The Rationale for Hearing Targeted Early CMV Screening:

Albert Park, MD
Chief Pediatric Otolaryngology, Professor
Primary Children’s Hospital
University of Utah
Nondisclosure:

- NIDCD R01 co-I Cochlear Implantation
- NIH U01 PI CMV multi-institutional study- pending
- Valganciclovir – not FDA approved for congenital CMV
The Story of DD:

- 19 mo child presented with progressively worsening hearing in Fall 2012.
- Failed newborn hearing screen and automated ABR at 3 weeks
  - **Click ABR** at 3 weeks: 30 dB nHL right and 25 dB nHL left
- Recommended FU 9 mo.
- PMH: enlarged ventricles 34 wks gestation in utero U/S
- U/S at birth- “germinolytic” cystic changes- in utero insult
Case History DD:

- Normal Otologic examination
- Repeat ABR right profound and left moderate SNHL
- Saliva CMV PCR- positive
- Neonatal Dry Blood Spot PCR- positive
- 6 week course of valganciclovir
- Left ear worsened to profound
- Bilateral Cochlear Implantation
- Explanted and reimplanted 2 years later
Epidemiology of cCMV on Hearing:

• Most common non-heredity cause of congenital hearing loss
• 4-6% congenital hearing loss (Stehel et al. 2008; Diener et al. 2017)
• 20% all pediatric hearing loss (Nance and Morton 2006)
CMV Not Commonly Tested!

No role for CMV testing?

Preciado et al. OHNS 2004
Proposed Role for Pediatric SNHL Evaluation

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

• Chart and database review
• Children 3 yrs or younger
• May 2008-September 2013
• Sequential diagnostic paradigm

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

• **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

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

• 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
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

• RESULTS:
• N=111 children w SNHL (2008-2013)
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

SNHL Etiology Based on CMV, Imaging and Genetic Evaluation

Largest group with a known etiology 30%

N=83

The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

- **Breakdown of CMV Patients (n=25)**
- Sixteen – confirmed CMV diagnosis
- Six of sixteen diagnosed via DBS testing
- Nine- probable CMV diagnosis
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

- 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
Cost Estimates Using Different Approaches for SNHL Evaluation:

<table>
<thead>
<tr>
<th>Cost $/100 patients</th>
<th>Type of Hearing Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMV</td>
<td>Mod-Sev, Sev-Prof</td>
</tr>
<tr>
<td>Imaging</td>
<td>Uni, ANSD, Overall</td>
</tr>
<tr>
<td>Genetic</td>
<td>Simultaneous</td>
</tr>
</tbody>
</table>

The graph shows the cost estimates for different hearing loss types using various approaches.
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

- 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
DD=Daisy Doutre

Former Representative
Ronda Menlove
Awareness of CMV:

- National survey 4184 participants (HealthStyles survey)
- 7% men and 13% women had heard of CMV
- High incidence of high risk behaviors for transmission

Comparison CMV Diagnosis with or without HT-CMV approach

Without HT-CMV

With HT-CMV

Newborn Hearing Screen

Passed

Failed

CMV negative

CMV positive

Hearing normal

Hearing Loss
Utah House Bill 81 (July 2013):

• DOH public education program to inform caregivers about CMV
• DOH education for providers and other organizations offering children’s programs
• Medical practitioners to test infants < 3 wks of age who fail two newborn screening tests for CMV and inform the parents cx and rx
National Map for Hearing Targeted Early CMV Screening (HT-CMV) 2013:
National Map for Hearing Targeted Early CMV Screening (HT-CMV)2017:

From National CMV Foundation Website February 2017
Almost 100 Birth Hospitals Implemented HT-CMV Screening
AAP Newsletter:

• December 2015
• Department Practice and Division of Quality
• Response to legislative efforts on CMV screening for newborns who fail an infant hearing test
AAP Newsletter:

• “No evidence ... supports treatment of newborns who test positive for CMV but are otherwise asymptomatic...”
AAP Newsletter:

• “Treatment currently is limited to off-label use of the antiviral drug valganciclovir which carries potential risks”
AAP Newsletter:

• “Clinicians practicing in the best, most up-to-date fashion ... face increased medical practice liability risk. If states continue down this path, it may threaten our ability to practice medicine in a manner consistent with the best available science...”
AAP Views:

• “These kinds of laws... may drive such treatment ...parents and providers often will feel that they must do something...In so doing, we may harm the children we are trying to help...”
AAP Position?

• No screening?
What is Treatment?

- **treatment** [trēt´ment]
- **1.** the management and care of a patient; see also **CARE**.
- **2.** the combating of a disease or disorder; called also **therapy**.

**Treatment Does Not Need to Mean Just Antiviral Therapy!**
Treatment From Early CMV Screening is...

- Helping the family of hearing impaired child
- Increases Detection rate of **Symptomatic** CMV infected children
- Protects at risk populations
- Focuses attention on CMV infected infants for progressive hearing loss
- Improves time to diagnose hearing loss for all CMV tested infants
- May improve hearing outcomes of CMV hearing impaired infants
- Reasonable cost
“Blindness separates people from things; deafness separates people from people.”

Helen Keller
Helping the Family:

• Parental response – surprise, sadness and concern

• Questions- cause of the hearing loss, likely impact on new family member, options for treatment

Kurtzer-White & Luterman, 2003; Yoshinaga-Itano & DeUzcategui, 2001; Young & Tattersall, 2007
Helping the Family even if the child doesn’t present with hearing loss:

- “I would want to have my baby tested for CMV even if my doctor or hospital didn’t do it routinely.” (84%)
- “I would want to know if my child has CMV even if he or she never develops problems.” (84%)
- “I would be willing to pay $20 to have my baby tested for CMV.” (87%)

CMV Testing is Time Sensitive:

- CMV testing requires child must be less than 3 weeks of life!
- Unlike Genetic testing, you cannot decide to wait until the child is older to make the diagnosis
Increasing the Detection Rate of the Symptomatic CMV Infected Infant:

- 10% fetal demise
- Prematurity
- Common features:
  - Hepatomegaly
  - Splenomegaly
  - Petechiae
  - Jaundice
  - Microcephaly
  - Chorioretinitis
  - Sensorineural hearing loss (50%)
Increasing the Detection Rate of the Symptomatic CMV Infected Infant:

• Minority symptomatic CMV cases diagnosed clinically!
• Vaudry et al., 2014; Townsend et al., 2011; McMullan et al. 2011
• <10% (Sorichetti et al. 2015)
• Since Utah Mandate- detected 5 CMV hearing impaired infants with CNS abnormalities
• Would not have been diagnosed otherwise
6 Weeks vs. 6 Months Valganciclovir Hearing Outcomes @ Two year Followup

Kimberlin et al. NEJM 2015

6 Weeks of Treatment

- Improved or Remained Normal: 36%
- Worse or remained abnormal: 64%

6 Months of Treatment

- Improved or Remained Normal: 77%
- Worse or remained abnormal: 23%

P = 0.04
### 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>0.0037</td>
</tr>
<tr>
<td>Receptive Communication Scale</td>
<td>5.2±0.5</td>
<td>7.3±0.5</td>
<td>0.0027</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.
Treating the Symptomatic cCMV Infected Infant:

• General consensus that this group would benefit from antiviral therapy
• Hearing targeted early CMV screening (Utah mandate) improves detection of this group
Protection of at Risk Groups:

- Child with congenital CMV will shed virus for months or years- “contagious”
- Pregnant moms or immunocompromised patient warned cCMV risk
- Hand washing, avoid kissing on lips, no sharing utensils
- 14 seronegative pregnant women -behavioral intervention resulted in no seroconversion
- 5000 seronegative pregnant women – behavioral intervention > 50% drop expected rate seroconversion

Focusing Attention on CMV Infected Infants at Risk for Progressive Hearing Loss:

- Utah HT-CMV screen identified CMV infected hearing impaired - >50% chance progressive loss
- Some have CMV but hearing initially normal - 15% chance of progressive loss
- Reduces the uncertainty of the CMV diagnosis
Comparison CMV Diagnosis with or without HT-CMV approach

Figure 1: Sequential Approach for Pediatric SNHL

Newborn Hearing Screen
- Passed
  - CMV negative
    - Hearing normal
  - CMV positive
    - Hearing Loss
- Failed
  - CMV negative
  - CMV positive
    - Hearing Loss
Focusing on Asymptomatic CMV Infected Infants:

- Example of Tracking hearing thresholds in a CMV infected child:
Impact HT-CMV Screening on Diagnostic Hearing Testing:

• Timely diagnostic hearing evaluation 56% (2 years prior) and 77% (2 years after law)!

• After the law, 86.6% diagnostic hearing evaluation among CMV screened vs 61.5% diagnostic hearing testing among non-CMV screened group

• HT-CMV benefits not just CMV infected but ALL children who fail their newborn hearing screen

Importance of Early Identification:

Average total language quotient for children with normal cognition by category of hearing loss and age of identification. solid bars= by 6 mo; shaded= after 6 mo.

# National Survey of Newborn Hearing Screening Programs:

## TABLE 1 Summary of Outcome Measures Reported by UNHSI Programs

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Weighted % (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborns screened before discharge</td>
<td>92 (25–100)</td>
</tr>
<tr>
<td>Newborns who did not pass screening before discharge</td>
<td>4 (1–34)</td>
</tr>
<tr>
<td>Newborns who were referred for a diagnostic evaluation&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Infants who needed a diagnostic evaluation and received one</td>
<td>2 (1–7)</td>
</tr>
<tr>
<td>Infants who needed a diagnostic evaluation and received one by the age of 3 mo</td>
<td>62 (15–95)</td>
</tr>
<tr>
<td>Infants who did not pass the hearing screening who had a medical home</td>
<td>80 (5–100)</td>
</tr>
<tr>
<td>Infants with confirmed hearing loss linked to EI&lt;sup&gt;b&lt;/sup&gt;</td>
<td>68 (10–100)</td>
</tr>
<tr>
<td>Infants with confirmed hearing loss linked to family-to-family support&lt;sup&gt;c&lt;/sup&gt;</td>
<td>40 (5–100)</td>
</tr>
</tbody>
</table>

<sup>a</sup> States and territories reported estimated percentages, which are weighted by the number of live births reported by the state or territory. States did not report estimates for all measures.

<sup>b</sup> This measure reflects the percentage of infants referred for diagnostic evaluation as a result of nonpass results in the hospital before discharge or nonpass results at an outpatient rescreening.

<sup>c</sup> Some programs reported rates that reflect the percentage of children referred to EI or family-to-family support, whereas others reported rates that reflect the percentage of children who received services through EI or family-to-family programs. When both rates were reported, we recorded the percentage that received services.
What about Antiviral Therapy?

• 26 day old infant presented with CMV induced SNHL
• Failed NBHS
• Saliva CMV PCR @ 3 wks age- positive
• ABR- normal right and left profound SNHL
• Ophthalmology exam- normal
Rationale for Antiviral Therapy:

- VGC x 6 weeks
- FU audio 2+ yrs after rx-stable hearing
- Speech progressing normally
Antiviral (VGC) treatment Hearing Impaired CMV Infected:

• 8 asymptomatic CMV patients underwent VGC + 3 asx treated before Utah law (n=11)
• Ave. age initial treatment 45± 22 days (28-101 days)
• Duration ave. 108±56 days (45-182 days)
• 3 (30%) neutropenia- 2 required reduction dose, 1 earlier cessation at 3 mo vs planned 6 mo (infected dacrocystocele).
• 4 elevation transaminase- 1 dose adjustment required
• Average follow-up period: 1.8 years (0.3-2.8)
Preliminary Outcomes from Antiviral Therapy:

- Total ears, Worse versus same, or improvement (NEJM 2015)
Randomized VGC Trial:

- NIH R01 study
- Asymptomatic CMV infected hearing impaired
- Randomized to VGC vs placebo
- Hearing and language outcomes
- Safety assessment
Randomized VGC Trial:

Asymptomatic cCMV Hearing Impaired Infants Randomized to Valganciclovir and No Treatment

- **Screening**
  - Key Inclusion Criteria: CMV positive hearing impaired infants

- **Randomization**
  - Arm 1: VGC
  - Arm 2: Untreated Controls

- **Day 0**
  - 6 mo after VGC started

- **12 mo of age**
  - Aim 1: Primary Endpoint (hearing)
  - Aim 2: Primary Endpoint (safety)
Collaborating Sites for CMV Trial:
Take Home Message:

• “No There is evidence ... supports treatment of newborns who test positive for CMV but are otherwise asymptomatic...”
  a. Provides providers and parents etiology for SNHL
  b. Increases opportunity to dx Sx cCMV patient
  c. Opportunity to educate family, prevent transmission to pregnant moms and immunocompromised patients
  d. Focus at risk patients for progressive loss
  e. Improves time to diagnose hearing loss for ALL infants who failed their newborn hearing screen
  f. Preliminary data promising for antiviral rx
  g. It is affordable
Universal vs. Hearing Targeted CMV Screening

Universal CMV screening (Uni-CMV)
- CMV testing
  - CMV positive
    - Hearing loss
    - No hearing loss
  - CMV negative

Hearing Targeted CMV screening (HT-CMV)
- Hearing Screening
  - Pass
  - Fail
    - CMV testing
      - CMV positive
        - Hearing loss
        - No hearing loss
      - CMV negative
Universal cCMV debate:

- Reminiscent of Newborn hearing debate

Universal Newborn Hearing Screening: Should We Leap Before We Look?

ABBREVIATIONS. NIH, National Institutes of Health; HRR, high-risk-register; ICN, intensive care nursery.

Across the nation pediatricians are being importuned, and indeed propelled, to implement universal newborn hearing screening, despite a total lack of information concerning ultimate costs and, particularly, risks. Without question, early detection of severe sensorineural hearing loss is a laudable goal, to be pursued devoutly. However, I would contend again, as Fred Bess and I argued in a commentary in Pediatrics 5 years ago, that universal newborn hearing screening in our present state of knowledge is not necessarily the only, or the best, or the most cost-effective way to achieve that goal, and more importantly, that the benefits of universal newborn hearing screening may be outweighed by its risks. The nagging question of ultimate costs and risks that Bess and I posed in that commentary remains unanswered, and in fact, virtually unaddressed.
Won’t we be missing a large number of children with cCMV?

A Targeted Approach for Congenital Cytomegalovirus Screening Within Newborn Hearing Screening

Karen B. Fowler, DrPH, Faye P. McCollister, EdD, Diane L. Sabo, PhD, Angela G. Shoup, PhD, Kris E. Owen, AuD, Julie L. Woodruff, AuD, Edith Cox, AuD, Lisa S. Mohamed, AuD, Daniel I. Choo, MD, Suresh B. Boppana, MD, on behalf of the CHIMES Study

Fowler et al. Pediatrics 2017
Universal vs HT-CMV Approach:

100,332 infants tested for cCMV infection in the CHIMES Study

CMV negative
\( (n = 99,883) \)
- Reasons for missing hearing screen
  \( (n = 381) \)
  - 253 infants not completed before hospital discharge
  - 88 infants died
  - 2 parental refusals
  - 38 infants with missing data
- 99,502 infants without cCMV infection who received a NHS test

CMV positive
\( (n = 449) \)
- Reasons for missing hearing screen
  \( (n = 6) \)
  - 3 infants not completed before hospital discharge
  - 3 infants died
- 443 infants with cCMV infection who received a NHS test
Universal vs HT-CMV Approach:

• NBHS identified 57% infants who had CMV-related SNHL in newborn period
• Newborn hearing screening methodology not presented
• Not clear methodology diagnostic ABR testing
• Need validation of newborns diagnosed with ABR testing with behavioral testing
Cost Effectiveness of Early CMV Screening:

Cost-effectiveness of Universal and Targeted Newborn Screening for Congenital Cytomegalovirus Infection

Soren Gantt, MD, PhD, MPH; Francois Dionne, PhD; Fred K. Kozak, MD; Oran Goshen, MD; David M. Goldfarb, MD; Albert H. Park, MD; Suresh B. Boppana, MD; Karen Fowler, DrPH
Cost Effectiveness Universal or HT-CMV Screening:

### Table 4. Estimated Mean Incremental Costs per Newborn to Identify Cases of cCMV Infection and Related Hearing Loss

<table>
<thead>
<tr>
<th>Cost to Identify 1 cCMV Infection</th>
<th>Universal 10/Test</th>
<th>Universal 50/Test</th>
<th>Universal 10/Case</th>
<th>Universal 50/Case</th>
<th>Targeted 10/Case</th>
<th>Targeted 50/Case</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2000</td>
<td>10,000</td>
<td>566</td>
<td>2832</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost to Identify 1 cCMV-related hearing loss</td>
<td>27,460</td>
<td><strong>90,038</strong></td>
<td>975</td>
<td>3916</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost to Prevent 1 Cochlear Implant</td>
<td>4064.157</td>
<td>12,620.277</td>
<td>39,401</td>
<td>271,947</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: cCMV, congenital cytomegalovirus.

- **All costs are in 2016 US dollars.**
- **Assumes valganciclovir hydrochloride treatment of only symptomatic**

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**Gantt et al. JAMA Pediatrics 2017**

<table>
<thead>
<tr>
<th>Cost (2001 US dollars)</th>
<th>None</th>
<th>Selective</th>
<th>Universal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cost of detection of deafness in cohort*</td>
<td>$69,200</td>
<td>$671,200</td>
<td><strong>$2,222,700</strong></td>
</tr>
<tr>
<td>Cost per infant whose deafness is diagnosed by 6 mo</td>
<td>$2300</td>
<td>$10,100</td>
<td><strong>$21,400</strong></td>
</tr>
<tr>
<td>Lifetime costs of all care related to deafness and lost productivity</td>
<td>$116,980,800</td>
<td>$115,520,600</td>
<td><strong>$114,648,300</strong></td>
</tr>
<tr>
<td>Cost per deaf child with normal language outcomes</td>
<td>$2,215,500</td>
<td>$1,978,100</td>
<td><strong>$1,769,300</strong></td>
</tr>
<tr>
<td>Incremental cost or saving (2001 US dollars)</td>
<td>-</td>
<td><strong>$16,400</strong></td>
<td>$44,300</td>
</tr>
<tr>
<td>Incremental cost per infant whose deafness is diagnosed 6 mo‡</td>
<td>-</td>
<td><strong>$1,460,200</strong></td>
<td>$872,300</td>
</tr>
</tbody>
</table>

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**Keren et al. Pediatrics 2002**
Universal cCMV vs HT-CMV Screening:

• No operational program currently following universal cCMV screening
• Several states and multiple institutions implementing HT-CMV screening
• Why is there no one implementing universal screening?
• No micro-cost data- estimates for screening may be too low
• “Normal” cCMV infants difficult to manage- one-third in HT-CMV cohort
What Can You Do?

• Talk to your Audiologists and Newborn Medical Directors
• Almost 100 hospitals performing HT-CMV screening
• Talk to your EDHI team- Implement DBS CMV PCR testing
• Every state has DBS that can be tested for CMV
• Join our CMV network: albert.park@hsc.utah.edu
Cytomegalovirus Clinical Group:

James Bale
Neurology

Stephanie McVicar
DOH

Marissa Diener
Family Studies

David Hillyard
ARUP

John Carey
Genetics

Krow Ampofo
Infectious Disease

Liz O’Brien
Lonnie Miner
Mariana Baserga
Roger Faix
Shrena Patel
Melanie
Boogaard

Tom Greene
Epidemiology

Sean Redmond
Speech and Lang.

Soren Gantt
Univ. BC
Infectious Disease

Mike Dean
Clinical Trials

Betsy Ostrander
Angela Shoup
Bradley Yoder
Elizabeth
Knacksteadt
Emily Thorell
Xiaoming Sheng
Shannon White
Claudia Fruin
Cathleen Zick
Jill Boettger
Typical Utah Rear Window:
Hearing-Targeted cCMV Screening in a County Hospital: The Parkland Experience

Angela Shoup, PhD  
Associate Professor, Otolaryngology  
Director Division of Communicative & Vestibular Disorders

Kris Owen, AuD  
Faculty Associate, Audiology  
Coordinator, Parkland Hospital UNHS Program

UT Southwestern Medical Center & Affiliated with Parkland Hospital and Children’s Health Dallas
The Parkland Hospital UNHS and HT-cCMV program

1986
Began screening babies at risk for hearing loss utilizing the HRR

1991/1992
Began screening all babies in the SCN & continued to screen based on HRR in WBN

1997
Committee organized to begin planning for a UNHS Program

1997
Pilot program in preparation for moving to UNHS

April 1999

September 1, 1999
UNHS & HT-cCMV

Cheryl Aldridge, PNP
Pam Ford, RN
Greg Jackson, MD
Abbott Laptook, MD
Kris Owen, AuD
Angela Shoup, PhD
Dale Talley, RN, MS, CPNP
Pablo Sanchez, MD
COLLABORATION
Parkland UNHS mission statement, 1999-present

- To provide every baby born at or transferred to Parkland with a hearing screening prior to discharge from the hospital;
- To connect babies referred by the hearing screening program with appropriate diagnostic services and examinations;
- To facilitate connection with early intervention services;
- To serve as a conduit of information to parents, other professionals, and the community regarding normal auditory behavior, speech and language development, and the importance of early intervention.
Parkland Statistics:
09/01/1999 – 08/31/2016

Screened: 237,535 (99%)

Referred: 2,057 (0.9%)

NH: 1202 (58.4% of refers)

LFU: 54 (2.6% of refers)

Deferred: 12 (0.6% of refers)

Confirmed AI: 789 (38.3% of refers; 0.33% of screened)
Parkland UNHS & HT-cCMV Protocol
cCMV Screen in Infants Born to HIV+ Mothers

CMV is short for cyto-megalo-virus

CMV is common

Most common virus transmitted from a pregnant woman to her unborn child

1 in 150 children are born with congenital CMV

1 in 3 pregnant women who get CMV will pass the virus to their unborn child

More common than the 29 combined metabolic and endocrine disorders in the recommended US newborn screening panel

2.6 MILLION CHILDREN worldwide are living with HIV. Most of these children were infected by their HIV-positive mothers during pregnancy, childbirth or breastfeeding.


Aids.gov
HT-cCMV Screening at Parkland

• Purpose of CMV screen for infants that refer on UNHS at Parkland:
  – Identify infants with cCMV & determine which infants with possible congenital hearing loss have cCMV
  – Support the families
    • Parent education
    • Assist with making appropriate treatment recommendations and referrals
    • Institute an appropriate monitoring plan
    • Provide prognostic information
HT-cCMV screen assists with meeting recommended guidelines

*Medical Evaluation*

Every infant with confirmed hearing loss and/or middle ear dysfunction should be referred for otologic and other medical evaluation. The purpose of these evaluations is to determine the etiology of hearing loss, to identify related physical conditions, and to provide recommendations for medical/surgical treatment as well as referral for other services. Essential components of the medical evaluation include clinical history, family history of childhood-onset permanent hearing loss, identification of syndromes associated with early- or late-onset permanent hearing loss, a physical examination, and indicated radiologic and laboratory studies (including genetic testing). Portions of the medical evaluation, such as urine culture for CMV, a leading cause of hearing loss, might even begin in the birth hospital, particularly for infants spending time in the NICU (Boppana et al., 2005; Nagy, Endreffy, Streitman, Pinter, & Pusztai, 2004; Roizen, 1999).
General interpretation of positive CMV screen

• Positive for cCMV: before 3 weeks of age
• Indeterminate: culture positive on specimen taken after 3 weeks of age with no previous CMV test before 3 weeks of age
• Acquired: culture positive for CMV on infant screened after 3 weeks of age who previously had a negative CMV culture
The Father of HT-cCMV Screening at Parkland Hospital:
Pablo J. Sanchez, MD

Current Affiliation: Infectious Diseases and Neonatology
Center for Perinatal Research
Nationwide Children’s Hospital
Columbus, OH
HT-cCMV Screening at Parkland: Inpatient

- All babies with a refer result on an inpatient hearing screen receive a CMV screen prior to discharge
- Parents are counseled prior to discharge about the CMV screen
HT-cCMV Screening at Parkland: Outpatient

- Repeat hearing screening
- cCMV screening
  - Results are reviewed prior to OP visit
  - If sample is not viable, obtain another sample at outpatient visit
  - If cCMV screen results are positive, a medical provider will discuss the results and follow-up recommendations with the parents
  - Connect family with Pediatric ID for follow-up and possible antiviral therapy
CHALLENGES & ISSUES
Collection of urine sample...
Saliva CMV screen
Babies with a refer result will be referred to Audiology for a final screening prior to discharge with the exception of those with a normal ABR. Families will be contacted with their results, and they will be scheduled for an appointment for an audiological assessment. This assessment will include a comprehensive hearing test and a detailed discussion of the results.

All babies with a refer result on the initial hearing screen by Audiology will receive a CytoMeningeal (CMV) screen prior to discharge from the hospital.

Babies with a positive CMV test will undergo further testing to determine the need for further treatment. This may include hearing follow-up and other medical interventions.

Purpose: To ensure that babies with hearing loss are identified and treated early.

Equipment:
- Eastern Medical Record (EMR)
- Monitoring and Auditory Brainstem Response (AABR) hearing screen
- Timely parental education and communication

Procedure:
- Well Baby Units
  1. An AABR screening and Critical Congenital Heart Defect (CCHD) screen will be completed prior to discharge.
  2. The baby will be taken to a quiet area for the hearing screen. The baby must be still and quiet during the hearing screen. The hearing technician will prop the baby for the screen and ensure the baby is in the best state for hearing screening.
  3. Once the hearing screen is complete, the hearing technician will discuss the results on the EMR screen attached. If the baby does not pass, the baby will be referred for further assessment.

Audiology will be notified by the Hearing Technician if a baby does not pass.
HT-cCMV Screening at Parkland

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total refer on UNHS</td>
<td>2057</td>
<td>0.9% with HS</td>
</tr>
<tr>
<td>Total HT-cCMV screen</td>
<td>1837</td>
<td>89% of refers on HS</td>
</tr>
<tr>
<td>cCMV positive</td>
<td>47</td>
<td>3% of cCMV screened</td>
</tr>
<tr>
<td>cCMV negative</td>
<td>1790</td>
<td>97% of cCMV screened</td>
</tr>
</tbody>
</table>
572 infants did not pass HS: 0.7% of 79,047 screened

483 (84%): cCMV screen

24 (5%): cCMV +

16 (67%) confirmed AI

4 (25%): clinical signs prompted cCMV screen

12 (75%): failed HS prompted cCMV screen

5 (83%): failed HS prompted cCMV screen

4 (33%): clinical signs of cCMV

8 (67%): no clinical signs of cCMV

6 (25%): NH

2 (8%): LFU

1 (17%): clinical signs prompted cCMV screen

5 (83%): failed HS prompted cCMV screen

2 (8%): LFU

Parkland HT-cCMV Results

09/01/1999-8/31/2004

- Live births: 79,575
- Hearing screened: 79,047 infants (99%)
- Did not pass: 572 (0.7%)
- Confirmed AI: 256 infants (0.3% of screened)
- cCMV +: 16 (6% of infants with confirmed AI)

09/01/1999-7/31/2016

- Live births: 240,080
- Hearing screened: 237,535 infants (99%)
- Did not pass: 2057 (0.9%)
- Confirmed AI: 789 infants (0.33% of screened)
- cCMV +: 47 (6% of infants with confirmed AI)

Stehel, Shoup, Owen, Jackson, Sendelbach, Boney, Sanchez (2008). Newborn hearing screening and detection of congenital cytomegalovirus infection. Pediatrics 121:970-975

Updated Data
Hearing Outcomes of HT-cCMV+ Infants

- 47 cCMV+
  - 16 WNL (34%)
  - 29 AI (62%)
  - 2 LFU (4%)
  - 15 U
  - 14 B
Hearing Outcomes of HT-cCMV+ Infants

- 16 WNL (34%)
- 5 WNL
- 1 U Mod
- 1 U Prof
- 1 B Prof
- 8 Current status UK
Hearing Outcomes of HT-cCMV+ Infants

47 cCMV +

16 WNL (34%)
29 AI (62%)
2 LFU (4%)

15 U
14 B
Hearing Outcomes of HT-cCMV+ Infants

- 29 AI (62%)
- 15 U
- 1 Mild
  - B Mod
  - 1 B Mod
  - 1 U Prof
  - 1 Current status UK
- 3 Mod
  - No change
  - 1 B mild/prof
  - 3 B Prof
- 1 Sev
  - No change
- 10 Prof
  - 5 no change
  - 1 Current status UK
Hearing Outcomes of HT-cCMV+ Infants

47 cCMV +

16 WNL (34%)

29 AI (62%)

2 LFU (4%)

15 U

14 B
Hearing Outcomes of HT-cCMV+ Infants

29 AI (62%)

14 B

1 Mod CHL
1 WNL
2 B Prof

4 Mod
2 B Prof
2 Current status UK

1 Sev
1 ANSD
1 WNL
7 Prof
B Prof
So, What Have We Learned Through 17 years of HT-cCMV?

• A CMV screen for all infants who refer on hearing screening can provide valuable information for managing those identified with hearing loss
• Appropriate monitoring/management can be implemented for those who initially do not pass HS and are found to be cCMV+
• CMV screening of only those infants who refer on hearing screening will miss many with cCMV who are asymptomatic for HL at birth
• Possible “false sense of security” in parents of infants that pass that may lead to delay in identification of delayed onset hearing loss
• 6% of infants with confirmed hearing loss in our population are positive for cCMV
Tips

• Insure you have strong provider support
• Insure you have a written protocol in place
• Specified individuals
  – Responsible for monitoring test results and notifying providers of positive outcomes
  – Responsible for following cCMV infants/families
• Educational materials available (written information) to provide the families
• Established protocol for follow-up
• Contingency plan for obtaining an additional sample if inpatient is not viable
Representatives of Maddie's Mission visited local state legislators to promote public education about cytomegalovirus. From left are: Farah Armstrong, Jenny Bailey, Sandra Salerno, Lillian Salerno, state Rep. Dr. John Zerwas, Becky Ghazi and Ann Blalock. Not pictured is Dr. Gail Demmler Harrison, CMV Expert at Baylor College of Medicine and Texas Children's Hospital.
Madeline Leigh Armstrong Act

A good plan violently executed now is better than a perfect plan next week.
– General George S. Patton
Only 9% of women know about CMV

Inform, Engage, & Advocate

16th Annual Early Hearing Detection & Intervention (EHDI) Meeting - February 26-28, 2017

In its 16th year, the EHDI Meeting has built a strong reputation for bringing together a wide variety of attendees including those who work in state Early Hearing Detection and Intervention programs; assist in EHDI efforts on the federal level; provide screening, diagnostic and early intervention support at the state/local level to young children with hearing loss and their families; champion Medical Home activities within each state; are parents of children with hearing loss; or are deaf or hard-of-hearing adults who are helping to expand opportunities for young children with hearing loss. EHDI Meeting participants will range from state and local programs to the federal level and from academics to families. Register today at ehdimeeting.org
Thank you for your attention!

The journey of a thousand miles begins with one step —- Lao Tzu