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

Save the Date!!!

Cytomegalovirus Public Health & Policy Conference

September 26-27, 2014
in Salt Lake City, Utah
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

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

Design: A retrospective review of the medical records for all children with a diagnosis of SNHL, seen from January 1, 1993, through December 30, 1996, at our institution.

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, 68.3% had a definite or probable cause of their SNHL identified; 19.9% had no possible causes, and 18.9% had no obvious cause. A family history of SNHL or premature infants 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 36.9%. However, syndromes commonly reported to be 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 3.97 years. The most useful diagnostic study was computed tomographic scanning.

Conclusions: Sensorineural hearing loss is fairly common in children. Extensive workups, often without clear direction, should be reordered based on the children with SNHL who otolaryngologists are now seeing. Inpatient screening programs, although identifying many children earlier, will also provide the opportunity to fine-tune the evaluation (i.e., cytomegalovirus titers and/or cultures at birth), 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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</tr>
</thead>
<tbody>
<tr>
<td>No. of children</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>85 (72.6)</td>
<td>81 (63.8)</td>
<td>69 (73.4)</td>
<td>159 (76.4)</td>
</tr>
<tr>
<td>Unknown cause</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>39 (33.3)</td>
<td>28 (22.0)</td>
<td>31 (33.0)</td>
<td>52 (24.6)</td>
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<tr>
<td>Family history</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>7 (6.0)</td>
<td>18 (14.2)</td>
<td>7 (7.4)</td>
<td>26 (12.3)</td>
</tr>
<tr>
<td>Inner ear defects</td>
<td>0</td>
<td>12 (9.4)</td>
<td>0</td>
<td>25 (11.8)</td>
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<tr>
<td>Preranal insult</td>
<td>16 (13.7)</td>
<td>16 (12.6)</td>
<td>14 (14.9)</td>
<td>40 (18.9)</td>
</tr>
<tr>
<td>TORCH infections</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>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>2 (1.7)</td>
<td>0</td>
<td>1 (1.2)</td>
<td>51 (24.2)</td>
</tr>
</tbody>
</table>
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

A diagnostic paradigm for childhood idiopathic sensorineural hearing loss

DIEGO A. PRECIADO, MD, LYNNIE Y.H. LIM, MD, ALIZA P. COHEN, MA, COLM MADDEN, MD, DAVID MYER, BS, CHRIS NGO, BS, JOHN K. BRADSHAW, MD, LOUISE LAWSON, PhD, DANIEL I. CHOO, 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. 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. Most (80%) of these cases are transmitted in an autosomal recessive manner.

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. 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 titers, 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%, 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 30% of children with SNHL. Of relevance in follow-up studies, in 1988, the one-in-one-and-one-half-year-old child's audiogram showed a bilateral SNHL.
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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:

- Primary CMV infection
- Seronegative mothers who develop infection during pregnancy
- Can transmit in seropositive mothers via reactivation of latent virus or reinfection with new strain
  - 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% or more of these infants have no sequelae
• 5% to 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

6 CMV-pos newborns

594 CMV-neg. newborns

400 Moms Seronegative Prior to Pregnancy

7 Moms acquire CMV

2 CMV-pos newborns

5 CMV-neg newborns

393 Moms don’t acquire CMV

393 CMV-neg 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:

Characteristics of CMV Induced Hearing Loss

Nature of Progressive SNHL:

Cumulative Percent SNHL by Age

Nature of CMV Induced SNHL (Summary):

• CMV makes up to 33% 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 as part of evaluation for pediatric hearing loss
• Sequential diagnostic paradigm
• Urine and later saliva CMV (2011) CMV PCR (Collaboration with David Hillyard –ARUP)
• DBS testing for infants > 3 weeks of age (Collaboration with Richard Harward/Harper Randall- DOH)
“New Current” Approach to Pediatric SNHL

1. History, physical examination, complete audiologic work-up
   - Diagnosis apparent (syndrome, AD, trauma, meningitis)
   - Diagnosis uncertain (idiopathic)

   - Appropriate treatment
   - CMV testing

2. GJB2 screen
   - Positive
     - Genetic counseling
   - Negative
     - Imaging
     - Lab tests as indicated
     - ECG (if severe to profound SNHL)

3. Imaging
   - Preferential seating
   - Serial audiograms

4. 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
- Universal Newborn hearing screen
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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

1. History, physical examination, complete audiologic work-up
   - Diagnosis apparent (syndrome, AD, trauma, meningitis)
   - Diagnosis uncertain (idiopathic)

2. CMV testing
   - Bilateral
   - Unilateral

3. GJB2 screen
   - Positive: Genetic counseling
   - Negative: Imaging, preferential seating, serial audiograms, lab tests as indicated, ECG (if severe to profound SNHL)

4. 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
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SNHL Etiology Based on CMV, Imaging and Genetic Evaluation

Largest group with a known etiology 30%

N=83

- CMV
- Idiopathic (largest group, 30%)
- Inner
- Genetic
- ANSD
- Other
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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 FU 305 days
  - 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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<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>
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<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>
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<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>
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<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>
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<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>
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</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 a 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 shed virus for months or years—“contagious”
- Good hygiene to minimize transmission to other people especially those at risk disease (pregnant mother or immunocompromised patients)
- Not share utensils, no kissing on the lips, no sharing of foods
Prevention of CMV:

• Small study 14 seronegative pregnant women w small children- behavioral intervention resulted in no seroconversion (Alder et al, 1996)

• N=5000 seronegative pregnant women – behavioral intervention resulted in reduction > 50% expected rate seroconversion (Picone et al. 2009; Vauloup-Fellous et al, 2009)
Other Benefits from Early CMV Diagnosis:

- Identify at risk group for repeated audiologic testing
- Obviates need other unnecessary testing (e.g. genetic testing > $611- connexin)
- May direct to other testing (e.g. MRI brain and ophthalmology)- ongoing studies- Young and Bale (UU)
- May impact on treatment (e.g. antiviral therapy)
Ganciclovir:

• 1\textsuperscript{st} antiviral agent approved for CMV treatment (1994)
• synthetic analogue of 2′-deoxy-guanosine
• Inhibits viral DNA polymerase
• Requires parenteral administration
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

Serial hearing testing baseline, 6 and 12 mo

Role for Antiviral Therapy?

• 21 of 25 (84%) improved or maintained normal hearing between baseline and 6 mo vs. 10 of 17 (59%) controls (p=0.06)

• None of 25 GCV rx’ed had worsening hearing vs 7 of 17 (41%) controls (p< 0.01)
Hearing Outcomes at 6 mo

Hearing Status

- Improved/no change: GCV treated (P < 0.01)
- Worse: No treatment (P = 0.06)

Comparison between GCV treated and No treatment groups.
Role for Antiviral Therapy?

- 50% treated group improved or stable hearing at 1 year versus 26% untreated group.
- 5 of 24 (21%) GCV rx’ed had worsening hearing vs 13 of 19 (68%) controls p< 0.01.
Hearing Outcomes at 12 mo

P=0.07

P<0.01

- GCV treated
- No treatment

improved/no change
worsened
Adverse Effects From GCV:

- 29 of 46 GCV rx’d (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 1st 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

• Abstract October 2013 and Grand rounds (Jan 9, 2014)

• Study Objectives:
  1. Compare impact hearing outcomes
  2. Compare impact neurologic outcomes
  3. Compare safety profile
  4. Correlate change in whole blood viral load with hearing and neurologic outcomes
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

CASG 112: 6 Wk v. 6 Mo PO Valganciclovir
Schematic of Study Design

- Enrollment
- Randomization
- Oral valganciclovir
- No treatment
- Oral placebo
- No treatment

ABR
- Valganciclovir vs. placebo to complete 6 mos of total therapy
- F/U weekly x 4 wks, then every two weeks x 8 wks, then every month x 3 mos
- 6 mos D/C study medication
- F/U at 7 mos
- F/U at 1 yr
- F/U at 2 yr

ABR/VRA
- Bayley III

IDWeek 2013, Late Breaker Abstract #43178
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**: 57% Improved or Remained Normal, 43% Worse or Remained Abnormal
- **6 Months of Treatment**: 73% Improved or Remained Normal, 27% Worse or Remained Abnormal

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

6 Weeks of Treatment

- Improved or Remained Normal: 64%
- 36%

6 Months of Treatment

- Improved or Remained Normal: 77%
- 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>
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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>
</tr>
</thead>
<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>
</tr>
<tr>
<td>Expressive Communication Scale</td>
<td>5.5±0.5</td>
<td>7.3±0.5</td>
<td>0.0158</td>
</tr>
<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 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 → 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
Conclusion:

• Rapidly evolving field
• Critical Primary Care physicians 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: