Novel Approaches to Ototoxicity Management across the Life Course

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Katharine Fernandez

Affiliation   NIDCD

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Carmen Brewer

Affiliation   National Institute on Deafness & Other Communication Disorders/NIH

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Johnnie Bass

Affiliation   Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Lisa Hunter

Affiliation   Cincinnati Children's Hospital Medical Center

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.

Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID 3003165

Submission Type Symposia

Topic Other

Status Submitted

Submitter Laura Dreisbach

Affiliation School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s) Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach

Novel Approaches to Ototoxicity Management across the Life Course

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Katharine Fernandez

Affiliation   NIDCD

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Carmen Brewer

Affiliation   National Institute on Deafness & Other Communication Disorders/NIH

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Johnnie Bass

Affiliation   Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lisa Hunter

Affiliation   Cincinnati Children's Hospital Medical Center

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.
Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Laura Dreisbach

Affiliation   School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach

Novel Approaches to Ototoxicity Management across the Life Course

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Katharine Fernandez

Affiliation   NIDCD

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Carmen Brewer

Affiliation   National Institute on Deafness & Other Communication Disorders/NIH

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Johnnie Bass

Affiliation   Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lisa Hunter

Affiliation   Cincinnati Children's Hospital Medical Center

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.

Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Laura Dreisbach

Affiliation   School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach

Novel Approaches to Ototoxicity Management across the Life Course

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Katharine Fernandez

Affiliation   NIDCD

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Carmen Brewer

Affiliation   National Institute on Deafness & Other Communication Disorders/NIH

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract   Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID 3003165

Submission Type Symposia

Topic Other

Status Submitted

Submitter Johnnie Bass

Affiliation Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s) Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lisa Hunter

Affiliation   Cincinnati Children's Hospital Medical Center

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract   Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.

Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID	3003165
Submission Type	Symposia
Topic	Other
Status	Submitted
Submitter	Laura Dreisbach
Affiliation	School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach

Novel Approaches to Ototoxicity Management across the Life Course

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Katharine Fernandez

Affiliation   NIDCD

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Carmen Brewer

Affiliation   National Institute on Deafness & Other Communication Disorders/NIH

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Johnnie Bass

Affiliation   Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Lisa Hunter

Affiliation   Cincinnati Children's Hospital Medical Center

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.
Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Laura Dreisbach

Affiliation   School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach

Novel Approaches to Ototoxicity Management across the Life Course

Submission ID 3003165

Submission Type Symposia

Topic Other

Status Submitted

Submitter Katharine Fernandez

Affiliation NIDCD

Participant(s) Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Carmen Brewer

Affiliation   National Institute on Deafness & Other Communication Disorders/NIH

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Johnnie Bass

Affiliation   Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID 3003165

Submission Type Symposia

Topic Other

Status Submitted

Submitter Lisa Hunter

Affiliation Cincinnati Children's Hospital Medical Center

Participant(s) Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.
Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Laura Dreisbach

Affiliation   School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach

Novel Approaches to Ototoxicity Management across the Life Course

Submission ID 3003165

Submission Type Symposia

Topic Other

Status Submitted

Submitter Katharine Fernandez

Affiliation NIDCD

Participant(s) Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Carmen Brewer

Affiliation   National Institute on Deafness & Other Communication Disorders/NIH

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Johnnie Bass

Affiliation   Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lisa Hunter

Affiliation   Cincinnati Children's Hospital Medical Center

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract   Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.

Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Laura Dreisbach

Affiliation   School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach

Novel Approaches to Ototoxicity Management across the Life Course

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Katharine Fernandez

Affiliation   NIDCD

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID 3003165

Submission Type Symposia

Topic Other

Status Submitted

Submitter Carmen Brewer

Affiliation National Institute on Deafness & Other Communication Disorders/NIH

Participant(s) Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Johnnie Bass

Affiliation   Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lisa Hunter

Affiliation   Cincinnati Children's Hospital Medical Center

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.

Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Laura Dreisbach

Affiliation   School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach

Novel Approaches to Ototoxicity Management across the Life Course

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Katharine Fernandez

Affiliation   NIDCD

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Carmen Brewer

Affiliation   National Institute on Deafness & Other Communication Disorders/NIH

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract   Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Johnnie Bass

Affiliation   Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract   Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lisa Hunter

Affiliation   Cincinnati Children's Hospital Medical Center

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.

Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID	3003165
Submission Type	Symposia
Topic	Other
Status	Submitted
Submitter	Laura Dreisbach
Affiliation	School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach

Novel Approaches to Ototoxicity Management across the Life Course

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Katharine Fernandez

Affiliation   NIDCD

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Carmen Brewer

Affiliation   National Institute on Deafness & Other Communication Disorders/NIH

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Johnnie Bass

Affiliation   Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Lisa Hunter

Affiliation   Cincinnati Children's Hospital Medical Center

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.
Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Laura Dreisbach

Affiliation   School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach

Novel Approaches to Ototoxicity Management across the Life Course

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Katharine Fernandez

Affiliation   NIDCD

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Session Description Drug-induced ototoxicity is an adverse event to life-saving therapeutic drugs that results in irreversible damage to the inner ear and auditory nerve, presenting as hearing loss and/or balance/vestibular dysfunction. Research has shown that early detection of toxicity through prospective ototoxicity monitoring provides the opportunity to consider modifications to treatment that may minimize or prevent permanent hearing loss or balance impairment. However, routine implementation of ototoxicity management in the clinical setting is often omitted from practice due to a lack of accepted standard protocols, largely driven by the lack of consensus on reliable monitoring tools and patient perceived benefit, as well as the lack of clinical resources for implementation of an effective program.

This symposium will provide a much-needed opportunity to present current research highlighting the effectiveness of monitoring tools for use in a variety of clinical settings across diverse populations while discussing issues related to the implementation of these measures into current clinical programs. Specifically, this symposium will convey the scope of cochleotoxicity and vestibulotoxicity in clinical practice with considerations of the range of treatment exposures, adverse events, and patient populations to address the complexities of ototoxicity management that inspire novel approaches to current and developing clinical practices. Emerging research efforts in clinical manifestations of ototoxicity on neurocognition. Applications of pharmacodynamic modeling for early detection, and approaches to prevention of hearing loss will be presented. Technological considerations for measurements made in the ear canal will be discussed as well as the application of various tools and interpretations to identify significant changes in the presence of ototoxic exposures. These contributions and considerations along with the understanding of the global burden of ototoxic hearing loss can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a

patient-centered focus across the continuum of care.

Presenter Diversity Speakers include practicing clinicians, clinical researchers, and scientists from across the United States specializing in the realm of ototoxicity management. Among the presenters, there is a variety of veteran ARO attendees and first-time attendees with an effort made to prioritize first-time ARO podium presenters. Two speakers are not members of ARO and one presenter belongs to an 'underrepresented population' specifically coming from a disadvantaged background according to NIH classifications. Presenters represent varied stages in their careers, ranging from postdoctoral fellows through full professors and clinical perspectives that span several years of service. Discussion will focus on practical aspects, including reliability, sensitivity, and specificity of clinical tests as they pertain to pediatric and adult populations, patient-perceived benefits of ototoxicity management as well as the larger societal benefits of universal adoption of ototoxicity monitoring and management protocols, and current service gaps, barriers, and solutions.

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the 2023 MidWinter Meeting for 2 weeks or 14 days.

Signature Katharine Fernandez

Novel Approaches to Ototoxicity Management across the Life Course

Complexities of Ototoxicity Management in Clinical Practice

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Carmen Brewer

Affiliation   National Institute on Deafness & Other Communication Disorders/NIH

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Medications commonly prescribed for anticancer treatments and some infections are known to cause auditory and vestibular/balance dysfunction known as ototoxicity. While ototoxicity is recognized to accompany the life-saving impact of these treatments, a parallel effort to manage ototoxicity has not become standard of care. Despite the well-established physical, socio-economic, and psychological consequences of hearing and balance dysfunction, clinical practice in management of patients receiving ototoxic agents is not consistent within or across countries. Early detection of ototoxicity through serial monitoring provides multidisciplinary care teams opportunities for identification of adverse effects, modifying treatment plans to mitigate hearing loss, and timely interventions. Preventing or minimizing ototoxicity is critical in order to preserve quality of life for patients receiving these treatments and to reduce the societal burden of hearing loss.

Ototoxicity management includes the full scope from diagnosis, monitoring, and rehabilitation to therapeutic treatment of individuals who experience hearing loss, tinnitus, or balance/vestibular difficulties following treatment exposures. Moreover, growing demands for audiologic care related to early detection of hearing loss and prevention, require design and implementation of new pathways that leverage advanced clinical tools to promote timely accessibility to individualized hearing health care while balancing important public hearing perspectives and care delivery models. Enhancements in clinical approaches to known practice gaps offer opportunities for innovation and research to further expand the audiologic practice with prevention of ototoxicity. This is essential for the earliest identification of ototoxicity or treatment-induced auditory and vestibular dysfunction. Timely detection can provide the patient/family and care teams opportunities to identify adverse effects and mitigate their subsequent impact. Moreover, emerging

approaches for earliest detection and prevention of ototoxicity can be incorporated in current practice to advance ototoxicity management from monitoring to diagnosis to interventions.

The primary objective of this presentation is to 1) convey the scope of ototoxicity in clinical practice (i.e., range of exposures and populations), and 2) summarize the complexities of ototoxicity management that inspire novel approaches to current and emerging clinical practice. These considerations can be used to advance development of feasible and effective ototoxicity management programs, direct research efforts, and prioritize a patient-centered focus across the continuum of care.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Carmen *	Brewer *	National Institute on Deafness & Other Communication Disorders/NIH
Gayla	Poling	Mayo Clinic, Department of Otolaryngology-Head and Neck Surgery

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Carmen C. Brewer

Novel Approaches to Ototoxicity Management across the Life Course

Global Estimates of Ototoxic Hearing Loss Associated with Exposure to Multidrug-Resistant Tuberculosis, Malaria, and Cancer Treatments

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Lauren Dillard

Affiliation   Medical University of South Carolina

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Multidrug-resistant tuberculosis (MDR-TB), malaria, and cancer are highly prevalent conditions worldwide and are commonly treated with ototoxic medications, placing many individuals globally at risk for ototoxic hearing loss (HL). Understanding the global burden of ototoxic HL can inform the policies, research, and clinical care needed to promote its primary prevention and management. The purpose of this study was twofold. First, to estimate the prevalence of ototoxic HL associated with treatment for MDR-TB (with aminoglycoside antibiotics), malaria (with antimalarials) and cancer (with platinum-based compounds cisplatin and/or carboplatin). Second, to estimate the annual global number of individuals i) exposed to ototoxic drugs to treat these conditions, and ii) HL cases associated with exposure.

Three separate systematic reviews and meta-analyses were conducted to estimate pooled prevalence (95% confidence interval [CI]) of HL associated with MDR-TB, malaria, and cancer treatments. To estimate the crude number exposed to ototoxic medications, we used global estimates of disease incidence, treatment, and mortality, provided by the World Health Organization, GLOBOCAN, and other relevant sources. For each condition, we estimated the crude global annual number of HL cases by multiplying the estimated number of exposed individuals (after accounting for mortality) by pooled prevalence estimates of ototoxic HL ascertained from meta-analyses. Sensitivity analyses present upper and lower estimates of annual HL cases for each condition. Sensitivity analyses were conducted by simultaneously varying several assumptions to create high and low estimates of exposures, which were combined with 95% CIs of pooled prevalence estimates of HL from meta-analyses.

For each condition, we present the crude estimated i) global annual number of individuals exposed to treatment, ii) pooled prevalence of HL associated with exposure to treatment with ototoxic drugs, and iii) global annual number of HL cases associated with exposure: MDR-TB exposed: 187,000; MDR-TB HL prevalence estimate: 40.6% (CI 32.8-66.6), MDR-TB HL cases: 76,000 (sensitivity analysis 59,000-211,000); Malaria exposed: 134 million, malaria HL prevalence estimate: 9.2% (CI 7.1-11.6), malaria HL cases: 12.3 million (sensitivity analysis 5.4-13.7 million); Cancer exposed: 1.02 million, cancer HL prevalence estimate: 43.2% (CI 37.9-48.6), cancer HL cases: 441,000 (sensitivity analysis 387,000-496,000).

Results demonstrate the high global caseload of potentially preventable HL and highlight the urgent need to prioritize primary and secondary global HL prevention associated with exposure to commonly used ototoxic medications. There exists uncertainty in global estimates that may be clarified by future research.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lauren *	Dillard *	Medical University of South Carolina

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lauren K. Dillard

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Manifestations of Cisplatin Ototoxicity and Its Effect on Neurocognition in Survivors of Childhood Cancer

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Johnnie Bass

Affiliation   Rehabilitation Services, St. Jude Children's Research Hospital

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Sensorineural hearing loss is a serious and permanent side effect of cisplatin chemotherapy that affects up to 60% of children who receive it as part of their treatment regimens for a variety of cancers. Approximately one-half of affected patients have moderate to severe hearing loss necessitating hearing aids or other interventions. Hearing loss from cisplatin is also associated with tinnitus, which affects the majority of patients exposed. Cisplatin induces a dose-dependent death of auditory hair cells in the cochlea after mitochondrial alkylation and release of reactive oxygen species and other proapoptotic factors. Cisplatin-induced ototoxicity is typically bilateral and initially impairs hearing in the high frequencies and commonly progresses to involve lower frequencies with increasing doses. Risk factors include increasing cumulative doses of cisplatin, young age, and cochlear exposure to radiation therapy. Cisplatin-induced ototoxicity typically occurs early after exposure to drug (hours to days) with further progression in hearing loss detected months to years after treatment.

Hearing loss is a significant treatment-related toxicity as it impairs speech recognition and intelligibility in developing children and has been associated with learning difficulties, poorer academic performance, reduced social-emotional attainment, and decreased quality of life. Recent studies have demonstrated an association between hearing loss and neurocognitive and academic deficits in childhood cancer survivors. The clinical manifestations of cisplatin-induced hearing loss will be briefly reviewed, and results from a recent study on the association between hearing loss and neurocognitive performance in a large cohort of childhood cancer survivors will be presented.

Enter all co-authors. You may search for any co-authors by using the search box. If you

cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Johnnie *	Bass *	Rehabilitation Services, St. Jude Children's Research Hospital

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Johnnie Bass

Novel Approaches to Ototoxicity Management across the Life Course

Clinical Presentation and Management of Ototoxicity Due to Aminoglycoside Treatments

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Angela Garinis

Affiliation   Oregon Health & Science University, Department of Otolaryngology

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides (e.g., gentamicin, amikacin, tobramycin) are highly potent, broad spectrum antibiotics widely and routinely used as a first-line treatment in patients with severe bacterial infections. Aminoglycoside antibiotics are well-documented, particularly when administered intravenously, to produce ototoxicity symptoms. Although aminoglycosides are effective at combating infections, they also have well-documented adverse events such as nephrotoxicity (kidney damage) and ototoxicity, including both vestibulotoxicity (balance/vestibular manifestations such as oscillopsia) and cochleotoxicity (tinnitus, hearing loss, difficulties listening in noise). It is not currently possible to predict which patient will ultimately develop ototoxicity after one or more courses of aminoglycoside treatment. Thus, early identification, prevention and mitigation of ototoxicity-related symptoms are recommended through the routine implementation of ototoxicity monitoring protocols.

Patients with cystic fibrosis (CF) are frequently prescribed antibiotics with known ototoxic adverse events. Clinical recommendations for implementing routine and guideline adherent ototoxicity management in patients with CF will be highlighted as an illustration of novel approaches to ototoxicity management of aminoglycoside treatments in the clinic. These are: 1) including questions about hearing, tinnitus and balance problems as part of the routine CF case history for all patients; 2) utilizing timely point-of-care measures; 3) establishing a baseline and conducting post-treatment evaluations for each course of intravenous ototoxic drug treatment; and 4) repeating annual hearing and vestibular evaluations for all patients with a history of ototoxic antibiotic exposure.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Angela *	Garinis *	Oregon Health & Science University, Department of Otolaryngology

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Angela C. Garinis

Novel Approaches to Ototoxicity Management across the Life Course

Evaluating the Vestibulotoxic Potential of Aminoglycosides in Patients Treated with Amikacin

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   John Lee

Affiliation   National Institute on Deafness and Other Communication Disorders, National Institutes of Health

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Aminoglycosides are broad-spectrum antibiotics used to manage recurrent respiratory infections and treat serious bacterial infections including multidrug-resistant tuberculosis and cystic fibrosis. Despite their robust antimicrobial efficiency and widespread clinical use, many of the FDA-approved aminoglycosides can induce toxic side effects including cochleotoxicity (i.e., outer hair cell death, permanent sensorineural hearing loss) and vestibulotoxicity (i.e., type I vestibular hair cell death, chronic disequilibrium).

While increasing attention has been given to identification, monitoring, and prevention of aminoglycoside-induced hearing loss, the vestibulotoxic potential of these drugs remains unclear. Reported incidences of vestibulotoxicity are highly variable, ranging from 0% to 60%, and a lack of comprehensive, routine vestibular testing has inhibited understanding of the vestibular changes induced by different aminoglycosides. Severe vestibular symptoms (i.e., vertigo) are not reported in most patients with vestibulotoxicity, due to both ears being equally affected. Symptoms more commonly associated with bilateral vestibular dysfunction (i.e., disequilibrium, postural instability) are often underappreciated and attributed to general deconditioning of patients during/after aminoglycoside treatment. As a result, many patients experiencing aminoglycoside-induced vestibulotoxicity likely go unevaluated. In addition, objective vestibular testing used to evaluate vestibulotoxicity is frequently limited to assessment of horizontal semicircular canal function. Clinical findings are often extrapolated to reflect the status of the entire vestibular periphery, and effects of ototoxic drugs on utricular, saccular, and anterior/posterior semicircular canal function

remain largely unknown. Histological analyses of temporal bones from patients exposed to aminoglycosides and animal studies suggest different aminoglycosides may preferentially affect different vestibular end organs. As a result, testing only horizontal canal function likely underestimates these drugs' vestibulotoxic potential.

The purpose of this clinical project was to develop a vestibulotoxicity monitoring protocol composed of functional tasks, objective tests, and questionnaires to comprehensively assess vestibulotoxic changes associated with aminoglycosides. Patients treated with IV and inhaled amikacin at the NIH underwent vestibular testing prior to treatment onset and at various post-treatment timepoints to evaluate the effects of amikacin on vestibular function. By monitoring vestibular function before and after all amikacin treatments, this study will ensure vestibular losses are properly identified and managed to minimize patients' risk of injury and falls. Results of this clinical study will also provide insight into the differential consequences of aminoglycosides on all vestibular end organs.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
John *	Lee *	National Institute on Deafness and Other Communication Disorders, National Institutes of Health

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature John Lee

Novel Approaches to Ototoxicity Management across the Life Course

Importance of Monitoring Tools and Pharmacodynamic Modeling for Aminoglycoside Ototoxicity

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Lisa Hunter

Affiliation   Cincinnati Children's Hospital Medical Center

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Patients treated with life-saving aminoglycoside antibiotics frequently experience adverse side effects of ototoxicity – permanent hearing loss and degraded speech communication. Cystic fibrosis (CF) is the most common life-threatening genetic disease in Caucasians and causes persistent lung infections in childhood that are frequently treated with aminoglycoside (AG) antibiotics, thus is an important patient group to target for prevention of ototoxicity. Currently, most patients with CF at risk are not monitored for ototoxic hearing loss. The lack of monitoring is primarily due to lack of availability and awareness of early detection methods, as well as treatment alternatives that can preserve hearing. There are critical gaps in our understanding of individual susceptibility for ototoxicity and access to effective tests that identify those at higher risk.

The long-term goal of our research program is to develop predictive models using novel auditory tests and pharmacodynamics (PD) for early detection and prevention of sensorineural hearing loss (SNHL) in at-risk individuals receiving aminoglycoside (AG) antibiotics. Newer methods to detect onset of ototoxicity include extended high frequency (EHF) transient otoacoustic emissions (TEOAE) and digits in noise (DIN) tests. DIN tests that can be automated or delivered remotely via the internet or through smartphones could fundamentally improve access to ototoxicity monitoring. Aims of this study are to (1) Optimize accurate detection of existing hearing loss at baseline and shifts that are due to ototoxicity using EHF chirp TEOAEs; (2) Determine accuracy of remotely delivered DIN to detect EHF hearing loss due to ototoxicity; (3) Determine if EHF hearing is related to higher cumulative AG exposures and set optimal dosing cut-off levels using PD models validated in CF to detect ototoxicity risk.

Results from prospective longitudinal monitoring with EHF TEOAE and DIN measures reveal temporal relationships to hearing threshold shifts. Pharmacodynamic models quantify individual differences in drug exposures that effectively predict hearing levels. Outcomes from improved monitoring will have an important positive impact because they will provide a better understanding of ototoxicity mechanisms, timing and risk factors that can be translated into improved ototoxicity monitoring. Clinical trials of drugs to protect the inner ear could be facilitated by expanded knowledge and availability of improved diagnostic and monitoring tools.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Lisa *	Hunter *	Cincinnati Children's Hospital Medical Center

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Lisa L. Hunter

Novel Approaches to Ototoxicity Management across the Life Course

Navigating Complexities of Ear Canal Acoustics in Ototoxicity Monitoring

Submission ID   3003165

Submission Type Symposia

Topic   Other

Status   Submitted

Submitter   Shawn Goodman

Affiliation   Department of Communication Sciences and Disorders, The University of Iowa

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract One of the longstanding challenges associated with measuring high frequency (> 8 kHz) otoacoustic emissions (OAEs) is the effect of ear canal acoustics on measured sound pressure levels. This issue directly impacts test-retest variability, a major determining factor in the sensitivity of ototoxicity monitoring protocols. When an OAE probe is sealed in the outer ear, the canal acts as a tube closed at one end and open at the other, resulting in standing wave resonances. As a result, at certain frequencies sound pressures measured at one end of the canal (the probe microphone near the ear canal entrance) do not match the sound pressures at the other end (the ear drum). The problem affects measurements of both stimulus levels as well as OAE levels.

Over the years, several solutions to this problem have been proposed, including use of a constant voltage, the depth compensation method, use of long "reflectionless" calibration tubes, and Thevenin-based source separation (to estimate forward pressure level and emitted pressure level). A brief overview of each method will be presented, along with references providing details of implementation. Advantages and disadvantages of the various methods will be discussed, including their relative theoretical accuracy and issues with practical implementation in ototoxicity monitoring.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Shawn Goodman

First Name	Last Name	Affiliation
Shawn *	Goodman *	Department of Communication Sciences and Disorders, The University of Iowa

Novel Approaches to Ototoxicity Management across the Life Course

Maximizing Measurements to Identify Significant Change in Ototoxicity Monitoring

Submission ID   3003165

Submission Type   Symposia

Topic   Other

Status   Submitted

Submitter   Laura Dreisbach

Affiliation   School of Speech, Language, and Hearing Sciences, San Diego State University

Participant(s)   Katharine Fernandez (Chair), Gayla Poling (Co-chair), Laura Dreisbach (Co-chair), Laura Dreisbach (Presenter), Carmen Brewer (Presenter), Lauren Dillard (Presenter), Johnnie Bass (Presenter), Angela Garinis (Presenter), John Lee (Presenter), Lisa Hunter (Presenter), Shawn Goodman (Presenter)

SUBMISSION DETAILS

Individual Abstract Most therapeutic treatments known to cause hearing loss initially damage basal cochlear regions. Identifying the tools to best reflect this damage across the lifespan are critical to the identification and management of these patients. One such tool, distortion-product otoacoustic emissions (DPOAEs), have the potential to quantify cochlear damage that has not yet been observed on the audiogram at both conventional (< 8 kHz) and extended high (> 10 kHz) frequencies.

DPOAE levels across the range of human hearing are repeatable over time in healthy newborns, children, and young adults, as well as a patient population rendering this metric an acceptable monitoring tool. The repeatability of DPOAE levels is enhanced with improved calibration techniques which provide more control over stimulus levels. Additionally, DPOAE paradigms utilizing varied stimulus levels to determine a threshold or varied ratios to calculate group delays are repeatable over time and have been used in individualized serial monitoring protocols in patients undergoing chemotherapy treatments with various platinum derivatives. To this end, the earliest signs of underlying cochlear damage were found at the highest frequencies with a response using a DPOAE concentrated discrete frequency sweep with high stimulus levels and detection thresholds.

While most efforts primarily focus on the repeatability of the DPOAE level, there are other attributes of DPOAE measures that are typically used for interpretation, namely the signal-to-noise ratio (SNR). Thus, the repeatability of DPOAE SNR values needs to be established to determine which attribute of DPOAEs should be used in monitoring programs. To answer this question DPOAE SNR

repeatability was assessed in the same populations where DPOAE level repeatability had been determined. While DPOAE SNR values were repeatable across four sessions, DPOAE levels were less variable allowing earlier indicators of cochlear damage.

Exploring various DPOAE paradigms and attributes across the lifespan and at the highest frequencies affords the clinician the most sensitive tools for the earliest detection of ototoxicity. As DPOAEs are a complex measure and minimally comprise two cochlear sources, further examinations are warranted to determine if these sources are differentially influenced by ototoxic exposures. Emerging DPOAE applications including targeted monitoring protocols to assess cochlear function at the highest frequencies and improved calibration techniques to ensure stable measurements have the potential to enhance clinical practice.

Enter all co-authors. You may search for any co-authors by using the search box. If you cannot find a co-author in this database, you may type them into the grid below. Please use the arrows to move authorship into the correct order. This is the order that will be printed in any program materials.

* Presenting Author

First Name	Last Name	Affiliation
Laura *	Dreisbach *	School of Speech, Language, and Hearing Sciences, San Diego State University

In-Person Participation I intend to participate in the MidWinter Meeting in-person for the entirety of the scheduled meeting.

Video Consent & Release of Rights I have read and agree to the above terms and conditions. My presentation can be recorded and available post the conclusion of the MidWinter Meeting for 2 weeks or 14 days.

Signature Laura Dreisbach