linked deafness.

Study Design: Case series.

Methods: A retrospective chart review was performed of all patients at a tertiary care facility who underwent CI between January 2006 and July 2011.

Results: A total of 4 patients were identified with characteristic radiographic findings of X-linked deafness. Audiometric findings at presentation were described. A modified cochleostomy was utilized to ensure electrode insertion within the scala tympani avoiding the internal auditory canal. Fluoroscopy was utilized to visual electrode progression during insertion. Complete insertion was accomplished in all patients. Cochlear implant performance for each patient was detailed.

Conclusions: Utilizing the techniques described, patients with X-linked deafness may successfully undergo CI with excellent potential for auditory rehabilitation.

Define Professional Practice Gap & Educational Need: 1) Paucity of data regarding the audiologic and radiographic presentation of patients with X-linked deafness; 2) lack of awareness of surgical techniques to prevent internal auditory canal insertion of the cochlear implant electrode in patients with X-linked deafness; 3) minimal data on post-operative outcomes in this patient population

Learning Objective: At the conclusion of this presentation, the participants should be able to (1) describe the potential audiological presentation of patients with X-linked deafness, (2) detail surgical techniques for cochlear implantation in patients with cochlear findings characteristic of X-linked deafness, and (3) describe expectations for performance outcome following cochlear implantation (CI) in patients with X-linked deafness.

Desired Result: Attendees will have 1) increased knowledge of the audiologic and radiographic presentation, diagnosis and post-operative outcomes of patients with X-linked deafness and 2) be able to recognize and prevent unintentional IAC insertions during cochlear implantation.

Medical Knowledge Practice-Based Learning

IRB or LACUC Approval: 11281

The Round Window: Is It the 'Cochleostomy' of Choice? Experience in 120 Consecutive Cochlear Implant Patients

David A. Gudis, MD, Douglas C. Bigelow, MD Michael J. Ruckenstein, MD

Objective: To demonstrate that round window insertion (RWI) for cochlear implantation with current multichannel electrodes is a reliable, effective, and safe technique; to demonstrate that RWI patient performance is equivalent to cochleostomy implantation.

Study design: Retrospective cohort of two years of consecutive cochlear implants.

Setting: Academic tertiary care referral center

Patients: 120 patients (65 female:55 male, age 19-92 years) underwent 129 consecutive cochlear implant procedures (9 bilateral) over a twoyear period. Devices included 82 Cochlear, 40 Med El, and 7 Advanced Bionics implants.

Intervention(s): Subsequent to a full audiometric assessment, patients underwent a mastoidectomy with facial recess approach whereby the primary surgical objective was to perform a RWI. When the surgeon was unable to access the round window safely, a cochleostomy was performed anterior and inferior to the round window. Post-operative performance was measured with HINT and/or AZ-Bio testing.

Main outcome measure(s): Surgical feasibility of safely performing a RWI; perioperative and post-operative complications; post-operative audiometric performance.

Results: In 109 out of 129 procedures (84.5%), a RWI was performed without any major post-operative complications. In 20 out of 129 procedures (15.5%), a separate cochleostomy was readily performed by the same approach. Both patient groups demonstrate post-operative performance similar to each other and to other reported series. Reasons for RWI failure included facial nerve or jugular bulb location and cochlear ossification. Acoustic hearing was preserved in 4 out of 4 RWI patients enrolled in a separate hearing-preservation trial.

Conclusions: RWI represents a reliable, effective, and safe technique for cochlear implantation.

Define Professional Practice Gap & Educational Need: 1. Inconsistency among surgeons regarding optimal insertion technique for cochlear implants. 2. Lack of agreement regarding anatomical feasibility of round window insertion for cochlear implants. 3. Lack of contemporary knowledge regarding comparison of performance data for cochlear implant patients based on method of insertion.

Learning Objective: 1. To understand the potential advantages and disadvantages of round window insertion for cochlear implantation. 2. To understand the post-operative performance of cochlear implant patients based on method of insertion. 3. To understand the anatomy of the facial recess approach and round window insertion. 4. To understand the surgical technique of round window insertion in detail.

Desired Result: 1. Attendees may apply the knowledge of this presentation to reconsider or modify their current surgical approach to cochlear implantation. 2. Attendees may better understand the advantages of round window insertion versus cochleostomy for cochlear implants.

Patient Care Medical Knowledge

IRB or IACUC Approval: 802604

Minimal Access Cochlear Implant Fixation: Tight Pocket with a Plate

Clough Shelton, MD, Frank M. Warren, MD

Objective: Minimal access approaches for cochlear implants have recently gained popularity, offering a smaller incision and minimal hair shave. Thinner internal receivers now available are adaptable for these approaches. However, conventional boney fixation of the internal receiver is difficult through this limited exposure and some minimal access techniques rely on soft tissue fixation only. Inadequate fixation can result in device migration, extrusion and electrode migration.

We compare wound complications and electrode migration for a group undergoing conventional exposure [10 cm incision, formation of a boney well and hold down sutures secured to bone] with a group undergoing minimal access with plate fixation [4 cm incision and device fixation using a titanium plate screwed to skull].

Study design: retrospective case review

Setting: Tertiary referral center

Patients: adults and children undergoing primary cochlear implant surgery using either technique

Intervention(s): therapeutic

Main outcome measure(s): Wound complications including device exposure or extrusion, electrode migration, wound breakdown, abscess, or cellulitis.

Results: There were 237 implants in the conventional group and 103 in the minimal access with plate group. The conventional group suffered a complication rate of 2.5% and the minimal access with plate group experienced a complication rate of 1%.

Conclusions: Cochlear implant surgery using the minimal access with plate fixation results in a similar wound complication rate as the conventional approach.

Define Professional Practice Gap & Educational Need: Inconsistencies within cochlear implant fixation

Learning Objective: Learn new fixation techniques

Desired Result: Be aware of new fixation options

Patient Care

IRB or IACUC Approval: IRB 00045048

Management of Electrode Exposure after Cochlear Implantation

Evan Walgama, MD, J. Walter Kutz, Jr., MD Peter S. Roland, MD, Brandon Isaacson, MD

Background: Exposure of a cochlear implant electrode array in the middle ear or external auditory canal is an uncommon complication. The limited evidence in the literature suggests that revision surgery can be performed successfully. We report a series of patients who elected to pursue conservative management as their implant was still functioning.

Objective: To evaluate observation as a strategy in the management of electrode exposure after cochlear implantation.

Study design: Retrospective case series

Setting: Tertiary neurotology practice

Patients: Patients with cochlear implant electrode exposure in the middle ear or external auditory canal who elected not to undergo revision surgery.

Main outcome measure: Length of follow-up without deterioration of implant function and without serious complication.

Results: Four patients between ages 4 and 85 elected not to undergo revision surgery for electrode exposure after cochlear implantation. One patient presented with a poorly functioning implant, but after reprogramming the implant returned to its baseline performance. Three other patients required no reprogramming and were managed medically without deterioration of implant function. Follow up time was between 2 and 5 years. There were no serious complications in any patient related to their cochlear implant.

Conclusions: Careful observation of patients with an exposed electrode after cochlear implantation and a functioning implant appears to be a reasonable management option.

Define Professional Practice Gap & Educational Need: 1. Lack of awareness of management options for complications of cochlear implantation

Learning Objective: Understand strategies in the management of electrode exposure, a complication of cochlear implantation.

Desired Result: Physicians will apply a spectrum of reported experience when counseling patients with electrode exposure after cochlear implantation regarding their treatment options.

Patient Care Medical Knowledge Practice-Based Learning Interpersonal and Commun

IRB or IACUC Approval: IRB approval was obtained prior to commencement of this study.

Effects of Intracochlear Trauma on Long-Term Hearing Outcomes in Normal Hearing Gerbils

John M. Pike, BS, Oliver F. Adunka, MD Baishakhi Choudhury, MD, Omar Awan, BS Kristine Faulk, BS, Douglas C. Fitzpatrick, PhD

Hypothesis: Reductions in auditory potentials due to cochlear trauma during a cochlear implantation will be predictive of long-term hearing outcomes.

Background: Cochlear implants are increasingly being provided to patients with residual hearing but poor speech understanding. If the residual hearing is preserved, speech understanding can be improved, especially in background noise. We have developed a gerbil model of cochlear implantation and determined that reductions in the cochlear microphonic (CM) can be used as a marker of intracochlear trauma. However, it is not known if the degree of trauma correlates with hearing outcomes.

Methods: Insertions of a rigid electrode through the round window were performed in normal-hearing gerbils. Acoustically evoked auditory potentials were recorded at the round window to tone bursts of varying frequency and intensity prior to insertion, after insertion, and after a 4 week survival period. The animal was sacrificed and the cochlea was prepared as a whole mount to verify the degree of damage.

Results: Most experimental animals (1.3 mm insertion) showed an initial reduction in the CM at high frequencies (4-16 kHz). After survival the reductions either remained the same or increased, including spread to low frequencies. These cases showed damage to the basilar membrane. Control cases (0.4 mm insertion) showed no loss of response.

Conclusions: These results indicate that the recordings made at the time of surgery can partially predict the long-term outcome of damage induced by the initial implantation surgery. Ultimately, we plan to apply these results to provide real-time feedback during cochlear implantation.

Define Professional Practice Gap & Educational Need 1: Lack of knowledge regarding physiologic effects of cochlear implant insertion. 2. Lack of a reliable technique to measure cochlear function during an implantation surgery.

Learning Objective: At the conclusion of this presentation, the participants should understand patterns observed in acoustically evoked early auditory potentials upon cochlear implantation in normal hearing gerbils and the predictive potential this has for long-term outcomes.

Desired Result: Attendees will have a better knowledge of cochlear physiology and how it can be measured during the implantation procedure. Eventually, our lab hopes to implement the recording system in practice for cochlear implantation patients in order to assess acute damage and long-term outcomes.

Medical Knowledge

IACUC approved - protocol #: 11-150 Supported by NIH grant T32-D005360 and the MED-EL corporation.

Minimization of Cochlear Implant Artifact in Cortical Auditory Evoked Potentials in Children

David Bakhos, MD, S. Roux, E. Lescanne, MD, PhD F. Bonnet-Brilhaut, MD, PhD, N. Bruneau, PhD

Objectives: In congenitally deaf children fit with a cochlear implant, little is known about the maturation of the auditory cortex. Cortical auditory evoked potentials are a useful methodology to study the auditory performance of children with cochlear implants. Nevertheless, these recordings are contaminated with well-known physiological artifacts (blinking, muscle) but also by cochlear implant artifact. The cochlear implant induces an artifact in the temporal lobe area. When specific tones are presented, detection and analysis of electrical artifact are difficult or impossible to measure. The objective of this study was to evaluate the independent component analysis in order to minimize the artifact of the cochlear implant.

Study design: prospective study

Method: Five children, aged ranged from 18 months to 4 years, who were fitted with a cochlear implant for at least 6 months, were included in this study. The stimuli were pure tone (750 Hz, 200 ms duration, 70 dB SPL) presented with irregular interstimulus interval (1000 and 2000 ms) via loud speakers. Cortical auditory evoked potentials were recorded from 17 Ag-AgCl (Fz, Cz, Pz, Oz, F8, C4, T8, P8, P10, P04, F7, C3, T7, P7, P9, PO3, MO) electrodes referenced to the nose. Peak latency and amplitude of each deflection culminating at fronto-central and temporal sites were analyzed.

Main outcomes measures: P1-N1-P2 peak latencies and amplitude in cortical auditory evoked potential recorded from children fitted with cochlear implants.

Results: The use of independent component analysis permit to minimize the cochlear implant artifact for the five children. P1-N1-P2 was recorded in fronto-central and temporal sites. Even if the artifact cochlear implant was smaller, it was still present in temporal site ipsilateral to the implanted side.

Conclusion: Independent component analysis allows the study of cortical auditory evoked potential and permits longitudinal studies in cochlear implant users in order to study the maturation of the auditory cortex.

Define Professional Practice Gap & Educational Need: Lack of awareness.

Learning Objective: To minimize the artifact of the cochlear implant in cortical auditory potentials.

Desired Result: To identify PI-N1-P2-N2 complex in children with cochlear implant.

Practice-Based Learning

IRB Approval Number:

Programming Strategy and Outcomes in Cochlear Implant Patients with Auditory Neuropathy Spectrum Disorder

Stanley Pelosi, MD, Alejandro Rivas, MD David Haynes, MD, Marc L. Bennett, MD Robert F. Labadie, MD, PhD, Linda Hood, PhD Andrea Hedley-Williams, AuD, George B. Wanna, MD

Objective: Patients with auditory neuropathy spectrum disorder (ANSD) exhibit altered neural synchrony in response to auditory stimuli. It has been hypothesized that a slower rate of electrical stimulation in programming strategies for cochlear implant (CI) users with ANSD may enhance development of neural synchrony and speech perception abilities.

Study design: Retrospective case series

Setting: Tertiary otologic practice

Patients: 39 patients with ANSD were reviewed.

Intervention: 20 patients with ANSD underwent CI.

Main outcome measures: electrically-evoked compound action potentials (ECAP) at the time of implantation; post-CI neural stimulation rates over time; speech perception abilities over time using parent questionnaire, closed-set testing, and open-set measures.

Results: The average length of followup for all patients was 36 months (range 0-69). ANSD patients were more likely to have been premature or admitted to the neonatal intensive care unit (p<0.05). Measurable ECAP responses were present in 11/13 patients with available data. 12/19 post-CI patients with available data were able to achieve open-set speech perception scores greater than or equal to 60%. Neural stimulation rates ranged from 250 to 3700 Hz. There were no significant differences in neural stimulation rate and auditory development as assessed by parent questionnaire (p<0.05).

Conclusions: A wide range of speech perception abilities is observed in patients with ANSD following CI. Other patient variables may play a more significant role than CI programming strategy in the development of auditory skills for this population.

Define Professional Practice Gap & Educational Need: There exists an incomplete understanding of the neural mechanisms that contribute to auditory dysfunction in patients with auditory neuropathy spectrum disorder. The means by which auditory neuropathy patients derive benefit from cochlear implantation has also been inadequately explained. Patients with auditory neuropathy spectrum disorder and cochlear implants exhibit a wide range of auditory development over time. The mechanisms underlying speech perception outcomes in these patients are not well-understood. One hypothesis is that a lower rate of auditory stimulation may enhance auditory synchrony and development of speech perception abilities. However, to this point no studies have demonstrated a relationship between neural stimulation rate in programming strategies and auditory development in cochlear implant users with auditory neuropathy.

Learning Objective: We aim to demonstrate the relationship between neural stimulation rate in programming strategies for cochlear implant users with auditory neuropathy and development of speech perception abilities.

Desired Result: Our intended result is to determine whether a lower electrical stimulation rate will enhance auditory development in cochlear implant users with auditory neuropathy.

Patient Care

Medical Knowledge

Practice-Based Learning

IRB or IACUC Approval: 101743, 090155

Speech Perception Performance of Double Array Nucleus Multichannel Cochlear Implant Users With Standard and Duplicated Maps in Each of the Arrays

Ricardo F. Bento, MD, PhD, Maria Valeria S.G. Gomez, PhD Rubens V.B. Neto, MD, PhD, Robinson Koji Tsuji, MD, PhD Anna Carolina O. Fonseca, MD, Liliane S. Ikari, MD

Objective. The present investigation evaluated the speech perception performance of adult patients with ossified cochleas implanted with the Nucleus 24M Double Array cochlear implant, using standard and duplicated maps in each of the arrays.

Study design. Retrospective case review.

Setting. Tertiary referral center

Patients. Sixteen subjects received a Nucleus 24 Double array Cochlear implant. Nine of them filled the following inclusion criteria: post lingually deaf patients with bilateral severe to profound deafness; bilateral obliterated cochlea due to different etiologies shown by the CT scan; older than 14 years of age to be able to give reliable responses in all the behavioral tests with the three tested maps.

Intervention. Rehabilitative

Main outcome measures. Speech perception performance with the two arrays was compared to the performance with the basal array duplicated and apical array duplicated maps. Three maps were fitted: the default map with both arrays activated, a double channel map using only the electrodes of the basal array, and a double channel map programmed only with electrodes of the apical array. Test battery was composed of vowels, closed set word and sentence recognition in quiet.

Results. The performance was similar in the four-choice word test for all the map situations; nevertheless, in both vowel and in closed set sentence recognition the standard map with both electrode arrays activated showed the highest scores (p<0.05).

Conclusions. The present results suggest that the performance with two split electrode arrays is superior to the performance with one array, regardless the duplication of channels.

Define Professional Practice Gap & Educational Need: Lack of contemporary knowledge about Speech Perception Performance of Double Array Nucleus Multichannel Cochlear Implant in obliterated cochleas.

Learning Objective: Evaluate the speech perception performance of adult patients with ossified cochleas implanted with the Nucleus 24M Double Array cochlear implant, using standard and duplicated maps in each of the arrays.

Desired Result: When indicating a cochlear implant in ossified cochleas they will know that the performance with two split electrode arrays is superior to the performance with one array, regardless the duplication of channels.

Patient Care, Medical Knowledge

IRB or IACUC Approval: 633/04

Automatic, Image-based Cochlear Implant Electrode-to-Spiral Ganglion Position Analysis: Implications for Programming

Jack H. Noble, PhD, Benoit M. Dawant, PhD Rene H. Gifford, PhD, Robert F. Labadie, MD, PhD

Hypothesis: We can develop an approach for determining the position of implanted cochlear implant (CI) electrodes relative to stimulation targets (the nerves of the Spiral Ganglion (SG)) for customized programming of CIs.

Background: Electrode position-dependent CI programming schemes can potentially improve hearing outcomes by customizing frequency allocation tables. In this work, we present the first approach for such by accurately determining electrode position relative to SG. The approach is fully automatic and thus practical for clinical use.

Methods: Intra-cochlear anatomy (scala tympani (ST) and vestibuli (SV)) and stimulation targets (the SG) are identified in pre-operative CT, and the electrode array is identified in post-operative CT using advanced image processing techniques. Pre and post-operative images are aligned using automatic image registration techniques. Tonotopy is computed using a previously presented equation that maps characteristic frequencies of the SG. For each implanted electrode, we automatically compute intra-cochlear compartment (ST or SV), distance-to-SG, and the SG characteristic frequency at that closest point.

Results: Using pre and post-operative CT, the proposed techniques are able to accurately identify the electrode and anatomical structures and are able to predict programming relevant characteristics associated with electrode position. Graphical results of such will be shown.

Conclusions: The software we have developed can be used to test and/or apply electrode position-dependent CI programming schemes. For programming, the automatically computed information specifies the optimal set of active electrodes, frequency allocation table, and electrode signal levels. Future work will include studying hearing outcomes using customized, position-dependant frequency allocation tables.

Define Professional Practice Gap & Educational Need: While it is widely believed that electrode position-dependent CI programming schemes can potentially improve hearing outcomes by customizing frequency allocation tables, until now there has been no technology developed to accurately determine electrode position relative to stimulation targets (the spiral ganglion). In this presentation, we will introduce the first of such technology to bring awareness to the professional community that position dependent programming schemes are now feasible.

The learning objectives include: (1) a basic knowledge of how the software works, (2) how well the software performs, (3) how it can be used for position-dependent CI programming, and (4) how position-dependent programming schemes can lead to better hearing outcomes.

The desired result is to increase awareness in the community that positiondependent programming schemes are possible and may improve hearing outcome so that researchers can take more steps in this direction. Eventually, if this approach does improve hearing outcomes, the goal would be for it to replace the typical 'one-size-fits-all' type approach for CIprogramming and become standard of care procedure.

Medical Knowledge

IRB Approval Number: 090155

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Implantation of the Vestibular System: Monkey and Man

Justin S. Golub, MD, Leo Ling, PhD Steven M. Bierer, PhD, Kaibao Nie, PhD James O. Phillips, PhD, Jay T. Rubinstein, MD, PhD

Hypotheses: (1) All three semicircular canals may be implanted with a vestibular prosthesis (2) Auditory and vestibular function may be preserved (3) Stimulation will result in canal-appropriate eye movements.

Background: A variety of vestibular pathologies may potentially be treated with prosthetic stimulation of the semicircular canals. We implanted all three canals in a normal rhesus monkey and a single human with uncontrolled Meniere's disease as part of an FDA feasibility study.

Methods: The UW/Nucleus Vestibular Implant was implanted adjacent to the three ampullae of a normal adolescent rhesus macaque and a human subject with uncontrolled Meniere's disease. Auditory function was assessed with auditory brainstem response testing (monkey) or standard audiometry (human). Vestibular function was measured with rotary chair testing using a scleral coil (monkey) or videonystagmography (human) to measure the vestibulo-ocular reflex.

Results: Implantation of all semicircular canals was technically feasible in monkey and human, though due to size constraints is markedly easier in human. Auditory and vestibular function were preserved in the monkey but not in the human subject. Stimulation resulted in canalappropriate eye movements in both monkey and human. Slow phase velocities were substantially higher and current thresholds were lower in monkey.

Conclusions: It is technically feasible to functionally implant all semicircular canals while preserving auditory and vestibular function. The lack of preservation in the single human subject may be related to the small N, Meniere's pathology, or other unknown factors. Comparing findings between monkey and man will facilitate translation of this important technology to the clinical realm.

Define Professional Practice Gap & Educational Need: There is insufficient understanding of novel and experimental treatments for vestibular disorders, including prosthetic stimulation of the vestibular system.

Learning Objective: (1) Understand the surgical technique for placement of the UW/Nucleus Vestibular Implant. (2) Understand basic physiologic measures used to assess functionality of the prosthetic device. (3) Understand the possibility of preserving auditory and vestibular function. (4) Understand different results obtained with monkey and human implantation.

Desired Result: Attendees will be aware of prosthetic stimulation of the semicircular canals for treatment of vestibular disorders, including the advantages and potential hurdles.

Patient Care Medical Knowledge Practice-Based Learning

IRB or IACUC Approval: WIRB # University of Washington-UWVN001_1

List outside funding: NIDCD, the Coulter Foundation, Cochlear, Ltd, and a gift from Sara Kranwinkle.

Progress Report—Glutamate Receptors, Signaling and Gentamicin in the Mammalian Vestibular System PI: Katherine J. Rennie, PhD

Significant ototoxicity limits the use of aminoglycoside antibiotics. Several mechanisms may contribute to death of both auditory and vestibular hair cells. Aminoglycosides enter outer hair cells of the cochlea through apical mechano-transduction channels (Marcotti et al. 2005) and can also inhibit the basolateral KCNQ4-mediated current ($I_{K,n}$) by PIP2 sequestration (Leitner et al. 2011). To test if similar mechanisms occur in vestibular cells, we investigated the effects of aminoglycosides and KCNQ channel modulators on potassium currents ($I_{K,n}$) in type I vestibular hair cells.

Whole cell patch clamp recordings were made from hair cells isolated from postnatal gerbil semicircular canals. At birth vestibular hair cells have delayed rectifier K⁺ currents and by the third postnatal week type I vestibular hair cells also express a low-voltage activated K⁺ current that resembles IK,n in outer hair cells. Extracellular neomycin (1 mM) rapidly and significantly reduced peak outward I_K by 16 ± 4.0% (n = 9) in mature type I hair cells. Gentamicin reduced peak I_K by 16.1 ± 7.2 % (n = 8). Intracellular exposure to aminoglycosides was also investigated. Intracellular Neomycin (1 mM in the patch electrode solution) reduced I_K by 17 ± 5.6%. KCNQ channel modulators were also used to probe KCNO channels. XE991 (20 uM) did not reduce IK in mature type I hair cells and the neomycin-induced reduction in IK was not reversed by the KCNQ agonist flupirtine (10 uM). Application of intracellular poly-Dlysine, which sequesters phosphoinositodes, had no significant effect on I_K in type I hair cells. Extracellular 4-aminopyridine (4-AP, 1mM) blocked a component of I_K and application of extracellular aminoglycosides in the presence of 4-AP gave no further inhibition of I_{K} . In immature type I hair cells (postnatal days 5-8), extracellular neomycin reduced I_K by $19 \pm 3.4\%$ (n = 5). We confirmed with fluorescent imaging that externally applied Texas Red conjugated gentamicin (GTTR) was rapidly taken up by vestibular hair cells.

We conclude that aminoglycosides significantly reduce the 4-APsensitive K^+ current in both early postnatal and mature type I vestibular hair cells. Our results also suggest that K^+ current inhibition in type I hair cells differs from that seen in outer hair cells, since it does not appear to involve PIP2 sequestration or KCNQ channels.

Progress Report - AOS Research Grant: Ménière's Disease - A

Molecular Genetic Study PI: Richard Smith, MD

Familial Menière's Disease Exome

We have been identified a small nuclear family in which three siblings have definite Menière's Disease (MD); both parents are unaffected. To test the hypothesis of distant autozygosity by descent (ABD), we used the Affymetrix 6.0 SNP array (Affymetrix, Santa Clara, CA) to genotyped all persons in this family. ABD analysis was completed using dChip under the assumption of autosomal recessive inheritance. Multiple shared homozygous regions were

identified throughout the genome consistent with a distantly outbred family. Homozygous regions with a LOD score of 0.27 were then analyzed in detail. Concurrently, targeted capture of the exome was performed on one affected sibling with the Agilent SureSelect Human All Exon 50Mb Kit. Paired-end sequencing using a SOLiD 4 was performed on captured DNA, reads mapped to the human reference genome (hg19), and variants identified. Overall, 90.42% of variants were present in dbSNP. There was 96.06% concordance

between the Affymetrix 6.0 SNP array calls and the SOLiD 4 exome variant calls. Next, regions of homozygosity were identified from the sequence data and compared to the regions of ABD from the SNP array data. A composite list of ABD regions has been complied and sequence variants within those intervals are being prioritized for validation. Variants are being chosen for Sanger validation based on the following criteria: in regions of ABD, variants must be nonsynonymous, novel or rare (<1% frequency in dbSNP132). We will also consider two heterozygous variants must be validated and tested for familial segregation. Genes with variants passing all filters will be prioritized by putative function and cochlear or

endolymphatic sac expression. In addition, we will screen a singleton MD cohort and matched controls for common and rare variants as a test of the Common Disease Common Variant (CDCV) and Common Disease Rare Variant (CDRV) hypotheses. If a pathogenic variant is not identified, whole exome sequencing will be performed on the other affected siblings. Following mapping and variant identification, results of all three exomes will be compared and shared regions of homozygosity will be identified. Regions will be

confirmed with the Affymetrix 6.0 SNP array data. We anticipate that analysis of three exomes will yield fewer regions of shared homozygosity. In addition, the sequence data from all three exomes can be combined as another filtering strategy. If this approach does not yield a pathogenic variant, custom targeted sequence capture will be performed on all ABD intervals and regions of the exome with inadequate coverage for accurate variant detection. ABD intervals can be interrogated for large insertions or deletions although this is not anticipated to cause MD in this family as large insertions or deletions of the genome would be expected to result in a more complex phenotype.

Transcriptome of the Endolymphatic sac

Endolymphatic sac samples have been obtained during endolymphatic sac shunt surgery or translabyrinthine surgery and stored in RNALater (Ambion) at -80C. As 200ng of high quality

total RNA is required for library preparation RNA, extraction techniques to yield sufficient quality and quantity of RNA are being optimized. We continue to collect endolymphatic sac samples.

<u>Summary</u> We have completed our objectives for the first six months and are actively pursuing our objectives and completion of both aims in the next six months.

Progress Report- AOS Research Grant: Role of Dexamethasoneinduced Aquaporin 3 Regulation in Endolymphatic Hydrops PI: Sung K. Moon,, MD, PhD

A. Specific Aims

The long-term goal of this project is to elucidate the role of the endolymphatic sac (ES) in the endolymph homeostasis on a molecular level and to investigate the role of aquaporins (AQPs) in the pathophysiology of endolymphatic hydrops for the exploration of the way to prevent/manage Meniere's disease. We hypothesize that pendrin expression affects AQP3 expression since the ES light cells are considered to be involved in fluid regulation through the energy generated by abundant mitochondria like a tubular cell of the kidney. To address this hypothesis, we propose three specific aims as follows:

Define an effect of pendrin expression on AQP3 expression in the human ES cells.

Determine if dexamethasone affects water permeability through upregulation of AQP3 in the pendrin-positive ES cells

Determine an effect of systemic dexamethasone on endolymphatic hydrops associated with pendrin deficiency

B. Studies and Results.

- Karyotypic analysis (Cell Culture Characterization Services, Orion Township, MI) of the immortalized ES cells (clone #13, passage 23) showed that the immortalized ES cells are diploid human male, with most chromosome counts in the range of 44 to 47 (modal number 46).
- The human endolymphatic sac cell line was further characterized and was found to secrete osmotically active viscous molecules in response to EGF and retinoic acid.
- RT-PCR analysis demonstrated the vasopressin-induced up-regulation of AQP2 as well as V2R. In addition, vasopressin-induced V2R up-regulation was inhibited by MAPK inhibitors, such as MEK1 inhibitor (PD98509) and p38 MAPK inhibitor (SB203580).
- Temporal bone histopathological analysis showed the compartment anomaly in the cochlea of the Foxi1-deficient mice that show head tilt.
- Pendrin-positive cells appeared to express AQP3 more than the pendrinnegative cells.
- RT-PCR analysis showed that the human ES cell line expresses the glucocorticoid receptor, which appeared to be up-regulated in the round cells.

D. Plans

- We plan to determine if silencing of pendrin affect AQP3 expression in the human ES cell line.
- We plan to determine if dexamethasone up-regulate AQP3 expression in the pendrin-positive ES cells.
- We plan to determine if dexamethasone affect water permeability of the pendrin-positive ES cells.
- We plan to determine if the silencing of AQP3 inhibit dexamethasoneinduced increase in water permeability in the pendrin-positive ES cells.
- We plan to determine if pendrin deficiency affect AQP3 expression in the murine ES in vivo.
- We plan to determine if systemic dexamethasone up-regulate AQP3 expression in the murine ES in vivo.
- We plan to determine if systemic dexamethasone affect pendrin deficiencyassociated endolymphatic hydrops in vivo.

E. Publications

Lim DJ, Moon SK. Establishment of cell lines from the human middle and inner ear epithelial cells. Adv Exp Med Biol. 2011;720:15-25.

F. Generated Resources related to this project

We have submitted an application for the U.S. patent of the human endolymphatic sac cell line.

Progress Report: AOS Research Grant: Restoration of Hearing in the Otoferlin Knockout Mouse using Viral Gene Therapy PI: Aurash Alemi

We hypothesize that in vivo microinjection of adeno-associated virus with an otoferlin gene insert (AAV2-OTOF) into the cochlear endolymph of the OTOF knockout (KO) mouse will restore hearing and reverse the pathologic changes.

Our application of adeno-associated virus (AAV) as a vector for the introduction of otoferlin in the KO mouse has been challenged by the 4.5-5 kilobase (kb) adeno-associated viral packaging limitation. Because the otoferlin cDNA is almost 6kb, the intact gene cannot be efficiently packaged inside of AAV.

A hybrid dual AAV vector system has been developed, which shows promise as a possible solution to the AAV packaging limitation^{1, 2}. The hybrid dual AAV vector system employs 2 separate viruses which each contain the 5' and 3' halves of the target gene respectively as well as a bridging DNA sequence and splicing signals. Reconstitution of full-length gene of interest occurs by ITR-mediated head-to-tail vector genome concatamerization and/ or bridging DNA sequence-mediated homologous recombination¹.

The molecular cloning of the otoferlin gene has been the focus of much of our efforts to date. The full-length gene was bisected using PCR amplification into a 5' half (2.8kb) and a 3' half (3.2 kb). These gene constructs have each been cloned into their respective hybrid vector, with the 5' half flanking the cytomegalovirus (CMV) promoter and the 3' half flanking a polyA sequence. Additionally, because our previous gene therapy studies expressed VGLUT3 using the chick beta actin (CBA) promoter, we have also created constructs containing CBA to compare expression of the two promoters (unpublished). As a positive control for the hybrid dual vector system, a 5' half vector has also been constructed, which contains the full length GFP gene, which will be recombined with an empty 3' vector cassette to monitor recombination efficiency.

The plasmid DNA vector system has been transfected onto HEK-293 cells at various concentrations using Lipofectamine2000 (Invitrogen) with minimal evidence of otoferlin gene expression. Because of the low co-transfection rate and low reported efficiency of vector recombination *in vitro*, we have decided to move forward with AAV2 production, which has been found to have high transduction efficiency in inner hair cells *in vivo* as well as in *in vitro* studies³. The plasmids are currently in their final stage of preparation and viral production is set to begin by the MassGeneral Vector Core Group (Massachusetts General Hospital). Following receipt of the viruses, studies will begin on the otoferlin KO mouse as well as continuation of both qualitative and quantitative *in vitro* studies, which we expect to complete by the end of the funding cycle.

References:

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Progress Report: AOS Research Grant: Transgenic Over-expression of a Cochlin Mutant in the Inner Ear PI: Long-Sheng Chang, PhD; D. Bradley Welling, MD, PhD

Presently, the exact cause of Ménière's disease, which is characterized by severe sudden attacks of vertigo, tinnitus, aural fullness, and fluctuations in hearing, is not understood, and there is no cure for this disease. Studies have suggested the involvement of combined environmental and genetic factors. Although most cases of Ménière's disease are sporadic, about 7% of those affected have a family history of the disease, suggesting that the disease development in some patients may have a heritable component. The ultimate goal of our research is to uncover the biological mechanisms in the inner ear that cause familial Ménière's disease, ultimately leading to a better understanding of the pathophysiology of this disorder and the development of preventive strategies and more effective treatment. To approach this goal, we have undertaken two approaches. First, we plan to define the elements required for inner ear-specific expression in the promoter of the Cochlin (COCH) gene, whose mutations cause autosomal-dominantly inherited hearing loss associated with vestibular dysfunction, designated DFNA9. We have isolated a 1.1-kb human COCH promoter and used it to generate a COCH promoter-driven luciferase-expressing construct. The COCH promoter contains several potential ear- and brain-specific transcription factor-binding sites and could direct luciferase expression in cultured epithelial cells. We also generated a *COCH* promoter-driven Cre recombinase construct, which will be used to generate transgenic mice for inner ear-specific gene inactivation. Second, we have obtained three embryonic stem cell (ES) clones with a knockout (KO) allele for Slc45a3 (solute carrier family 45, member 3), which encodes a multipass membrane-bound, solute transporter. Mutations in several members of the solute carrier family have been implicated in hereditary hearing loss. By blastocyst injection, we generated chimeric mice from two of the $Slc45a3^{KO}$ ES clones. Through further mating, we obtained heterozygous $Slc45a3^{KO}$ mice. We are in the process of producing homozygous $Slc45a3^{KO}$ mice, which will be used to better understand the role of Slc45a3 in hearing and vestibular functions in the inner ear.

Progress Report: AOS Research Grant: p75NTR Signaling in Vestibular Schwannoma Cells PI: Iram Ahmad, MD

Neurofibromatosis type II (NF2) is characterized by bilateral vestibular schwannomas (VSs) and results from a mutation of the tumor suppressor gene merlin. We are studying the differences of VS cells compared with normal Schwan cells (SCs) that allow VS cells to proliferate and survive in the absence of axonal contact. Following loss of axonal contact, normal SCs upregulate p75NTR receptor expression, re-enter the cell cycle, and ultimately undergo apoptosis due, at least in part, to activation of p75NTR. We have previously found, like denervated SCs, VSs express higher levels of p75NTR compared with normal nerves. ProNGF, a high affinity ligand for p75NTR, induces apoptosis in normal SCs by activating c-Jun N-terminal kinase (JNK). By contrast, VS cells fail to die in the presence of proNGF. Furthermore, VS cells display persistent JNK activation that prevents apoptosis. ProNGF rescues VS cells with suppressed JNK signaling suggesting that, in contrast to its role in normal SCs, p75NTR promotes VS cell survival. We previously showed that p75NTR expression correlates with merlin inactivation and proliferation in normal SCs and that activation of p75NTR enhances proliferation of a schwannoma cell line. We have taken this to study nerves with a POSchD39-121 mutation in merlin. Our recent work has shown that p75NTR is increased in P0SchD39-121 mice compared to the wild-type. We performed sciatic nerve axotomies on mice and observed that loss of axonal contact results in merlin inactivation by S518 phosphorylation, correlated with increased proliferation and p75^{NTR} expression. To verify that loss of merlin function leads to increased $p75^{NTR}$ expression, we compared $p75^{NTR}$ levels in the sciatic nerves from wild-type and POSchD39-121 mice, which harbor an inactivating merlin mutation. We observed elevated p75^{NTR} expression in the uninjured nerves of P0SchD39-121 mice compared with nerves from wild-type mice. p75^{NTR} is elevated in uncut mutant mice nerves. We also assayed cell proliferation and apoptosis in the merlin mutant and wild-type nerve. We found that although p75NTR is elevated, the proliferation and apoptosis for these correlating nerves is not affected. We are continuing work on the effects of ProNGF on SC.

Progress Report: AOS Research Grant: Meniere's disease: physiological changes induced by low-dose gentamicin treatment PI: Felix E. Schweizer, PhD

The long-term goal of this project is to understand the physiological consequences on vestibular hair cells of low-dose gentamicin treatment used to treat intractable vertigo. Two aims were proposed for this funding period: 1); to test the hypothesis that exocytosis from vestibular hair cells is disrupted by gentamicin treatment, and 2); to test whether afferent fibers remain responsive to hair-cell released glutamate after low-dose gentamicin treatment. We have made progress and we have encountered unexpected difficulties.

Using the semi-intact preparation of the dissected utricle described in the proposal we have made capacitance recordings from type 1 and type 2 hair cells. We find that the capacitance increases are small and calcium dependent. Using acute external exposure to gentamicin we find that gentamicin blocks calcium currents and thus, also blocks exocytosis. While we observe recovery of both calcium currents and exocytosis, we do not yet have enough data to conclude whether exocytosis after gentamicin exposure is identical to baseline or whether there are changes to exocytosis beyond the reversible blocking of calcium channels. We have also tried to patch cells with gentamicin in the pipette but so far have been unsuccessful in seal formation. We are now trying to load the very tip of the pipette without gentamicin to avoid any membrane effects of gentamicin that might disrupt seal formation.

Patch clamping of vestibular hair cells, while not easy in the semi-intact tissue is clearly feasible in tissue obtained from younger animals. Unfortunately, we encountered considerable difficulties in obtaining data from animals older than 10 days. This is a serious issue since we want to determine whether exocytosis in hair cells from low-dose gentamicintreated animals is affected by gentamicin. It is possible that further experience with older tissue over the coming months will allow us to overcome this hurdle. However, we also have developed an alternative strategy of using acutely dissociated hair cells. We can successfully patch hair cells in a dissociated preparation from three week old animals and are in the process of testing older ages. In this preparation it appears that cell health is a crucial factor but we just recognized light exposure as a major contributor to cell health and hope this insight will make further progress easier. We do not yet have data from low-dose gentamicin treated animals (see next paragraph) but are confident that we will be able to complete specific aim 1 using this approach.

Lastly, we have injected animals with low-doses of gentamicin. We will use fiber recordings in the intact animal to test whether evoked responses are abolished but basal discharge remains unaffected. If so, we will apply NBQX, a selective AMPA receptor blocker to determine whether the basal activity is likely driven by glutamate acting on AMPA receptors. While this particular experiment does not conclusively demonstrate a function for hair cell released glutamate in driving basal discharge, it certainly would be very suggestive as hair cells are the major glutamate releasing cells in the vestibular epithelium. Together these experiments will go a long way towards addressing specific aim 2.

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Members Deceased Since Last Spring Meeting

Patrick Brookhouser, MD (Active 1988) Omaha, NE Date of Death: 9/3/2011