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Diagnosis of Auditory Neuropathy Spectrum Disorder in Children

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Outline

- Brief Overview
- Etiologies
- Counseling Families
- What to Do
- Case examples showing variability in presentation of ANSD

ANSD: Audiologic Findings

- Normal outer hair cell function as measured by present otoacoustic emissions (OAEs) or the presence of a cochlear microphonic (CM).
 - OAEs may be present initially but disappear over time, or be absent at time of diagnosis
(Starr et al, 1996)
- Abnormal auditory nerve response as observed by absent or markedly abnormal ABR
- Acoustic reflexes are absent in most cases
(Berlin et al 2005, 2010)

ANSD: Audiologic Findings

- Individuals affected by the disorder may perform differently than those with typical cochlear hearing loss
 - » “Typical” SNHL results in impaired frequency resolution
 - » AN is thought to affect timing of neural activity and
 - » Disrupt perception based on temporal cues
(Starr et al 1991,1996; Berlin et al.,1993; Hood, 1999; Zeng et al 1999, 2005; Kraus et al, 2000; Rance et al 2004)

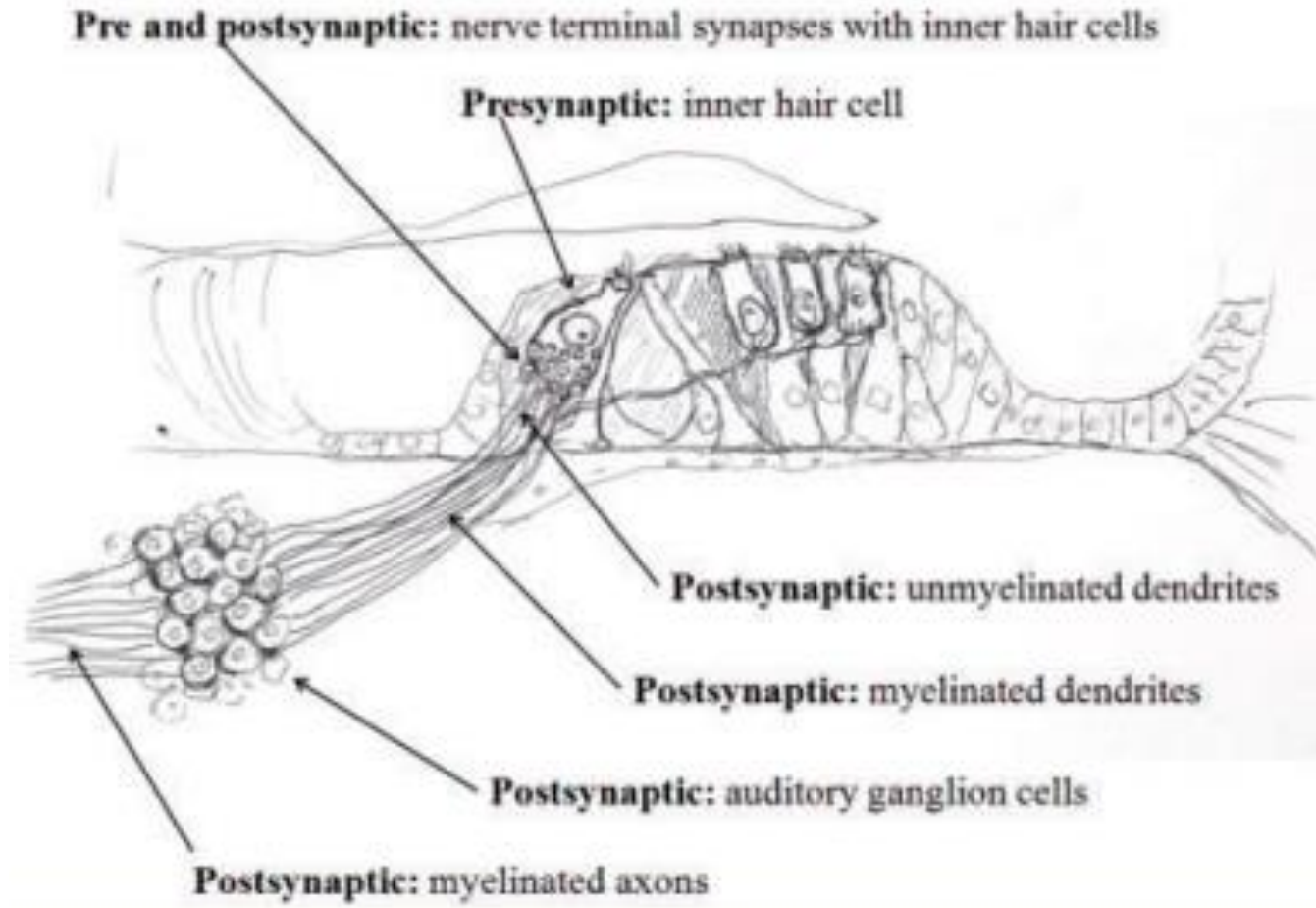
Clinical Characteristics Reported

- Pure tone thresholds ranging from normal to profound
- Disproportionately poor speech recognition abilities for the degree of hearing loss
- Difficulty hearing in noise
- Impaired temporal processing
- Hearing fluctuation
 - » Temperature sensitive AN reported by Starr et al
- Some individuals with AN have little or no communication difficulties while others are functionally deaf
- **Not all individuals diagnosed with ANSD experience the same problems or to the same degree**

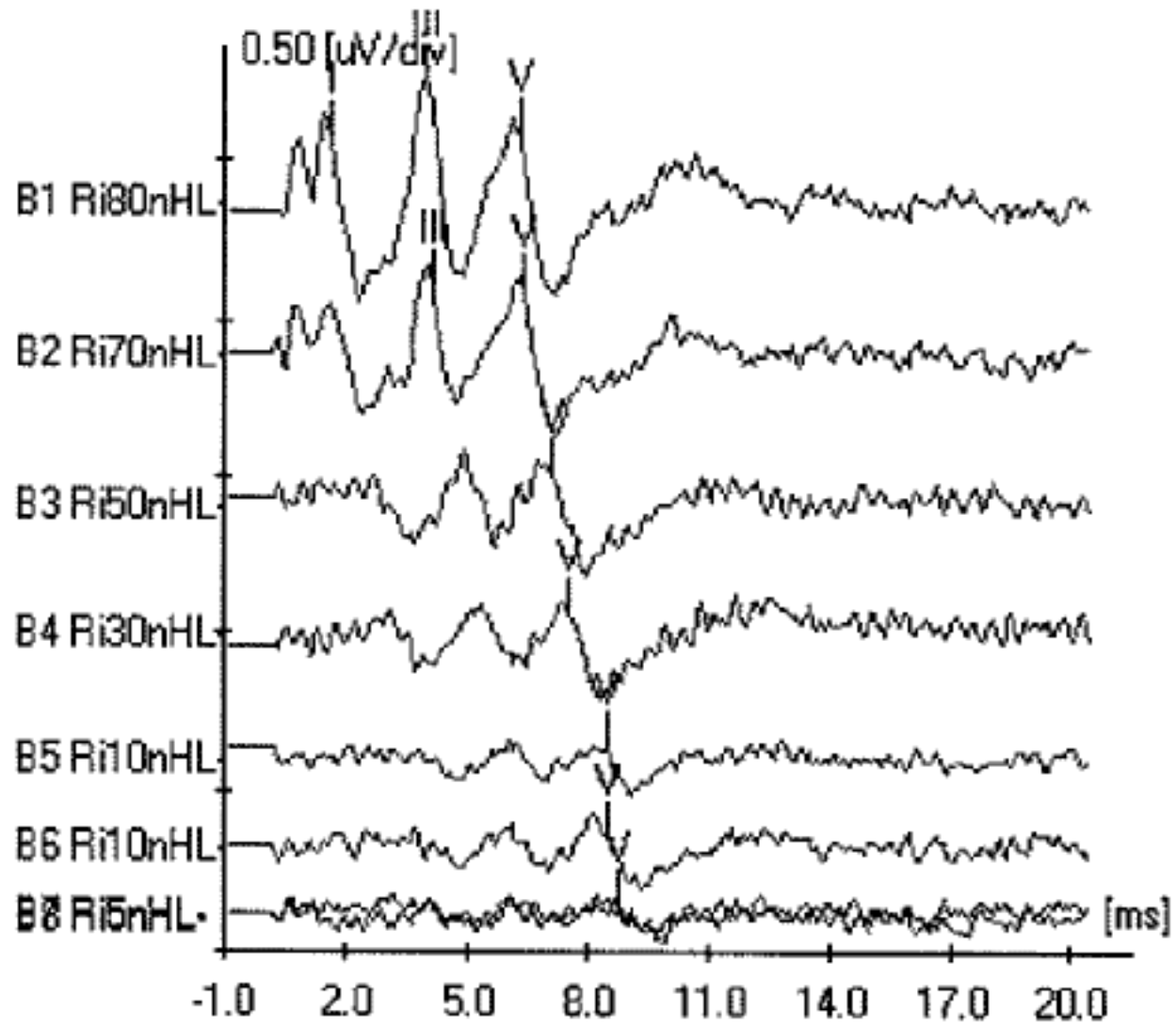
(Starr et al 1996, Zeng et al 1999, Kraus et al 2000, Rance et al; 2002; 2004; 2005, Zeng and Liu, 2006)



Auditory Neuropathy: Various Sites of Lesions

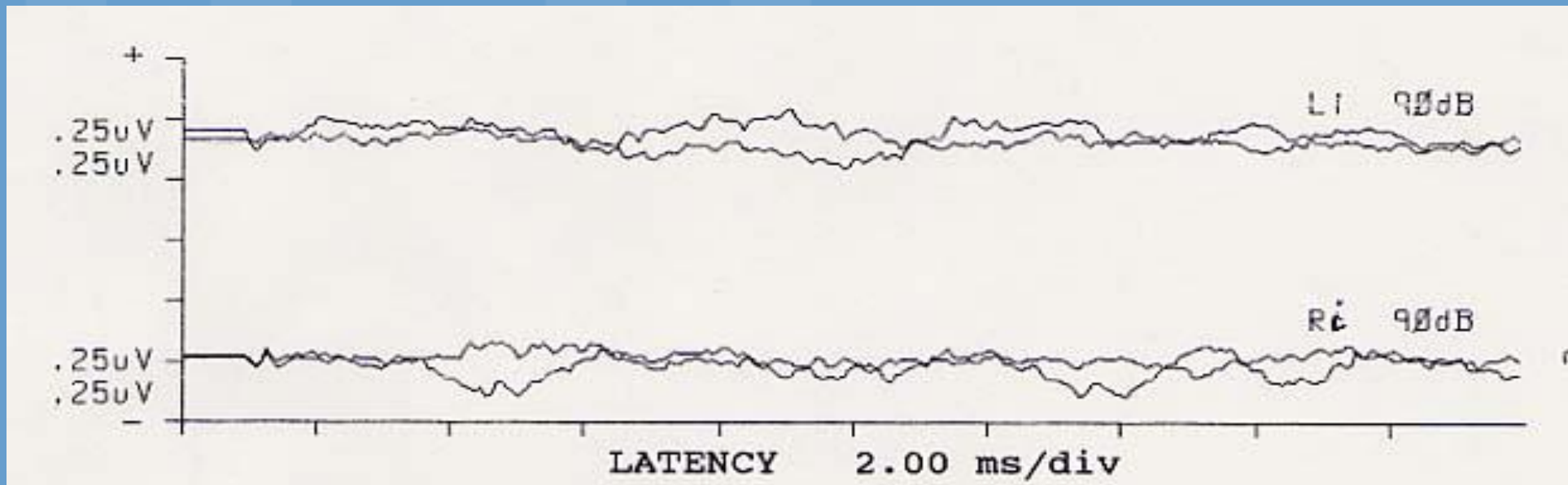


Normal ABR



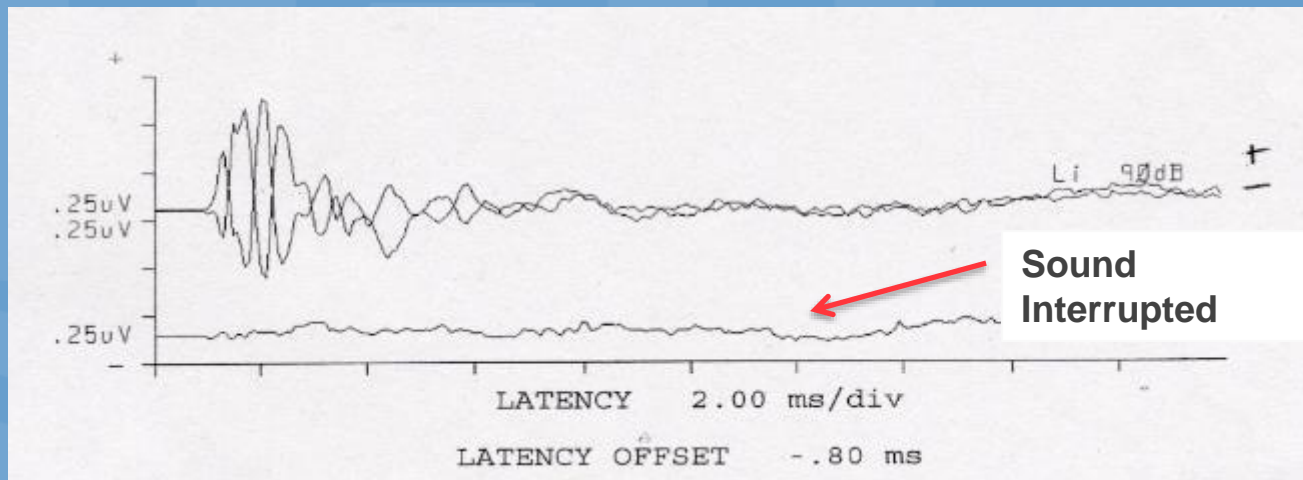
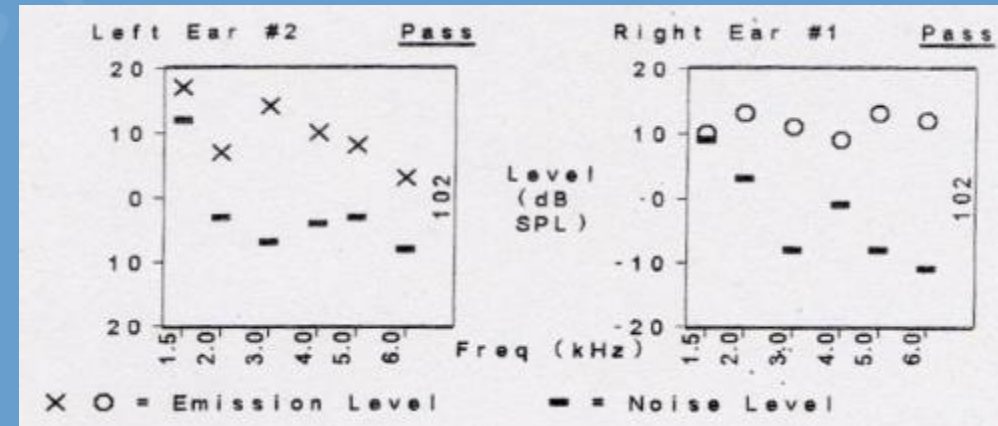
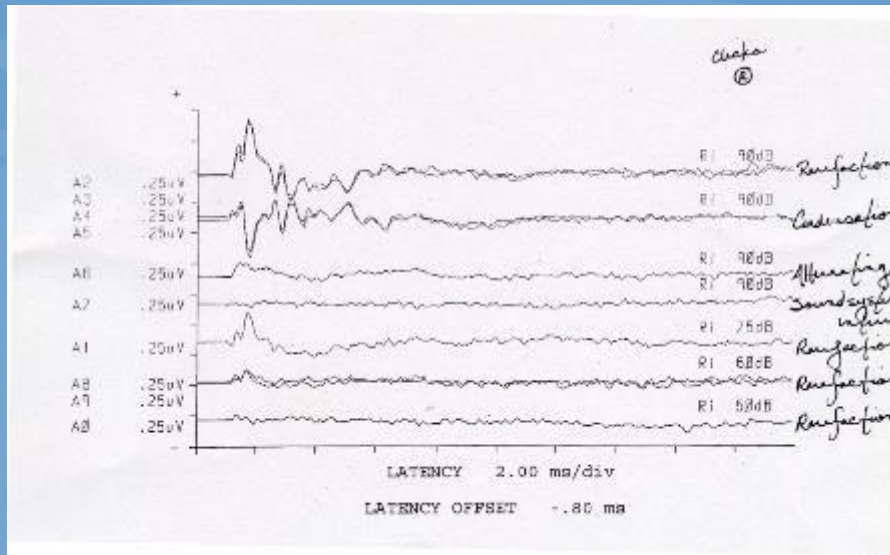


Absent ABR with No Cochlear Microphonic: Child with profound hearing loss



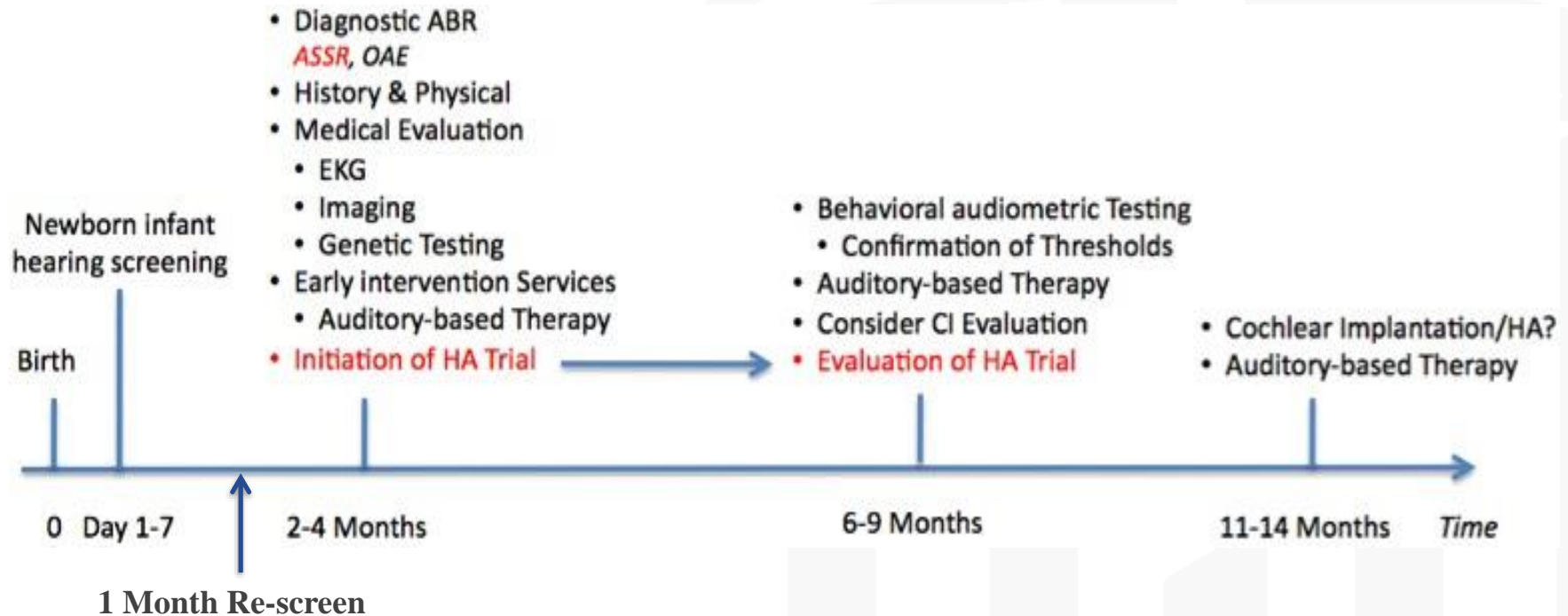
Typical Pattern of ANSD

Abnormal ABR with Present CM





Timeline Following Diagnosis of HL



ABR Protocol for Evaluating CM

- Must have adequate recording conditions
 - Infant ready to sleep (natural or sedated sleep)
 - Avoid electrodes positioned over transducer
- *Single polarity* clicks at 90dBnHL with rarefaction and condensation polarities. Caution: know your equipment and follow protocol to rule out ANSD
 - If using alternating polarity, be certain to look at rarefaction and condensation runs separately
- Tone bursts can also be evaluated but use caution in using present neural responses to estimate thresholds
- Must use insert earphones
 - Excessive stimulus artifact with standard headphones obscures cochlear microphonic
- Sound interrupted run with stimulus on but sound tube disconnected or clamped to check for stimulus artifact



Etiologies and Associations

➤ Genetic Etiologies:

» Syndromic:

- Charcot-Marie-Tooth disease
- Friedrich's Ataxia; Hereditary motor and sensory neuropathy (HSMN)
- Brown Vialetto-Van Laere syndrome

» Non-syndromic:

- Recessive genetic mutations:
 - » Otoferlin (OTOF), Pejvakin (PJKV)
- Autosomal dominant mutations:
 - » (AUNA1) (onset of auditory symptoms in late teens): (OPA1) (optic neuropathy and moderate HL)

➤ Perinatal Conditions:

- » Hyperbilirubinemia
- » Hypoxia
- » Low birth weight

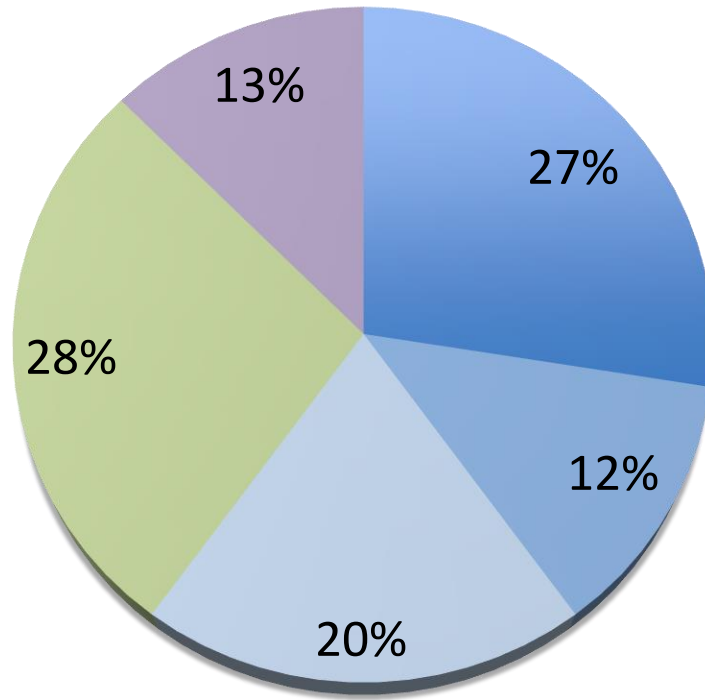
Etiologies and Associations

- Congenital Conditions:
 - » Cochlear Nerve Deficiency (Buchman et al 2006)
- Mitochondrial Disorders
- Infectious Processes
 - » Viral Infections (e.g. mumps, meningitis)
- Head injury
 - » Shaken baby syndrome

Rance (2005);Rapin & Gravel (2003);Starr et al. (2003); Hayes 2011



Gestational Age at Birth (n=35)



- Extremely preterm (< 28 weeks)
- Very preterm (28- < 32 weeks)
- Moderately preterm (32- < 37 weeks)
- Full term (≥ 37 weeks)
- Unknown

*Challenges in Early Management of Children with ANSD:
Analysis of the Timeline from Diagnosis to Intervention*
Kim Holden, B.S., Patricia Roush, AuD

Brown-Vialetto-Van Laere Syndrome 2

- Mutations in SLC52A2 are associated with a rare neurologic, autosomal recessive disorder: Brown-Vialetto Van Laere Syndrome
- Brown-Vialetto-Van Laere Syndrome 2 (BVVLS2) is a progressive neurodegenerative disease that is a consequence of severe riboflavin (vitamin B2) deficiency.
- Prevalence very low
- Patients mostly present with hearing loss, bulbar palsy and respiratory compromise
- Age of onset varies from infancy to adulthood
- Untreated BVVL is a rare and often fatal disorder
- All patients to date have been diagnosed with ANSD

(Bosch et al 2012)



Brown-Vialetto Van Laere Syndrome 2 (BVVLS2)

- Previously, no effective treatment but in past few years researchers discovered that high doses of vitamin B2 in some patients have had dramatic effects on halting progression of disease, especially when started early in disease course.
- A small subset of children diagnosed with ANSD will have conditions associated with progressive neurologic disease such as Brown Vialetto Van Laere .
- Although Brown Vialetto Van Laere is a rare disorder; it is likely undiagnosed in some children and adults.
- Brown Vialetto Van Laere or other progressive neurologic diseases should be considered in differential diagnosis for children who present with ANSD

Typical Audiologic Test Battery

- Auditory Brainstem Response (ABR)
- Acoustic Immittance Measures
 - » Tympanometry
 - » Acoustic Reflex Testing
- Otoacoustic Emissions Testing
- Behavioral Audiometry
 - » VRA, BOA, play audiometry
- Speech Recognition Testing
- Cortical Evoked Potentials as needed

Otologic Examination

- Medical History
- Ear Exam
- Etiology
- Evaluate for other associated problems
 - » Seizures
 - » Motor delays
 - » Visual problems
 - » Ear canal problems
 - » Otitis media
- Radiologic Studies (MRI/CT)
 - » Inner ear malformations
 - » Cochlear nerve integrity
- Consider neurology and genetics consults
- Other studies as needed

Cochlear Nerve Deficiency (CND) (May present with ANSD pattern)

- Small or absent VIII nerve
- Must perform MRI to determine if VIII nerve is small or absent
- CT may show normal internal auditory canal when cochlear nerve is absent
- In cases when there is question of CND both CT and MRI imaging may be needed
- Imaging is especially important when behavioral audiometry shows profound hearing loss

UNC Children with Characteristics of ANSD and Available MRI (2009)

N=140

- 35/140 (25%) Cochlear Nerve Deficiency (CND)
(absent or small cochlear nerve) in one or both ears
 - » Unilateral (n=24; 69%)
 - » Bilateral (n=11; 31%)

Buchman, C, Roush P, Teagle H, Brown C, Zdanski C, Grose J.
Auditory neuropathy characteristics in children with cochlear
nerve deficiency. *Ear Hear.* 2006 Aug;27(4):399-408



Can Cortical Evoked Potentials (CAEPs) Help?

- ABR evaluates outer ear to lower brainstem
- CAEP evaluates outer ear to auditory cortex
- CAEPs not as reliant on timing as earlier evoked potentials and may be present when ABR is not
(Hood, 1998, Rapin and Gravel, 2003)
- Unlike ABR must be completed in awake (but quiet) infants
(Cone Wesson and Wunderlich, 2003)
- Further CAEP research needed with normal infants and infants with SNHL and ANSD

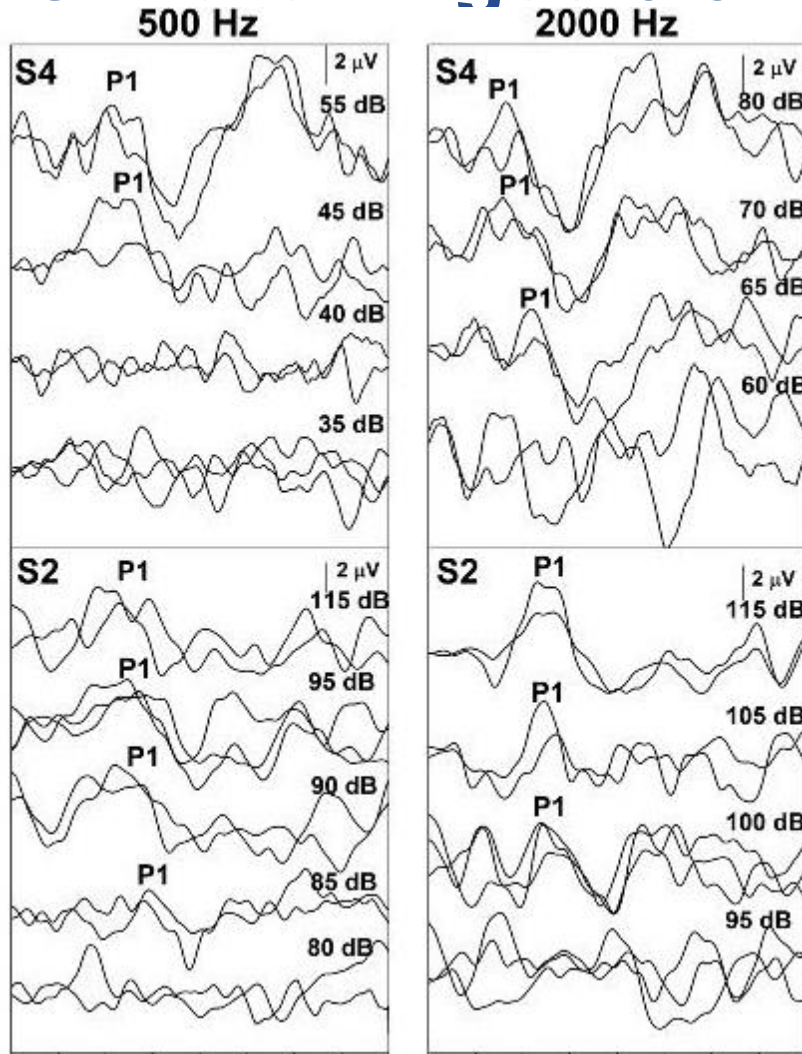


Objective Hearing Threshold Estimation in Children With Auditory Neuropathy Spectrum Disorder

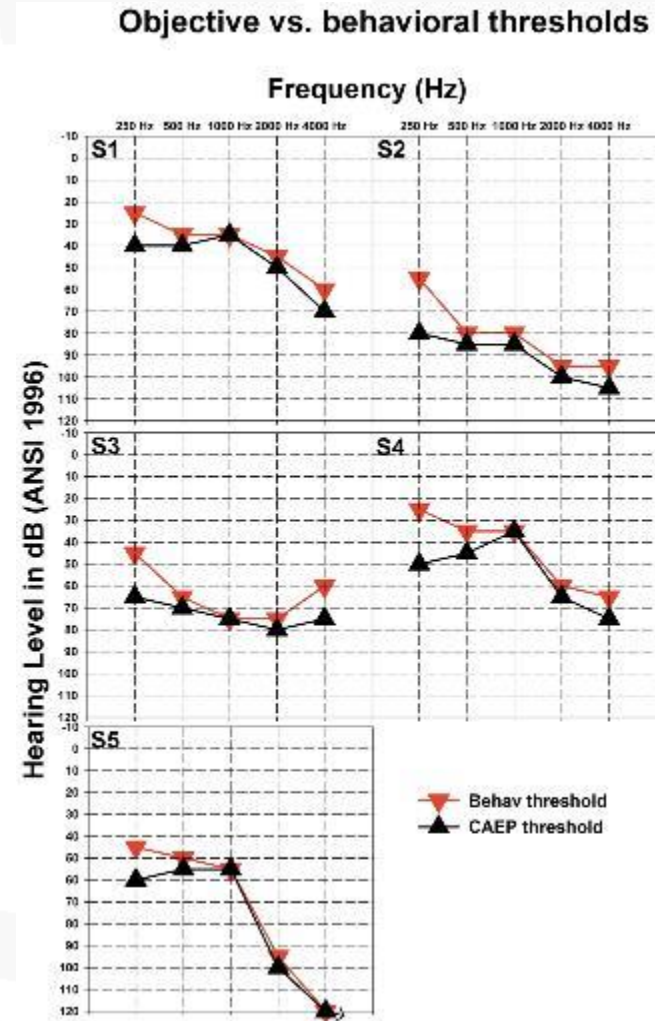
Shuman He, MD, PhD; Holly F. B. Teagle, AuD; Patricia Roush, AuD; John H. Grose, PhD; Craig A. Buchman, MD

The Laryngoscope. 2013 Nov;123(11):2859-61

CAEP Threshold Estimation in ANSD 5 Children Ages 6.5-11.3 Years



P. Roush 2017



Summary of UNC Protocol for Management of Infants with ANSD

- Diagnose ANSD using ABR with single polarity clicks
- Counsel family about recommended steps in first year of life
- Enroll in early intervention
- Complete otologic exam including imaging with MRI (and CT if needed)
- Attempt behavioral audiometry with VRA beginning at 6-7 months developmental age
- Fit child with hearing aids as soon as behavioral thresholds have been established

Summary of UNC Protocol for Management of Infants with ANSD

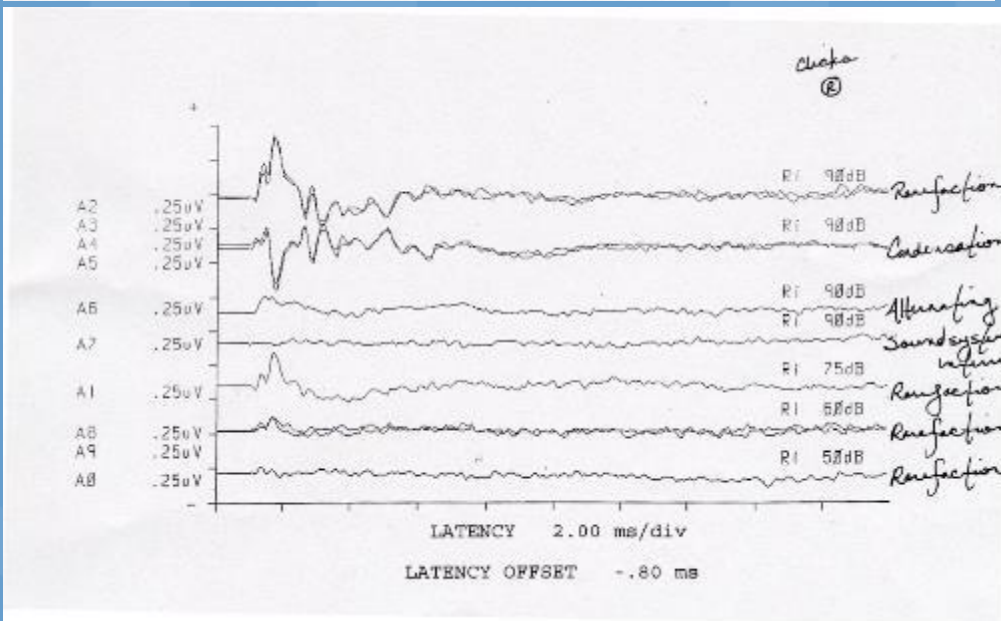
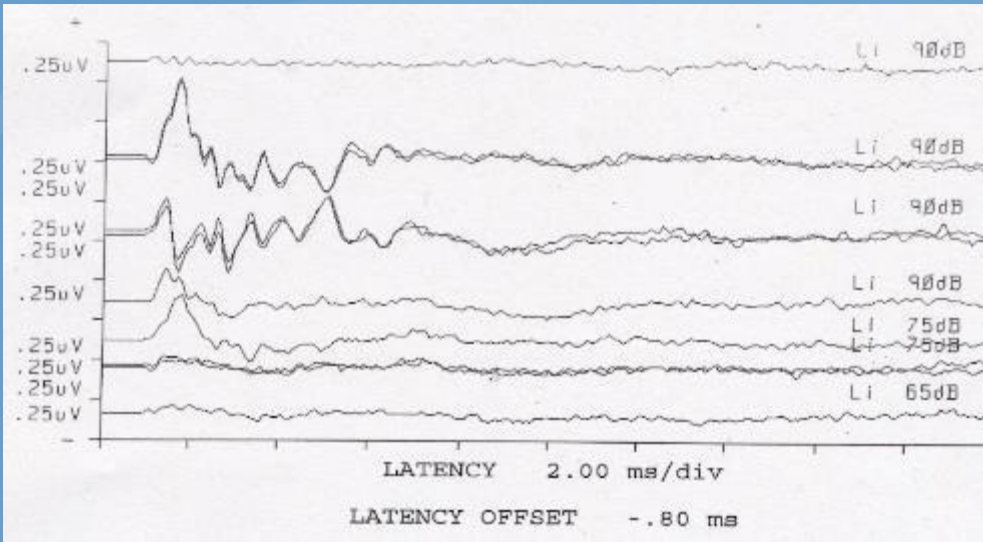
- Set hearing aids to match targets for gain and output using prescriptive formula, measured RECDs and HA verification
- Perform hierarchical battery of speech perception tests
- Regularly communicate with early intervention teacher and parent re communication progress
- Evaluate and monitor progress and take action if child falling behind
- Consider CI if benefit from amplification insufficient for continued progress in communication skill development
- Use cortical evoked potentials to aid with management when needed
- Refer for comprehensive developmental evaluation when child has complex needs



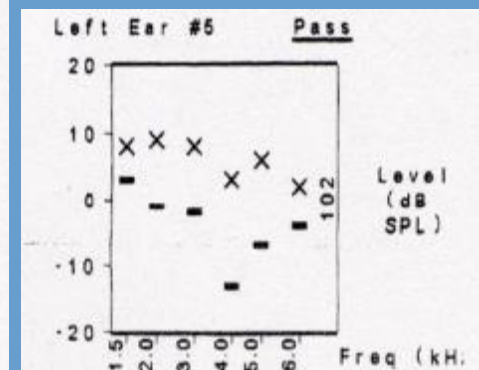
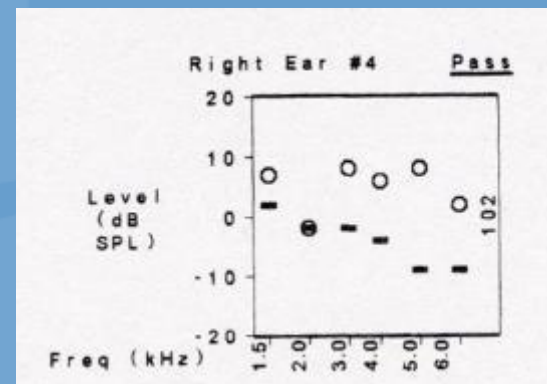
Variable Presentations of ANSD

Case Examples

Case #1: Present CM and OAEs

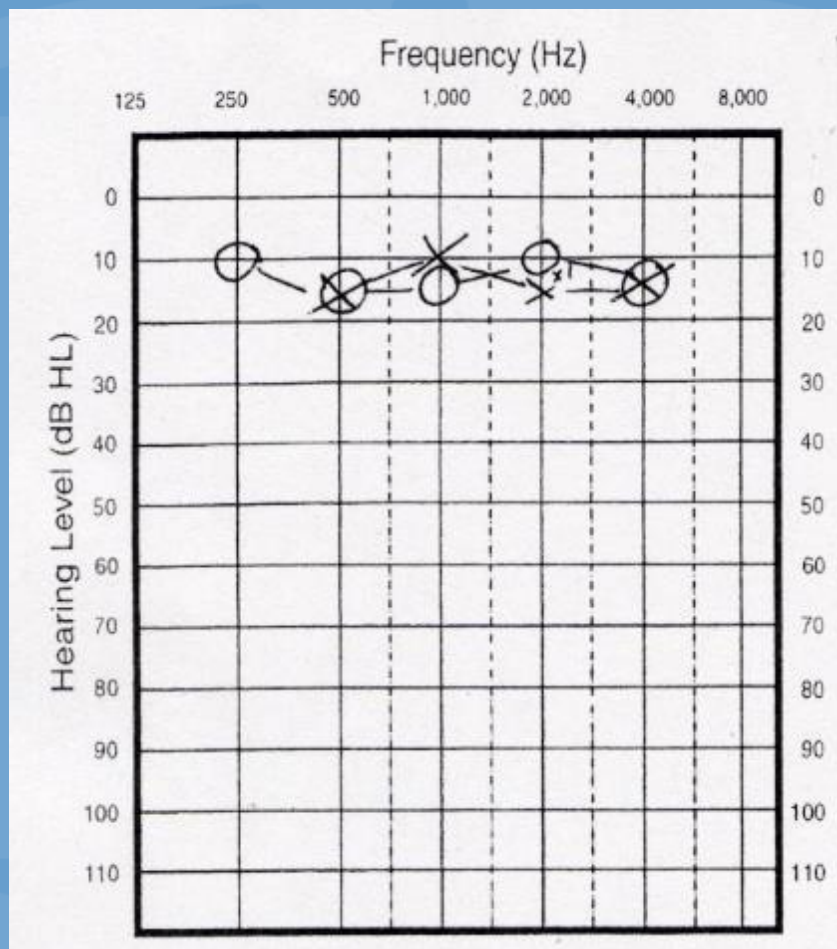


- 24 wk preemie, 940 grams
- NICU 4 months, ventilated
- ABR at 4 and 5 months of age abnormal
- ABR repeated at 18 months-no change

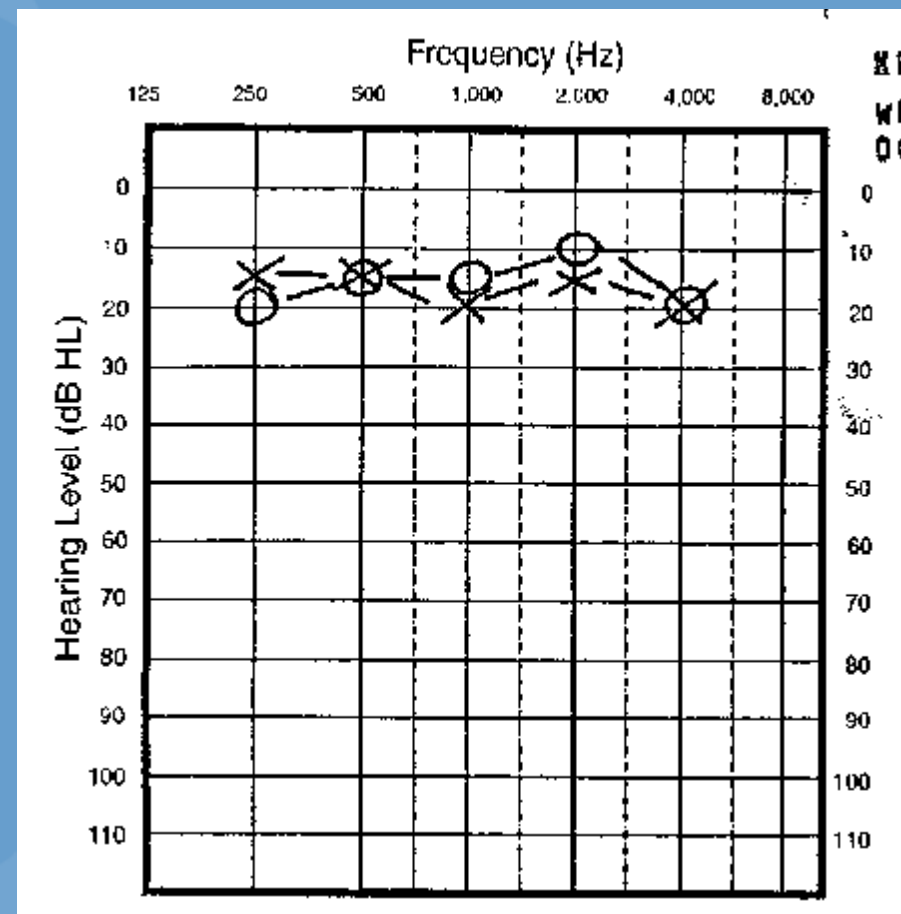


Case #1

Normal thresholds, Present CM and OAEs



Audiogram at 14 months



Audiogram at 18 months

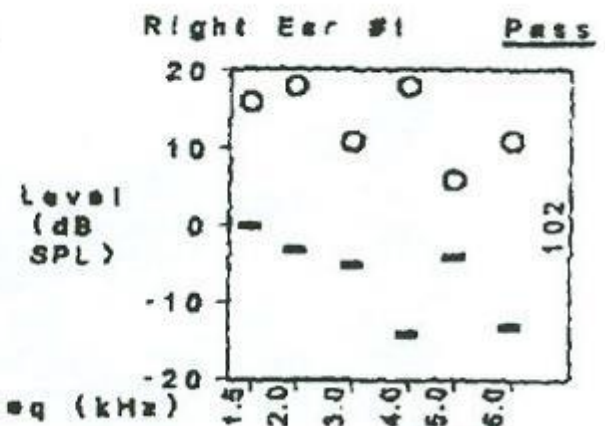
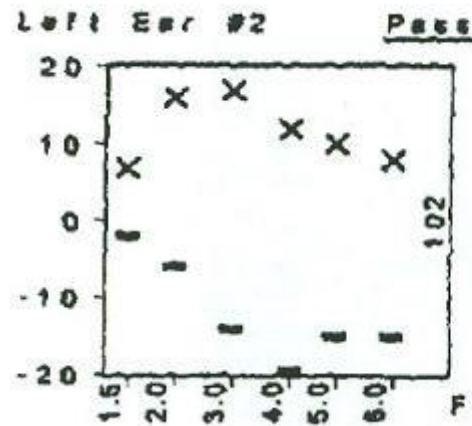
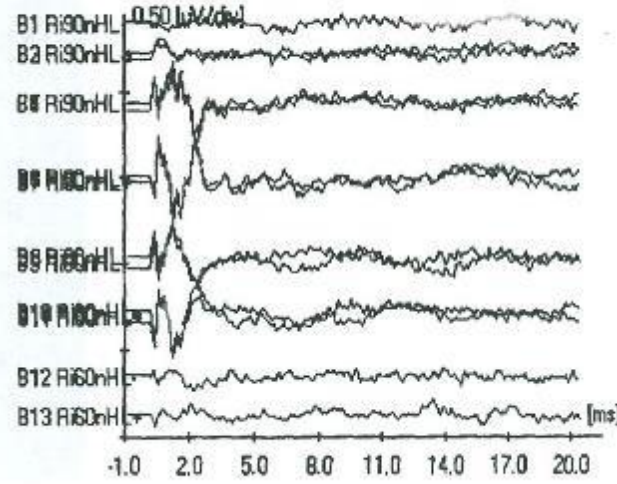
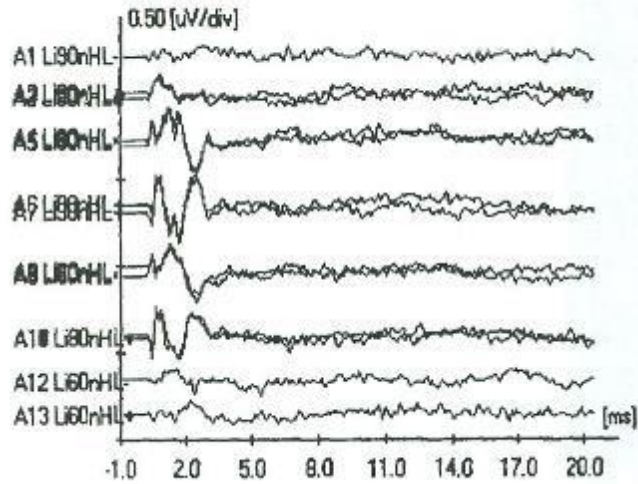
Case #1

Speech Perception Test Results

- Age 2 yrs-11 months:
 - ESP monosyllabic word test (closed set test of speech perception):
 - 12/12 correct for each ear at 50dBHL
- Age 5 years:
 - PBK words: 80% and 84% at 60dBHL for right and left ears
- Will continue to monitor hearing thresholds, auditory, speech and language abilities

Case #2

Abnormal ABR with Present CM and OAEs

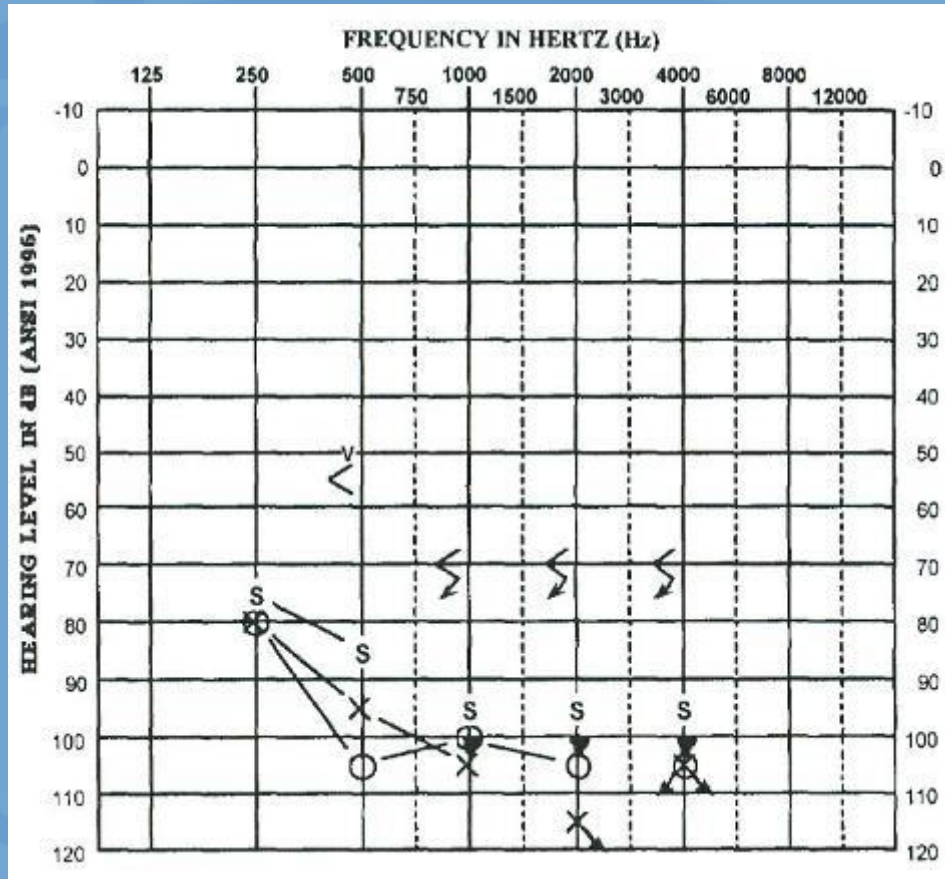


Case #2

Child with Profound Bilateral HL
Present CM and OAEs



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Ear exam: *Normal*

EKG: *Normal*

MRI: *Normal*

Connexin test: *Negative*

Otoferlin test: **POSITIVE**

Received CI at 24
months of age

Case # 3 Background

- 25 weeks gestation
- Ventilated for 6 weeks
- Oxygen 3 ½ months
- Hyperbilirubinemia
 - » Treated with lights, exchange transfusion
- Treated with antibiotics and diuretics
- Hospitalized 4 ½ months
- No family history of hearing loss
- Did not pass newborn hearing screen at hospital discharge
- Initially diagnosed with profound bilateral SNHL at an outside clinic and fitted with high gain hearing aids

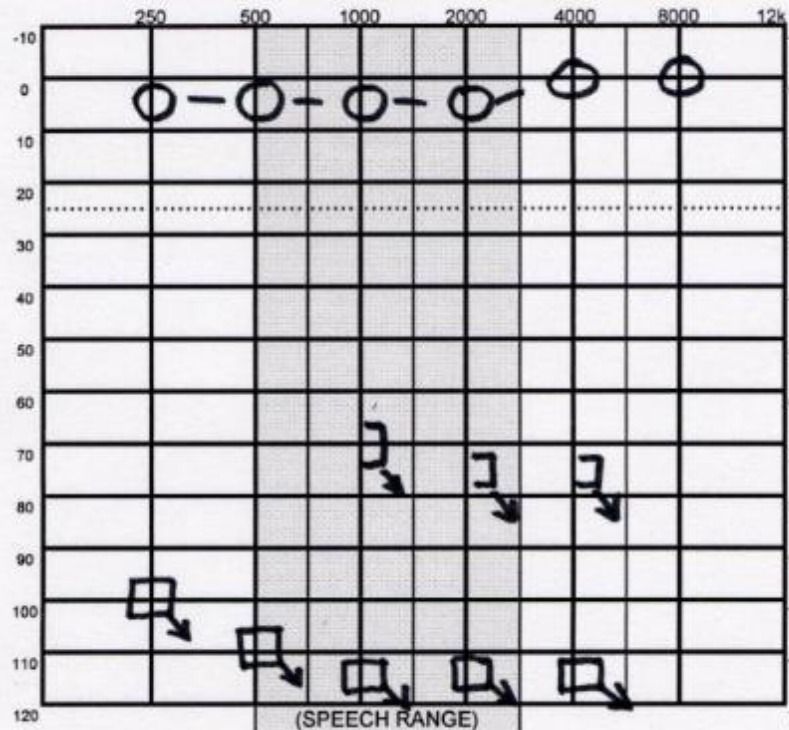
Case #4

- Child born at full term
- No family history of hearing loss
- Presented to clinic with left profound unilateral hearing loss at 4 years of age.
- Passed newborn hearing screen using OAEs

Case # 4



PURE TONE AUDIOMETRY (RE: ANSI 1969)



	RIGHT (RED)	LEFT (BLUE)
Air	O	X
Air (Opp. Ear Masked)	Δ	□
Bone	<	>
Bone (Opp. Ear Masked)	[]
No Response	↓	↓
SOUND FIELD	S	
AGED	R	L

TEST	
STANDARD	
PLAY	
COR/VRA	
BOA	
SITE	
BOOTH	
OTHER	

RELIABILITY	
EXCELLENT	
GOOD	
FAIR	
POOR	

Left Ear #3

TYMPANOMETRY

CONTRA (Phone Ear)	.5k Hz	1k Hz	2k Hz	4k Hz
RIGHT (AD)				
LEFT (AS)				

IPSI (Probe Ear)	.5k Hz	1k Hz	2k Hz	4k Hz
RIGHT (AD)	85	85	85	
LEFT (AS)	NR	NR	NR	

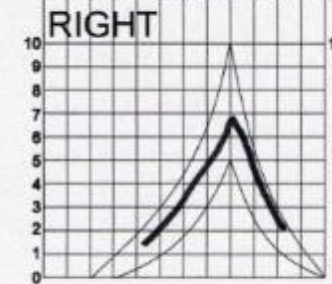
REFLEX DECAY @ 1k Hz STATIC COMPLIANCE

RIGHT (AD)		
LEFT (AS)		

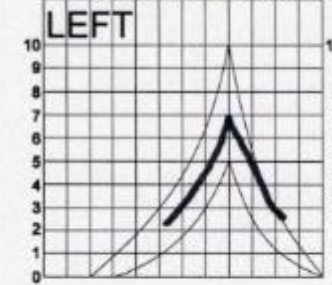
MODE

STANDARD EARPHONES	
INSERT EARPHONES	
SOUND FIELD TESTING	
ASSISTED EVALUATION	

-300 -200 -100 0 100 200

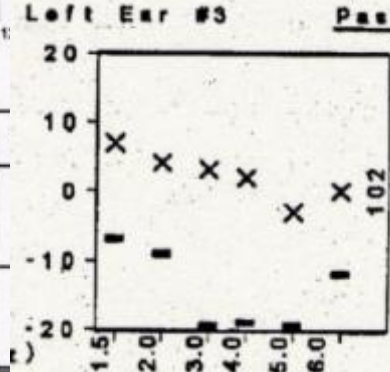


-300 -200 -100 0 100 200

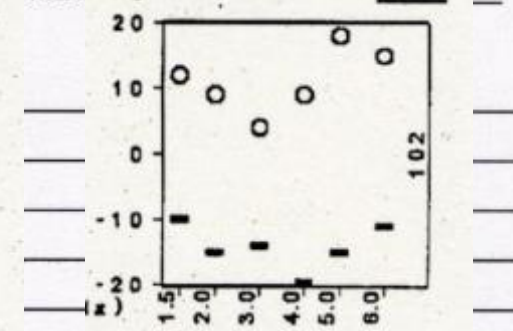


SPEECH AUDIOMETRY

	PTA	SRT/SAT	SPEECH RECOGNITION		SPEECH RECOGNITION		MCL
			%	dB HL	%	dB HL	
RIGHT (AD)		0	100	50			
masking							
LEFT (AS)		NR	CNT				
masking							



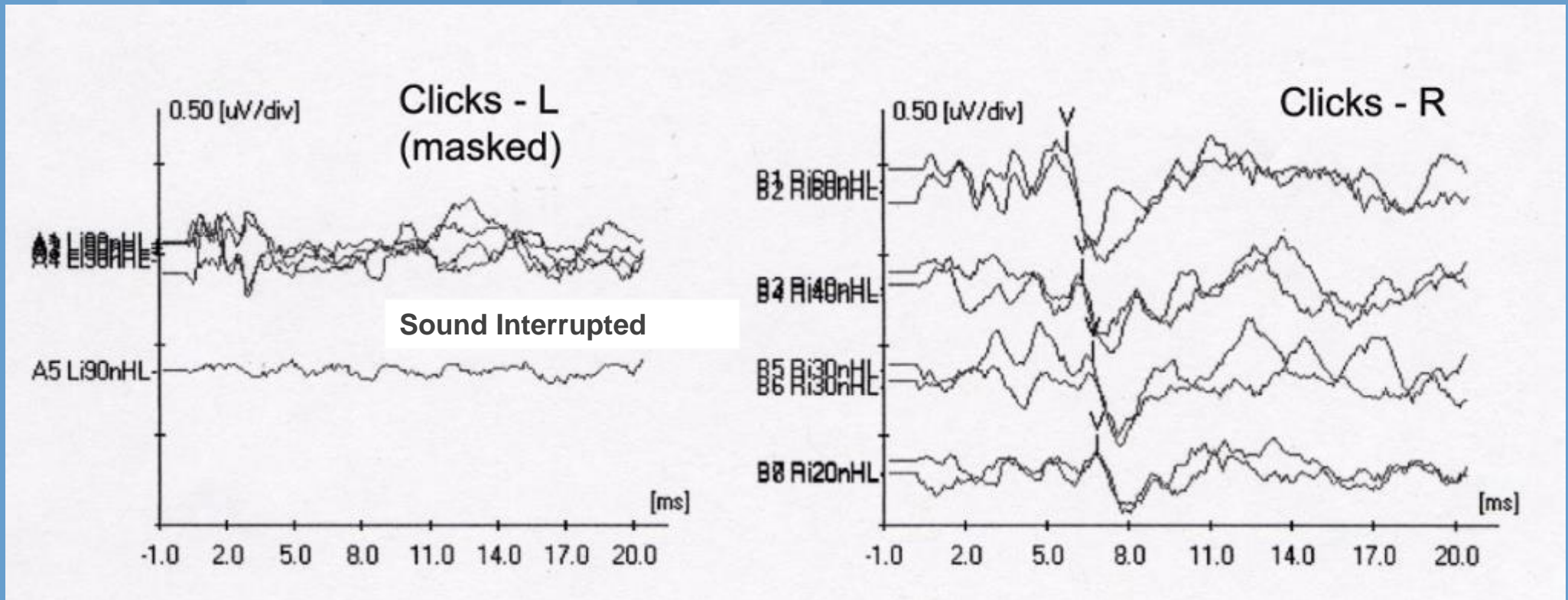
Pass MET Right Ear #1 Pass





Case #4

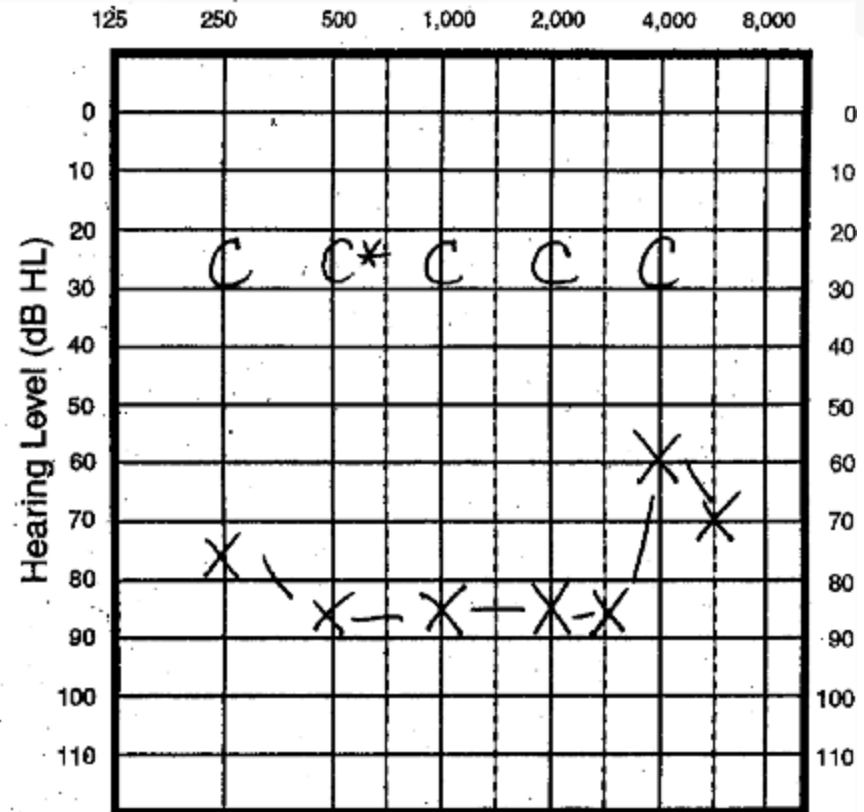
ABR Completed at Age 4 years



MRI results consistent with absent VIII nerve on left

Case #5: 8 year old with ANSD

- Child with progressive neurologic disease
- Speech recognition scores 5 years post CI in right ear:
 - » 6 % words: 38% phonemes
- Recently began wearing HA again in non-CI ear
- Mom reports increased benefit compared to CI alone
- Many additional medical issues:
 - » Ataxic (in wheelchair now)
 - » Optic neuropathy (only sees at close range)
- Late diagnosis of Brown Vialetto Van Laere syndrome





Five Cases with ANSD pattern on ABR...Five Different Outcomes

1. Normal hearing sensitivity no device needed, limited services required
2. Child with profound bilateral hearing loss; doing well with CI
3. Child with moderate HL benefitting from amplification
4. Child with unilateral profound HL and absent cochlear nerve
5. Child with progressive neurologic disease; limited benefit from either HA or CI alone; child feels best benefit from CI and HA combined

Counseling in ANSD: What Do We Say to Families?

- Child has an auditory disorder; difficult to know prognosis at time of ABR evaluation
- Degree of deficit may be mild or severe
 - a small number have normal hearing sensitivity
- Results of behavioral testing are necessary before specific recommendations can be made
- Hearing aid use is helpful in some cases but not in others; benefit can only be determined with appropriate fitting and consistent use
- Cochlear implantation may be a better option if adequate benefit from amplification not received



Counseling in ANSD: What Do We Say to Families?

- Frequent follow up visits will be necessary
- Child should be enrolled in early intervention as soon as family is ready
- Most effective communication strategy will need to be determined with input from family, teachers, therapists, and audiologist
- We will work together as a team to find a solution for their child's hearing disorder

Counseling in ANSD: What Do We Say to Families?

- Information provided to families should be based on current evidence and not “hearsay”
- Important that we are confident in our knowledge of disorder or refer to those who are
- While it is more difficult than with non-AN hearing loss to provide “prognosis” for family, there is a lot of useful information that needs to be provided to families at time of diagnosis.
- Families need to be reassured that help is available and be informed of a timeline for the first year following diagnosis



BC Early Hearing Program Video for Families

<https://www.youtube.com/watch?v=IX8IVJgiC3U>

Trastorno en el Espectro de la Neuropatía Auditiva



El Trastorno en el Espectro de la Neuropatía Auditiva (ANSD) es una pérdida de audición sensorineural menos común

Conclusions

- ANSD is more complicated than originally thought and population more heterogeneous
- It's unlikely that a single approach to management will meet the needs of all children.
- Some children will benefit from hearing aids either in the short term or the long term, others will require cochlear implantation.
- Visual methods to support communication may be required for some children even those who have received cochlear implants

Conclusions

- The available clinical evidence does not support withholding audibility from infants with ANSD. Although audibility does not ensure good speech recognition, lack of audibility is certain to result in poor speech recognition.
- Important to consider the needs of the whole child, not only the auditory neuropathy diagnosis.
- Important to use team approach to carefully monitor child's progress in meeting communication goals.



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Gracias!

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