Congenital Cytomegalovirus Infection: Hearing Loss Characteristics, Audiological Management, and Fostering Parent Partnerships

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Studies of etiology of HL seldom include routine screening for CMV

Routine screening for CMV not conducted for newborns, except when babies are enrolled in research projects

Most congenital CMV is asymptomatic (90%)

No representative audiometric pattern
  - Hearing loss can be unilateral or bilateral, stable, progressive, delayed in onset, or fluctuating
CONGENITAL CYTOMEGALOVIRUS INFECTION

- Most common congenital infection in humans although not easily spread
- Clinical observation of infection in the newborn period identifies <5% of all infants with congenital CMV infection
- Newborn morbidity/mortality + late sequelae – hearing loss, mental retardation, cerebral palsy, impaired vision
- Leading cause of non-hereditary sensorineural hearing loss in children
- Leading infectious cause of brain damage in US children
WHAT WE KNOW

- Accounting for approximately 1/3 of sensorineural hearing loss in young children
- Frequent late onset hearing loss
- Frequent progression of hearing loss
- Frequent fluctuating hearing loss
- Majority of children with congenital cmv infection never identified
CMV is a Leading Cause of Childhood Hearing Loss

- 21 – 25% of all pediatric hearing loss (Morton, 2006)
- 35% of all pediatric hearing loss (Dahle, 2000, UAB data)
- Leading cause of unilateral hearing loss (Nance)
- Major cause of pediatric hearing loss including unilateral hearing loss (Ross, 2008)
- 11.3% of children with Asymptomatic CMV have hearing loss (Fowler, 1999)
- 36.4% of children with Symptomatic CMV have hearing loss (Fowler, 1999)
What Is the Public Health Impact of Congenital CMV Infection?

**Incidence at Birth**
(186 per 100,000)

- Clinically apparent infection, 10%
- Other environmental causes, 14%
- Other genetic causes, 44%
- Nonsyndromic, 30%
- GjB2 mutation, 21%
- Pendred’s syndrome, 3%
- Clinically inapparent infection, 11%

**Prevalence at 4 Years**
(270 per 100,000)

- Clinically apparent infection, 7%
- Late-onset, 10%
- Clinically inapparent infection, 8%
- Other environmental causes, 14%
- Other genetic causes, 33%
- Nonsyndromic, 22%
- Syndromic, 11%
- EVA SLC26A4+, 5%
- EVA SLC26A4-, 7%
- GjB2 mutation, 21%
- mtA1555G, 1%
- Total genetic contribution 68%
- Other genetic causes, 33%
- Nonsyndromic, 22%
- Syndromic, 11%
- GjB2 mutation, 21%
- CMV, 25%

**Total genetic contribution** 54%

*Morton and Nance NEJM 2006*
ISSUES BEING ADDRESSED

- Newborn diagnosis and screening
- Antiviral treatment of the newborn
- Prevention of maternal and congenital CMV infection
- Management of sequelae
ANNUAL CONGENITAL CMV INFECTION

- Range – .5 % to 1.5 %
- Average – 1 %
- With annual birthrate of 4 million
- 40,000 US children born with infection annually
SOURCES OF INFECTION

- Transplacental
- Intrapartum
- Breast milk
- Nosocomial/transfusion
DIAGNOSIS

- Isolation of CMV from the urine or saliva of the neonate within first two weeks of life
- Presence of CMV IgM from the blood of the neonate
- Use of Blood Spot
- Detection of Cytomegalic Inclusion Bodies from affected tissue (rarely used)
TYPES OF CONGENITAL CMV INFECTION

- Symptomatic 5-10 %
- Asymptomatic – 90-95 %
  - Primary – First time infection
  - Recurrent – Reactivation of infection, seropositive before pregnancy
PRIMARY MATERNAL CMV INFECTION DURING PREGNANCY

• 95% clinically inapparent

• 35% transmitted to fetus

• No clear relationship between gestational age and transmission

• Fetal damage more likely in first 26 weeks, (32%) than later (15%)
HIGH RISK FOR PRIMARY MATERNAL AND CONGENITAL CMV INFECTION

- Teen mothers
- Exposure to young children:
  - Day care workers
  - mothers
- Sexual activity
RECURRENT CMV INFECTION

- Can cause symptomatic infection in infants
- Can cause similar sequelae to primary infection
CHARACTERISTICS OF CONGENITAL SYMPTOMATIC CMV INFECTION

- Hepatosplenomegaly
- Microcephaly
- Thrombocytopenia
- Petechiae
- Jaundice with conjugated hyperbilirubinemia
SEQUELAE OF SYMPTOMATIC CONGENITAL CMV INFECTION

- Seizures
- Chorioretinitis
- Periventricular calcifications
- Sensorineural hearing loss
- Motor deficits
SEQUELAE OF ASYMPTOMATIC CONGENITAL CMV INFECTION

- Hearing loss
- Chorioretinitis
- Seizures
CHARACTERISTICS ASSOCIATED WITH INCREASED RISK OF SEQUELAE

- Primary maternal infection
- Symptomatic congenital CMV infection
- Presence of neonatal neurological abnormalities
- Abnormal head CT scan
- Chorioretinitis in the newborn
Review of Congenital CMV and Hearing Loss Research

- 1960s - CID/symptomatic CMV infection and hearing loss first reported. Medearis, 1964; McCracken, et al. 1969
- 3.9% at birth will have hearing loss; 8.3% at 6 yrs
  - Symptomatic infection – 16.5% HL at birth; 36.4% at 6 yrs
  - Asymptomatic infection – 2.9% HL at birth; 11.3% at 6 yrs
UAB Investigation of Congenital CMV Infection and Hearing Loss

- NICHD Program Project Grant – 24 years
- NIDCD CMV and Hearing Loss Grant – 7 years
- NIDCD Multi Site Study – 7 years, current
- Multiple publications, different cohorts of subject study group, various authors over a long time span
- Audiological protocol changes with new technology
NIDCD CMV Grant, UAB

- Multi-site investigation, 7 sites
- 100,000 newborns to be screened for congenital CMV infection
- Link newborn hearing results
- Evaluate methods for CMV screening
  - Saliva vs. dried blood spots (DBS)
- Audiological follow up of CMV positive infants for 4 years
A Sound Tomorrow Starts Today

The CHIMES Study
Karen B. Fowler
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Diane Sabo

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Components of Audiological Assessment

- Auditory Brainstem Response (ABR) tone bursts, bone conduction
- Otoacoustic emissions (OAE)
- Immittance with high frequency probe for subjects less than 7 months of age, only when conductive involvement needs greater definition
- Behavioral assessment
  - Visual Reinforcement Audiometry (VRA)
  - Play Audiometry
ABR Assessment at First Visit

- Early assessment at 3-6 weeks of age
  - Objective
    - Obtain valid/accurate estimates of ear specific, frequency-specific hearing thresholds for each ear
    - Characterize type of permanent loss as baseline

- Case history/parent observation report

- Otoscopic inspection

- OAE
  - Medical referral if testing deferred because of otologic problems
Schedule for Behavioral Audiological Assessment

- Visual Reinforcement Audiometry scheduled at 7, 12, 18, and 24 month follow-up visits
- Play Audiometry scheduled at 24, 30, 36, and 42 month follow-up visit
Monitoring for Hearing Loss

- Behavioral tests can be difficult with the very young
- Masking may be a problem
- Monitoring with Electrophysiological tests becomes expensive
- Counseling for parent and child necessary
Intervention Counseling

- Need for parent centered communication options
- Need for professional counseling referral if need arises, know limitations.
HEARING LOSS RESULTING FROM CONGENITAL CMV INFECTION

- 4 Million - Annual Birth Rate
- 1 Percent - Average CMV Infection Rate
- 40,000 - Children Infected
- 4,000 - Symptomatic CMV (40.7% with HI)
- 36,000 - Asymptomatic CMV (7.4% with HI)
- 4,292 - Children born annually with/develop HI from CMV
- 3/1,000 - Hearing loss in newborn population
- 35.76 - % of hearing loss due to CMV

Adapted from Dahle et al, 2000
# Hearing Loss and CMV

<table>
<thead>
<tr>
<th>SUBJECTS</th>
<th>ASYMPTOMATIC</th>
<th>SYMPTOMATIC</th>
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<tbody>
<tr>
<td>SUBJECTS</td>
<td>651</td>
<td>209</td>
</tr>
<tr>
<td>Subjects with HL</td>
<td>48(7.4%)</td>
<td>85(40.7%)</td>
</tr>
<tr>
<td>Unilateral HL</td>
<td>25(52.1%)</td>
<td>28(32.9%)</td>
</tr>
<tr>
<td>Bilateral HL</td>
<td>23(47.9%)</td>
<td>57(67.1%)</td>
</tr>
<tr>
<td>High Frequency</td>
<td>18(37.5%)</td>
<td>11(12.9%)</td>
</tr>
<tr>
<td>Delayed Onset</td>
<td>18(37.5%)</td>
<td>23(27.1%)</td>
</tr>
<tr>
<td>Age Range</td>
<td>24-182 Months</td>
<td>6-197 Months</td>
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<tr>
<td>Progression</td>
<td>26(54.2%)</td>
<td>46(54.1%)</td>
</tr>
<tr>
<td>Age Range</td>
<td>3-186 Months</td>
<td>2-209 Months</td>
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CMV Case Study (1)
CMV Case Study (2)
CMV Case Study (3)
Sudden Delayed Onset Hearing Loss at Six Years Secondary to SX CMV (4)
Progression of Unilateral HL in 10 Children: ASX CMV (5)
Unilateral Hearing Loss and Congenital CMV Infection

- Approximately 40% of CMV related hearing loss is unilateral.
- Since CMV related HL is often progressive and/or delayed in onset, it is not uncommon for HL resulting from CMV to be identified after the newborn period.
- With universal newborn hearing screening, when HL is detected early, CMV cultures taken within the first 2 weeks of life can assist with detection of CMV infection.
Demographics for Children with Congenital CMV and Unilateral HL

- 45% female
- 69% black
- 74% public or no insurance for hospital care
  - Demographic characteristics for children with unilateral hearing loss did not differ overall from the total group of 934 children with congenital CMV infection
Unilateral Hearing Loss and CMV

• Asymptomatic CMV – 53% unilateral
  ◦ 40% with progression of hearing loss
  ◦ 63% of loss in the Right ear

• Symptomatic CMV - 35% unilateral
  ◦ 52% with progression of hearing loss
  ◦ 55% of loss in the Right ear
Progression of Unilateral to Bilateral Loss in Children with Congenital CMV

- 11% developed some degree of HL in their good ear
<table>
<thead>
<tr>
<th>Condition</th>
<th>SX (93%)</th>
<th>ASX (7%)</th>
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<tbody>
<tr>
<td>Infant death</td>
<td>10%</td>
<td>0</td>
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<tr>
<td>Hearing loss</td>
<td>60%</td>
<td>7–15%</td>
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<tr>
<td>Mental retardation</td>
<td>45%</td>
<td>2–10%</td>
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<tr>
<td>Cerebral palsy</td>
<td>35%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Chorioretinitis</td>
<td>15%</td>
<td>1–2%</td>
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</table>
CMV MANAGEMENT CONCERNS

- Frequency of viral reactivation
- Frequency of monitoring
- Protocol for medical treatment
- Side effects of drugs
- Need for long term treatment
- Long term subject compliance
- Emotional needs of parent and child
Management of Children with Congenital CMV HL

- Maintain long term subject compliance with a defined monitoring protocol
- Use carefully defined audiological protocols in order to avoid variations in HL results because of examiner variability in test procedures used
- Provide information to all caregivers regarding the characteristics of CMV related HL and the importance of their role in monitoring hearing
Addressing Challenges to Monitoring and Defining Progressive and Delayed Onset HL

- Develop standardized procedures for collection and recording of audiological assessment data
- Develop detailed Manual of Procedures (MOP) for audiology clinic policies and procedures
- Develop audiology protocols establishing optimal and minimal goals for audiology assessment results at visits
- Review and observation of audiologists in a practice by experienced pediatric audiologist/supervisor
- Detailed patient retention plan with patient database and data forms (Appointment history & missed appointment forms/action)
Challenges to Monitoring and Defining Progressive and Delayed Onset HL(2)

- Variability of hearing loss: progression, delay in onset, and fluctuation requires frequent assessment
- Otitis media resulting in conductive overlay for sensorineural hearing loss, delay in getting baseline assessment data
- Parental compliance with repeat assessments
Identification and Management of Progressive and Delayed Onset Hearing Loss

- Other Potential Factors Contributing to Changes in Hearing Results
  - Middle ear disease
  - Other disease factors
  - Anatomical factors
  - Hereditary factors
  - Treatment factors
  - Trauma
Newborn Hearing Screening/Follow-up “MISSES” May Lead to Invalid Assumptions re HL Stability

- Mild HL < 30-40 dB HL
- Some unusual configurations of HL
  - Low-frequency hearing loss (OAE and ABR)
  - Steeply sloping high frequency HL
  - Mid-frequency HL
- Profound HL when early follow-up results (OAE) confirm presence of middle ear dysfunction and cloud presence of sensory neural HL
- AN if use only OAE technology
Additional Factors Leading to Invalid Assumptions about Stability of HL

- Inappropriate audiological technique related to chronological age vs. mental age (8 months ca vs. 4 months ma)
- Inconsistent audiological technique by multiple examiners
- Other developmental problems – motor, vision, etc
- Equipment calibration problems
MANAGEMENT OF INTERVENTION FOR HEARING LOSS

- Interdisciplinary assessment to identify any additional conditions
- Early intervention program referral
- Training to empower child/parent to optimize learning opportunities
- Parent training about federal legislation/state/local regulations developed to address needs of children with disabilities
Helping Parents Understand

- The importance of Audiological Monitoring
- The probability of progressive and delayed onset hearing loss
- The importance of their role in monitoring for changes in their child’s hearing and speech and language
  - Setting up routine “tests” of hearing
  - Observing their child’s attention to auditory detail
  - Listening for changes in their child’s speech and language
Conveying Information to Parents about CMV and Hearing Loss

- Considerations for practitioners
  - presentation method
    - Most parents have never heard about CMV, use basic information
    - Guilt is common, convey information that this is the most common congenital infection in humans and about 60-80% of adults have this virus
    - Be straight forward/honest about probability for progression/delayed onset loss
    - Use latest research information
    - Listen to parents and allow ample time for questions
Parent’s Ability to Synthesize Information

- Determines how the information will be accepted
- Determines how recommendations and monitoring will be carried out
Challenges and Observations (1)

- Too much information to convey in one session
- Double whammy - disease and HL
- Emotional Component - Did I do this, Is my child infectious?
- Knowledge base of examiner and parent often incomplete
- Resources for information are available, over 40 years of research findings
- Observing parents for indicators for guidance in counseling
  - Too much, stop
  - I want more
  - I don’t understand
  - I don’t believe you
  - I need to ask questions, I want to participate
Challenges and Observations (2)

- Observations of Parents for Indicators and Guidance in Counseling
- Up Front, This is Your Time and an Opportunity for Us to Learn. We can Proceed as you Wish
  - Too much, stop
  - I want more
  - I don’t understand
  - I don’t believe you
  - I want to ask questions, I want to participate
Guidance Is General, Sessions Require Individualized Adaptations Suited to Family Needs

- Every Session is Different
- Every Audiologist is Different
- Every Family is Different
- Every Child is Different
- Every Hearing Loss is Different
General Considerations

- Be prepared
- Be honest
- Be respectful
- Be committed
- Be responsible
- Provide documentation
Objectives for Counseling Parents About Hearing Status for Children With Congenital CMV Infection (I)

- Understand Auditory Function
- Understand Importance Of Audition on Development
- Understand Measurement of Hearing
- Understand Basics of Hearing Loss
- Understand Current Status of Hearing
- Understand Impact on Learning
- Understand Intervention Choices, Multiple, Not Exclusionary
Objectives For Counseling Parents about Hearing Status for Children With Congenital CMV Infection (2)

- Understand Resources
- Understand CMV Infection and Potential Impact On Hearing: Normal, Progression, Delay in Onset, and/or Fluctuations
- No known Predictors Except for Type of Infection (ASX or SX) and Gestational Timing of Infection
- Understand Need for Long Term Monitoring
- Understand Parental Role/Responsibility
- Understand CMV is Common Infection with 60-80 % of Adults Positive
Goals for Audiological Counseling

- Knowledge about audiogram
- Knowledge about hearing loss
- Impact on speech development, social development, cognitive development
  - Frequency - Speech banana, words/sound examples
  - Intensity – audio recording
  - Configuration – impact on speech perception
  - Speech awareness, threshold, discrimination
Getting Prepared: Audiologist

- Know types of CMV infection and impact on hearing
  - **Symptomatic CMV Infection**, born with microcephaly, enlarged liver and spleen, jaundice, petechiae, more likely to have hearing loss as well as problems with cognitive, motor, and vision function. Only 5-10% of children born with CMV are symptomatic and about 50-60% have hearing loss.
  - **Asymptomatic CMV Infection** – About 95% of children born with CMV are ASX. Hearing loss is most frequently occurring problem. About 7% have hearing loss. May have vision problems also.
Getting Prepared: Audiologist

- Review all prior reports available: medical, developmental, vision function, genetics, social service
- Collect resources for potential distribution: printed, electronic, and video on CMV and hearing
- Format contract to review with parent for continued audiological service provision over an extended period of time
- Locate intervention service centers in close proximity to family home for possible site visits
- Locate parent support group with other parents of children with hearing loss from CMV
- Schedule social service initial contact for review of family needs
Getting Prepared: Initial Session

- Assess parents preferred mode of Communication, have resources available
- Comprehensive audiological history
- Assess parent perceptions about their child’s hearing, knowledge about CMV
- Assess parents learning style
- Determine parent objectives for session
- Involve parents in assessment
Environment for Sharing Information

- Typical office/desk not conducive to free flowing conversation
- Arrange for close proximity face to face contact without barrier of desk
- Arrange for age appropriate play engagement of child with high chair, table chair, or activity center with appropriate toys (zip locked/disinfected for each individual client)
Environment for Sharing Information

- Avoid distractions, have sign on door
- Provide reasonable accommodations, hand sanitizer, tissue, water, magazines, directions to bathroom/with changing table.
- Be aware of body language and make sincere efforts to establish rapport
- Ask for parental input up front regarding their impressions about hearing. Place emphasis on parent centered services.
Frequently Asked Questions

- Where did this infection come from?
- Did I give this infection to my child?
- Is my child infectious to other children, to pregnant women? How long will my child shed this virus?
- Why do some children with congenital CMV infection get by with no problems?
- What makes the hearing loss get worse?
- How long do we have to worry about delayed onset?
- Will my child be allowed to go to a regular school program? Will my child have to be isolated?
- Will my child be able to talk?
- Will my child be normal?
Helping Parents Become Partners in the Monitoring/Intervention Process

- Be straightforward
- Let parents know you are available to help
- Help parents understand how important their role is in obtaining the best services for their child
- Listen to concerns
- Provide the best information research has to offer to answer questions
Helping Parents Detect Changes in Hearing

- Learn to differentiate auditory responsiveness vs. visual responsiveness
- Learn to hear speech sounds produced by child/observe child’s responses to speech
- Set up ”standard” hearing observation sites within the home
- Develop and use observation/documentation reports
- Document any changes in auditory responsiveness or speech behavior
- Provide number of person to call to schedule an appointment for prompt reassessment
MONITORING FOR BEHAVIORAL CHANGES SUGGESTING PROGRESSIVE HEARING LOSS

- Withdrawal
- Acting out behaviors
- Uncharacteristic irritability
- Inability to understand speech in noise
- Difficulty localizing sound
- Preference for increased volume setting
- Changes in acoustic characteristics of speech
- Complaints of broken amplification
Resources on CMV & Preventing Infections During Pregnancy

Centers for Disease Control and Prevention (CDC) CMV Homepage
http://www.cdc.gov/cmv/

CDC Podcast on Congenital CMV
http://www2.cdc.gov/podcasts/player.asp?f=7925

CDC 10 Tips for Preventing Infections During Pregnancy
http://www.cdc.gov/ncbddd/pregnancy_gateway/infection.htm

Ross, 2008
Selected Resources For Additional Information

- Infanthearing.org (NCHAM)
- Babyhearing.org (Boy’s Town Hearing Research)
- National Institute on Deafness and Communication Disorders (NIDCD)
- CDC Infant hearing web site, CMV home page
- ASHA web site
- Listen-up.org
- Agbell.org
- Handsandvoices.org
- Translation into many languages: worldlingo.com
Resources for Parents on Congenital CMV

National Congenital CMV Disease Registry
http://www.bcm.edu/pedi/infect/cmv

Stop CMV
http://www.stopcmv.com/

Lisa Saunders: What you need to know about CMV
http://www.authorlisasaunders.com/mycustompage0042.htm

CMVKids
http://cmvkids.com/

CMVSupport (United Kingdom)
http://www.cmvsupport.org/modules/news/
What We Want to Know

- What causes progressive’ fluctuating, and delayed onset hearing loss
- What is the role of newborn hearing screening in relation to detection of CMV infection
- What causes the hearing loss and what factors predispose some infants to hearing loss
Thanks for all each of you do for children with hearing loss and their families. We make a difference.