MASSACHUSETTS EYE AND EAR

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Congenital CMV Pediatric Case Studies

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CMV Definition

- Cytomeglovirus (CMV) is the most common infectious cause of birth defects in the United States.
- According to the CDC, 1/200 infants is born with congenital CMV infection.
  - 10-15% symptomatic congenital CMV
  - 85-90% asymptomatic congenital CMV
    - » Isolated hearing loss is considered asymptomatic
    - » 15% of asymptomatic congenital CMV will develop late onset hearing loss

Identification

- 10-15% of babies with cCMV have signs at birth
  - Hearing loss
  - Petechiae (pinpoint, round spots that appear on the skin as a result of bleeding)
  - Jaundice
  - Microcephaly
  - Intrauterine growth restriction (IUGR)
  - Hepatosplenomegaly (enlargement of the liver and spleen)
  - Seizures
  - Retinitis

CMV is short for cyto-megalo-virus

CMV is serious

Leading non-genetic cause of childhood hearing loss

Every hour, 1 child is permanently disabled by CMV

CMV also causes:

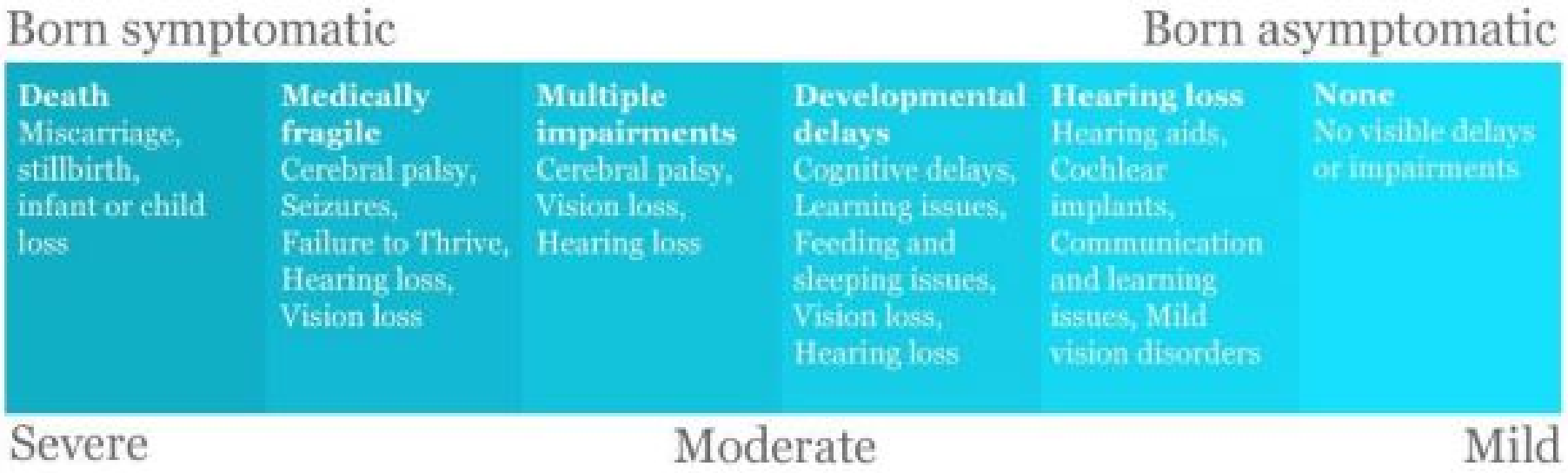
Vision loss
Microcephaly
Behavior issues
Mental disability
Cerebral Palsy
Seizures

90%
of babies born with CMV will appear healthy at birth

400
children die from CMV every year

Scientific research has found a connection between CMV and miscarriage

NATIONAL CMV FOUNDATION



National CMV Foundation

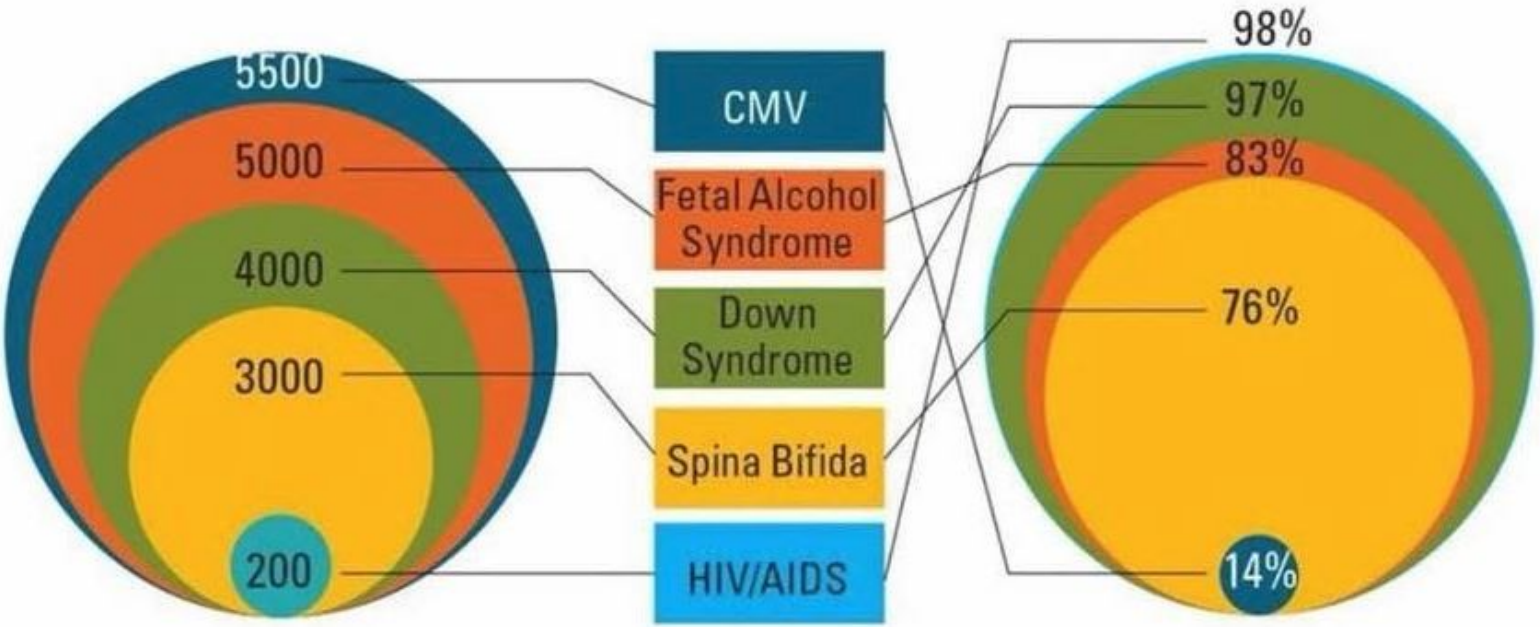
Prevention: Awareness

- Most people don't realize that they have been infected with CMV
- One of highest risk groups are pregnant women who have not contracted CMV prior to pregnancy
- CMV is very common in home and daycare settings.
  - Pregnant day care providers in Germany are not allowed to work during pregnancy to help prevent primary infection
- Studies estimate that as many as 70% of healthy children between 1-3 years of age are infected with CMV

CYTOMEGALOVIRUS (CMV)

US children born with or developing long-term medical conditions each year

Women's awareness of these diseases



From National CMV Foundation (www.nationalCMV.org

Prevention: Recommendations for Pregnant Women

- Wash your hands often with soap and water- especially after changing diapers, feeding a young child or wiping noses.
- Do not share food, drinks, or eating utensils with young children.
- Do not put a pacifier in the your mouth.
- Do not share a toothbrush with a young child.
- Avoid contact with saliva when kissing a child.
- Clean toys, countertops, and other surfaces that come into contact with children's urine or saliva.

Targeted cCMV Screening

- Hearing Screening (UNHS) Referral
- IUGR (Low birth weight) or other risk factors
  - Laboratory testing is needed to confirm cCMV
  - Testing must be performed within three weeks to confirm congenital infection
  - Testing performed via urine, saliva (cheek swab), or blood using polymerase chain reaction (PCR)
  - Urine or saliva testing-most accurate
  - Cheek swab screening done at MGH (98% sensitivity)

MEE/MGH cCMV Protocols for Isolated SNHL

- MEE Pediatric Otology and MGH-Pediatric Infectious Disease
  - Infectious Disease prescribes the antivirals
  - All babies with symptomatic CMV receive the antivirals
- Referrals to:
  - Opthalmology
  - Neurology
  - Audiology
  - Otology/ID
  - Early Intervention

cCMV –Treatment with Valganciclovir

- Symptomatic CMV
  - Automatic treatment for 6 months
    - Thought to improve neural transmissions
- Asymptomatic CMV (isolated hearing loss)
  - Parental decision
  - 6 week course, if baby is doing well, continue for 6 months

In the United States

- No consensus on how to treat asymptomatic CMV (isolated hearing loss)

ValEar Clinical Trial

- Randomized Controlled Trial of Valganciclovir for Asymptomatic Cytomegalovirus Infected Hearing Impaired Infants.

- “The study is trying to see if children treated with an antiviral medication (Valganciclovir) will have better hearing and language outcomes when compared with children that had no antiviral treatment.” (valear.org)

Study Procedures Overview

- 6 months of study drug (valganciclovir or placebo)
- Blood draws to monitor safety and to look at how the drug works in the body
- Phone surveys to assess speech and communication when the patient is around 14 and 22 months of age
- The study team will be obtaining data from hearing exams that occur during the study period
- At visits answering questions related to patient's past medical history, medication use, family history, study drug use, and any doctor or hospital visits while taking the study drug

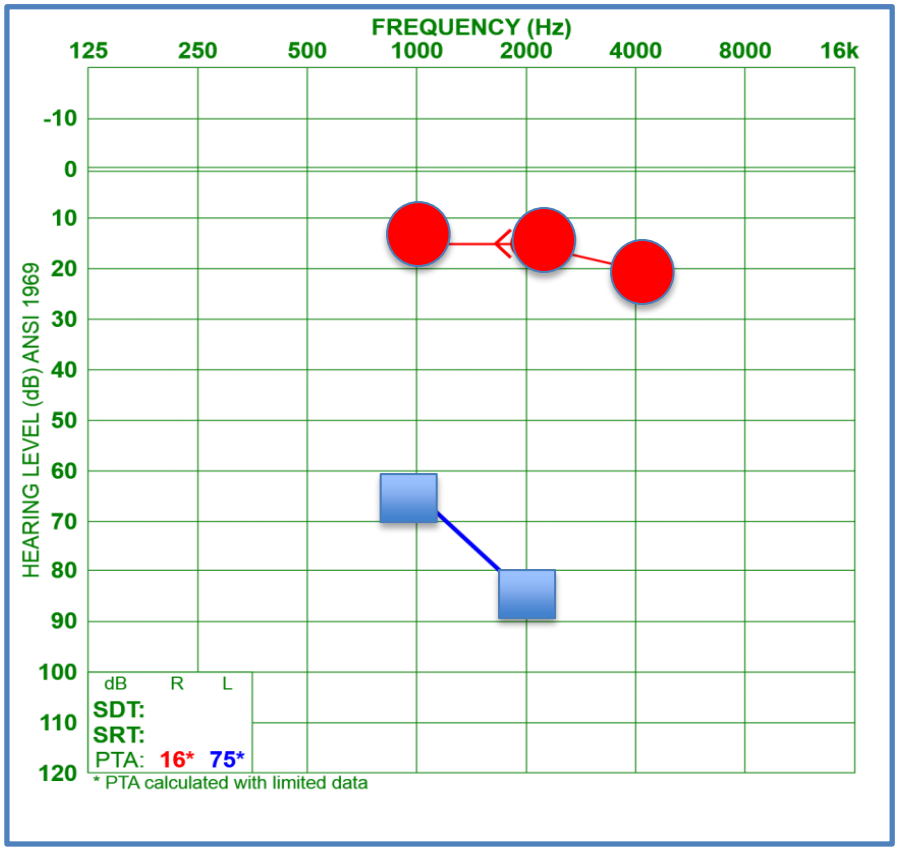
MEE Pediatric Case Studies

Case 1

- Left ear refer on newborn hearing screening.
- Did not receive antiviral treatment

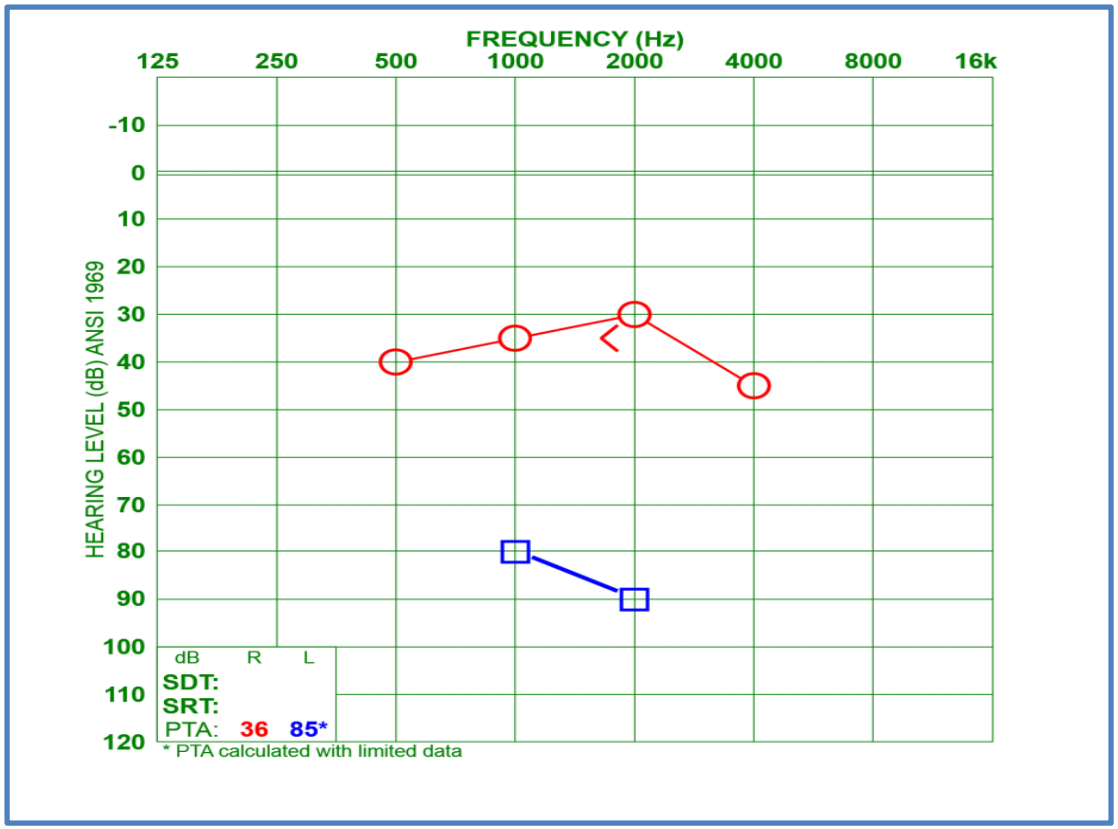
5 months: Normal hearing right ear; Moderate to severe hearing loss left ear.

- Testing via ABR



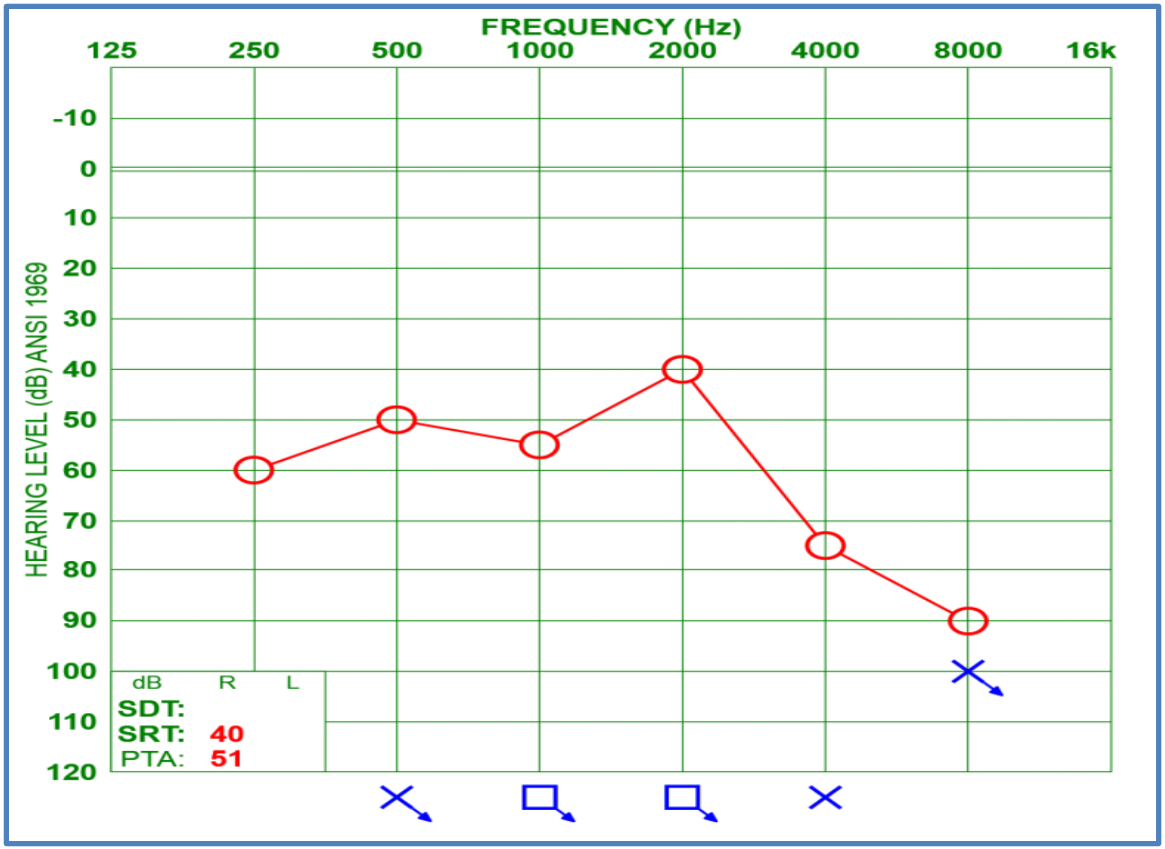
17 months: Mild hearing loss right ear; Stable in the left.

- Began use of hearing aid in the right ear.



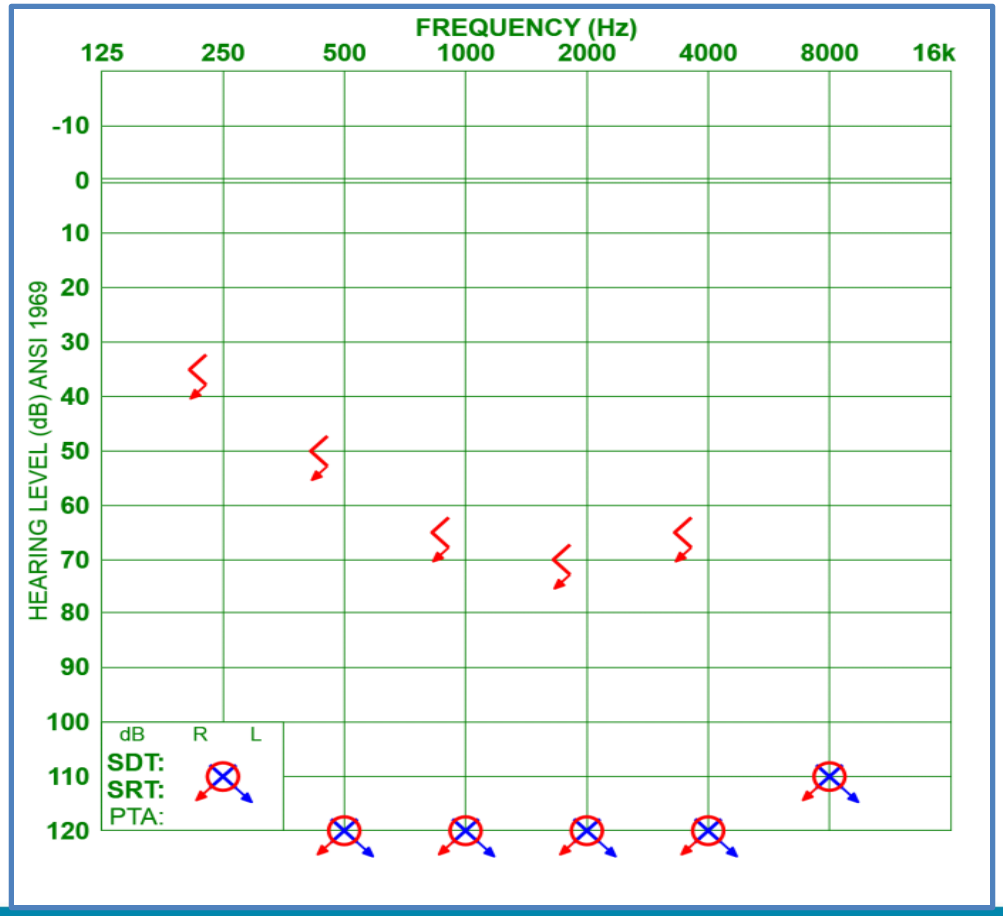
27 months: Moderate hearing loss right ear; profound left.

-Results were confirmed by ABR one month later.



2.5 years: Profound hearing loss in both ears.

Patient reported that her right hearing aid was broken:



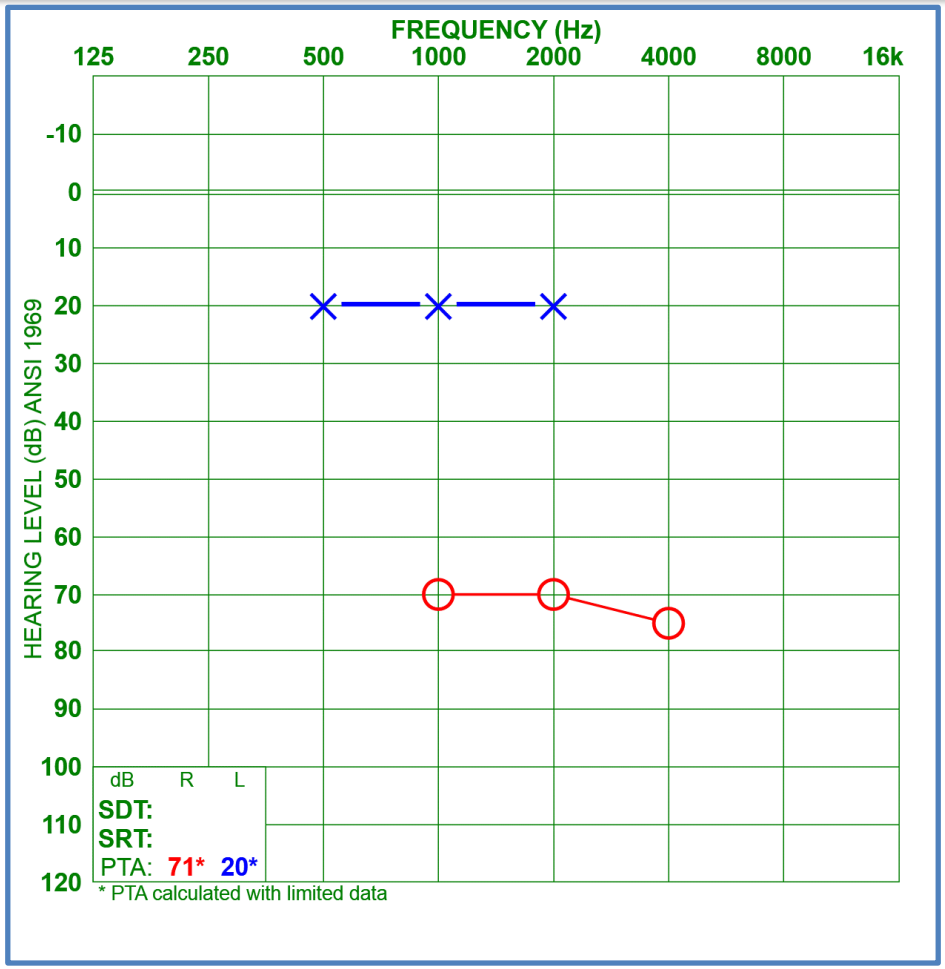
History

- 3 years: Cochlear implant for the right ear.
- 6 years: Patient is enrolled in an auditory-oral educational kindergarten program.
- 7 years: Cochlear implant for the left ear.
- Documented speech and language delay related to history of hearing loss.
- Patient receives excellent benefit from her bilateral cochlear implants.

Case 2

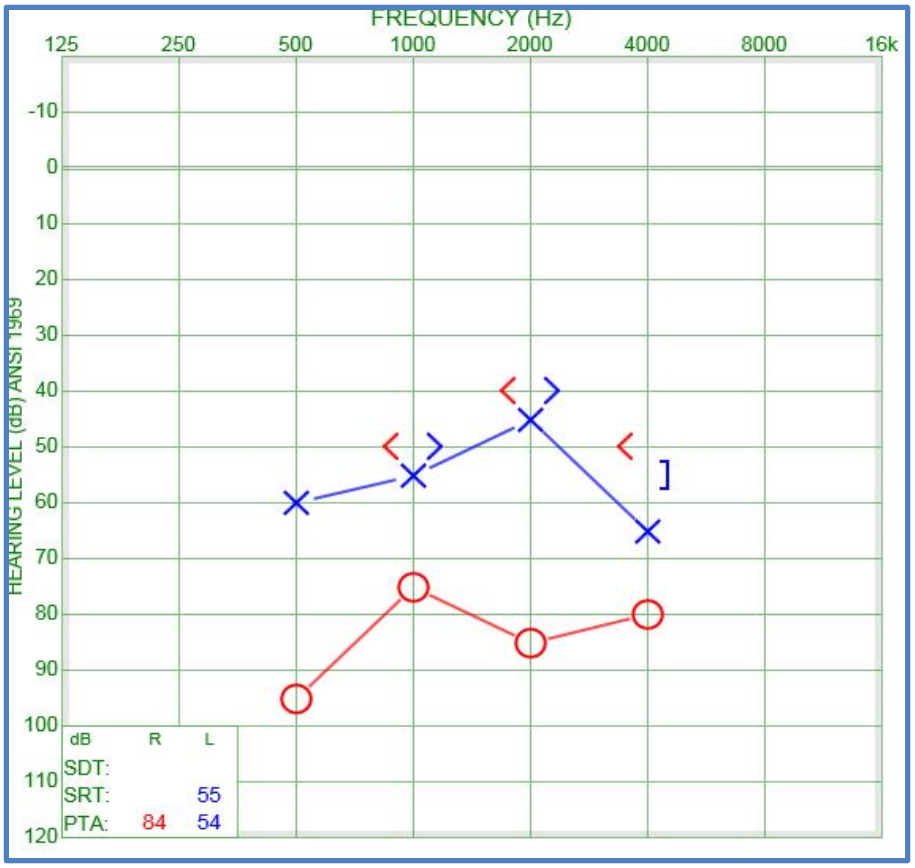
- Passed newborn hearing screening in both ears.
- Enrolled in Early Intervention due to delayed speech and language development. Referred for hearing test.
- Did not receive antiviral treatment.

2.5 years: Normal hearing left ear; moderate to severe hearing loss right ear.



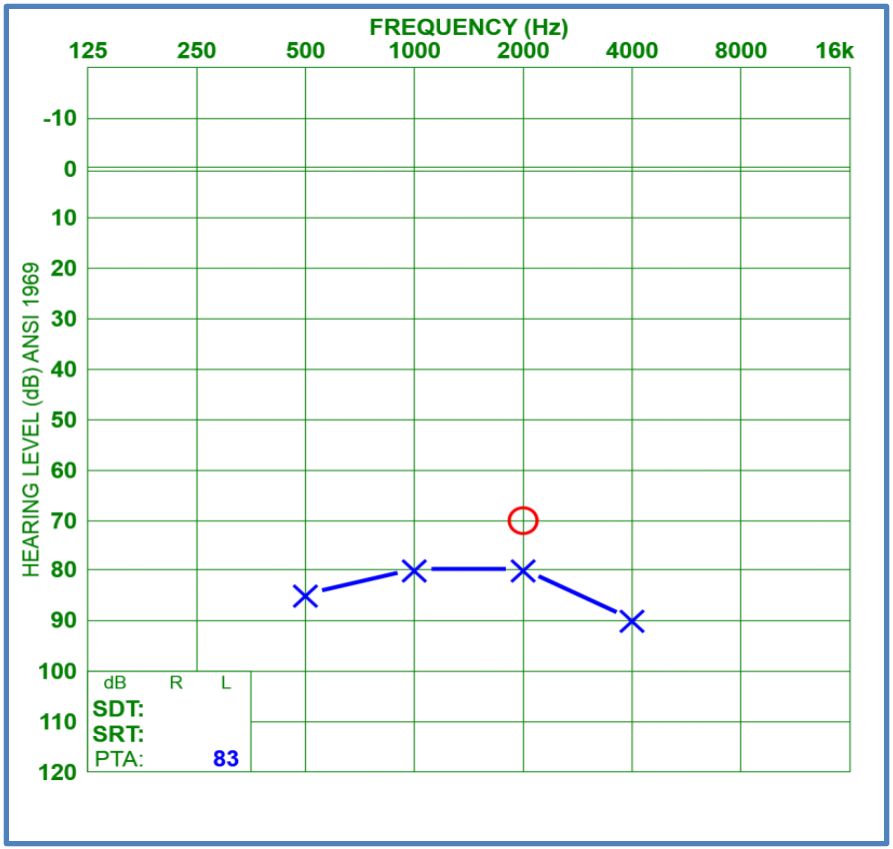
3 years: Moderate hearing loss left ear; severe hearing loss right ear.

Parents report concern regarding delayed speech/language development.



4 years: Severe to profound hearing loss left ear; severe hearing loss right ear.

- Patient attending school for the deaf.



Follow-Up

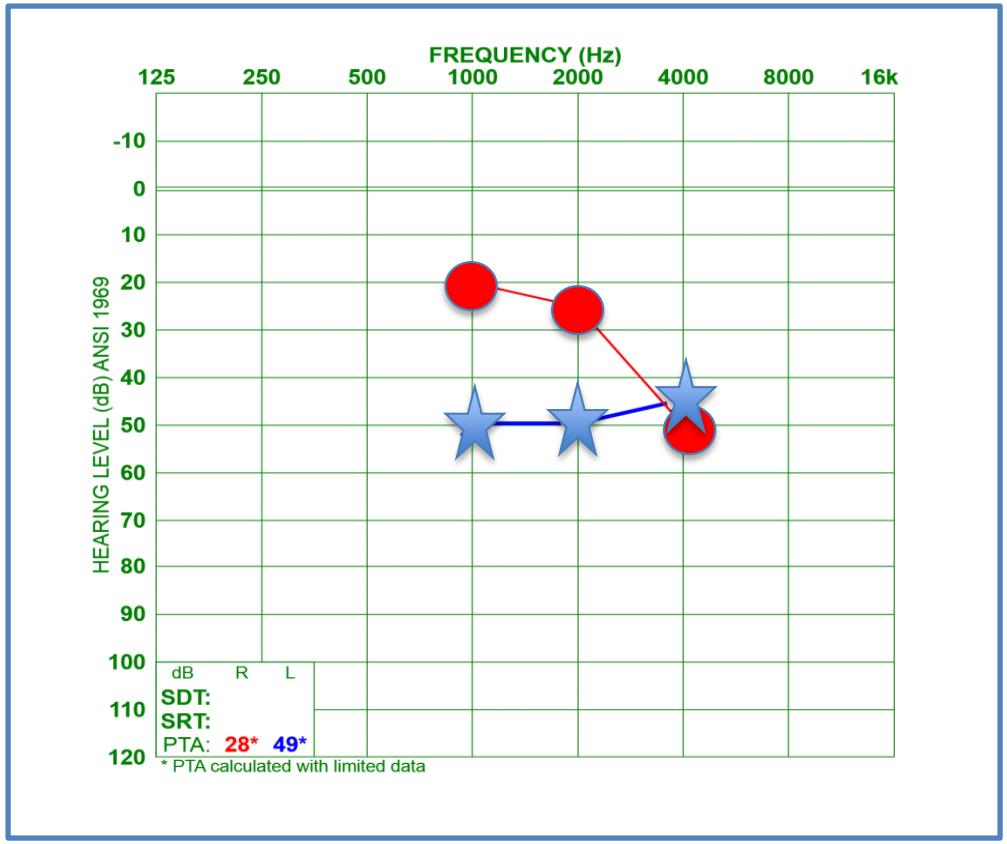
- 5 years: Cochlear implant for the right ear.
- 6 years: Left ear word recognition ability is 2%.
- 7 years: Cochlear implant for the left ear.
- Patient receives excellent benefit from her bilateral cochlear implants.

Case 3

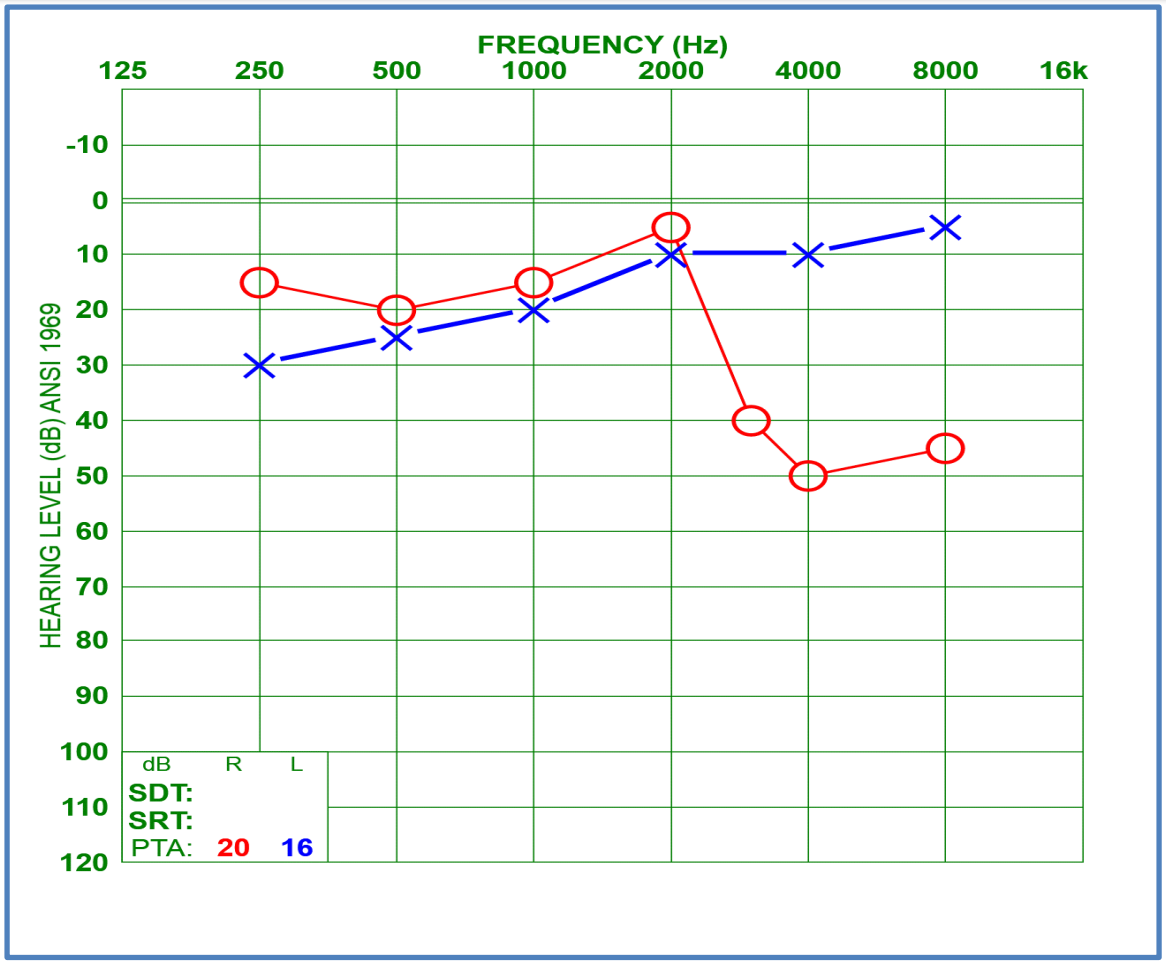
- Left ear refer on newborn hearing screening.
- Isolated hearing loss-considered asymptomatic.
- Treated with antivirals.

Testing at 2 weeks: Slight to moderate sloping hearing loss right ear; moderate hearing loss left ear.

Testing via ABR

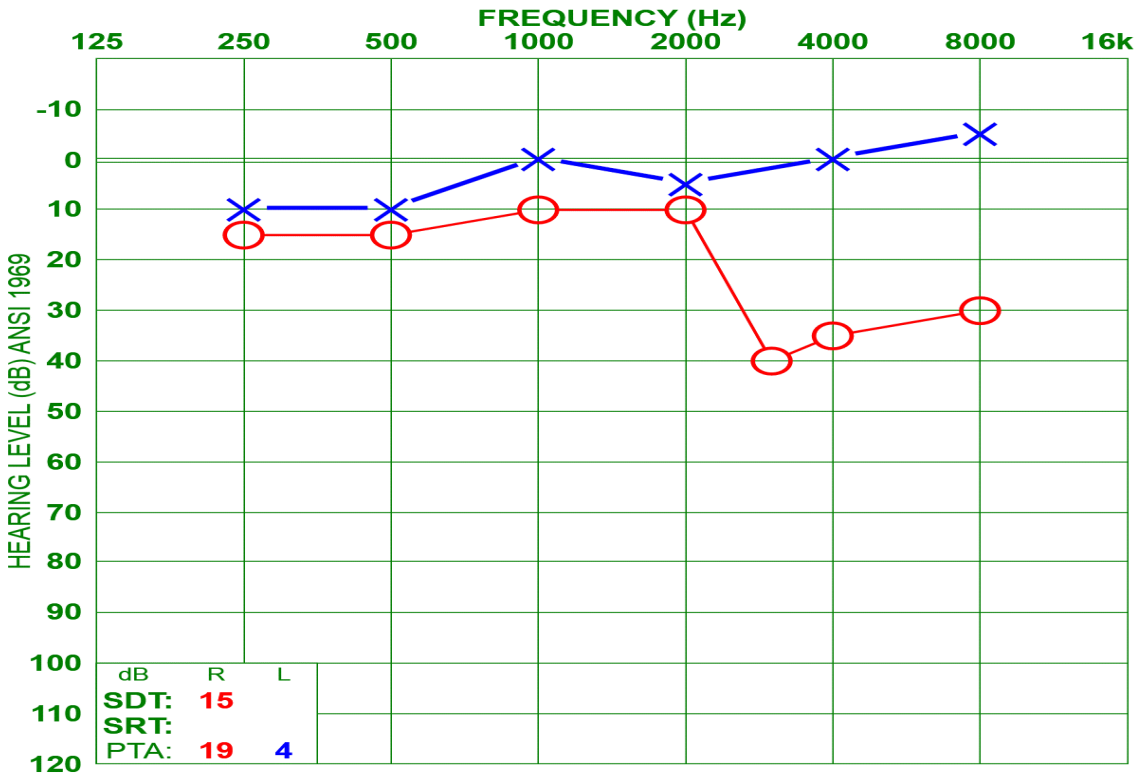


8 months: Ended antiviral treatment. Hearing improved in both ears.



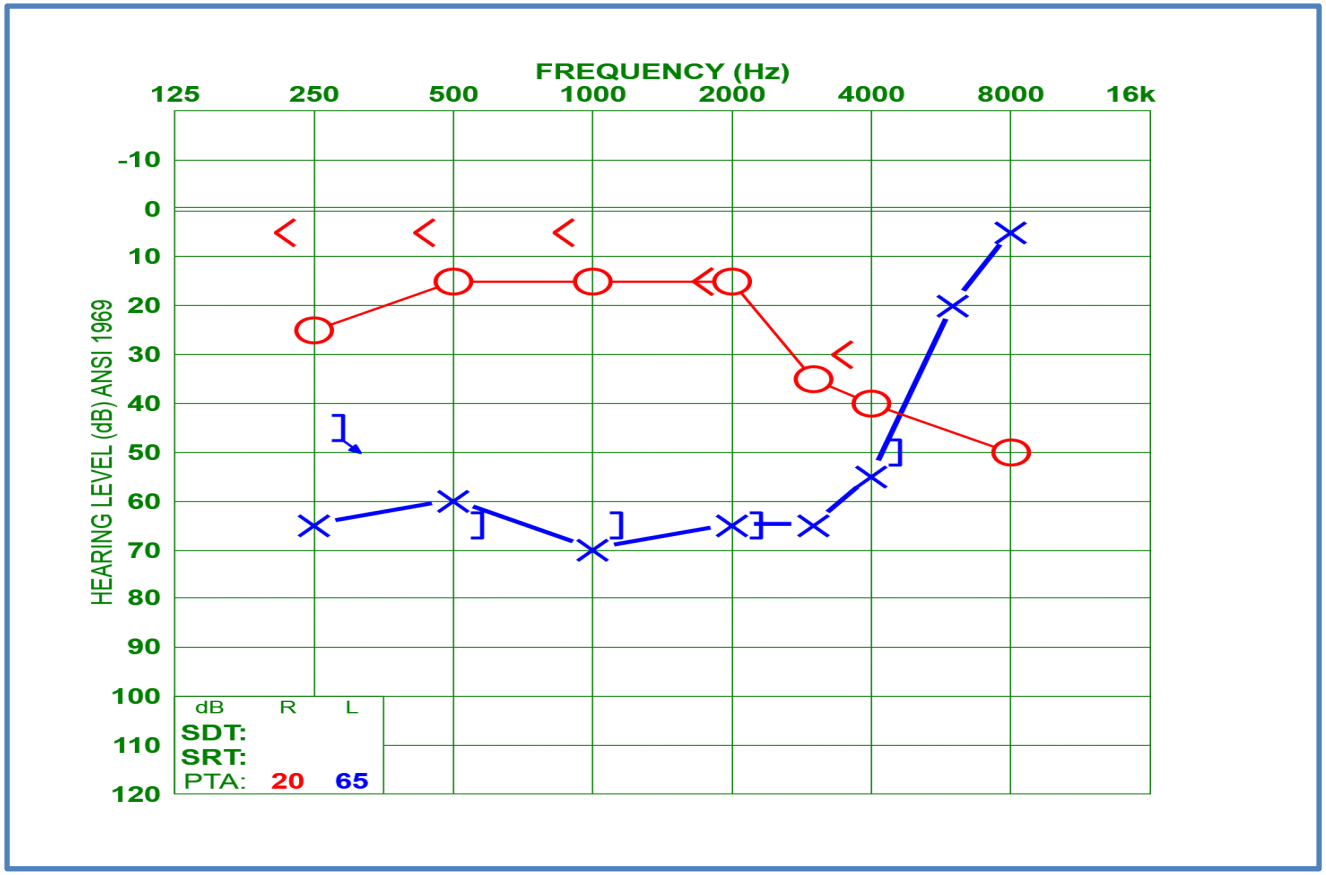
14-28 months: Stable hearing-5 audiograms.

- Normal hearing left, high frequency HL right



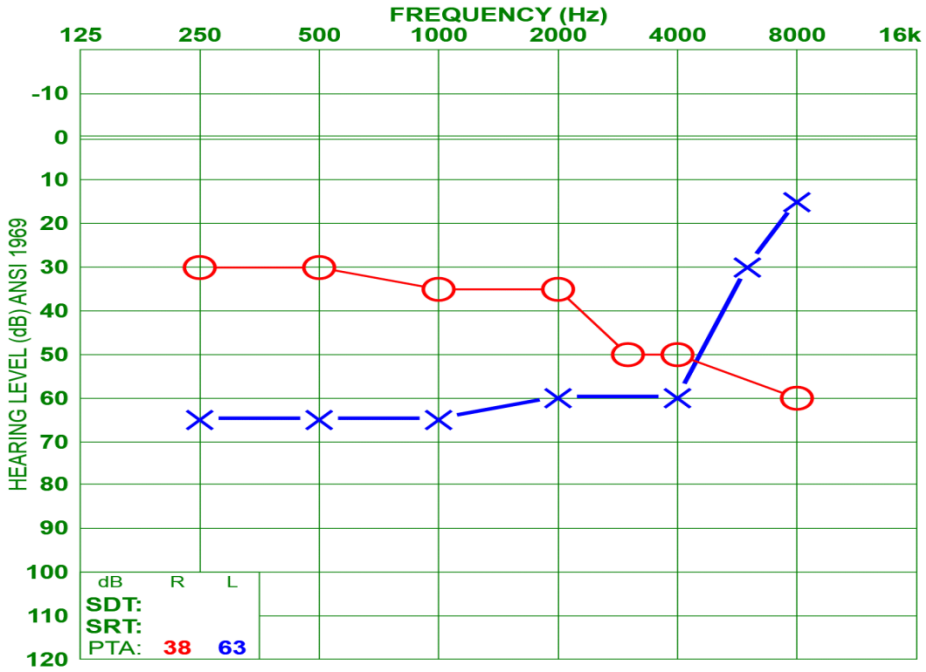
3 years: Left ear decrease to moderate loss. Normal sloping to moderate loss right ear. Second round of antiviral treatment.

- WIPI: 80% right. Began second round of antiviral treatment.



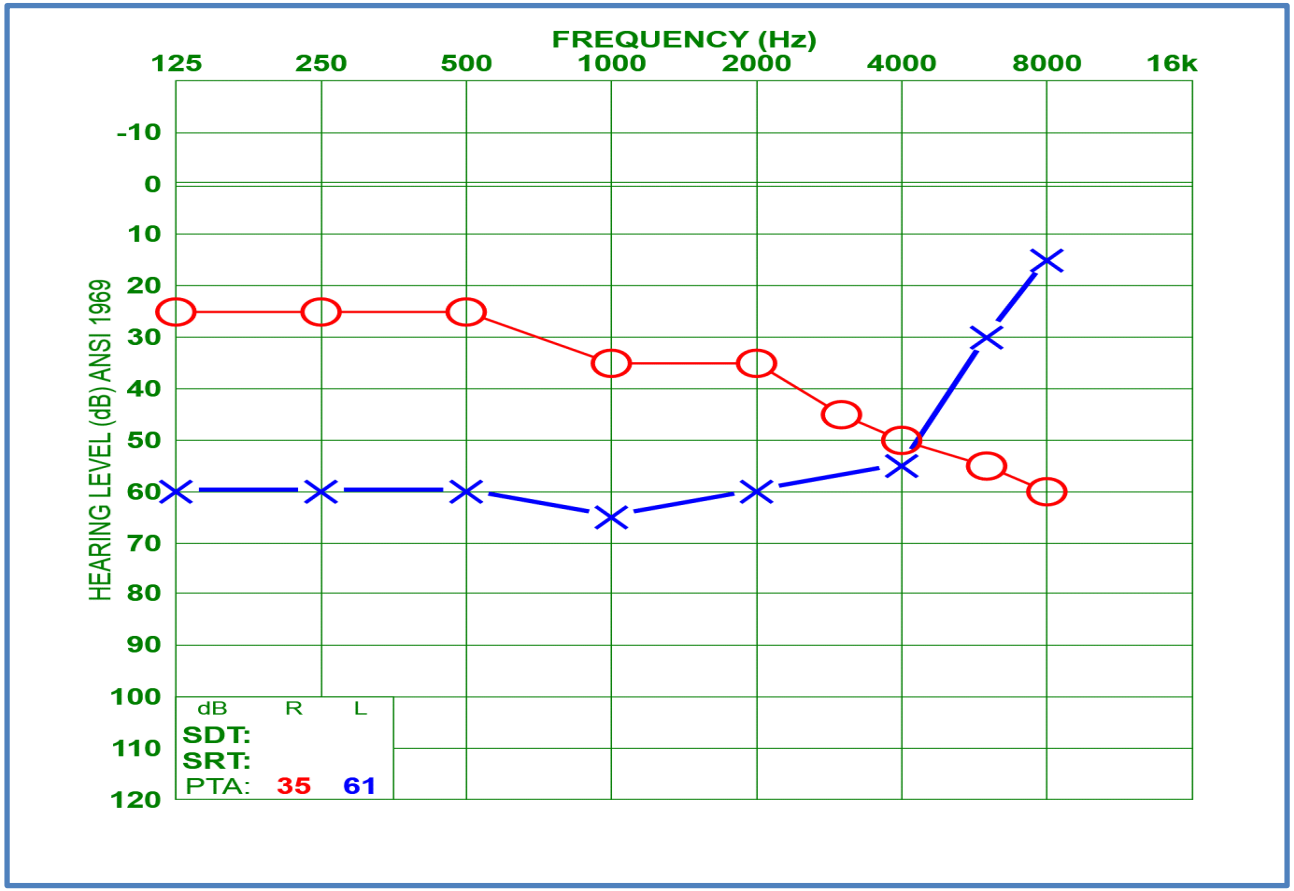
3.5 years: Decreased hearing in the right ear to mild/moderate loss. Moderate hearing loss in the left ear.

-Hearing aid fit for the right ear; cochlear implant recommended for the left ear. Word recognition: CNC-72% right; ESP, Cat 2 left



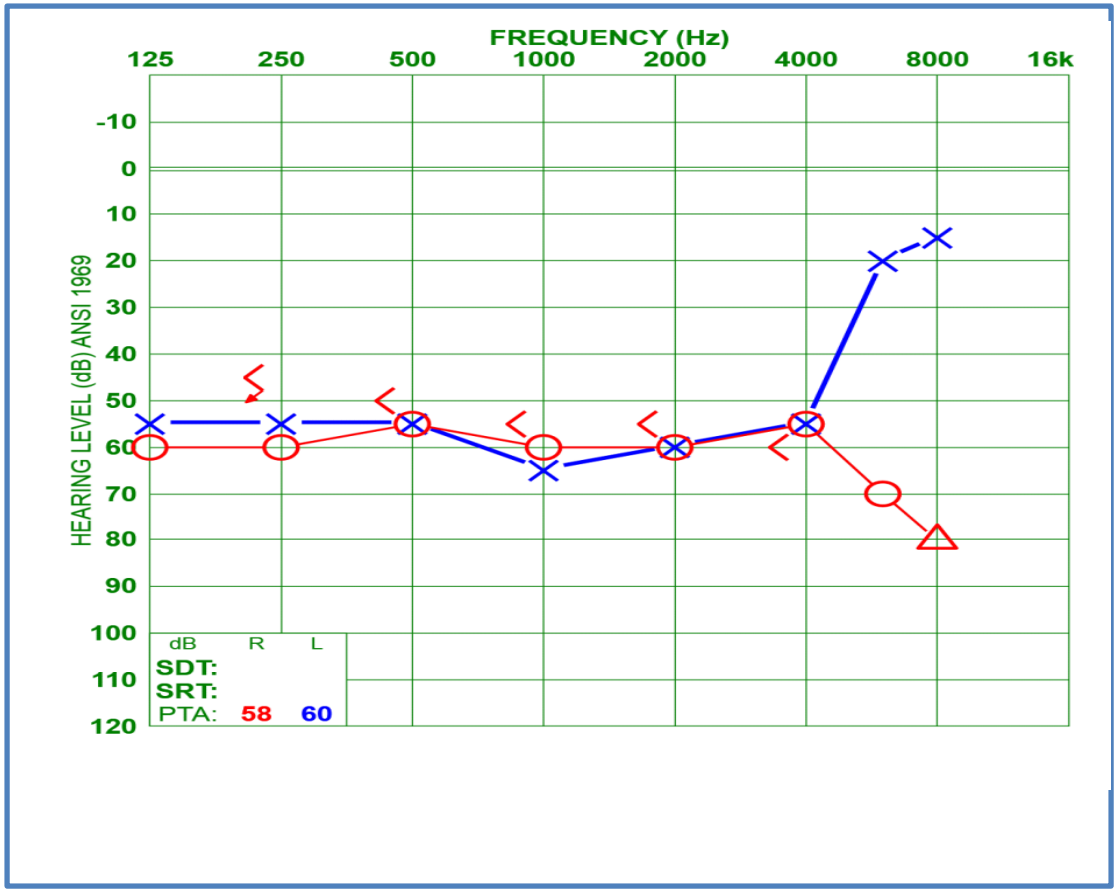
4 to 5 years: Hearing is stable. 14 audiograms.

- CNC-80% right; ESP cat 2 left. Uses right hearing aid; left CI recommended.



5 years: Right ear decrease to moderate/severe, now same as left ear. Poor word recognition.

- Word recognition (CNC) on right ear: Reduced from 78% to 2% in three months. ESP Cat 2 on the left ear.



5 years, 3 months: Cochlear implant for the left ear.

- Speech and language development has been normal. Attending a mainstreamed pre-school class with support from teacher of the deaf.

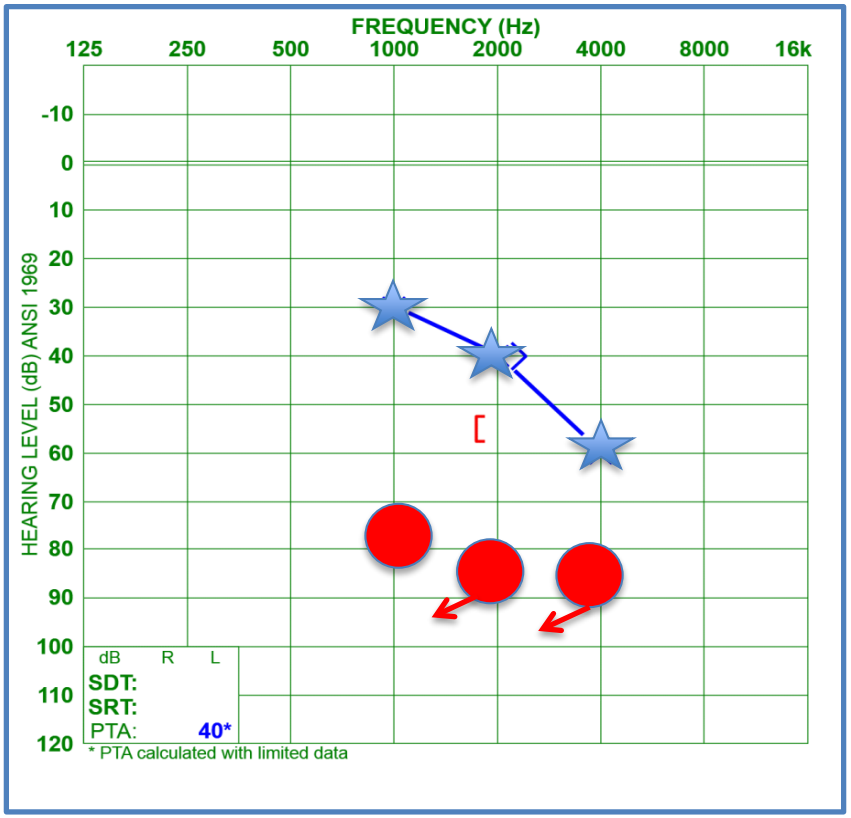
- Good benefit from left cochlear implant. Right cochlear implant recommended.

Case 4

- Right ear refer on newborn hearing screening.
- 13 days: Began antiviral treatment-oral valgancyclovir.
- Speech and language development has been normal to date.

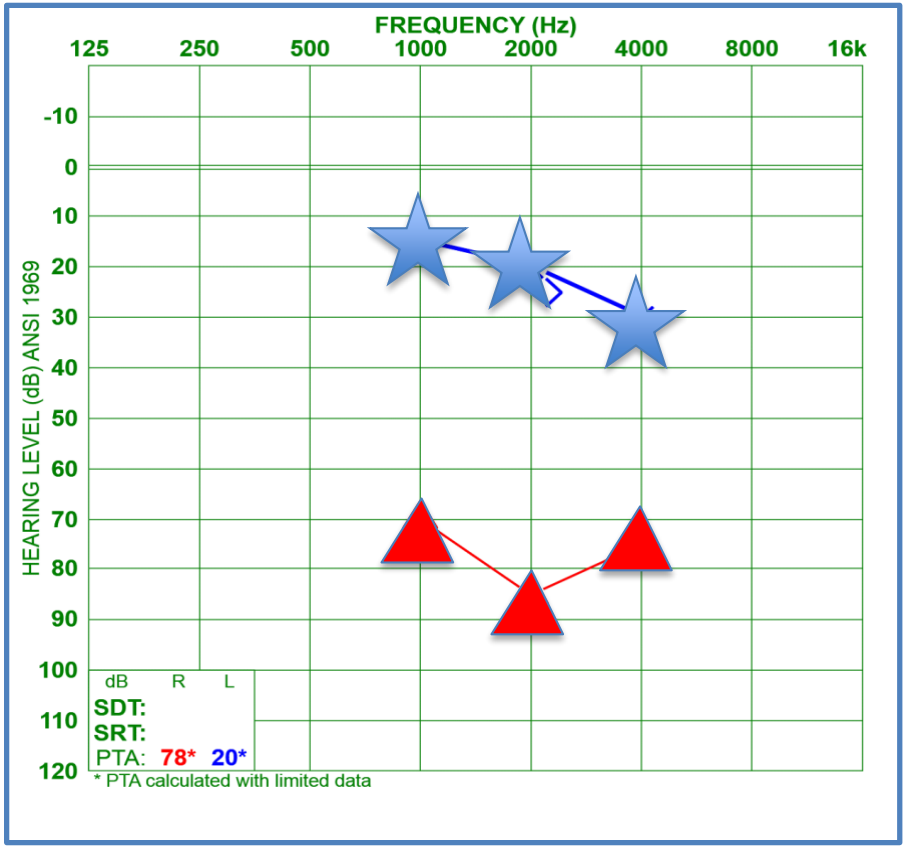
•9 days: Mild hearing loss left ear; severe hearing loss right ear.

- ABR before treatment



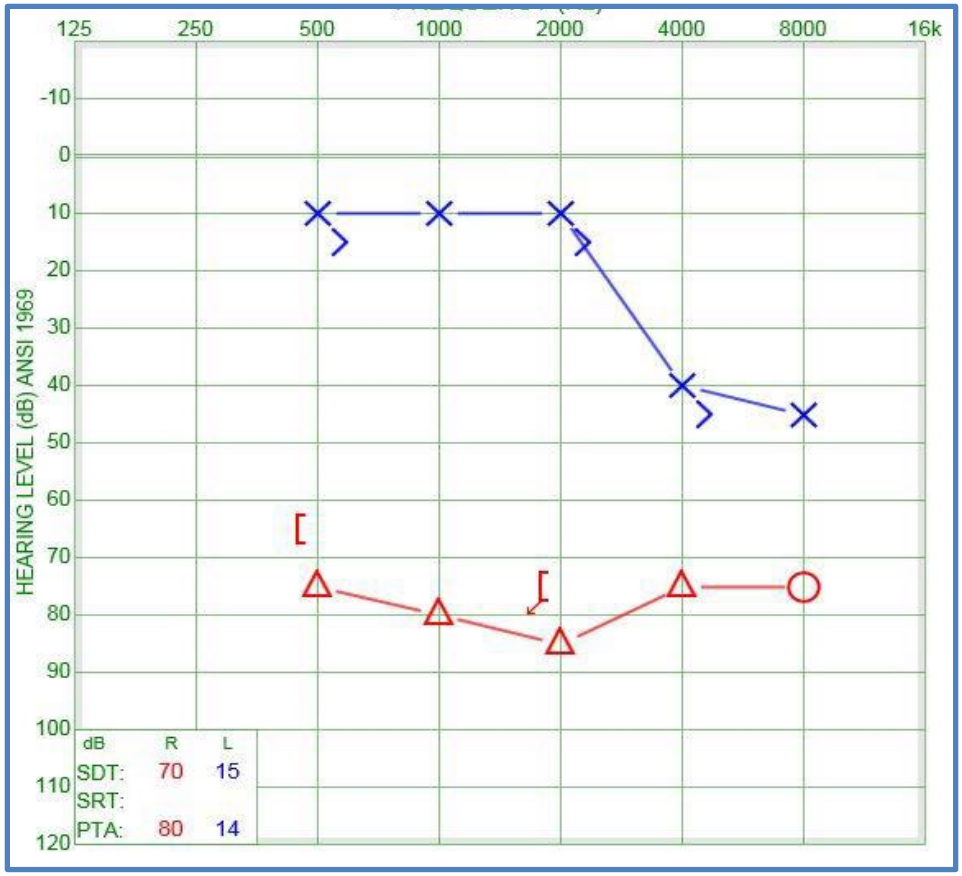
•4 months: Improved hearing in both ears.

-After treatment.



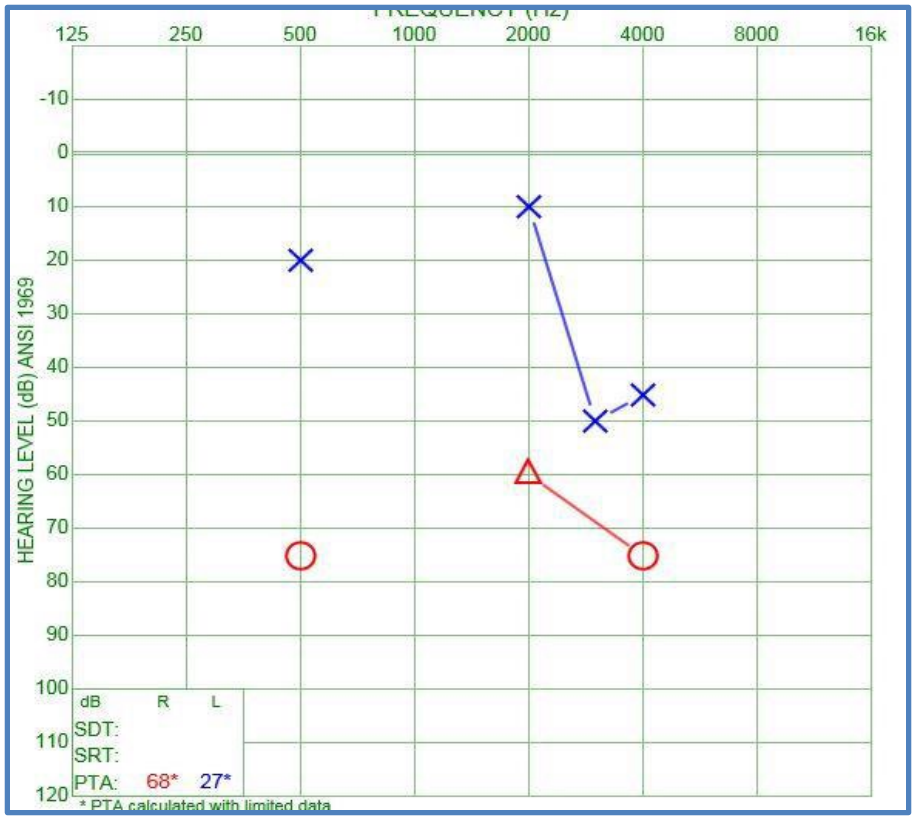
9 months

- Stable hearing.



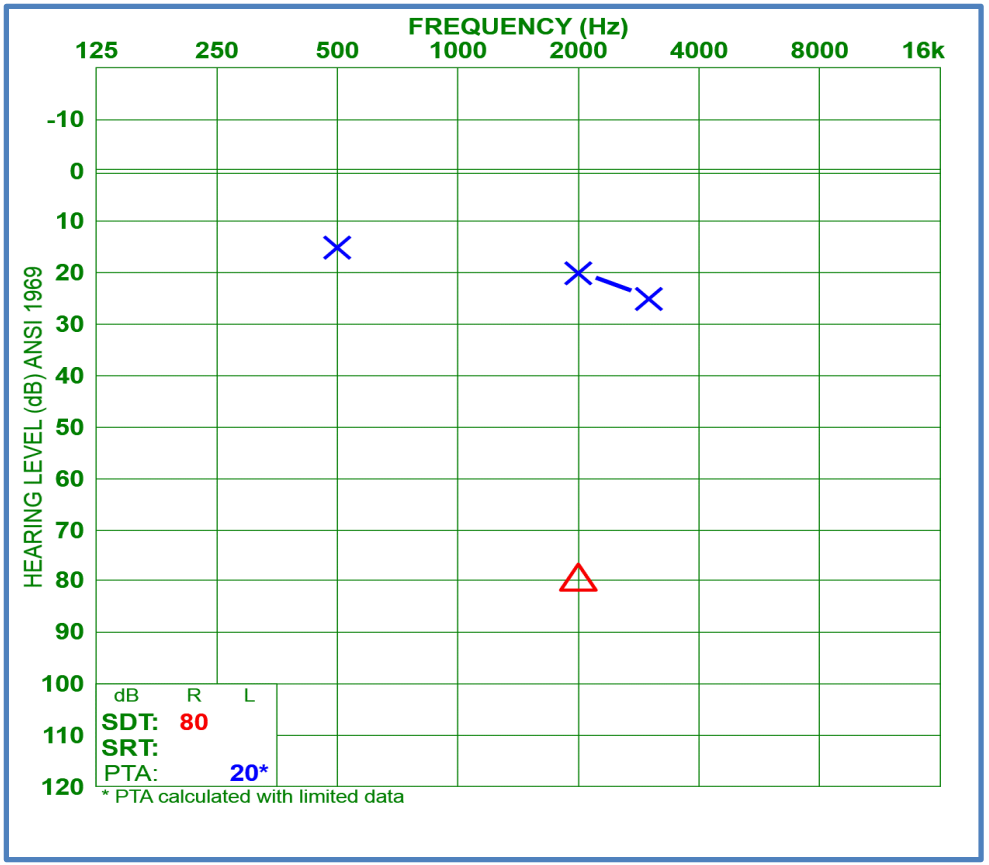
11 months

- Decreased hearing, bilateral otitis media.



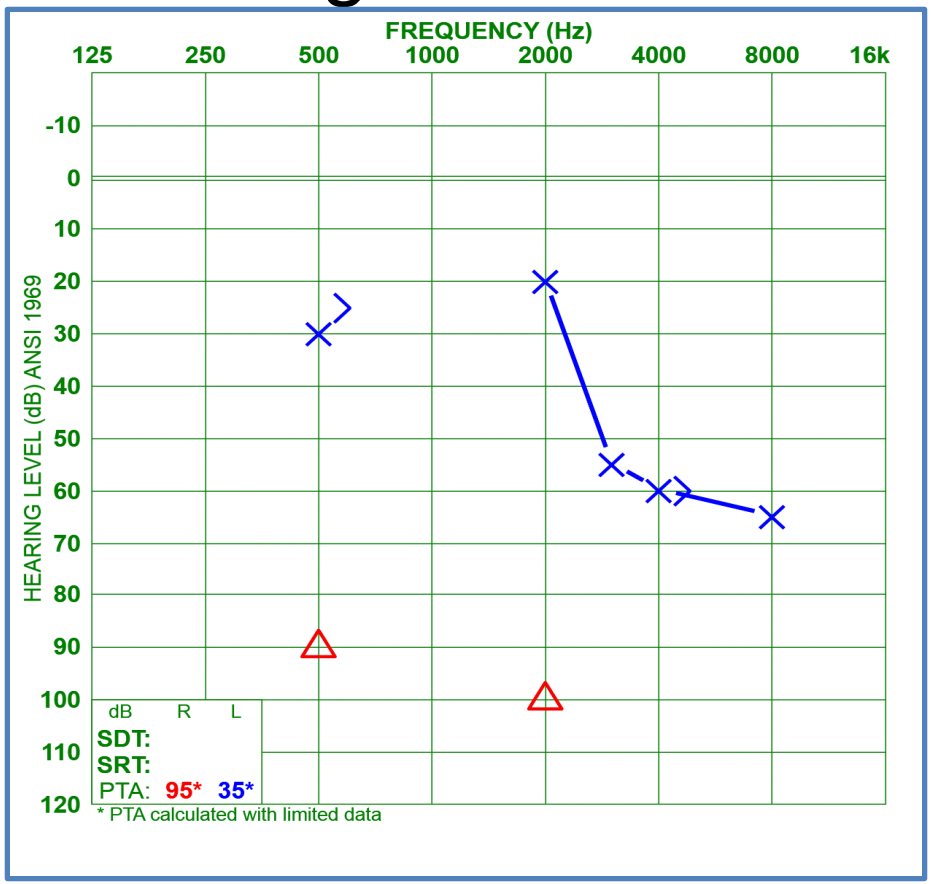
•18 months

- Improved hearing and resolved OM in both ears.



21 months

- Decreased hearing in both ears.



Case 4 recommendations

- Cochlear implant for the right ear.
- Amplification in the left ear as needed.
- Monitoring audiograms-at least every three months or if change is suspected.
- Continue with Early Intervention.

Discussion

- **Prior to anti-viral treatment:**
  - More rapid progression of hearing loss.
  - Severe to profound by age three.
  - Less vigorous monitoring schedule due to unknowns regarding progression of hearing loss.
  - Less timely intervention which led to interruptions in access to audibility, adversely affecting speech/language development.

Discussion

- **After anti-viral treatment:**
  - Longer time periods of normal hearing in at least one ear
  - Allows access to speech sounds during critical speech/language learning period, increasing the probability of meeting milestones.
  - Measurement of word recognition ability is critical.
  - Frequent monitoring is needed even after hearing improvement and cessation of treatment for evidence of reactivation of virus

Conclusions

- CMV testing should be incorporated into all Universal Newborn Hearing Screening Program protocols.
- Treatment can improve hearing during the critical period for speech and language acquisition.
- Hearing improvement may not be permanent.

Conclusions

- Consistent and frequent monitoring of these patients will allow for quick and active intervention.
- Aggressive intervention should be considered in cases of unilateral hearing loss. Earlier implantation of poorer ear should be considered to lessen or prevent a disruptive period of poor hearing and speech understanding.
- Excellent benefit from cochlear implants noted for this population.