

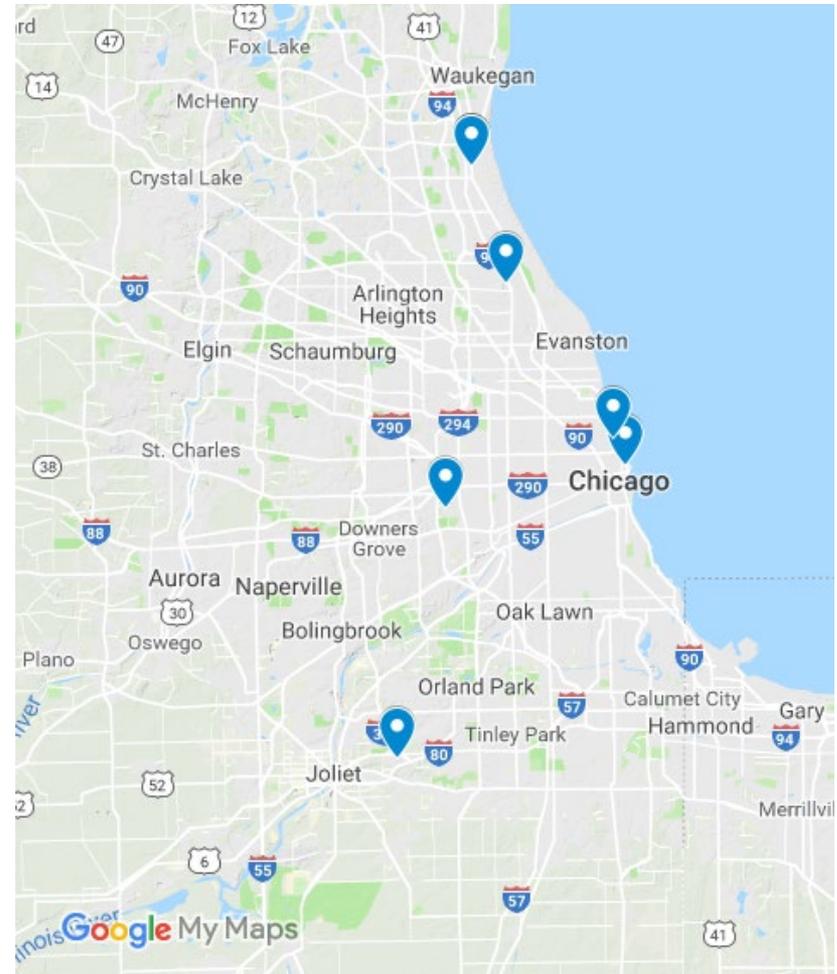
Development of an Audiological Testing and Monitoring Protocol for Patients with Congenital CMV

Ann & Robert H. Lurie
Children's Hospital of Chicago
Audiology Department
Kristen Cortese, Au.D., CCC-A &
Lisa Weber, Au.D., CCC-A
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Lurie Children's Department of Audiology

- 6 locations
 - Chicago (2 locations), Lake Forest, Northbrook, Westchester and New Lenox
 - Main Hospital in downtown Chicago
 - Specialty Care Center
 - Level III NICU
 - Not a birthing facility



Lurie Children's



Lurie Children's Audiology Team



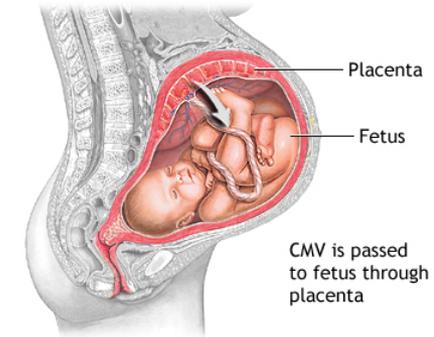
Presentation Objectives

- Review congenital cytomegalovirus (cCMV) infection including:
 - How it is diagnosed
 - Possible symptoms
 - Specialties involved in treatment & management
- Describe the difference between symptomatic and asymptomatic cCMV infection
- Explain the process of developing an evidence based protocol for audiological monitoring of patients with cCMV
- Present case studies



Congenital Cytomegalovirus (cCMV)

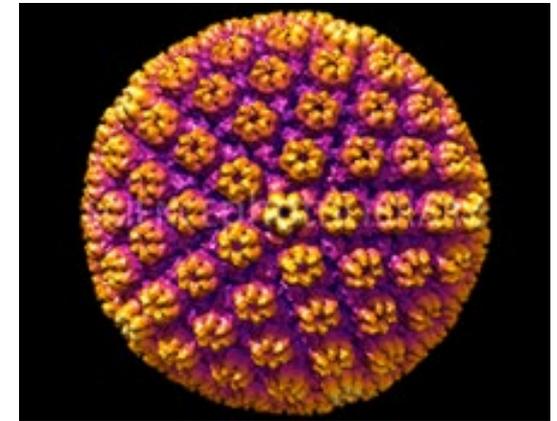
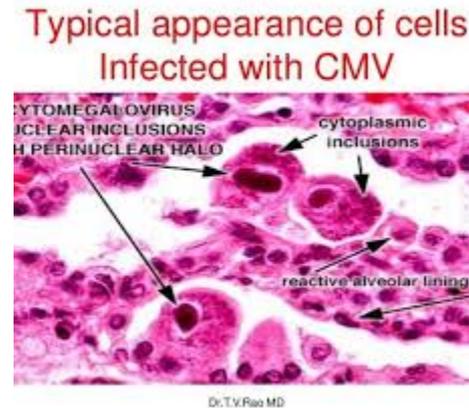
- CMV is a common virus of the herpes family. Once infected the body retains the virus for life.
- Congenital CMV or (cCMV) occurs when the CMV virus is transmitted to fetus in utero
 - Primary infection
 - Reactivation/reinfection



- Affects approximately 20,000 (up to 40,000) infants born each year in the US and over 1 million newborns globally
- Major contributor to permanent neurologic and cognitive deficits in childhood

Congenital Cytomegalovirus (cCMV)

- The only way to differentiate a congenital infection from a postnatal infection is to complete testing prenatally, or within the first 3 weeks or 21 days of life
- Amniocentesis
 - Higher sensitivity after 21 weeks gestation
- Urine
 - High sensitivity
- Saliva
 - High sensitivity
- Dried Blood Spots
 - Lower sensitivity
 - Some states not allowing



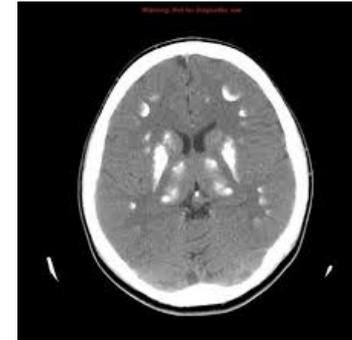
Specialties Involved in Treatment & Management

- Neonatal Intensive Care Unit (NICU) Physicians
- Primary Care Physicians (PCP)
- Infectious Disease (ID)
- Ophthalmology
- Radiology
- Neurology
- Audiology
- Otolaryngology
- Early Intervention Providers



Symptomatic cCMV

- Approximately 10% of infants
- Present clinical abnormalities at birth
 - 40-60% of these infants will experience long term issues from these symptoms
 - These mainly include:
 - Motor & cognitive deficits
 - Vision loss
 - Hearing loss
 - Patients have one or more of the following symptoms



Baby with Typical Head Size

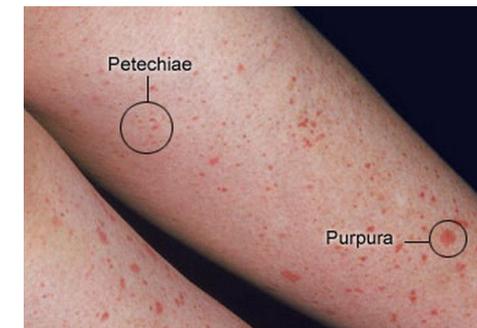
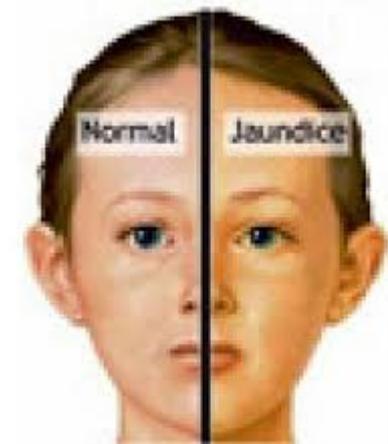
Baby with Microcephaly

Baby with Severe Microcephaly



Symptomatic cCMV: Possible Symptoms

- Central Nervous System Involvement
- Cerebral palsy
- Microcephaly
- Seizures
- Intracranial calcifications
- Hydrocephaly
- Cognitive impairment
- Hypotonia
- Poor feeding
- Poor temperature control
- Chorioretinitis
- Optic atrophy
- Pale optic nerves
- Petechiae
- Jaundice
- Hepatosplenomegaly
- Hepatitis (hepatomegaly)
- Thrombocytopenia
- Intrauterine growth restriction (IUGR)
- Sensorineural (SNHL) Hearing loss



Asymptomatic cCMV

- Approximately 90% of infants
- No clinical abnormalities at birth
 - Can have some cCMV related symptoms, but even less infants have permanent symptoms
 - Cognitive impairment
 - Retinitis
 - Children who are asymptomatic may go undetected and unidentified

Asymptomatic cCMV with Isolated SNHL

- Hearing loss can be the ONLY SYMPTOM of cCMV
 - An infant with SNHL and no additional symptoms is still considered asymptomatic



cCMV and Hearing Loss

- cCMV is second only to genetic causes as the leading cause of permanent hearing loss in children



Illinois cCMV Legislation



- Public Act 099-0424 in Illinois
 - Effective Date January 1, 2016
- If a newborn infant fails the 2 initial hearing screenings in the hospital, then the hospital performing that screening shall provide to the parents of the newborn infant information regarding (i) birth defects caused by cCMV (ii) testing opportunities and options for cCMV, including the opportunity to test for CMV before leaving the hospital; and (iii) early intervention services
- No current state or universal guidelines for medical or audiological management of this patient population

Our Audiology Team Needed to Determine

- 1) What should be our protocol for audiological testing and monitoring of patients diagnosed with cCMV?
- 2) Should the follow-up be different or the same for patients with symptomatic vs. asymptomatic infections?



Protocol Development

- Steps Completed:

- Review of current literature
- Discussion with the Audiology Clinical Quality Team (CQT)
- Meeting with the Infectious Disease (ID) Department
- Insight from Lurie Children's otolaryngologist, Dr. Nancy Young, Audiology Department medical director



Literature Review: Symptomatic vs. Asymptomatic Hearing Losses

Symptomatic cCMV (10% of Infants)	Asymptomatic cCMV (90% of Infants)
Occurs at a higher rate (1/3)	Occurs at a lower rate (1/10)
Generally earlier onset	Generally later onset
Generally greater degree of severity	Generally lesser degree of severity
More bilateral hearing losses	More unilateral losses

Literature Review: cCMV Hearing Loss Characteristics

- **Asymmetric, progressive, fluctuating and late onset**
 - Approximately 50% is **progressive**
 - Rate of progression appears similar regardless of symptomatic vs. asymptomatic status
 - Later progression in symptomatic group
 - Approximately 33-50% is **late onset**
 - Median age occurs later in asymptomatic children
 - Usually occurs before 6 years of age, mainly within the first year of life, but hearing loss at an older age has been reported

(Fowler, 2013 & Goderis et al, 2014)

Current Protocol and Procedures

- For infants & children with a diagnosis of cCMV
 - Initial evaluation natural sleep diagnostic ABR
 - Follow-up every 3 months during the first year of life, every 6 months until age 3, and yearly until age 5
 - Same follow-up symptomatic and asymptomatic infants/children
- For infants who fail newborn hearing screening and have not had testing for cCMV
 - Inpatient – refer to medical team
 - Outpatient – refer back to PCP

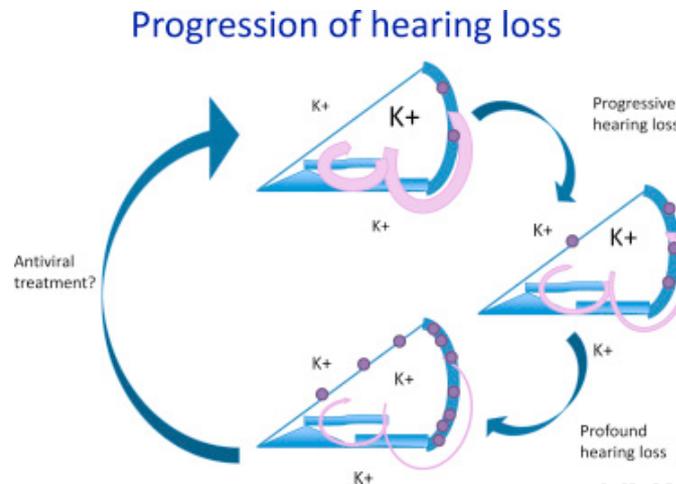


An Interdisciplinary Approach

- Lurie Children's Infectious Disease has a multi-institutional referral model for prompt specialty care of neonates with cCMV
- Referred infants are scheduled within 24-48 hours
- Evaluations Completed:
 - Infectious Disease: Physical evaluation and lab work
 - Ophthalmology: Eye exam
 - Radiology: Neuroimaging of the head
 - Neurology: Neurological evaluation if warranted
 - Audiology: Natural sleep diagnostic ABR
 - Coordinated with Otolaryngology if patient has already been diagnosed with a hearing loss

Treatment and Management

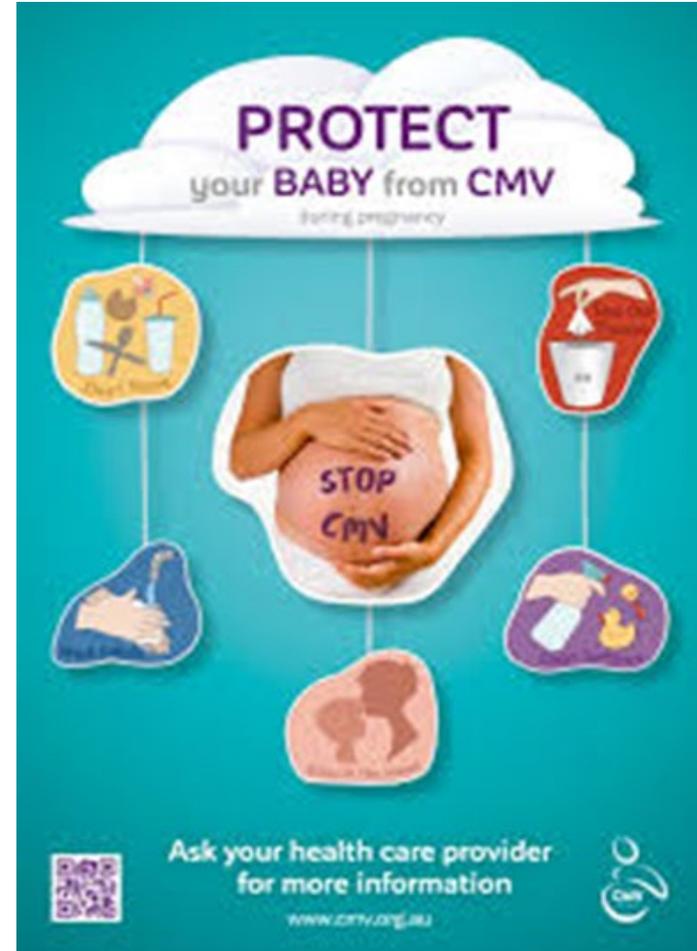
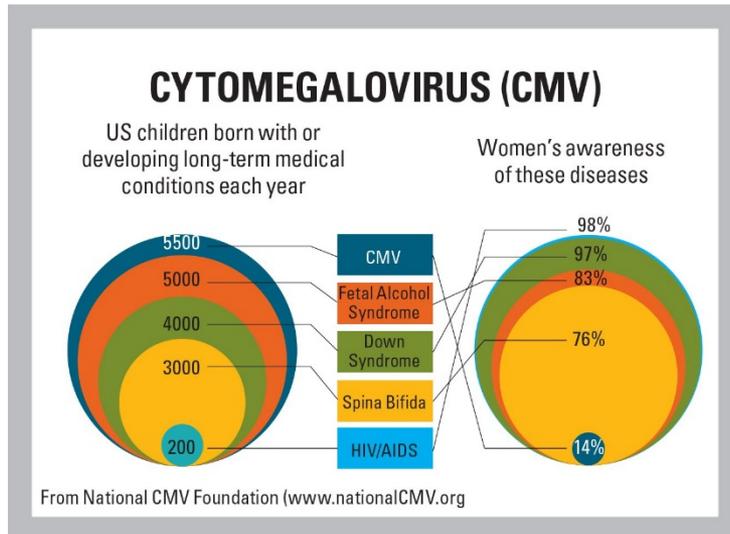
- If the infant is symptomatic OR asymptomatic with isolated hearing loss, antiviral therapy with oral valganciclovir is discussed
 - Studies have shown that among infants with symptomatic cCMV disease, 6 months of oral valganciclovir therapy had a moderately favorable effect on long-term audiological and neurodevelopmental outcomes and was not associated with an excess risk for adverse side effects



(Kunberlin et al, 2015)

How to Prevent cCMV

Can reduce the risk of by educating pregnant mothers
Women of childbearing age often have little information about CMV, let alone accurate information about CMV





Case Studies

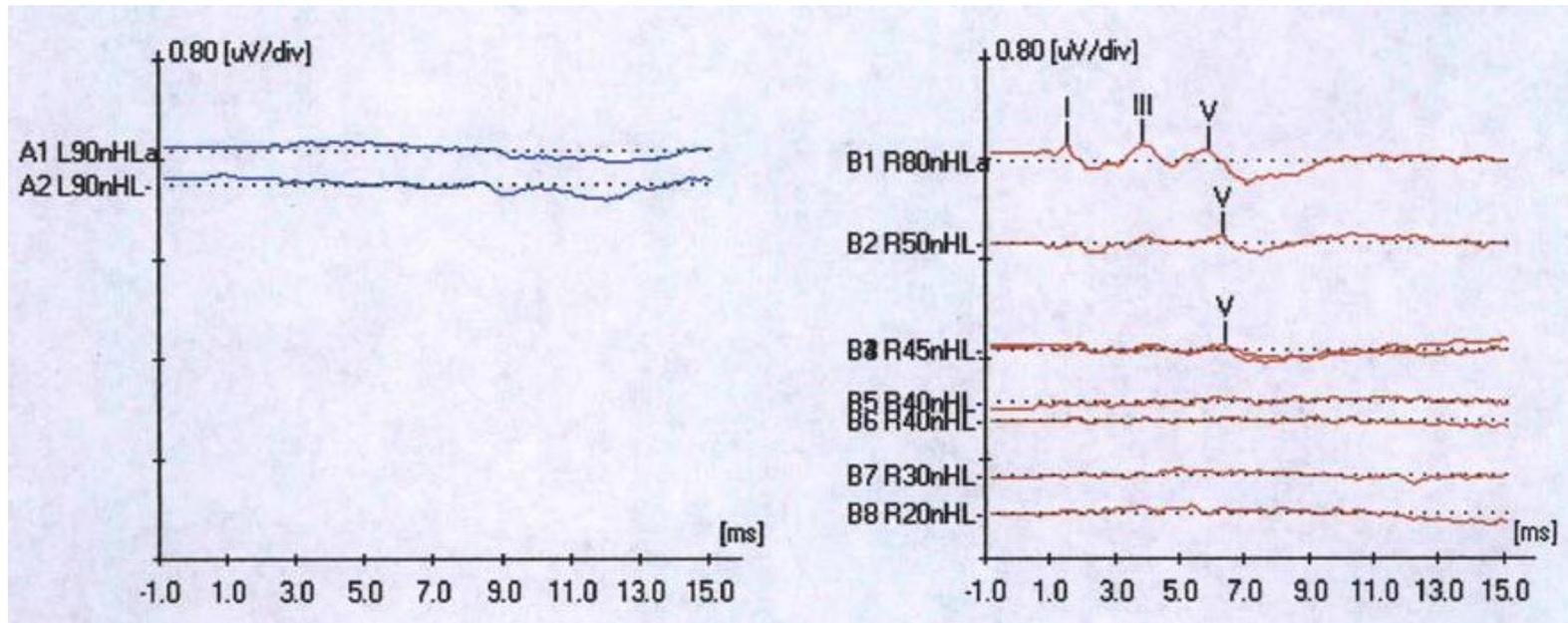


Case Study #1

- Birth: PASSED the NBHS in both ears
- By 3 months of age: Head ultrasound revealed cerebral calcifications and cysts, positive urine cCMV test
 - Patient is **symptomatic**
- 3 months of age: Natural sleep ABR
 - RE: Normal hearing
 - LE: Borderline normal to possible mild hearing loss
 - Both Ears: Distortion product otoacoustic emissions (DPOAEs) present in both ears
- 18 months of age: Behavioral testing attempted
 - RE: DPOAEs essentially present
 - LE: DPOAEs essentially absent
 - Audiological testing unsuccessful and sedated ABR recommended

Case Study #1:

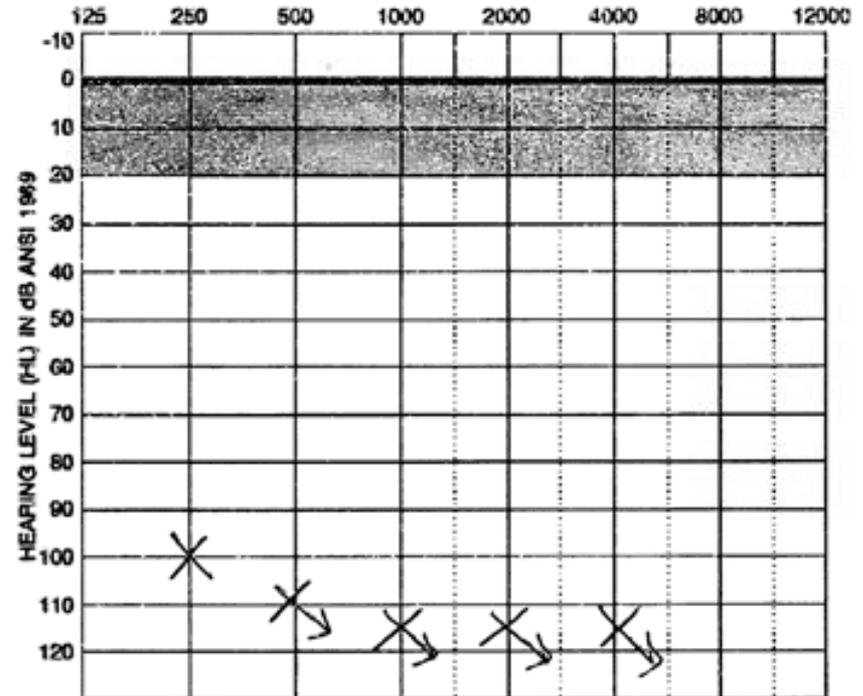
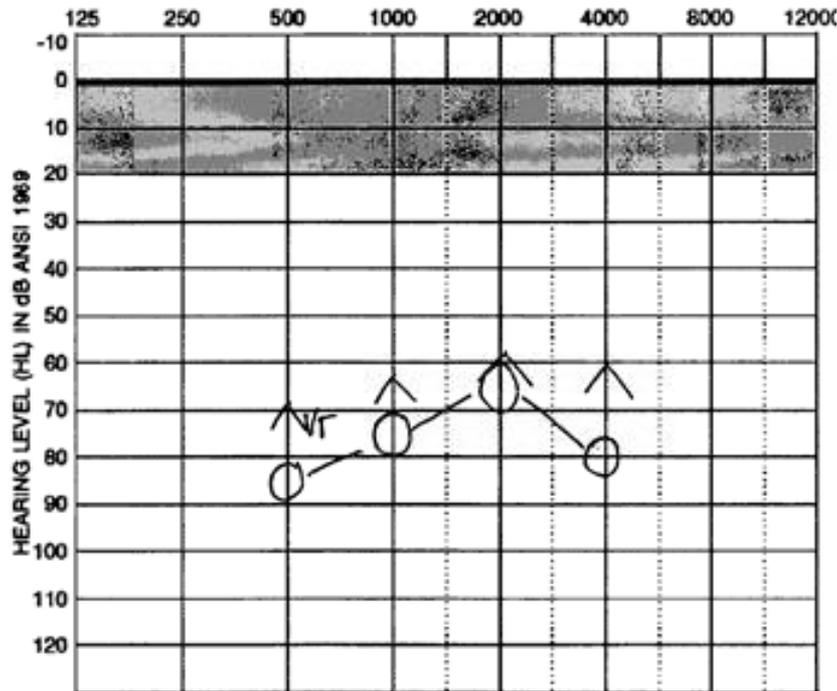
- From 3 months of age to 2 years of age:
 - RE: Normal hearing > mild SNHL
 - LE: Borderline normal to possible mild > moderate to profound SNHL



- 2 years of age: Hearing aids dispensed

Case Study #1

- From 3 years of age to 4 years of age:
 - RE: Mild to moderate SNHL > moderately-severe to severe SNHL
 - LE: Severe to profound SNHL > profound SNHL



- Cochlear implant evaluation begins

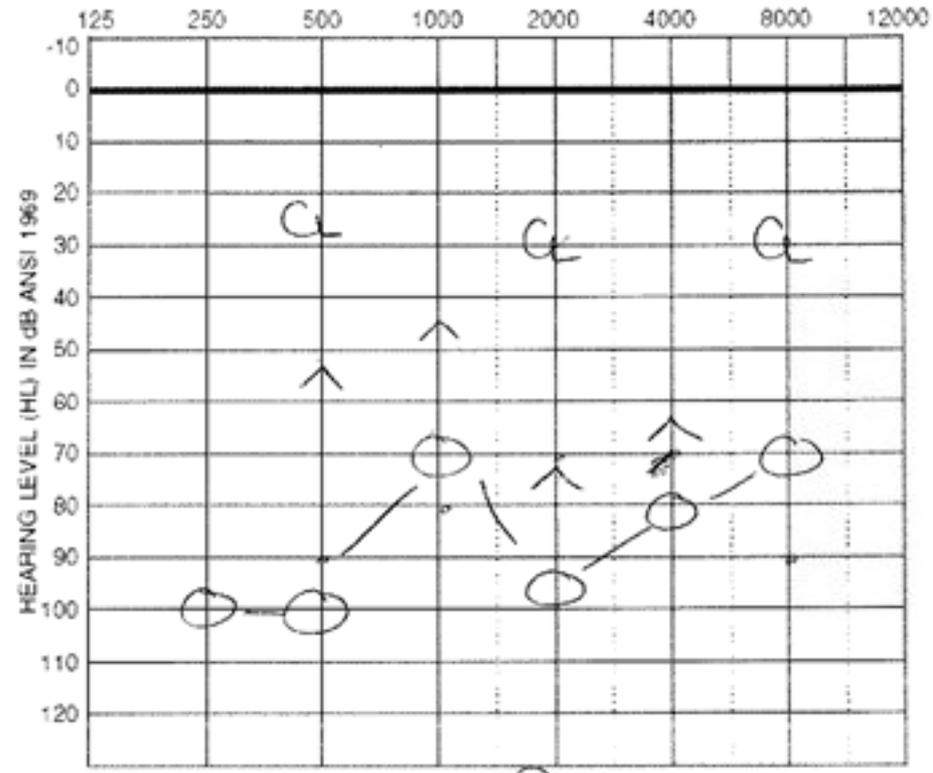
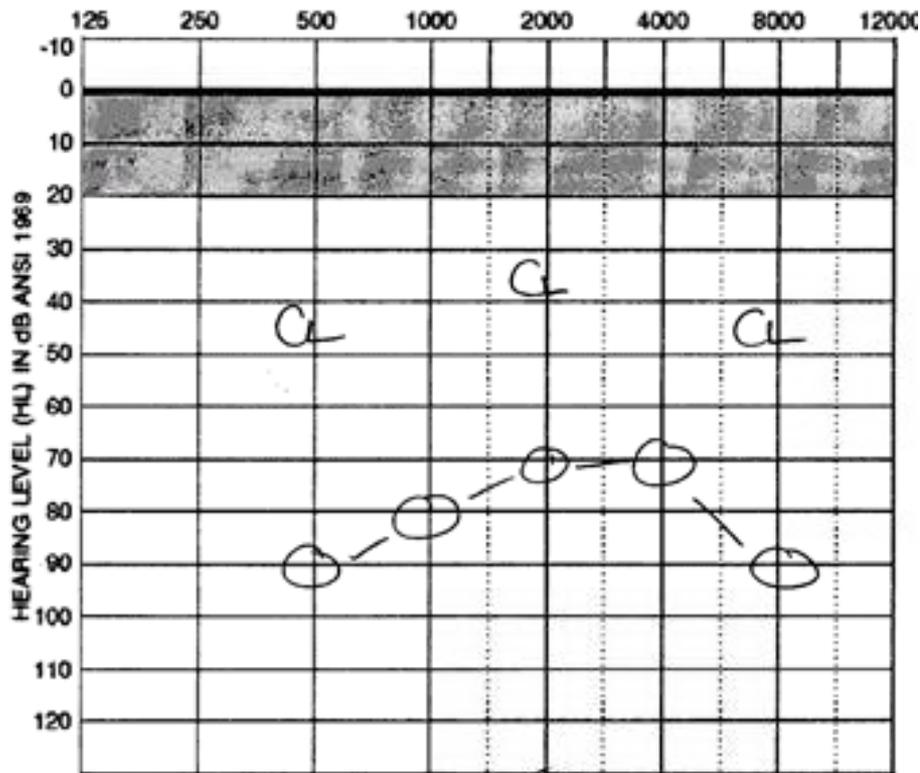
Case Study #1

- 5 years of age:
 - Left cochlear implant surgery and initial stimulation
- 7 years of age:
 - Right cochlear implant surgery and initial stimulation



Case Study #1

- From 5 years of age to 7 years of age:
 - Fluctuation and progression in unaided hearing



Case Study #2

- Birth: Failed NBHS and tested positive for cCMV at birth
- 9 days of age: Evaluated by Infectious Disease (ID), Ophthalmology and received an ultrasound of the head (same day).
 - Patient found to be **asymptomatic with isolated SNHL**
- 3 weeks of age: Diagnosed with a profound SNHL in both ears

Right Ear - ASSR Results	Recorded ASSR Threshold	Estimated Behavioral Threshold**
500 Hz	111 dB HL	101 dBeHL
1000 Hz	113 dB HL	103 dBeHL
2000 Hz	116 dB HL	106 dBeHL
4000 Hz	112 dB HL	102 dBeHL

Left Ear - ASSR Results	Recorded ASSR Threshold	Estimated Behavioral Threshold**
500 Hz	106 dB HL	96 dBeHL
1000 Hz	108 dB HL	98 dBeHL
2000 Hz	121 dB HL	111 dBeHL
4000 Hz	122 dB HL	112 dBeHL

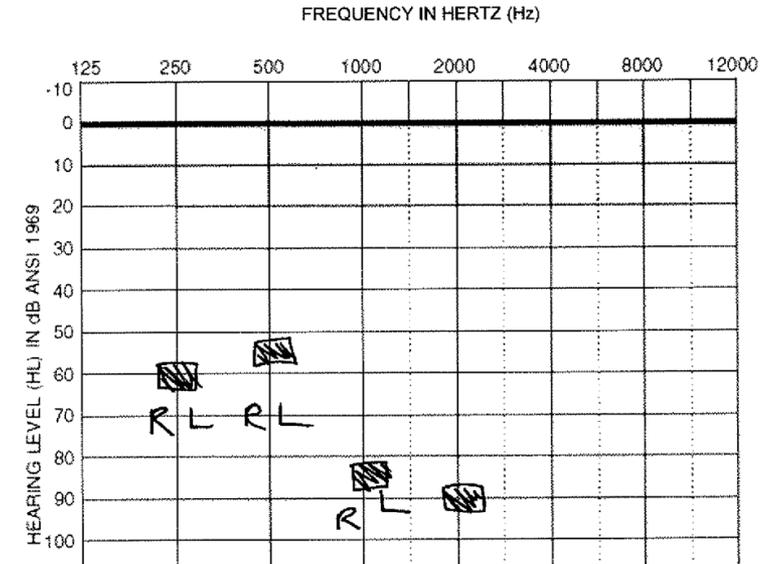
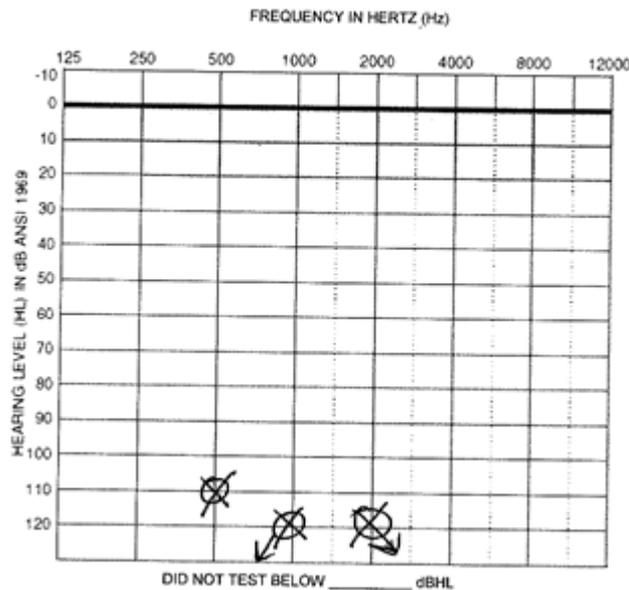
Case Study #2

- 5 weeks of age: Evaluated by Otolaryngology
- 6 weeks of age: Fit with binaural hearing aids



Case Study #2

- 6 months of age: Cochlear implant evaluation process began



- LittleEars Questionnaire: 2/35; This score indicates that the child's auditory behavior is not age-appropriate
- Receives DT-H therapy from local provider
 - Responds only to loud noisemakers (drums, cymbals, shakers)
 - No response to name or voices
 - No consistent responses to music
 - Very visual; watches faces and mouths

Case Study #3

- Birth: Failed NBHS
 - No risk factors for hearing loss
- 3 weeks of age: Natural sleep ABR testing was incomplete
- 5 weeks of age: Natural sleep ABR & ASSR confirms a profound bilateral SNHL
 - Patient referred back to PCP

Case Study #3

- 5 weeks age: Positive cCMV test
- 6 weeks of age: Evaluated by Infectious Disease (ID), Ophthalmology and received a head ultrasound (same day)
 - Patient found to be **asymptomatic with isolated SNHL**
- 2 months of age: Evaluated by Otolaryngology and dispensed with binaural amplification (same day)

In Conclusion

- The connection of hearing loss and cCMV is well known
- Audiology has a significant role in regards to monitoring, treatment and management
- Early Hearing Detection & Intervention (EHDI) may lead to a diagnosis of cCMV that may have gone undetected
- We hope that our protocol evolves with:
 - Additional research in the area of treatment
 - Universal newborn screening for cCMV
 - A vaccination

Questions????



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