Unilateral Hearing Loss Caused by Congenital Cytomegalovirus Infection

Faye P. McCollister, EdD
University of Alabama, Emeritus
National Center for Hearing Assessment and Management

Karen Fowler, DrPH
Department of Pediatrics
University of Alabama, Birmingham

Infrequent Identification of Congenital Cytomegalovirus Infection & HL

- 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

Pass, 1999

Congenital Cytomegalovirus Infection

- Leading (nongenetic) cause of sensorineural hearing loss in children
- 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)
- 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)

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%)

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

CLINICAL IMPACT OF CONGENITAL CMV INFECTION for SX and ASX

	Frequency of sequelae	
	Symptomatic (7%)	Asymptomatic (93%)
Infant death	10%	0
Hearing loss	60%	7–15%
Mental retardation	45%	2–10%
Cerebral palsy	35%	<1%
Chorioretinitis	15%	1–2%

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

Pass, 1999

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

UAB Study of HEARING LOSS IN CHILDREN WITH CONGENITAL CMV INFECTION

- Longitudinal study-- 24 years
- First hearing article published in1977
- Ss identified 1st week of life
- Age at time of audiologic evaluation: 1 month to 19 yrs; mean age of 5 yrs
- Audiologic evaluations every 3 months in 1st year, every 6 months until 2.5-3 yrs and yearly thereafter

Dahle et al. 2000

Hearing Loss and CMV

SUBJECTS	ASYMPTOMATIC	SYMPTOMATIC
SUBJECTS	651	209
Subjects with HL	48(7.4%)	85(40.7%)
Unilateral HL	25(52.1%)	28(32.9%)
Bilateral HL	23(47.9%)	57(67.1%)
High Frequency	18(37.5%)	11(12.9%)
Delayed Onset	18(37.5%)	23(27.1%)
Age Range	24-182 Months	6-197 Months
Progression	26(54.2%)	46(54.1%)
Age Range	3-186 Months	2-209 Months

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

AUDIOLOGICAL PROTOCOL

- ABR : Click, TB of 500 & 4000 HZ until 9 months
- Air and bone conduction if AC>25 dBnHL
- Immittance
- VRA after 5 months until 2.5 to three years

Dahle, et al, 2000

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

UAB Study of Congenital CMV and HL: Unilateral Hearing Loss

	Asymptomatic	Symptomatic
Degree of Loss	Onset and Last Visit	Onset and Last Visit
Minimal (15-25)	11.1%→11.1%%	0→0
Mild (26-40)	19.4%→5.5%	23.3→9.3%
Moderate (41-55)	11.1%→8.3%	14.0%→9.3%
Moderate-Severe (56-70)	8.3%→2.8%	30.2%→9.3%
Severe (71-90)	5.5%→13.9%	11.6%→23.3%
Profound (>90)	2.5%→38.9%	20.9%→41.9%
High Frequency(4K,8K)	25.0%→19.4%	0→0

Fowler, Unpublished Dat

UAB Study of Congenital CMV and HL

	Asymptomatic	Symptomatic
Subjects	710	223
Hearing Loss	8.9 % (63)	42.6% (95)
Unilateral HL	55.6% (35)	46.3% (44)

Fowler, unpublished data

UAB Study of Congenital CMV and HL: Unilateral Hearing Loss Demographics

	Asymptomatic	Symptomatic
Sex, Male	48.6%	59.1%
Race, Black	82.9%	50.0%
Insurance, Public	85.7%	59.1%
Referral	20.6%	61.9%

Fowler, unpublished data

Uab Study of Congenital CMV and HL: Unilateral Hearing Loss

	Asymptomatic	Symptomatic
HL, Right Ear	58.1%	39.4%
HL, Onset at Birth	48.6%	79.5%
HL, Late Onset	41.9%	27.3%
HL, Late Onset, Age Range	9–182 mo	6–94 mo

Fowler, unpublished data

UAB Study of Congenital CMV and HL: Unilateral Hearing Loss

	Asymptomatic	Symptomatic
Progression of HL, Affected Ear	38.7%	39.4%
Progression of HL to Bilateral	11.4%	25.0%
Progression of HL, Age Range	3–138 mo	9–197 mo

Fowler, unpublished da

Treatment of Sudden onset or Progressive Hearing Loss

- Immunosuppressant Drugs
- Dexamethazone
  - Side effects in children
- Antiviral Drugs
  - Does not cure virus, but stops virus replication

Management of Children with Congenital CMV and Unilateral 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

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

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

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 followup results (OAE) confirm presence of middle ear dysfunction and cloud presence of sensory neural HL
- AN if use only OAE technology

Challenges to Monitoring and Defining Progressive and Delayed Onset HL

- Variability of hearing loss: progression, delay in onset, and fluctuation requires frequent assessment
- Otitis media resulting in conductive overlay for sn hearing loss, delay in getting baseline assessment data
- Parental compliance with repeat assessments

Monitoring Behavior for Development of Unilateral Hearing Loss in Children

- Has difficulty localizing sounds, seems to turn in the wrong direction to find sound or comply with request
- Child turns face of parent toward their visual field
- Does not seem to hear as well in noisy listening situations
- Seems to learn at a slower rate
- Does not awaken when ear with better hearing is blocked against bedding and ear with hearing loss is not blocked

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)

Percentages of Sensorineural Hearing Losses That are Unilateral

Kinney (1953)	1307	48%
Brookhouser, Worthington & Kelly (1991)	1829	37%
Wadkin, Baldwin, Laoide (1990)	171	35%
Dahle (2000)	133	40%

Counseling Parents of Children With Unilateral Hearing Loss

- Avoid noise exposure
- Avoid ototoxic medications unless essential
- Obtain prompt medical attention for otitis media
- Radiologic evaluation and laboratory test results

Child Has Severe Unilateral HL , Attends Educational Program for Normal Hearing Students

- Evidence suggests children with unilateral loss are at greater risk for developing bilateral loss (Brookhouser, 2002)
- Development of bilateral loss may/may not be evident to caregivers and educational service providers
- Children with unilateral loss may not be eligible and/or do not necessarily receive services known to be beneficial; need consultation from audiologist and interventionist for IEP/IFSP
- Infection control in educational setting for normal hearing children may become an issue

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

Following Children With Risk Indicators For Progressive/Late Onset Hearing Loss May Result in Management Problems

- Population is Large
- Pediatricians May Feel Causes Undue Stress
- Tracking is Major Problem
- Compliance is Major Problem
- Repeated Assessments May be Expensive
- Many Clinics Have Waiting Lists
- Parents May Not See Need, Especially if Hearing is Normal

Benefits For Family and Their Child Far Outweigh the Management Problems

- Receive information about the etiology and characteristics of their child's hearing loss and resources for additional information
- Able to network with parents of other children with progressive/delayed onset hearing loss
- Receive early intervention
- Influences the way HL is managed
- Early identification/intervention results in …….

Helping Parents Become Partners in the Monitoring/Intervention Process

- Be straight forward
- 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

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
- ASHA web site
- Listen-up.org
- Agbell.org
- Handsandvoices.org
- Translation into many languages: worldlingo.com

Resources on Infant and Childhood Hearing Loss

Early Hearing Detection and Intervention (EHDI)
http://www.cdc.gov/ncbddd/ehdi/

National Center on Hearing Assessment and Management (NCHAM)
http://www.infanthearing.org

Boy's Town Hearing Research
http://www.babyhearing.org

National Institute on Deafness & Communication Disorders (NIDCD)
http://www.nidcd.nih.gov/

Hands and Voices
http://www.handsandvoices.org

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

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

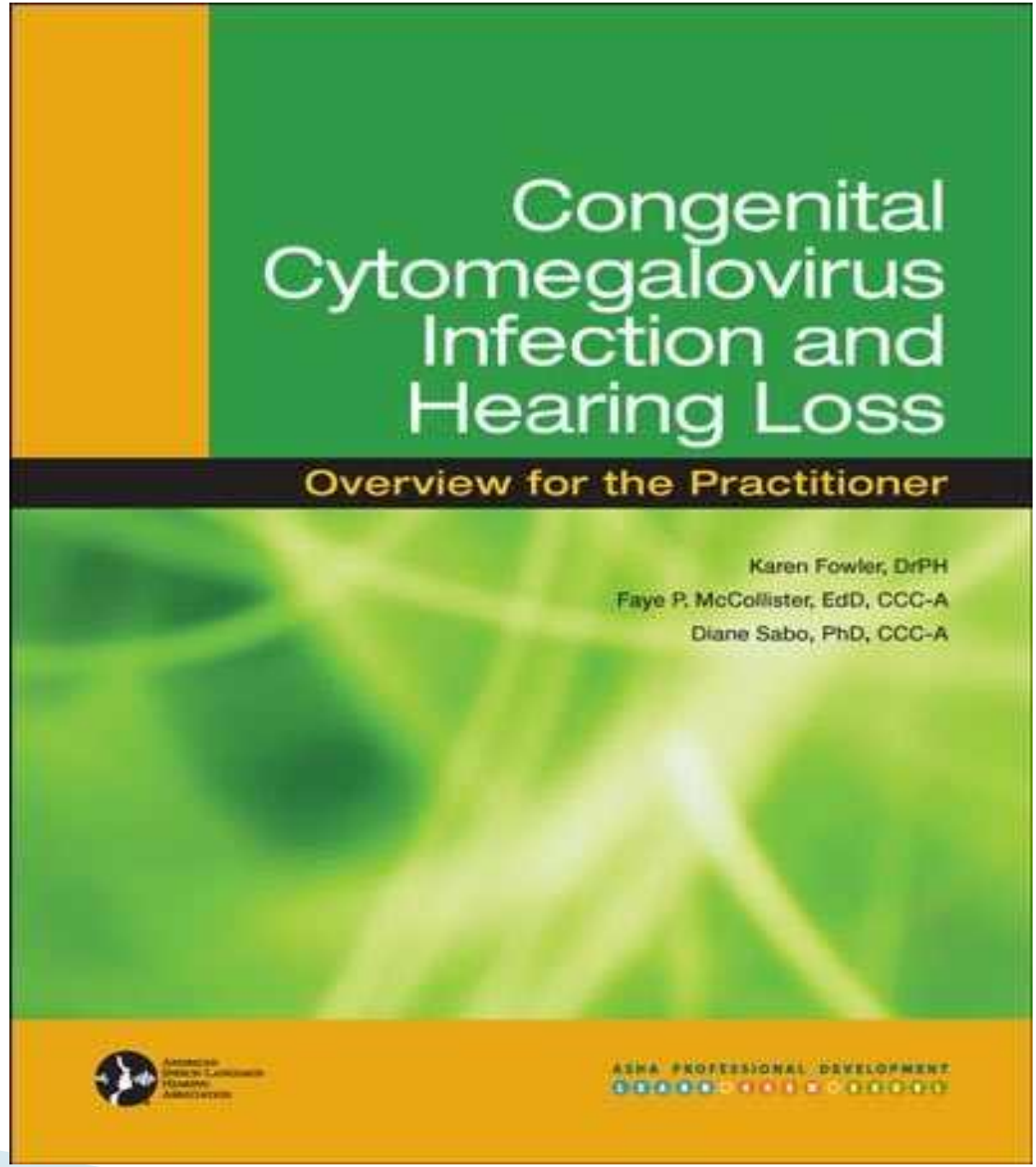
CMVKids
http://cmvkids.com/

CMVSupport (United Kingdom)
http://www.cmvsupport.org/modules/news/

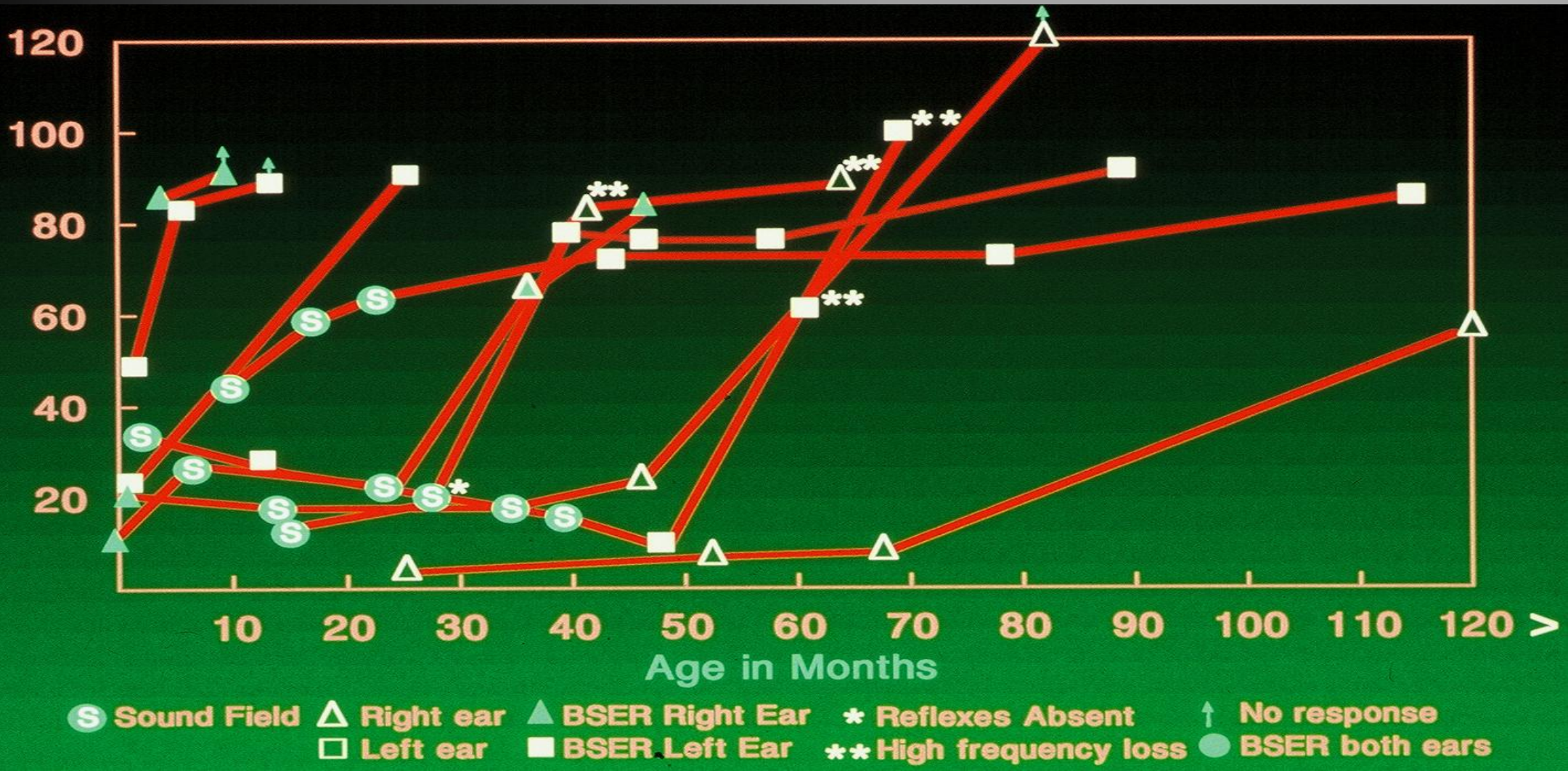
Handouts and Information for Parents

- CHIMES Study Website, UAB
- Signs and Symptoms of Hearing Loss
- Characteristics of Progressive Hearing Loss
- Is my child infectious
- Will my child develop other problems

Karen B. Fowler
Diane Sabo
Faye McCollister
fmc901@earthlink.net



Progression of Unilateral HL In 10 Children: ASX CMV



CMV Case Study :Unilateral HL