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Parent Story: Jasmine Webster
Hearing and Congenital CMV: Overview of Screening, Diagnosis and Interprofessional Care for Infants and Children

Albert Park, MD
Angela Shoup, PhD
Objective:

• Impact CMV on Hearing
• Screening and diagnostic tests for hearing
• Importance of a team approach
• Surveillance Pearls
Sensorineural Hearing Loss and CMV:

• Most common sequelae from cCMV- 12.6%
• Most common cause of nonhereditary SNHL
• May account up to 20% pediatric SNHL
• CMV Screening

NIH Valganciclovir Ear Trial:

- **Aim 1**: Compare the hearing and language outcomes of cCMV-infected with isolated hearing loss treated with VGCV to untreated infants via a multi-institutional double-blinded placebo controlled clinical trial.

- **Aim 2**: To evaluate the safety of antiviral VGCV therapy for cCMV-infected infants with isolated hearing loss.

- **Aim 3**: Evaluate the pharmacokinetics of valganciclovir using pharmacometric modeling to develop a population pK model.
Study Design:

Asymptomatic cCMV Hearing Impaired Infants Randomized to Valganciclovir and No Treatment

<table>
<thead>
<tr>
<th>Screening</th>
<th>Randomization</th>
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| Key Inclusion Criteria: CMV positive hearing impaired infants | Arm 1: VGC
| Arm 2: Untreated Controls | Aim 1: Primary Endpoint (hearing)
| Aim 2: Primary Endpoint (safety) |

Day 0 1-6 mo of age 6 mo after VGC started 8 mo post randomization (9-14 mo of age)

Aim 3: Pharmacokinetics
Over Thirty Institutions Started HT-CMV Screening!
Three Common Screening Approaches:

Any institution or hospital can implement an early CMV screening program.
**Expanded Targeted Screening Approach:**

<table>
<thead>
<tr>
<th>Failed hearing screen</th>
<th>Elevated transaminase</th>
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<tbody>
<tr>
<td>Maternal CMV infection</td>
<td>Elevated direct bilirubin</td>
</tr>
<tr>
<td>SGA</td>
<td>Petechial rash</td>
</tr>
<tr>
<td>Unexplained hydrops</td>
<td>HUS imaging suggestive CMV</td>
</tr>
<tr>
<td>Intracranial calcifications</td>
<td>Unexplained thrombocytopenia</td>
</tr>
<tr>
<td>Intrabdominal calcifications</td>
<td>Unexplained HSM</td>
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</tbody>
</table>
Results from Expanded Targeted Screening:

- 754 of 85,553 (0.8%) newborns underwent CMV testing based on expanded targeted screening
- 21 (2.8%)/754 tested positive CMV
- 14 cases sCMV/100k
- 4.2 cases cCMV/100k – no screening process
- Expect 26 sCMV/100k based on 0.3% incidence and 10% sCMV rate

Case:

• 2 mo cCMV infant with right moderate and left mild SNHL (isolated SNHL)
• How often should you recheck this child?
• If the child is not cooperative, what frequencies and which ear should be prioritized?
Methods:

- Asymptomatic cCMV patients with isolated SNHL were selected for the study*
  - 2 populations: congenital/early-onset or delayed-onset
- Audiologic assessments (ABR, behavioral audiometry, and tympanometry) were conducted by trained audiologists blinded to CMV status
- Hearing loss by ABR defined as >25 dB for click or any tone burst frequency at 1, 2, or 4 kHz
- Hearing loss by behavioral testing was defined as >20 dB at 1, 2, or 4 kHz
- SNHL was analyzed by laterality, ie better- and poorer-hearing ear
- Hearing change by ear was analyzed at 12 months and 18 years of age
- Clinically significant worsening in hearing >10 dB in click ABR, >15 dB in 1 frequency, or >10 dB change in 2+ frequencies

Results:

• Most congenital/early-onset SNHL patients had worsening hearing thresholds in the poorer-hearing ear and no change in the better-hearing ear by 12 months of age.

• The poorer-hearing ear worsened earlier and more precipitously than the better-hearing ear in most patients with congenital/early-onset SNHL through childhood.

• Delayed-onset SNHL patients also demonstrated earlier and more precipitous worsening hearing in the poorer-hearing ear, however, the overall progression was slower and the degree of loss was less severe.

Results:

- Same database to evaluate hearing loss trajectory for symptomatic and asymptomatic cCMV infected children
- n=96 symptomatic and n=92 asymptomatic
- Severity worsened for all cCMV children at ALL frequencies tested (0.5, 1, 2 and 4 kHz)

Lanzieri et al. Hearing Trajectory in Children with Congenital Cytomegalovirus Infection. Otolaryngology-HNS Journal, 2018
Recommendations:

• Monitoring individual hearing thresholds in both ears is important for appropriate interventions and future evaluation and efficacy of antiviral treatment.
• All frequencies will worsen if progression occurs. Can use DPOAE for surveillance.

• Surveillance should continue through adolescence
• Utah: every 3 mo x 3 years then every 6 mo thru 6 years of age
• Would then recommend at least annually afterwards
Conclusion:

- Hearing most common sequelae from CMV
- Any child can undergo hearing testing regardless of age
- Long-term follow-up important
- Need to test both ears
Your feedback is important!

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The National Technical Resource Center for Early Hearing Detection and Intervention (EHDI) Programs