The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

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Nondisclosure:

- Triological Career Development Award-murine model of CMV induced SNHL
- Industry supported grant (Otonomy)
- Multiinstitutional study CYP2D6 adenotonsillectomy clinical trial
- None of these grant relevant to this presentation
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss
Objectives:

• CMV induced SNHL not recognized in literature
• If you look for CMV in these patients, you will find it often
• There are compelling reasons for early CMV diagnosis
• The advantages of the Utah CMV law
• The limitations of the law
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

“Progress is impossible without change, and those who cannot change their minds cannot change anything.”

George Bernard Shaw
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

Events in 1999:
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

Billings and Kenna. Arch. OHNS 1999

Causes of Pediatric Sensorineural Hearing Loss

Yesterday and Today

Kathleen R. Billings, MD, Margaret A. Kenna, MD

Objectives: To ascertain the present common causes of sensorineural hearing loss (SNHL) in children and compare them with those of previous reports.


Setting: A tertiary care children’s hospital.

Patients: Three hundred one children, aged 1 week through 18 years, who presented for evaluation of SNHL.

Results: Of the 301 children, 66.1% had a definitive or probable cause of their SNHL identified; 18.9%, 1 or more possible causes; and 15.0%, no obvious cause. A family history of SNHL, prematurity, and/or complicated perinatal course was found in 28.6% of patients. Named syndromes, multiple congenital anomalies, meningitis, or prenatal maternal factors, including maternal prenatal substance abuse, were present in another 38.3%. However, syndromes and abnormalities associated with SNHL, such as Waardenburg syndrome, were seen in less than 1% of patients. The average age at diagnosis was 3.02 years for the bilateral moderate or severe SNHL, for unilateral SNHL, the average age was 3.87 years. The most useful diagnostic study was computed tomography scanning.

Conclusions: Sensorineural hearing loss is fairly common in children. Extensive workups, often without clear direction, should be considered based on the children with SNHL who are examined by otolaryngologists. In fact, some studies have shown that many children earlier, will also provide the opportunity to fine-tune the evaluation (i.e., cytomegalovirus and other cultures) by finally increasing the diagnostic yield.


Table 2. Epidemiologic Features of Previous Studies for Children With Bilateral Moderate to Severe SNHL

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of children</td>
<td></td>
<td>117 (100.0)</td>
<td>127 (100.0)</td>
<td>94 (100.0)</td>
<td>211 (100.0)</td>
</tr>
<tr>
<td>Known cause</td>
<td></td>
<td>85 (72.6)</td>
<td>81 (65.8)</td>
<td>69 (73.4)</td>
<td>159 (75.4)</td>
</tr>
<tr>
<td>Unknown cause</td>
<td></td>
<td>32 (27.4)</td>
<td>46 (36.2)</td>
<td>25 (26.6)</td>
<td>52 (24.6)</td>
</tr>
<tr>
<td>Genetic</td>
<td></td>
<td>39 (33.3)</td>
<td>28 (22.0)</td>
<td>31 (33.0)</td>
<td>52 (24.6)</td>
</tr>
<tr>
<td>Family history</td>
<td></td>
<td>32 (27.4)</td>
<td>10 (7.9)</td>
<td>25 (26.6)</td>
<td>26 (12.3)</td>
</tr>
<tr>
<td>Syndromal</td>
<td></td>
<td>7 (6.0)</td>
<td>18 (14.2)</td>
<td>7 (7.4)</td>
<td>26 (12.3)</td>
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<tr>
<td>Inner ear defects</td>
<td></td>
<td>0</td>
<td>12 (9.4)</td>
<td>0</td>
<td>25 (11.8)</td>
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<tr>
<td>Prenatal insult</td>
<td></td>
<td>16 (13.7)</td>
<td>16 (12.6)</td>
<td>14 (14.9)</td>
<td>40 (19.0)</td>
</tr>
<tr>
<td>TORCH infections</td>
<td></td>
<td>19 (16.2)</td>
<td>25 (19.7)</td>
<td>17 (18.1)</td>
<td>3 (1.4)</td>
</tr>
<tr>
<td>Meningitis</td>
<td></td>
<td>3 (2.6)</td>
<td>16 (12.6)</td>
<td>7 (7.4)</td>
<td>12 (5.7)</td>
</tr>
<tr>
<td>Chronic otitis media</td>
<td></td>
<td>2 (1.7)</td>
<td>0</td>
<td>1 (1.2)</td>
<td>51 (24.2)</td>
</tr>
</tbody>
</table>
A diagnostic paradigm for childhood idiopathic sensorineural hearing loss

DIEGO A. PRECIADO, MD, LYNN H.Y. LIM, MD, ALIZA P. COHEN, MA, COLM MADDEN, MD, DAVID MYER, BS, CHRIS NGO, BS, JOHN K. BRADSHAW, MD, LOUISE LAWSON, PhD, DANIEL I. CHO0, MD, and JOHN H. GREINWALD, JR, MD, Cincinnati, Ohio

OBJECTIVE: Our objective was to determine the diagnostic yield of laboratory testing, radiological imaging, and GJB2 mutation screening in a large cohort of patients with differing severities of idiopathic sensorineural hearing loss (SNHL).

DESIGN AND SETTING: We undertook a retrospective study of patients presenting with SNHL at our institution from 1993 to 2002.

RESULTS: Laboratory testing had an extremely low yield. Patients with unilateral SNHL had a significantly higher imaging yield than those with bilateral. The diagnostic yield of GJB2 screening was significantly higher in patients with severe to profound SNHL than in those with less severe SNHL. However, a relatively large number of patients with mild to moderate SNHL had positive GJB2 screens.

CONCLUSIONS: Based on diagnostic yields, we propose a cost-effective stepwise diagnostic paradigm to replace the more commonly used and costly simultaneous testing approach. EBM rating: C. (Otolaryngol Head Neck Surg 2004;131: 804-9.)

Moderate to profound congenital sensorineural hearing loss (SNHL) in the United States is estimated to occur in 1 to 2 per 1000 births.1 Its etiology has historically been classified as either hereditary or acquired. Improvements in prenatal, neonatal, and pediatric care have, however, led to a decrease in the incidence of acquired etiologies, and it is now estimated that up to 50% of all cases are genetic in origin.2 Most (80%) of these cases are transmitted in an autosomal recessive manner.3

Determination of the specific etiology of childhood SNHL is sometimes made from case history review or physical examination. In 22% to 35% of cases, the review may reveal environmental causes such as intrauterine infections, ototoxic medications, maternal or neonatal metabolic disorders, maternal illicit drug use, prematurity, low Apgar scores, or exposure to teratogens.4 Physical examination may show dysmorphisms and syndromes that may be associated with SNHL. More frequently, the etiology of SNHL cannot be diagnosed on history and physical examination alone and remains unknown. To assist in the diagnosis of patients with idiopathic SNHL, clinicians often enlist the collaboration of other specialists, and typically order an extensive battery of laboratory tests, including complete blood count (CBC), thyroid function tests, erythrocyte sedimentation rate (ESR), urinalysis, syphilis antibody blood tests, cholesterol and triglyceride blood levels, blood chemistries, and an electrocardiogram (ECG). Though the SNHL-specific diagnostic yield of these tests has been reported to be as low as 0% to 2%,4,5 this simultaneous diagnostic approach to laboratory testing continues to be used.

High-resolution radiographic imaging studies and genetic testing are now added to this protocol and performed concurrently. An invaluable diagnostic tool, temporal bone imaging has revealed abnormalities in up to 39% of children with SNHL.4 Of relevance in genetic testing is a study performed late 1990's

Preciado et al.
Otolaryngology-HNS
2004; 131: 804-9
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No role for CMV testing?
What is Cytomegalovirus?

- A Herpesvirus
- Species specific (only infects humans)
- CMV most common cause of nonhereditary SNHL
- May account up to 33% pediatric SNHL\(^1\)
- Cost C-CMV greater than $4 billion/yr in US

Transmission Mother to Fetus:

- Seronegative moms
- Seropositive moms
- Infant presentation
  - Symptomatic (evident at birth) — 5%-10%
  - Asymptomatic (silent at birth) — 90%-95%
CMV: Symptomatic Congenital Infection

- 10% fetal demise
- Prematurity
- Common features:
  - Hepatomegaly
  - Splenomegaly
  - Petechiae
  - Jaundice
  - Microcephaly
  - Chorioretinitis
  - Sensorineural hearing loss (50%)
CMV: Asymptomatic Congenital Infection

• >90%
• 5-15% have sensorineural hearing loss that can be evident at birth or appear later in childhood
Disease Burden of CMV in the US:


1000 Live Birth Pregnancies

600 Mom Seropositive Prior to Pregnancy
- 594 CMV-neg. newborns
- 6 CMV-pos newborns

400 Moms Seronegative Prior to Pregnancy
- 7 Moms acquire CMV
- 393 Moms don’t acquire CMV
  - 5 CMV-neg newborns
  - 393 CMV-neg newborns

2 CMV-pos newborns

5 CMV-pos newborns

1-2* children with permanent disabilities

*2/3 children will be asymptomatic at birth
**Why Seropositivity can result in Congenital Infection?**

<table>
<thead>
<tr>
<th>Infection with Different CMV strain between pregnancies</th>
<th>Mothers of Infected Infants (n= 16)</th>
<th>Mothers of Uninfected Infants (n=30)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>10 (62%)</td>
<td>3 (13%)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>No</td>
<td>6 (38%)</td>
<td>26 (87%)</td>
<td></td>
</tr>
</tbody>
</table>

**Acquisition of new CMV strains increases number of mothers with infected infants**

NEJM 2001; 344: 1366-1371
Challenge of Vaccination:

• No commercially licensed vaccine available for CMV

“The Challenge with vaccination for congenital CMV is the need for a vaccine to be better than nature.”

David Kimberlin
Audiologic Sequelae from Congenital CMV:

• Grosse et al. 2008
• Morton et al. 2006
Audiologic Sequelae from Congenital CMV:

Characteristics of CMV Induced Hearing Loss

Nature of Progressive SNHL:

Nature of CMV Induced SNHL (Summary):

• CMV makes up to 21% cases of pediatric SNHL
• Can present at birth but frequently presents later in life
• Type and severity of hearing loss variable
• Progression and fluctuation of HL common
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss – Utah Experience

• What happens if you look for CMV?
• May 2008 started to incorporate CMV testing
• Sequential diagnostic paradigm
“New Current” Approach to Pediatric SNHL

History, physical examination, complete audiologic work-up

- Diagnosis apparent (syndrome, AD, trauma, meningitis)
  - Appropriate treatment
  - GJB2 screen
    - Positive: Genetic counseling
    - Negative: Imaging
      - Lab tests as indicated
      - ECG (if severe to profound SNHL)
      - Imaging
        - Preferential seating
        - Serial audiograms
- Diagnosis uncertain (idiopathic)
  - CMV testing
  - Bilateral: Unilateral
    - Imaging
      - Preferential seating
      - Serial audiograms

FM, HA and/or CI
- Preferential seating
- Ophthalmology evaluation
- Speech therapy
- Audiology rehabilitation
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• Chart and database review
• Children 3 yrs or younger
• May 2008-September 2013
• Sequential diagnostic paradigm
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- **Confirmed Diagnosis** - positive urine or saliva CMV PCR infant < 3 weeks OR positive result infant > 3 weeks AND positive DBS

- **Probable Diagnosis** - positive urine or saliva > 3 weeks of age AND CNS findings or progressive SNHL
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• Those with negative CMV testing underwent imaging, genetics evaluation +/- EKG

• Cost analysis of the diagnostic testing (Multihospital Standardized Cost Accounting System):
  - MRI t-bone $1591
  - GJB2 testing $611
  - CMV PCR saliva or urine $66
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• RESULTS:
• N=111 children w SNHL (2008-2013)
“New Current” Approach to Pediatric SNHL

History, physical examination, complete audiologic work-up

- Diagnosis apparent (syndrome, AD, trauma, meningitis)
- Diagnosis uncertain (idiopathic)

- Appropriate treatment
- CMV testing
  - Bilateral
  - Unilateral

- GJB2 screen
  - Positive
    - Genetic counseling
  - Negative
    - Imaging
      - Preferential seating
      - Serial audiograms
    - Imaging Lab tests as indicated
      - ECG (if severe to profound SNHL)

- FM, HA and/or CI
- Preferential seating
- Ophthalmology evaluation
- Speech therapy
- Audiology rehabilitation
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SNHL Etiology Based On History, Examination and Audiology

N=26
“New Current” Approach to Pediatric SNHL

History, physical examination, complete audiologic work-up

- Diagnosis apparent (syndrome, AD, trauma, meningitis)
  - Appropriate treatment
  - GJB2 screen
    - Positive
      - Genetic counseling
    - Negative
      - Imaging
        - Lab tests as indicated
        - ECG (if severe to profound SNHL)
  - CMV testing
- Diagnosis uncertain (idiopathic)
  - Bilateral
  - Unilateral
  - Imaging
    - Preferential seating
    - Serial audiograms
  - FM, HA and/or CI
  - Preferential seating
  - Ophthalmology evaluation
  - Speech therapy
  - Audiology rehabilitation
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SNHL Etiology Based on CMV, Imaging and Genetic Evaluation

- Largest group with a known etiology: 30%
- N=83
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- Breakdown of CMV Patients (n=25)
  - Sixteen – confirmed CMV diagnosis
  - Six of sixteen diagnosed via DBS testing
  - Nine- probable CMV diagnosis
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- Characteristics of CMV Induced SNHL Patients:
- Average age initial evaluation 352 days (range 24-1387 days)!
- Only 5 infants evaluated at one month of age or younger
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• Distribution of CMV vs SNHL Groups:

![Comparison Hearing Distribution CMV vs Overall SNHL Group](chart.png)
# Cost Estimates of Alternative SNHL Evaluation Approaches Based on Diagnostic Yield (Based on Testing 100 children with SNHL)

<table>
<thead>
<tr>
<th>Testing</th>
<th>Bilateral Mild</th>
<th>Bilateral Mod-Severe</th>
<th>Bilateral Severe-Prof</th>
<th>Unilateral</th>
<th>ANSD</th>
<th>Overall</th>
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</thead>
<tbody>
<tr>
<td>GJB2 screen¹</td>
<td>15%</td>
<td>5%</td>
<td>37.7%</td>
<td>0%</td>
<td>0%</td>
<td>19%</td>
</tr>
<tr>
<td>Imaging</td>
<td>0%</td>
<td>8%</td>
<td>0%</td>
<td>18%</td>
<td>50%</td>
<td>11%</td>
</tr>
<tr>
<td>CMV PCR</td>
<td>20%</td>
<td>23%</td>
<td>36%</td>
<td>36%</td>
<td>17%</td>
<td>30%</td>
</tr>
<tr>
<td>Simultaneous</td>
<td>$226,907</td>
<td>$226,907</td>
<td>$226,907</td>
<td>$226,907</td>
<td>$226,907</td>
<td>$226,907</td>
</tr>
<tr>
<td>GJB2 screen</td>
<td>$66811</td>
<td>$218,619</td>
<td>$163,920</td>
<td>N/A</td>
<td>N/A</td>
<td>$195,413</td>
</tr>
<tr>
<td>Imaging</td>
<td>N/A</td>
<td>$221,482</td>
<td>N/A</td>
<td>$164,490</td>
<td>$162,426</td>
<td>$214,023</td>
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<tr>
<td>CMV PCR</td>
<td>$55,579</td>
<td>$176,249</td>
<td>$147,617</td>
<td>$147,617</td>
<td>$189,464</td>
<td>$160,832</td>
</tr>
</tbody>
</table>

¹Diagnostic yield based on Preciado et al. and Dent et al. study
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• Conclusion:
  • Diagnostic Paradigm incorporating early CMV testing has high yield (30%)
  • DBS testing can diagnose infants > 3 weeks of age
  • Average age of initial evaluation significant challenge for diagnosis
  • Early CMV testing – lower cost than imaging or genetic testing
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- Is CMV diagnosis for SNHL patients helpful?
- Are we jumping the gun?
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“Prevention is better than cure.”

Desiderius Erasmus
Prevention of CMV:

• Child with congenital CMV will shred virus for months or years-“contagious”
• Good hygiene
Prevention of CMV:

- 14 seronegative pregnant women - behavioral intervention resulted in no seroconversion
- 5000 seronegative pregnant women – behavioral intervention > 50% drop expected rate seroconversion

Other Benefits from Early CMV Diagnosis:

- Identify at risk group - audiologic testing
- Obviates need other unnecessary testing
- May direct to other testing
- May impact on treatment (e.g. antiviral therapy)
Ganciclovir:

- 1st antiviral agent approved for CMV treatment (1994)
- Synthetic analogue of 2’-deoxy-guanosine
- Inhibits viral DNA polymerase
- Requires parenteral administration

![Ganciclovir molecule](image)
Role for Antiviral Therapy?

n=100 neonates with Sx-CMV < 1 mo age

IV GCV x 6 wks

No Treatment

Serial hearing testing baseline 6 and 12 mo

Hearing Outcomes at 6 mo

- Improved/no change: 80% for GCV treated, 60% for no treatment. $P<0.01$
- Worsened: 10% for GCV treated, 20% for no treatment. $P=0.06$

GCV treated
No treatment

Hearing Status: improved/no change vs. worsened
Hearing Outcomes at 12 mo

- Improved/no change: GCV treated vs. No treatment: P=0.07
- Worsened: GCV treated vs. No treatment: P<0.01
Adverse Effects From GCV:

- 29 of 46 GCV rx’ed (63%) had grade 3 or 4 neutropenia during rx vs 9 of 43 (21%) controls  \( p < 0.01 \)
- Mean time onset neutropenia: 14 days for both
- 3 GCV recipients had catheter infections
- 1 GCV recipient transient Gm (-) septicemia
Conclusions from Study:

• GCV therapy begun within 1\textsuperscript{st} mo life in symptomatically infected infants prevents hearing deterioration at 6 mo and may prevent at > 1 year

• Almost 2/3 treated infants have significant neutropenia during therapy.
Limitations of the Study:

• Of the 100 enrolled patients from 18 CASG sites, only 42 met all the study entry criteria.
• Large number of patients not evaluated for the primary end point may affect results.
• Applies to children with “symptomatic CMV”.
• Relevance to “real” world- e.g. having families stay in house for 6 wk IV therapy.
• Concerns with GCV- neutropenia, gonadal toxicity and carcinogenicity in animal models.
Valganciclovir:

- L-valyl ester prodrug of ganciclovir
- After oral administration, it is rapidly converted to ganciclovir by intestinal and hepatic esterases
Six Months versus 6 weeks Valganciclovir (VGC) for infants with Symptomatic CMV

- Confirmation CMV from urine or throat swab-culture, shell vial or PCR
- Symptomatic CMV (1 or more): thrombocytopenia, petechiae, HSM, IUGR, hepatitis, CNS involvement (hearing loss, radiographic, CMV in CSF)
- <30 days
- Weight > 1800 grams
- Gestational age > 32 weeks
Six Months versus 6 weeks Valganciclovir (VGC) for infants with Symptomatic CMV
6 Weeks vs. 6 Months Valganciclovir Hearing Outcomes @ 6 mo

6 Weeks of Treatment

- Improved or Remained Normal: 55%
- Worse or Remained Abnormal: 45%

6 Months of Treatment

- Improved or Remained Normal: 63%
- Worse or Remained Abnormal: 37%

P = 0.19
6 Weeks vs. 6 Months Valganciclovir
Hearing Outcomes @ 12 mo

6 Weeks of Treatment
- Improved or Remained Normal: 57%
- Worse or Remained Abnormal: 43%

6 Months of Treatment
- Improved or Remained Normal: 73%
- Worse or Remained Abnormal: 27%

P = 0.01
6 Weeks vs. 6 Months Valganciclovir
Hearing Outcomes @ 24 mo

6 Weeks of Treatment
- Improved or Remained Normal: 64%
- Other: 36%

6 Months of Treatment
- Improved or Remained Normal: 77%
- Other: 23%

P = 0.04
## Bayley III Developmental Scale Qualitative Descriptors of Composite Scores

<table>
<thead>
<tr>
<th>Composite</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>130 and above</td>
<td>Very superior</td>
</tr>
<tr>
<td>120-129</td>
<td>Superior</td>
</tr>
<tr>
<td>110-119</td>
<td>High average</td>
</tr>
<tr>
<td>90-109</td>
<td>Average</td>
</tr>
<tr>
<td>80-89</td>
<td>Low Average</td>
</tr>
<tr>
<td>70-79</td>
<td>Borderline</td>
</tr>
<tr>
<td>69 and below</td>
<td>Extremely low</td>
</tr>
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</table>
### 6 Weeks vs. 6 Months Valganciclovir Bayley III Outcomes 24 mo.

<table>
<thead>
<tr>
<th></th>
<th>6 Week Therapy</th>
<th>6 Month Therapy</th>
<th>Adjusted P-value</th>
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<tbody>
<tr>
<td>Cognitive Composite</td>
<td>76.0±2.6</td>
<td>84.4±2.6</td>
<td>0.0236</td>
</tr>
<tr>
<td>Language Composite</td>
<td>72.5±2.9</td>
<td>84.6±2.9</td>
<td><strong>0.0037</strong></td>
</tr>
<tr>
<td>Receptive Communication Scale</td>
<td>5.2±0.5</td>
<td>7.3±0.5</td>
<td><strong>0.0027</strong></td>
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<tr>
<td>Expressive Communication Scale</td>
<td>5.5±0.5</td>
<td>7.3±0.5</td>
<td>0.0158</td>
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<tr>
<td>Motor Composite</td>
<td>74.1±3.2</td>
<td>85.5±3.3</td>
<td>0.0130</td>
</tr>
<tr>
<td>Fine Motor Scale</td>
<td>6.4±0.6</td>
<td>8.0±0.6</td>
<td>0.0566</td>
</tr>
<tr>
<td>Gross Motor Scale</td>
<td>5.3±0.5</td>
<td>7.0±0.5</td>
<td>0.0198</td>
</tr>
</tbody>
</table>

P-values < 0.0071 (=0.05/7) considered statistically significant using Bonferroni adjustment for multiple testing.
Neutropenia by Group:

Percent Neutropenia by Group

- Grade 3: P > 0.6
- Grade 4: P > 0.6
- Total: P > 0.6

Legend:
- VGC 6 wk
- Placebo 1.5-6 mo
- VGC 1.5-6 mo
Neutropenia from VGC Trial

- Three subjects had VGC dose temporarily held for ANC < 500 (All first 6 wk treatment)
- No excess neutropenia with continuation of VGC treatment from 6 weeks to 6 mo compared to placebo
Conclusion from 6 wk vs 6 mo VGC Trial:

• 6 mo VGC rx infants w sx congenital CMV improves audiologic and neurodevelopmental outcomes to at least 2 years of age
• Less neutropenia seen during first 6 weeks than seen in an earlier CASG study of IV GCV
• No excess neutropenia w continuation of VGC from 6 weeks to 6 mo. compared to placebo
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

“Medical science has proven time and again that when the resources are provided, great progress in the treatment, cure, and prevention of disease can occur.”

Michael J. Fox
Utah CMV Law:

• Passed July 2013
• Charges Utah Dept Health oversee
  1. Educational programs to increase awareness of this condition
  2. CMV testing newborns who fail 2\textsuperscript{nd} hearing screen at 3 weeks of age or younger
Awareness of CMV:

- Survey 4184 participants (HealthStyles survey)
- 7% men and 13% women had heard of CMV
- High incidence of high risk behaviors for transmission
Incorporation NBHS for CMV testing (Advantage):

• Uses an existing screening program to diagnosis a common cause of SNHL (NBHS)
• The number of infants undergoing CMV testing is manageable
• The method of testing is easy to perform
• The cost of testing is relatively inexpensive
• Identifies subset of children with congenital CMV who may benefit from antiviral therapy
Incorporation NBHS for CMV testing (Disadvantage):

- Not all children are screened for congenital CMV infection
- Majority of children who will develop CMV induced SNHL are not tested
- Many families unaware their child has CMV
- Lost opportunity for education, prevention and antiviral therapy
Should we be looking at universal CMV screening?

• NO

• No evidence to support antiviral therapy for CMV infected children without hearing loss

• Significant cost to implement (DBS assay not a good option- poor sensitivity)

• Logistical hurdles
Proposed Approach for Early Detection:

• 3 week old fails NBHS x2 \(\rightarrow\) CMV saliva PCR-positive
• Early intervention services
• Family provided education on CMV
• Audiologic evaluation (ABR) for possible SNHL
• MRI brain/temporal bone
• Antiviral therapy option presented if confirmed SNHL
Early Results from CMV legislation:

- Awareness still a challenge
- Some infants have undergone blood PCR CMV testing not saliva or urine
- 2 false positive saliva CMV results
- Know of 10 infants diagnosed with congenital CMV from Utah law
Early Results from CMV legislation:

Percent Infants Who Undergo Audiologic Diagnostic Testing by 3 mo of age

Groups Compared

- Historical
- CMV tested
- CMV positive
Conclusion:

• Rapidly evolving field
• Critical providers, EDHI personnel and caregivers know about CMV
• Diagnosis not difficult
• May be more cost effective as first test for hearing loss etiology
• Increasing evidence early diagnosis potential to improve patient and at risk population outcomes
Acknowledgements: