EHDI Conference
March 2, 2010

Medical Diagnoses Driven by UNHS

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Children's Hospital Boston

Congenital Cytomegalovirus (CMV) and Hearing Loss

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What is Cytomegalovirus (CMV)?

- CMV is a type of herpes virus that often causes an asymptomatic infection in people who are otherwise healthy.
- After becoming infected, the virus remains in the body, dormant for the rest of the person's life.

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Types of CMV

- Congenital CMV
  - Infected before birth from either a primary or recurrent maternal infection
- Perinatal CMV
  - Occurring during the periods before, during, or after the time of birth
  - Exposure to infected cervical secretions, breast milk, or blood products

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Congenital CMV

- Most common congenital infection
- 40,000 children are born with CMV infection in the US each year.
- Contributes to approximately 400 deaths.
- 8,000 children are diagnosed with permanent disabilities (sensorineural hearing loss, vision impairment, and/or developmental delay).

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Treatment

- Currently no cure for CMV.
- Antiviral drugs help with the progression of hearing loss, pneumonia, and retinitis.
- Two drugs commonly used
  - Valganciclovir (intravenous)
  - Ganciclovir (oral)

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- Newborn Hearing Screen
  - Unilateral refer
  - Bilateral refer
- Diagnostic ABR
  - Newly identified hearing loss
    - Cheek swab for CMV testing
    - Consultation with Otolaryngology Team
    - Repeat ABR every 4 – 8 weeks

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Case Study (HM)

- Born full term
- Healthy pregnancy and delivery
- Transferred to the NICU at 4 days of life due to petechiae involving head and trunk.

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Case Study (HM)

- Thrombocytopenia
- Calcification throughout the brain
- Abdominal ultrasound revealed calcifications of the gallbladder.
- Congenital CMV was diagnosed.

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NHS/ABR - First week of life

- Referred bilaterally on the Newborn Hearing Screen (NHS)
- Diagnostic ABR revealed a severe hearing loss bilaterally.
- Absent Distortion Product Otoacoustic Emissions (DPOAEs) bilaterally

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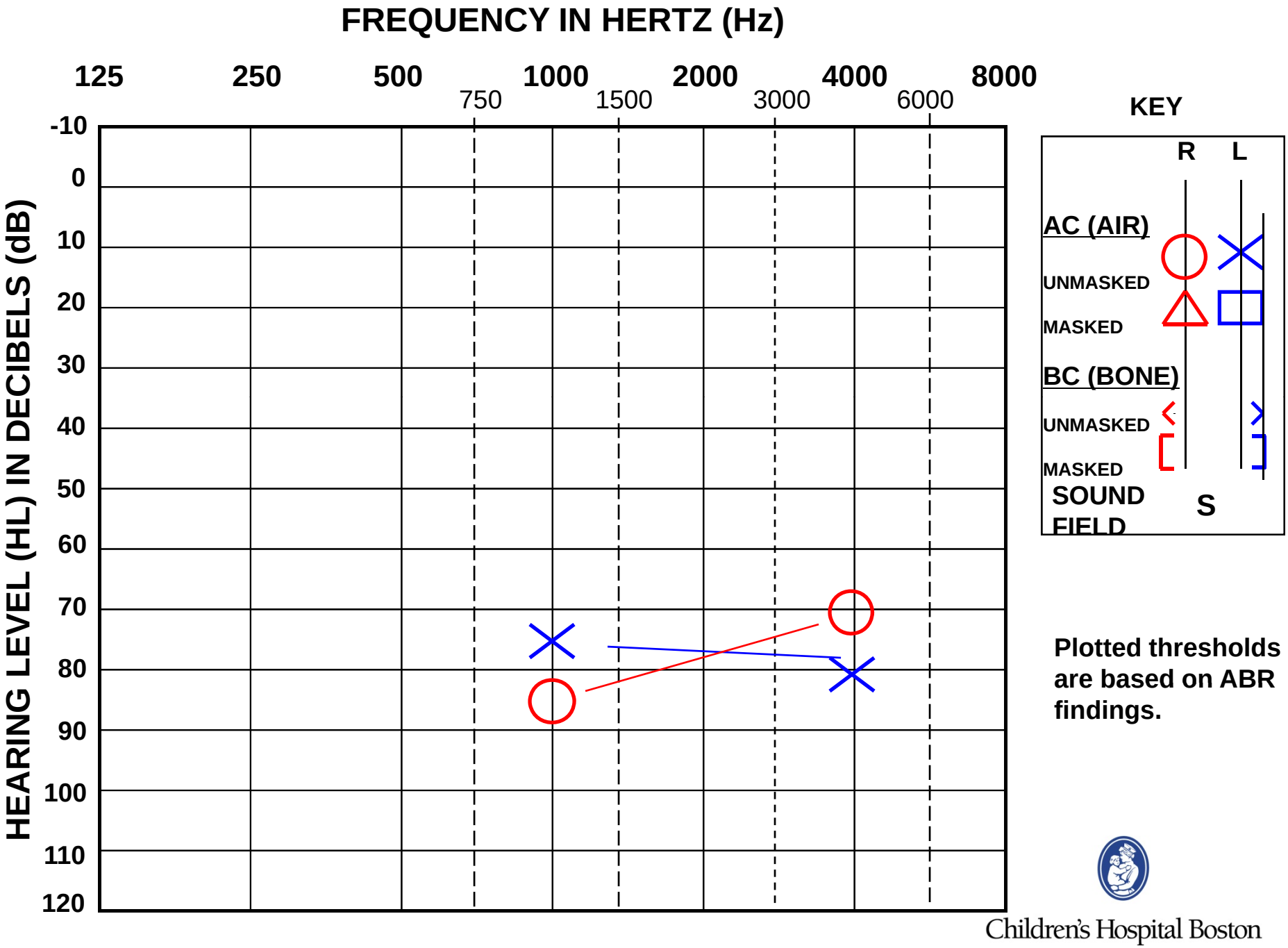

Plotted thresholds are based on ABR findings.

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ABR - 5 weeks of age

- Inpatient evaluation
- Hospitalized for anemia
- Currently taking Ganciclovir
- Parents report no concerns regarding hearing.
- Examination of the ears by an otolaryngologist was performed prior to this appointment.

  - Middle ears were clear.

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ABR - 5 weeks of age

Testing Results/Impressions:

- ABR results revealed a moderately-severe hearing loss bilaterally.
- Limited testing as patient woke up
- Improvement in hearing thresholds

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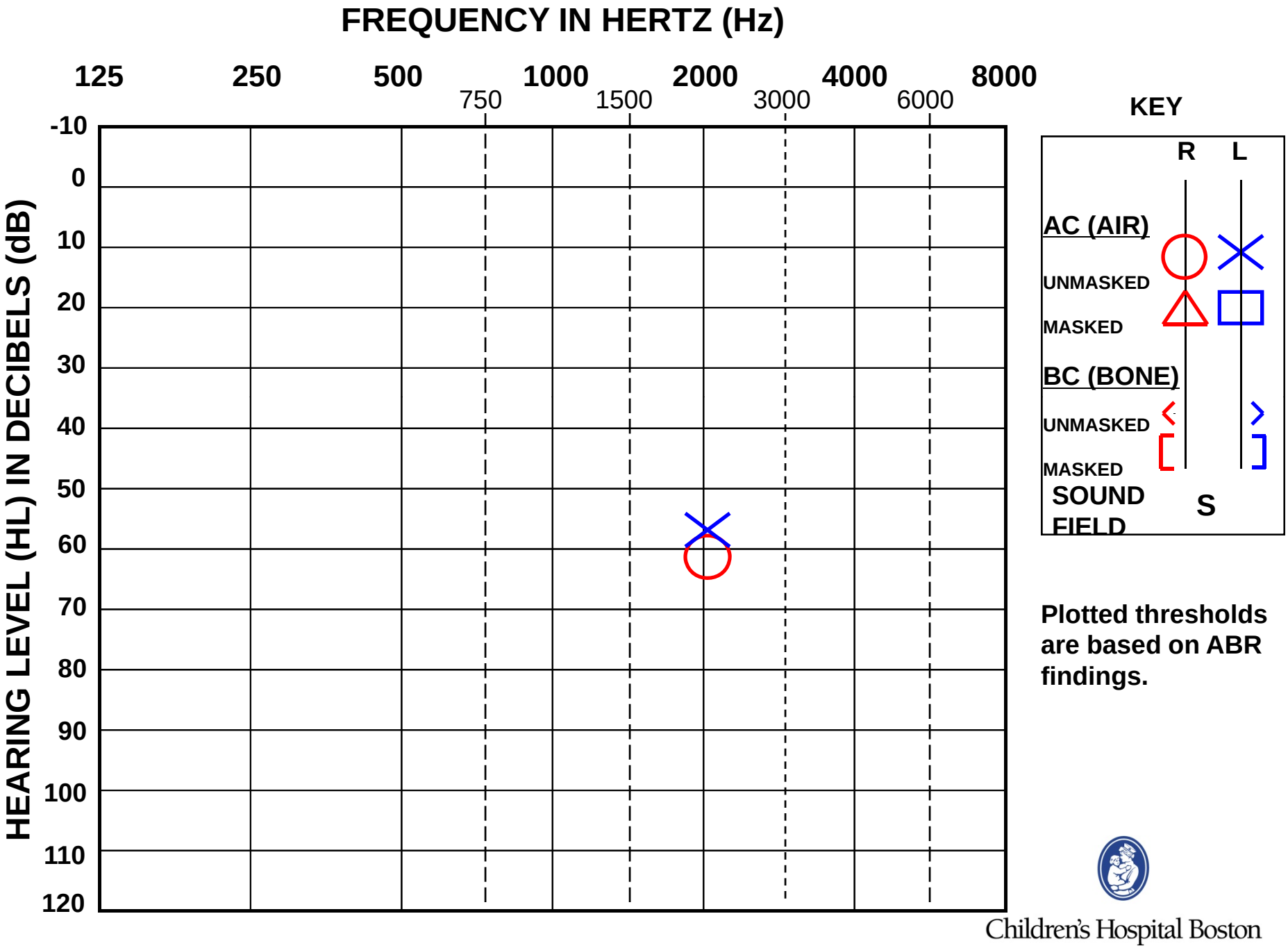

Plotted thresholds are based on ABR findings.

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ABR – 9 and 17 weeks of age

- Outpatient visit
- Still taking Ganciclovir; began smaller doses at 17 weeks of age
- Doing well at both visits, per parent report

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ABR – 9 and 17 weeks of age

Testing Results:

- ABR results:
  - Right ear: Mild high frequency hearing loss
  - Left ear: Normal hearing
- DPOAE results:
  - Right ear: Present 2K-3K Hz, absent 4K-8K Hz
  - Left ear: Present 2K-8K Hz

-Normal tympanograms for both ears

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ABR – 9 and 17 weeks of age

Testing Impressions:

- 9 weeks: Significant improvement in hearing thresholds in comparison to previous testing
- 17 weeks: Noted stability in hearing sensitivity

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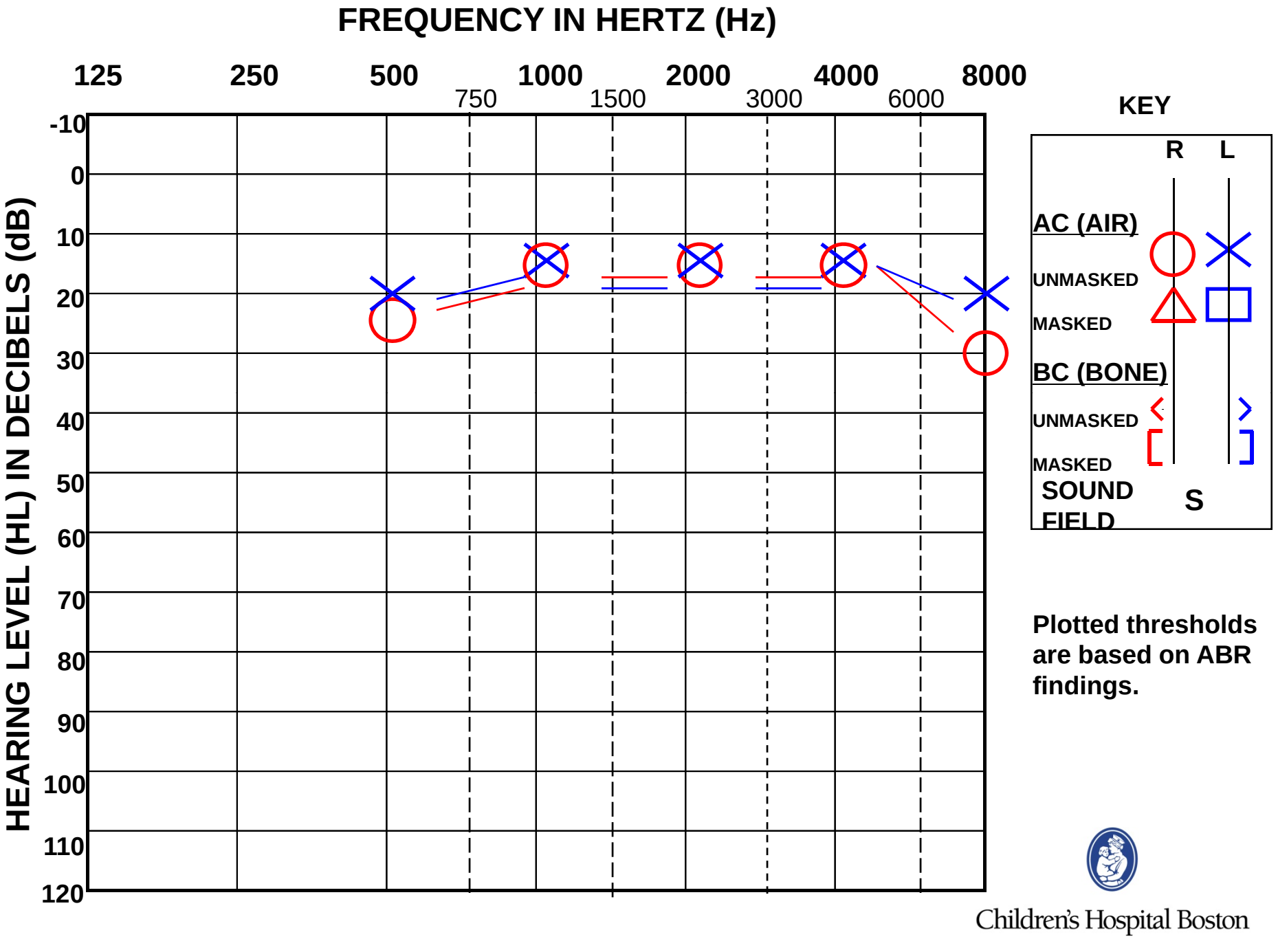

Plotted thresholds are based on ABR findings.

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Future Management

- Audiological follow-up via unsedated ABR testing to monitor hearing sensitivity
- Otologic care per managing otolaryngologist
- Medical management per Infectious Disease (ID) protocol

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Conclusion

- Children diagnosed with CMV are at risk for permanent developmental delay and impairments, including hearing loss.
- Early identification of a CMV diagnosis is crucial so that treatment may be prescribed before irreversible damage occurs.
- Hearing loss associated with CMV can improve with appropriate treatment.
- Audiological follow-up is critical.

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Questions to Consider

- Should all mothers be tested for CMV?
- Should CMV be a part of newborn screening?
  - Use of the dried blood spot
- Should we develop a universal CMV protocol for all babies who refer on the NHS?
- Need for future research

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Profound bilateral sensorineural hearing loss: is that all? (Part 1)

Marilyn Neault, PhD

March 2, 2010

Thank you to Margaret Kenna, MD, Greg Licameli, MD, Heidi Rehm, PhD, and Jennifer Harris, AuD

Is that all?

- Baby girl born to 19 year old mother, healthy pregnancy, full-term birth
- Mother's half-sibling has mild hearing loss
- Bilateral refer on newborn hearing screen
- Diagnostic ABR → profound bilateral sensorineural hearing loss
- Connexin 26 and connexin 30 negative
- Normal ophthalmology exam at 6 months, recheck recommended

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Next chapter

- Parents begin using ASL with baby
- Right cochlear implant surgery at 12 months
- Parents requested test for Usher Syndrome at 17 months because the child was not walking well
- Result: two mutations in the myosin 7A gene (Usher Syndrome Type 1B)

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Sister act

- At the time Usher Syndrome was diagnosed, baby sister had just been born
- Baby sister: bilateral refer on NBS, profound bilateral sensorineural hearing loss
- Autosomal recessive inheritance
- Genetic testing showed the same two mutations on the myosin 7A gene as her sister (F1963del and G1942X)
- G1942X is a novel mutation

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Parental decisions

- Baby sister also received cochlear implant surgery at 12 months
- Parents considering 2nd implants for both girls
- Both use ASL and are developing spoken language

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Usher Syndrome

- Hearing loss at birth
- Vision loss later from retinitis pigmentosa
- 3 - 6.2 per 100,000 in general population
- 0.6 - 28% in deaf population
- Still usually late diagnosis
- Limited availability of genetic testing
- Heterogeneous presentation

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Usher Syndrome

(3-6% of childhood deafness)

Traditional classification

	Hearing Loss	**Vestibular System**	**Retinitis Pigmentosa**
Type I	Congenital profound	Congenital balance problems; absent responses, late walkers (average 20 months)	Onset pre-puberty
Type II	Congenital mild-severe sloping	Normal	Onset in teens-20s
Type III	Progressive later onset	Variable, often progressive balance problems	Variable onset

9 genes pinpointed for Usher so far, and there are more

- Type 1 Usher syndrome:
  MY07A, *USH1C*, *CDH23*, *PCDH15*, *SANS*
- Type 2 Usher syndrome:
  USH2A, *VLGR1, WHRN*
- Type 3 Usher syndrome:
  USH3A

Testing labs listed at www.genetests.org

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Interventions

- Hearing aids
- Cochlear implants
  - Early diagnosis may tip the scales towards CI in families who might not have opted for it in other circumstances
  - Early bilateral CI gives chance for localization
- Physical therapy
- Mobility training
- Vision specialist if vision loss begins early
- Sunglasses, Vitamin A (for Usher Type 2), DHA (fish oil / flax) being studied

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Genetic Testing for Usher Syndrome

- Conservative approach
  - HL with retinal abnormalities (positive ERG test, DAT or pigmentary changes)
- Less conservative approach
  - Profound congenital hearing loss with delayed walking
- Even less conservative approach
  - Test infants and children with moderate to profound SNHL if Cx26 (and possibly Cx30) negative
  - Test infants and children with any bilateral SNHL
- No matter which approach, need genetic counseling

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Parental needs

- Genetic / medical explanations (available)
- Advice for daily living: when and what to tell the child? how make environment safe? (less available)
- Connections with other parents of young children with Usher (rarely local)
  - www.hearseehope.com
- Adult role models with Usher Syndrome and early cochlear implantation (rare)

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Profound bilateral sensorineural hearing loss: is that all? (Part 2)

Marilyn Neault, PhD

March 2, 2010

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Baby Boy

- Full term healthy baby, bilateral refer
- Somalian parents, little English, interpreter used for all visits
- Diagnostic ABR at 7 weeks showed profound bilateral sensorineural hearing loss
- Parents: “We accept it. It is from God.”

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Medical evaluation

- As part of routine workup for profound SNHL, otolaryngologist recommended an electrocardiogram
- Result: markedly prolonged QT interval
- Genetic testing:
  homozygous deletion in the LQT1 gene
- Diagnosis:
  Jervell and Lange-Nielsen Syndrome (JLN)
- Incidence 1 / 160,000 to 1 / 600,000
- Autosomal recessive inheritance

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Interventions for hearing loss

- Audiogram showed no response to any sound
- Brief trial of loaned hearing aids, no response
- Family Sign Language Program
- Cochlear implant at 2 years 9 months (VERY difficult decision for parents)
- Child is a late walker (>24 months)

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Importance of JLN diagnosis

- Long QT in EKG means high risk of fainting and even sudden death
- Caregivers must be aware
- Long QT should be known pre-anesthesia for CI
- Treatment: medication (beta blocker)
- Must avoid QT-prolonging medications
- Cardiologist recommended implanting a defibrillator (parents declined)
- Parents were tested for long QT → mother has it and is now medicated

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Take-home messages

- Medical workup and genetic testing are good for more than satisfying curiosity
- Other important conditions can be found apart from the hearing loss
- Other family members may also have the related condition and be unaware

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Results of an Atypical ABR:

Refer from UNHS

Cheryl Edwards, AuD

March 2, 2010

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History

- Born full term, without complication
- Referred in left ear only on AABR screen
- Seen for Dx ABR at 7 weeks of age
- No parental concerns re: hearing
- No family history reported at that time

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Results

- 1000 Hz tympanograms
  - Normal bilaterally
- Ipsi MEMR
  - present 500 Hz – 2000 Hz, left
  - DNT, right
- DPOAEs
  - Present bilaterally
    - 1500 Hz – 8000 Hz, right; 2000 Hz – 8000 Hz, left

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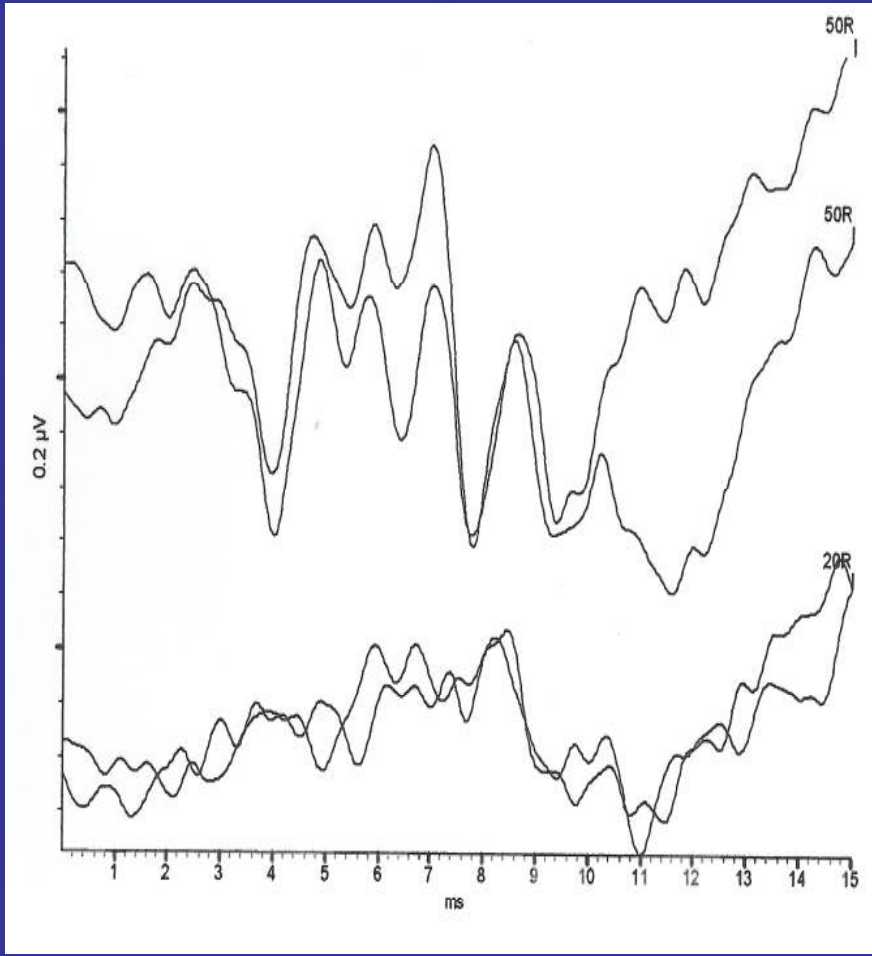
Right Ear



- Click stimuli at 50 dBnHL and 20 dBnHL
- Click rate decreased from 51.1/sec to 21.1/sec
- Tone Burst ABR elicited Wave V thresholds within normal limits from 1000 Hz – 8000 Hz.

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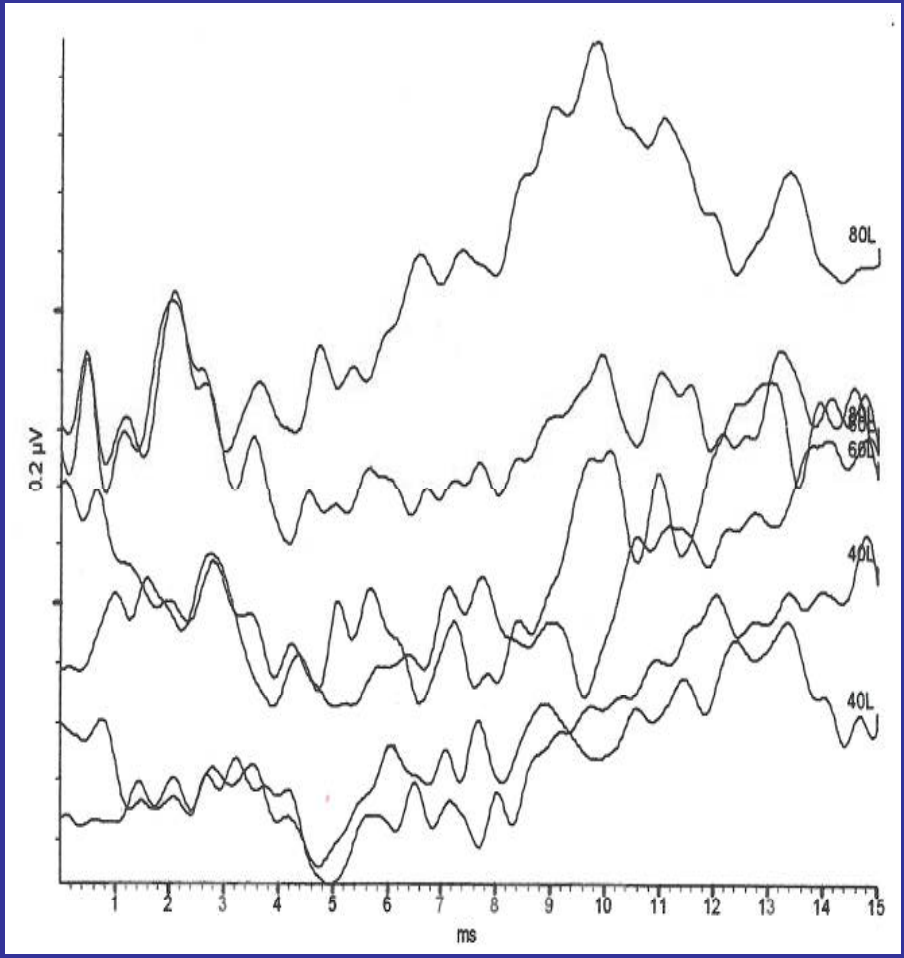
Left Ear



- Wave I with latency-intensity function to 40 dBnHL.
- Comparison of condensation and rarefaction polarities did not yield an abnormal CM

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Follow-up

- Referred to Otolaryngology; imaging deferred until after second ABR
- Testing at 3 months:
  - Tympanograms: Normal
  - Ipsi MEMR: present, right; absent, left
  - ABR: Same responses, morphology worse
    - Slowed rate to 11.1/sec in the left ear
- Otolaryngology: recommended MRI

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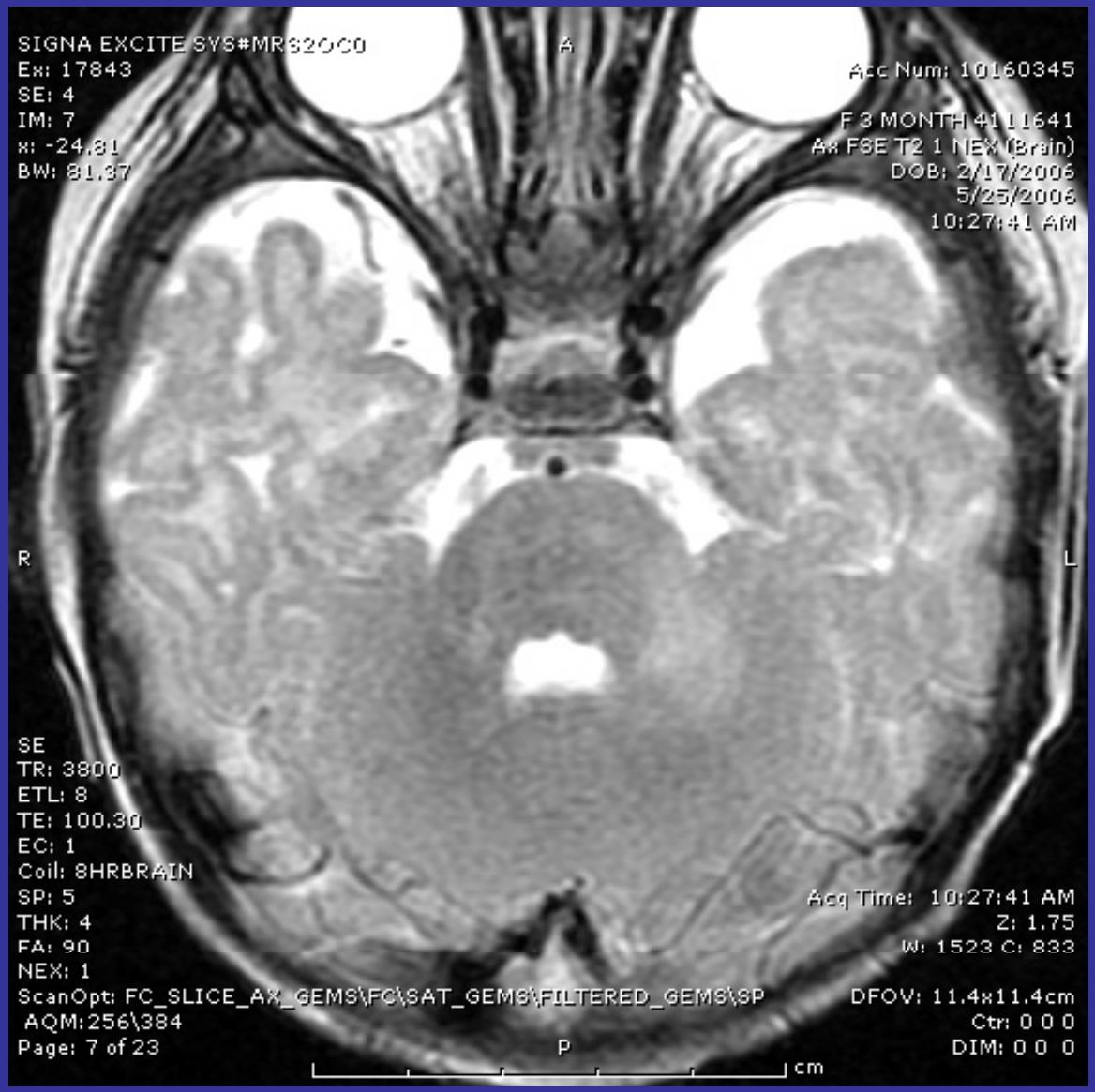
MRI – 3 months



0.6 cm x 0.6 cm
x 0.9 cm

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Radiology/Neurosurgery

- Unknown if mass is a tumor or vascular malformation (hemangioma)
- Felt that left ABR is affected due to involvement of the cerebellar peduncle
- Due to location, biopsy was deferred and monitoring via MRI recommended

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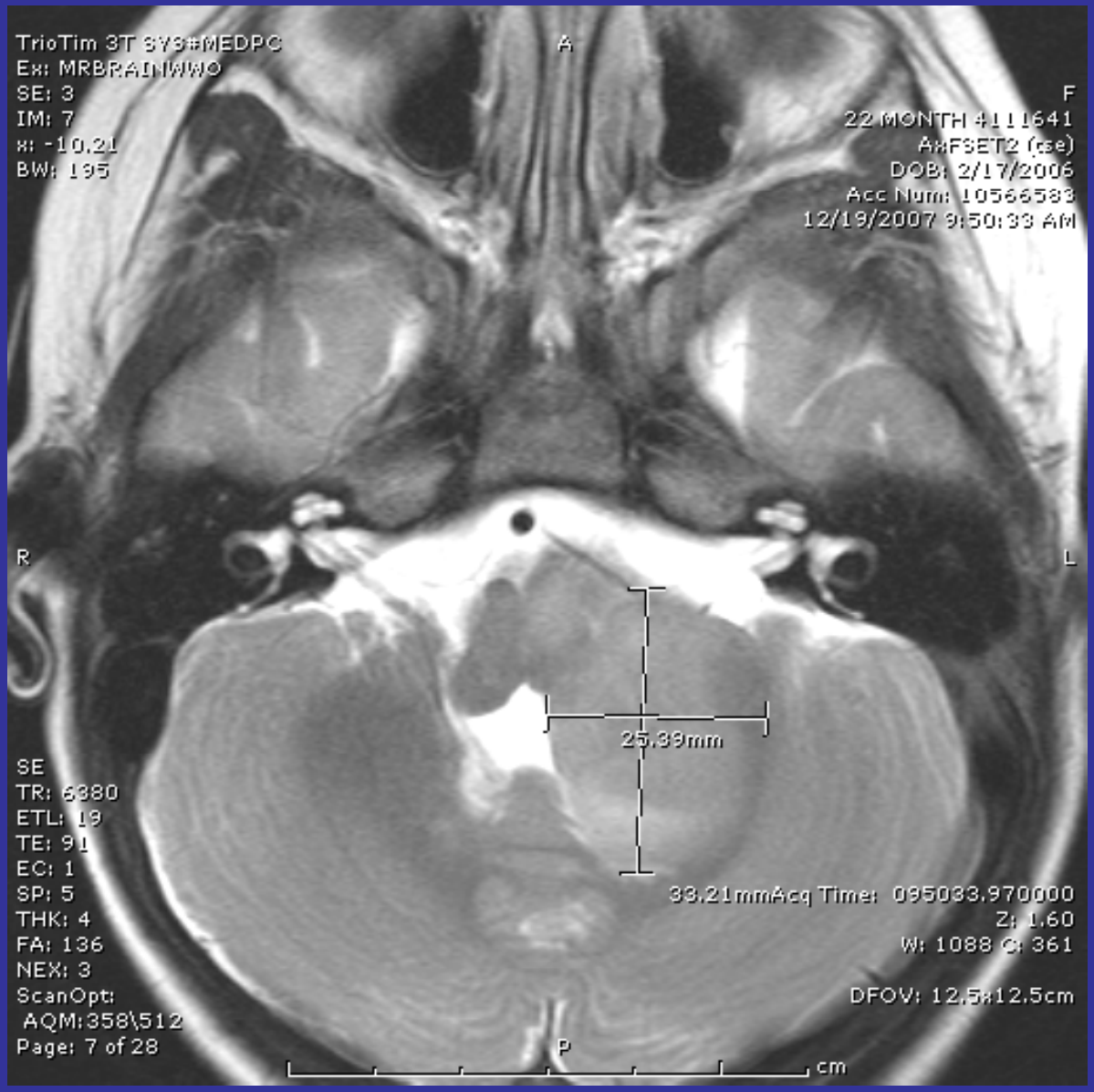
MRI – 22 months



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Biopsy completed at 12 months

- Low grade pilocytic astrocytoma
  - Extends into cerebellum, dorsal pons and lower medulla
- Chemotherapy initiated at 14 months
  - Vincristine and carboplatin
- Mass has remained stable at 2.6 x 2.0 cm

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Status: age 2 years

- Hearing
  - Evaluated every 3 months
  - Normal in sound field
  - SAT of 40 dB HL in the left ear
    - Not a big fan of the headphones
- Social and engaging
- 200 words, can sing ABCs
- OT/PT every 2 weeks
- Mobility increased, gait “unstable”
- Intermittent nystagmus, eye crossing
  - Using glasses

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Conclusions

- What if OAEs had been used for screening …or follow-up
- Close collaboration with ORL, Genetics, Neurology, Neurosurgery, Ophthalmology, Radiology

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Thank you!

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