Improving the Diagnosis of Conductive Hearing Loss in Children with Otitis Media

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Thank you to...

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# Mechanisms of hearing loss resulting from middle-ear fluid

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<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Ear Side</th>
<th>Fluid?</th>
<th>Ear Fluid</th>
<th>Mucoid/Serous</th>
<th>Amount</th>
<th>SO Prediction</th>
<th>PO Prediction</th>
</tr>
</thead>
<tbody>
<tr>
<td>P001</td>
<td>6 yrs</td>
<td>L Y</td>
<td>Mucoid</td>
<td>Full</td>
<td>MEE</td>
<td>MEE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P002</td>
<td>11 mos</td>
<td>L Y</td>
<td>Mucoid</td>
<td>Full</td>
<td>MEE</td>
<td>MEE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P003</td>
<td>2 yrs</td>
<td>L Y</td>
<td>Mucoid</td>
<td>Full</td>
<td>Retracted TM</td>
<td>MEE</td>
<td></td>
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<tr>
<td>P004</td>
<td>5 yrs</td>
<td>L Y</td>
<td>Mucoid</td>
<td>Full</td>
<td>Retracted TM, MEE</td>
<td>n/a</td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>R Y</td>
<td>Mucoid</td>
<td>3/4 Full (A-F Line)</td>
<td>Serous Fluid</td>
<td>n/a</td>
<td></td>
<td></td>
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<tr>
<td>P005</td>
<td>10 mos</td>
<td>L N</td>
<td>Mucoid</td>
<td>serous fluid, immobile TM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>R N</td>
<td>Mucoid</td>
<td>mobile, dry</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P006</td>
<td>14 mos</td>
<td>L N</td>
<td>Mucoid</td>
<td>Serous Fluid</td>
<td>Fluid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P007</td>
<td>10 mos</td>
<td>L Y</td>
<td>Mucoid</td>
<td>Full</td>
<td>immobile, mucoid, full</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P008</td>
<td>3 yrs</td>
<td>L Y</td>
<td>Mucoid</td>
<td>Full</td>
<td>mobile, mucoid, full</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P009</td>
<td>1 yr</td>
<td>L Y</td>
<td>Mucoid</td>
<td>Full</td>
<td>MEE</td>
<td>effusion, complete</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Available online at www.sciencedirect.com

www.elsevier.com/locate/heares
A Clinical Dilemma: Patient A

![Image of ear anatomy]

**Tymp 226 Hz Left**

- **Volume**: 0.68 ml
- **Compliance**: - ml
- **Pressure**: - daPa
- **Gradient**: - daPa

**Hearing Level (dB)**:

- **Frequency (Hz)**: 750, 1.5k, 3k, 6k, 12.5k

- **Hearing Level**: -120 to 0 dB
A Clinical Dilemma: Patient B

Why does Patient A have hearing loss, but Patient B does not?
A Clinical Dilemma: Patient C

No reliable behavioral thresholds could be obtained

- Do they have hearing loss? Do they not?
- Does it matter?
Invited Review

Evaluating the Perceptual and Pathophysiological Consequences of Auditory Deprivation in Early Postnatal Life: A Comparison of Basic and Clinical Studies

Jonathan P. Whittington1,9 and Daniel B. Polley1,2,3

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Figure 3. Masking-level differences (MLDs) as a function of age. Panels show data from the sequential tests. Circles represent children in the control group, and triangles represent children with a history of otitis media with effusion. The white region depicts the 95% confidence interval for the normal group.

From Hall et al., 1995
The Problem (s)

• OM has many forms
  • Tons of variability

• Limited knowledge of how these variables are related
  • Do effusion characteristics impact hearing loss? Prognosis/resolution?

• What variables are important to consider for management and how do we identify/measure them?

• How does variability influence whether there are long-term behavioral (or otherwise) consequences of OM?
Otitis Media

Long-Term Behavioral Outcomes
Deficits in Speech, Language, Auditory Processing, Binaural Hearing, Hearing in Noise, Spatial Hearing, Academic Struggles, Increased Listening Effort

OM Variables
- Effusion Volume
- Effusion Viscosity
- Presence of Infection
- Bacterial or Viral

Presentation Variables
- Unilateral or Bilateral

Hearing Loss Variables
- Presence of Absence
- Unilateral or Bilateral
- Magnitude of HL
- Symmetric of Asymmetric

Prognosis Variables
- Persist or Resolve
- Stable or Fluctuating
Cumulative Auditory Deprivation

Otitis Media

Patient Variables
- Age
- SES
- Maternal Education

Long-Term Behavioral Outcomes

OM Variables
- Effusion Volume
- Effusion Viscosity
- Presence of Infection
- Bacterial or Viral

Presentation Variables
- Unilateral or Bilateral

Hearing Loss Variables
- Presence of Absence
- Unilateral or Bilateral
- Magnitude of HL
- Symmetric of Asymmetric

Prognosis Variables
- Persist or Resolve
- Stable or Fluctuating
Research Plan

- **Short-Term Research Plan:** Understand how variables in OM are related and influence cumulative auditory deprivation and determine ways to measure variables that are important to cumulative auditory deprivation.

- **Long-Term Research Plan:** Determine what factors of OM put children at risk for long-term deficits and develop ways to identify them in clinic as early as possible to better inform management decisions.
Research Program Approach
Participants

• Children with OM (primarily OME) having tubes placed (mean age 34 months)
  • Participate in a large battery of assessments within 48 hours of tube placement, with repeated measurements of middle-ear status on the morning of surgery to confirm no change. We then characterize several OM-related variables during surgery.

• Age matched normal hearing control children with no recent history of OM

• SNHL ruled out in all participants
Repeat initial visit in 3 months if AOM/OME resolves or earlier/more frequently as clinical course indicates.

**BTNRH ENT or Pediatrician Diagnoses AOM or OME**

**Plan: Watch & Wait**

**Plan: Tube Placement**

**Initial Visit (1-2 hours)**
Takes place within 72 hours following diagnosis

1) WAI
2) 226 Hz Tymps
3) DPOAEs & TEOAEs
4) Behavioral Audiometry (Air & Bone)

**Initial Visit (1-2 hours)**
Takes place within 48 hours prior to tube placement

1) WAI
2) 226 Hz Tymps
3) DPOAEs & TEOAEs
4) Behavioral Audiometry (Air & Bone)
5) ABR (if > 4 yrs)

**Day of Surgery**

1) Pre-Op WAI & 226 Hz Tymps
2) Pre- & Post-Myringotomy 226 Hz Tymps
3) Pre- & Post-Myringotomy Subjective Description of Effusion Characteristics
4) Collection of Effusion
5) Quantification of effusion volume, viscosity, and purulence

**Post-Op Visit**
Takes place ~1 month post-op
Repeat all testing from Initial Visit
Wideband Acoustic Immittance (WAI)

- Measurements are made in response to wideband sounds (200 – 8000 Hz)
- FDA approved
- **Absorbance**: Portion of the energy being absorbed by the ear
Effusion Collection & Analyses
Effusion Characteristic Variability

Diagnosis of OME in Clinic

5 - 57 days

- Effusion at Tube Placement in OR = 61%
- No Effusion at Tube Placement in OR = 39%

- Volume
  - Partial Effusion = 39%
  - Full Effusion = 61%

- Viscosity
  - Mucoid = 87%
  - Serous = 10%
  - Purulent = 3%

Effusion volume ultimately characterized as clear, partial, or full.

Al-Salim et al 2021
Effusion Volume Drives Hearing Loss

![Graph showing the effect of effusion volume on hearing loss]

- Normal
- Clear/Empty
- Partial Effusion
- Full Effusion

Al-Salim et al 2021
Can’t Predict Effusion Volume from Tympanometry

Al-Salim et al 2021

Full Mucoid Effusion

½ Mucoid Effusion (Partial)
Effusion volume impacts DPOAEs, but somewhat differently than it does for hearing levels.

Separation between empty and partial ears, likely due to influence of both forward and reverse transmission for DPOAEs.

Al-Salim et al 2021
Unlike Tympanometry, WAI Absorbance Shows Significant Promise in Predicting Effusion Volume

The influence of OME on auditory mechanics is highly variable when we look across frequency!

Merchant et al 2021
Predictions Are Also Strong in Individual WAI Data

Results of a machine learning algorithm trained on 70% of the data (reduced using a PCA) and validated on 30% of the unseen data: high AUCs for effusion present vs absent and full vs. partial, moderate for clear vs. normal.

<table>
<thead>
<tr>
<th>Effusion Present versus Absent</th>
<th>Partial versus Full Effusion</th>
<th>Clear versus Normal Ears</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation Confusion Matrix</td>
<td>Validation Confusion Matrix</td>
<td>Validation Confusion Matrix</td>
</tr>
<tr>
<td>Accuracy: 95%, Sensitivity:</td>
<td>Accuracy: 89%, Sensitivity:</td>
<td>Accuracy: 65%, Sensitivity:</td>
</tr>
<tr>
<td>95%, Specificity: 95%, AUC:</td>
<td>89%, Specificity: 88%, AUC:</td>
<td>67%, Specificity: 62%, AUC:</td>
</tr>
<tr>
<td>0.988</td>
<td>0.944</td>
<td>0.689</td>
</tr>
<tr>
<td>Present: 8459</td>
<td>Full: 8459</td>
<td>Clear: 3642</td>
</tr>
<tr>
<td>Absent: 439</td>
<td>Partial: 439</td>
<td>Normal: 1788</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>541</td>
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<tr>
<td></td>
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<td>9561</td>
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<td></td>
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<td>541</td>
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<tr>
<td></td>
<td></td>
<td>9561</td>
</tr>
</tbody>
</table>
Combining Absorbance with a Computational Model Improves Accuracy

- Computational model (a simple lumped element model) that we fit the WAI data to. Meant to represent the gross underlying mechanics. Parameters represent mechanical aspects that can change due to pathology.

- We use various parameters to isolate specific mechanical changes and improve predictions. Here, isolating middle ear impedance (as opposed to ear-canal impedance) improved AUCs for the clear/normal distinction.

<table>
<thead>
<tr>
<th>AUC Values for Various Approaches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decision Variable</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Absorbance</td>
</tr>
<tr>
<td>Zme estimate</td>
</tr>
</tbody>
</table>

Merchant & Neely, 2021
Unlike Tympanometry, WAI Absorbance Shows Significant Promise in Predicting Effusion Volume
WBT vs Tympanometry, Case 2

**Left:** Likely little to no effusion, just negative pressure, normal to near normal hearing.

**Right:** Full effusion/AOM, likely mild to moderate HL.

Left: Likely little to no effusion, just negative pressure, normal to near normal hearing.
Why are these data exciting to us?

- Wide range of HL for OME. Knowledge of HL is important for management (and likely long-term behavioral outcomes). But testing hearing is hard in this age range!
- Relationship between volume, HL, and WAI absorbance may allow us to infer how a child is hearing.

Al-Salim et al 2021
Merchant et al 2021

![Graph showing mean absorbance by effusion volume in OME Ears](chart.png)
Tymp 226 Hz Right

Tymp 226 Hz Left

Volume: 0.60 ml
Pressure: - daPa
Compliance: - ml
Gradient: - daPa

Volume: 0.67 ml
Pressure: - daPa
Compliance: - ml
Gradient: - daPa

Adult
10%-90%

ABS
10%-90%

kHz

kHz
When thing’s don’t add up…

- 8-year-old male
- Seen in clinic for suspected otitis media
- Bilateral Flat Tymps
- Bilateral CHL
- ENT couldn’t visualize fluid, but assumed it was present, and scheduled for BMT
- Enrolled in BTNRH OM Study
When things don’t add up…

[Graphs and data showing various measurements and results related to hearing tests.]
Is audiometric assessment of children with OME challenging? Yes! Especially for ear specific information, even in an ideal research setting.

<table>
<thead>
<tr>
<th>Ear Specific Audiometric Test Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit</td>
</tr>
<tr>
<td>n</td>
</tr>
<tr>
<td>Clinic</td>
</tr>
<tr>
<td>Research</td>
</tr>
</tbody>
</table>

While sound field data is certainly very useful clinically, ear specific information may be particularly important in this population because:

1. OME status in one ear is not well correlated with the contralateral ear.
2. Sound field data could miss a hearing loss in one ear.
3. Deficits in processes like binaural hearing are likely influenced by how both ears are hearing.

Merchant et al., 2024
Is WAI Absorbance Easier? (Yes! Much!)

WAI Test Success

| Percent |  |
|---------|--
| No      | 3.78% |
| Yes     | 96.22% |

Merchant et al., 2024
In Progress...Directly estimating CHL from WAI

• What if instead of estimating volume from WAI to infer something about hearing, we could directly estimate CHL from an individual WAI Absorbance tracing?

• Goal: Develop a WAI-based acoustic estimate of the CHL caused by OM within 3-5 dB HL. Preliminary data suggests that this is achievable by combining WAI with computational modeling.

Merchant & Neely, 2023
In Progress…Directly estimating CHL from WAI

- We used a relatively simple electrical analog model of ear-canal acoustics and middle-ear mechanics to model individual WAI absorbance data and predict the magnitude of the CHL.

- Using this method, we can achieve a correlation between CHL and 4PTA of 95% and a prediction error, quantified as the mean absolute difference, of 3.2 dB.
In Progress: (Patented) Machine Learning Outputs for WBT Interpretation
Reporting

WBT Testing:
"Wideband tympanometry (WBT) testing was completed today. This test utilizes a broadband click stimulus to measure how effectively sound is transmitted through the middle-ear system. WBT absorbance refers to the amount of sound energy that is absorbed by the middle ear across frequencies."

WBT Results:
1. Normal Findings

"WBT absorbance findings are generally within normal limits across the frequency range, suggesting normal middle-ear function."

2. OME (in children)

Full effusion
"WBT absorbance is largely reduced across most frequencies, with a slight peak noted between 4-6 kHz. Findings suggest that the middle-ear space is likely fully filled with fluid, which often leads to a mild-moderate degree of transient conductive hearing loss."

Partial effusion
"WAI absorbance is partially, but not completely, reduced across the frequency range, suggesting that the middle-ear space may be partially filled with fluid. On occasion, this finding may contribute to a slight transient conductive hearing loss; however, hearing sensitivity may also remain unaffected."

3. Patent Tube/Perforation

"WAI absorbance is elevated in the low-frequency range, suggesting a patent tube or tympanic membrane perforation. This finding is further supported by the large ear canal volume measured."
In Progress…

Monitoring OME & CHL via Mobile Testing

• Improved knowledge of what is happening with a given episode of OME is helpful, but may not tell us much about long-term outcomes or cumulative auditory deprivation. Need longitudinal data for that.

• Goal of our Mobile OM (MOM) Project: Understand the trajectory of OME episodes and prognostic value of WAI

• Initial Audiologic Assessment Battery
  • Otoscopy
  • 226 Hz Tympanometry
  • Wideband Acoustic Immittance
  • Distortion Product Otoacoustic Emissions (DPOAEs): 1-10 kHz
  • Behavioral Pure-Tone Audiometry

• Weekly Monitoring Assessment
  • Otoscopy
  • 226 Hz Tympanometry
  • Wideband Acoustic Immittance
  • Distortion Product Otoacoustic Emissions (DPOAEs): 1-10 kHz
Case Studies
Case Study - Control

Control 2 - Initial

Control 2 - Week 2

Control 2 - Week 4
Case Study 1

**Subject 5 - Initial**

**Subject 5 - Week 1**

**Subject 5 - Week 2**
Case Study 2

Subject 3 - Initial

Subject 3 - Week 2

Subject 3 - Week 5
Results

Tympanometry Status Across Visits (By Jerger Type)

Tymp Type

A

B

C

Effusion Volume Across Visits

Volume

Clear

Partial

Full

OM Group

Control
Results

OM Group

Control
Key Takeaways

- WAI shows strong potential in differentiating volume of an effusion.
  - The same cannot be said of 226 Hz tympanometry.

- This is significant, as volume of the effusion also appears to be a driving factor as to whether and how much CHL is present.
  - Having a tool that could predict whether a substantial CHL is present would be valuable given the challenging nature of behavioral audiometric assessment in the age group where OM is most common.

- Preliminary data suggest that WAI may be able to directly predict CHL levels in children with OME, providing an ear-specific estimate of hearing that is otherwise not often available.

- WAI is sensitive to subtle shifts in middle-ear mechanics that are not identified using standard tympanometry.
Thank you for your attention!

Postdoctoral Training

The purpose of this program, directed by Morita Chatterjee, Ph.D. and co-directed by Karla McGregor, Ph.D., is to furnish postdoctoral fellows an opportunity to develop and broaden their research capabilities in one or a combination of scientific disciplines related to human communication and its disorders. A number of exceptional features associated with the program are particularly advantageous to trainees, including:

- A training faculty of full-time scientists to serve as sponsors
- A staff of research-oriented clinicians with access to a large and varied patient population
- Modern, well-equipped laboratories and diagnostic clinics
- A stimulating mix of fundamental and clinically relevant research projects
- A strong core support staff

A T32 institutional postdoctoral training grant from National Institutes of Health (NIH) provides stipends for three trainees in behavioral and clinical translational research appointments with mentors listed below. Additional positions may on occasion be available in those labs or in other research areas including biology, physiology and genetics based on other funding outside of the T32 grant.

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