

Auditory Neuropathy Spectrum Disorder in Children: Diagnosis and Management



Indianapolis, Indiana
February 21, 2020

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Kalamazoo, Michigan 1977

- Audiologists at community speech and hearing clinic performed annual hearing evaluations for college aged students at a vocational/tech school
- Auditory Brainstem Response (ABR) evaluations and Otoacoustic Emissions (OAE) testing were not available at that time
- Audiologists I worked with asked me to test the hearing of one of the students they had tested in previous years
 - 19 year old with ASL as his primary mode of communication
 - No ability to understand spoken language
 - Pure tone audiometry showed hearing levels within normal limits
 - He could detect speech at soft levels but could not understand words
- Central deafness or ANSD?
- Today, we have many more assessment tools available to help us with the diagnosis and management of auditory neuropathy but still many questions that need to be answered



Outline

- Overview and Definitions
- Diagnosis
- Etiologies and Associations
- Variations in Presentation
- Management Protocols
- Counseling Families



Auditory Neuropathy A Definition:



A form of hearing loss characterized by abnormal auditory nerve response as indicated by absent or abnormal auditory brainstem response (ABR) and evidence of normal outer hair cell function as measured by presence of a cochlear microphonic in the ABR or present otoacoustic emissions

-Santarelli, 2010



ANSD: Audiologic Findings

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

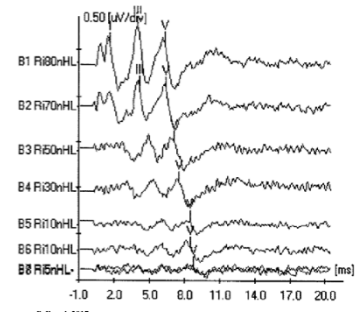
ANSD: Audiologic Findings

- Individuals affected by the disorder may perform differently than those with typical cochlear hearing loss
 - 'Typical' sensorineural hearing loss (SNHL) results in impaired frequency resolution
 - Auditory neuropathy is thought to affect timing of neural activity and disrupt perception based on temporal cues (likely varying degrees)

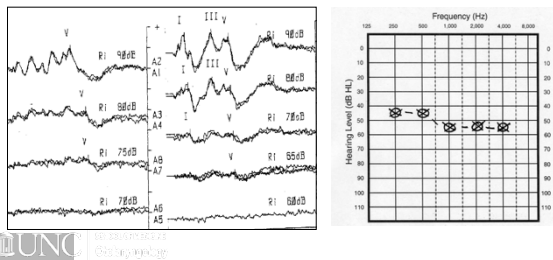
(Starr et al 1991,1996; Berlin et al.,1993; Hood, 1999; Zeng et al 1999, 2005; Kraus et al, 2000; Rance et al 2004)

Diagnosis and Early Controversies

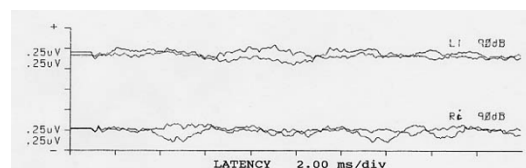
Normal ABR



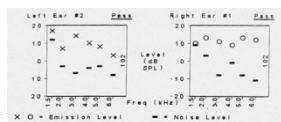
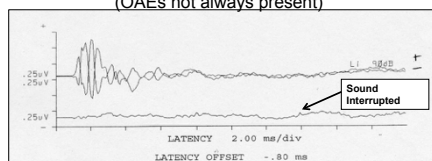
Estimated thresholds from tone burst ABR in non-AN type hearing loss



Child with profound hearing loss (not ANSD): Absent ABR with no cochlear microphonic:

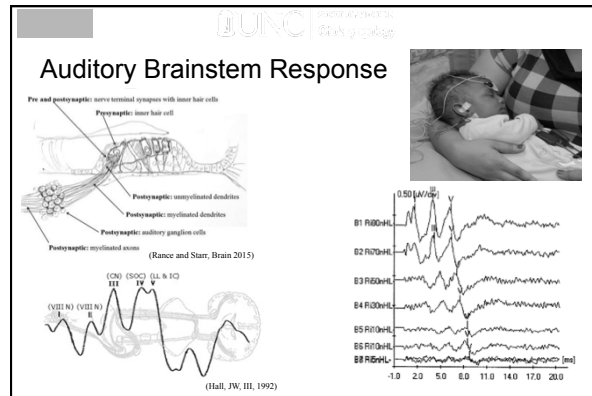


Typical Pattern with ANSD Abnormal ABR with Present CM (OAEs not always present)



What is a Cochlear Microphonic (CM)?

- Pre-neural response (occurs before Wave I in the ABR)
- Unlike the ABR, the CM shows a direct phase relationship to the acoustic wave form. When the polarity of the stimulus is changed there is a reversal of CM waveform
- Considered to have limited clinical use in past; renewed interest in diagnosis of ANSD
- CM can be recorded in normal ears, ears with "typical SNHL" and ears with ANSD
- Significance in ANSD is when CM is present when neural response is absent or markedly abnormal



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
- Tone bursts can also be evaluated but use caution in using present neural responses to estimate thresholds in case of ANSD
- 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

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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 (but only in a sub-set of cases)
 - 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)

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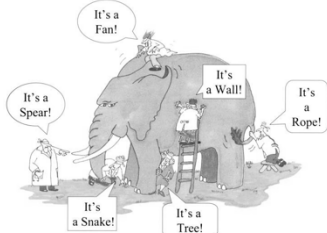
Early Controversies

- Are Hearing aids of any benefit?
 - Should we aid both ears?
 - Should we provide 'low gain' amplification?
- Do cochlear implants work in cases of ANSD?
- Is sign language necessary for all children with AN?
- Does AN resolve over time?
- Do hearing levels fluctuate from day to day or minute to minute?

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Auditory Neuropathy: Early 2000's...




Downloaded on 11/14/18 from: <http://www.pinkconcussions.com/blogreal/2015/12/6/the-6-blind-men-and-the-elephant-the-story-of-concussion>

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Auditory Neuropathy Spectrum Disorder (ANSD)

*Guidelines Development Conference:
 Identification of Infants and Children with Auditory Neuropathy*
 Lake Como, Italy, June 19-21, 2008



Kai Uus, Barbara Cone, Yvonne Sininger, Pat Roush, Deborah Hayes, Charles Berlin, Ferdi Grandori, Jon Shalloo

Not pictured: Arnie Starr, Christine Pett, Gary Rance

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Guidelines: Identification and Management of Infants and Young Children with Auditory Neuropathy Spectrum Disorder

Lake Como, Italy, June 19-21, 2008

- Terminology
- Diagnostic Criteria
- Comprehensive Assessments
- Audiological Test Battery
- Amplification Strategies
- Considerations for Cochlear Implantation
- Habilitation for Communication Development
- Screening
- Monitoring Infants with "Transient" ANSD
- Counseling Families of Infants with ANSD

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Auditory Neuropathy Spectrum Disorder (ANSD)

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Guidelines available at:
[http://www.thechildrenshospital.org/pdf/
 Guidelines%20for%20Auditory%20Neuropathy
 %20-%20BDCCH.pdf](http://www.thechildrenshospital.org/pdf/Guidelines%20for%20Auditory%20Neuropathy%20-%20BDCCH.pdf)
 (Children's Hospital of Colorado website)

Etiologies and Associations

Etiologies and Associations

Genetic Etiologies:

- Isolated AN:
 - Otoferlin (OTOF) – DFNB9 (recessive)
 - Pejvakini (PJKV) – DFNB59 (recessive)
 - AUNA1- DIAPH 3 (dominant) - (onset of auditory symptoms in late teens, progressing to profound in 5th decade of life)
- Non-isolated AN:
 - Friedreich's Ataxia (FDRA) (recessive)
 - Hereditary motor and sensory neuropathies (HMSN) e.g Charcot-Marie-Tooth disease (dominant and recessive types)
 - (OPA1) (optic neuropathy and moderate HL; several types)(dominant)
 - Leber's (LHON)-MTND4 (optic neuropathy; mild to moderate HL)
 - (AUNX1) AIFM1 (x-linked recessive)
 - Brown Vialetto-Van Laere syndrome (BBVL) – SLC52A2, SLC52A3 (recessive)

Santarelli 2010

Etiologies and Associations

Pre and Perinatal Conditions:

- Prematurity (Inner hair cell loss?)
- Hyperbilirubinemia
- Hypoxia
- Low birth weight

Postnatal Conditions:

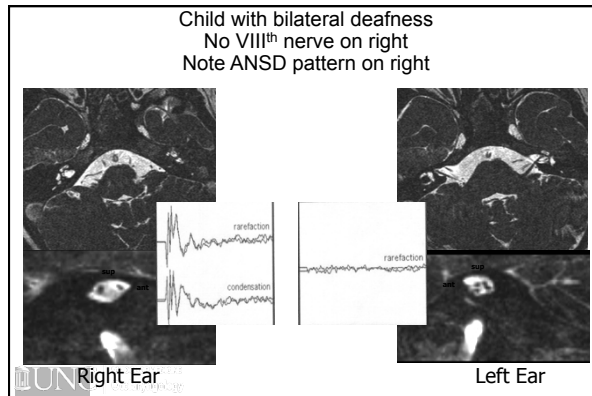
- Infectious processes
- Viral infections (e.g. mumps, meningitis)
- Head injury (shaken baby syndrome)

Rance (2005);Rapin & Gravel (2003);Starr (2003); Hayes 2011, Ammatuzzi (2001)

Etiologies and Associations

Cochlear Nerve Deficiency:

- 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

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Characteristics of children seen at UNC with ANSD

Records review of 261 children with ANSD from 1999-2017:

- 42% female, 58% male
- 89% failed NBHS in one or both ears; 11% passed
- 67.8% bilateral ANSD; 32.2% unilateral
- 15.3% of ANSD cases had cochlear nerve hypoplasia/aplasia identified by MRI and/or CT
- >50% of cases presenting with unilateral ANSD pattern had cochlear nerve hypoplasia/aplasia
 - Not surprisingly this group had lower associated co-morbidities compared to all children with ANSD

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Characteristics of children seen at UNC with ANSD

- For 243 with information on gestational age (GA):
 - 48% were born preterm at/or less than 30 weeks
 - 21% were born between 31-37 weeks GA
 - Among 74 infants with ANSD with reported hyperbilirubinemia, 82% were born preterm at or below 37 weeks GA
 - 5 infants had documented kernicterus, only one of whom was born at term

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Table 6-1. Etiologies Commonly Associated with Auditory Neuropathy and the Likely Pathological Locus in Each Case

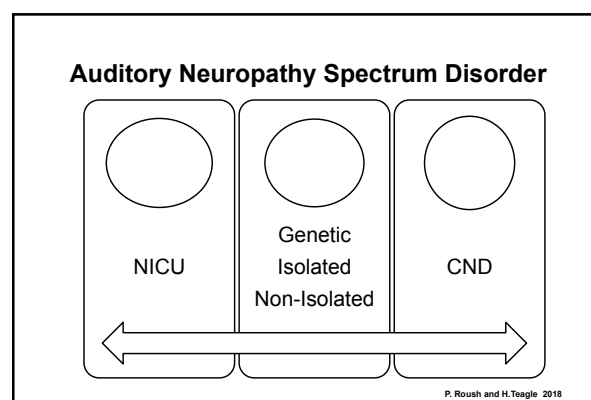
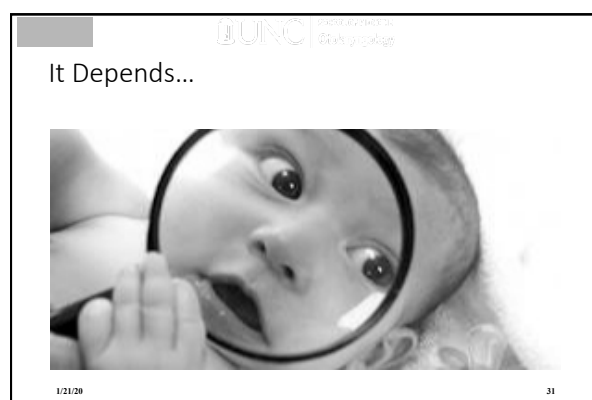
Etiology	Representative Example	Locus	Key References
Congenital Malformation	Hypoplasia	Auditory nerve	Buchman et al., 2006
Trauma	Hypoxia	Inner hair cell	Amatuzzi et al., 2001 Nash et al., 2014
Toxic-Metabolic Disorder	Kernicterus	Ganglion cells	Rance et al., 1999 Shapiro, 2003 Nash et al., 2014
Neoplasm	Acoustic neuroma	Auditory nerve	Laury et al., 2009
Genetic Mutation Affecting Neural Function	Charcot-Marie-Tooth disease	Dendrites and axons	Starr et al., 1996, 2003
	Autosomal Dominant Optic Atrophy (OPA1)	Dendrites	Yu-Wai-Man et al., 2010 Santarelli et al., 2015
Genetic Mutation Affecting Synaptic Function	Otoferlin (OTOF) mutation	Ribbon synapse	Starr et al., 1998 Moser et al., 2013
Mitochondrial Disorder	Friedreich ataxia	Dendrites and axons	Rance et al., 2008
	Mohr-Tranebjærg syndrome	Dendrites and axons	Marshall et al., 2001 P. Roush 2017

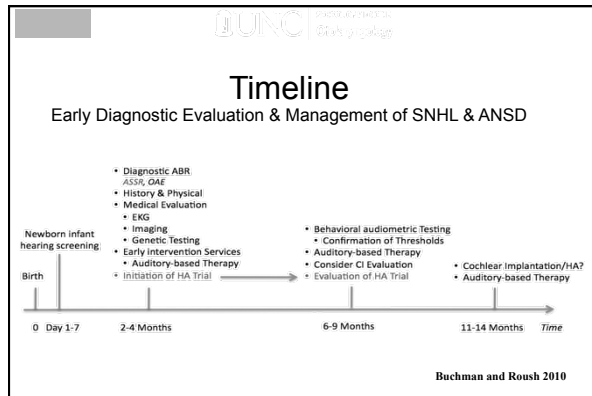
Pre and postsynaptic: nerve terminal synapses with inner hair cells

C. Rance 2018 in Auditory Processing Disorders: Assessment, Management, and Treatment, Third Edition
edited by Donna Geffner, Deborah Ross-Swain

What to do...

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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
- Referral to Genetics or Neurology when indicated

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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
- CAEP testing when needed

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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

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Cortical Evoked Potentials (CAEP)



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

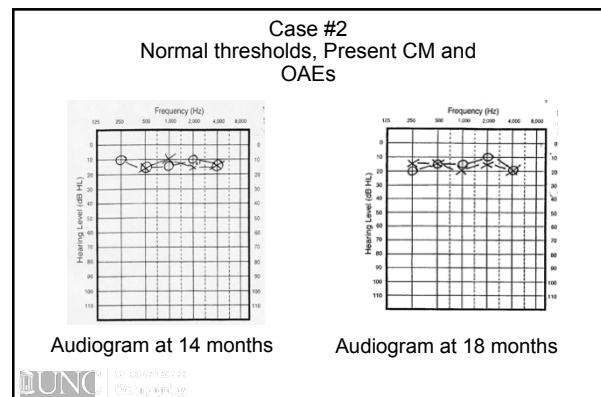
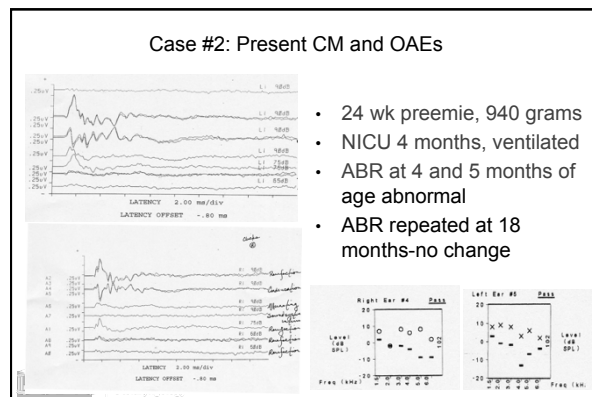
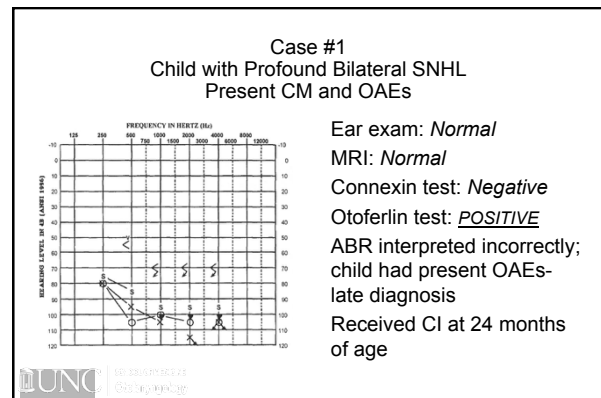
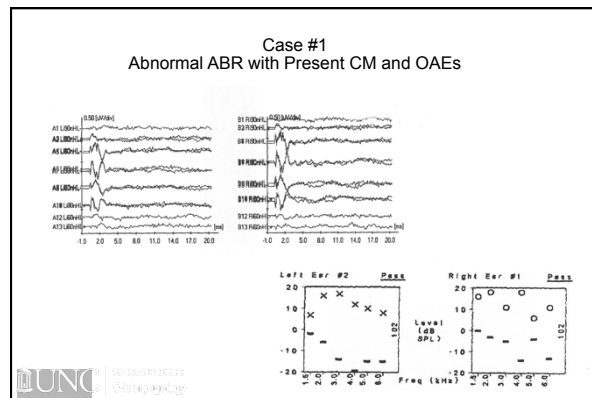
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Summary of UNC Protocol for Management of Infants with ANSD

- 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
- Consider CI if benefit from amplification insufficient for continued progress in communication skill development
- Use CAEP to aid with management when needed
- Refer for comprehensive developmental evaluation when child has complex needs

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Case Examples



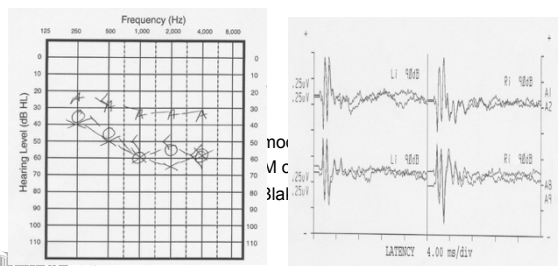
Case #2 Speech Perception Test Results

- 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

Case # 3 Background

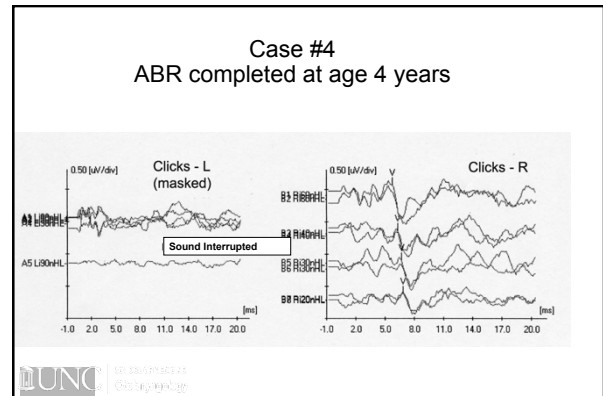
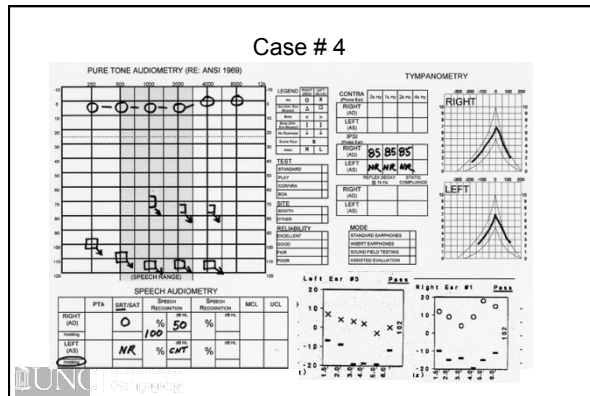
- 25 weeks gestation
- Ventilated for 6 weeks
- Oxygen 3 ½ months
- Hyperbilirubinemia
 - Treated with lights, exchange transfusion
- Treated with antibiotics and diuretics
- Hospitalized 4 ½ months
- No family history of hearing loss
- Did not pass newborn hearing screen at hospital discharge
- Initially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

Case #3 Child with moderate hearing loss CM present, absent OAEs



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 (continued)

- Results of MRI:
 - Right ear: Normal inner ear anatomy
 - Left ear: Consistent with small or absent nerve VIII
- At age 7 years child has above average speech and language development, no academic problems
- Managed as we do other cases with profound unilateral hearing loss.

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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 Vialotto Van Laere syndrome

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

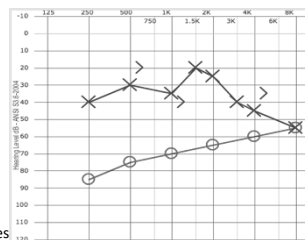
1. Child with profound bilateral hearing loss; doing well with CI
2. Normal hearing sensitivity no device needed, limited services required
3. Child with moderate HL benefitting from amplification
4. Child with unilateral profound HL and absent cochlear nerve
5. Child with progressive neurologic disease;
 - Limited benefit from either HA or CI alone;
 - Child feels she receives the greatest benefit from combined use of CI and HA
 - Supplemental visual communications system is needed
 - Child is using cued speech

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Initial behavioral audiometry at age 4 1/2

- SRT:
 - Left: 25dBHL
 - Right: CNT
- Recorded PBKs:
 - Left: 48%
 - Right: CNT
- Tympanometry
 - Large physical volume consistent with patent tubes



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Factors that may affect outcomes

- Age at diagnosis and treatment
- Appropriateness of device fitting
- Consistency of use
- Quality of intervention
- Extent of family involvement
- Cognitive abilities of child
- Presence of other medical conditions



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Outcomes

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Impact of the Presence of Auditory Neuropathy Spectrum Disorder (ANSD) on Outcomes of Children at Three Years of Age

Ching, T., Day, J, Gardner-Berry, Hou, S, Seeto, M, Wong, A., and Zhang, V.
International Journal of Audiology 2013;52:S55-S64

Study Aim:

To determine influence of ANSD on speech, language and psycho-social development of children at 3 years of age.

- 47 participants
 - 27 using hearing aids, 19 using CI, 1 no device
- 37 % had disabilities in addition to HL

Conclusion:

No significant difference in performance levels or variability between children with and without ANSD, both for children who use hearing aids and children who use CI

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Children with Auditory Neuropathy Spectrum Disorder fitted with hearing aids applying the American Academy of Audiology Pediatric Amplification Guideline: Current Practice and Outcomes.

Compared speech production, speech perception, and language of 12 children with ANSD and 22 children with similar degrees of mild-to-moderately severe sensorineural hearing loss (SNHL)

- Children were participants in the OCHL study and were fitted with HAS according to AAA Pediatric Amplification Guide

Results:

- Children with ANSD displayed functional speech perception abilities in quiet
- No significant differences found on language or articulation measures between the two groups

Walker, E.A., McCreery, R.W., Spratford, M., Roush, P.A.,
Journal of the American Academy of Audiology 2015, (3), 204-18.

Auditory Performance and Electrical Stimulation Measures in Cochlear Implant Recipients With Auditory Neuropathy Compared With Severe to Profound Sensorineural Hearing Loss

Attias et al, Ear and Hearing 2016

Study Aim:

- To compare auditory and speech outcomes and electrical parameters after CI between children with isolated AN and children with SNHL
 - 16 patients with 'isolated AN' (5-12.2 yrs of age)
 - 16 control patients with SNHL
 - Matched for duration of deafness, age at CI, type of CI
 - Implanted for at least 3.4 yrs (on average 8 yrs post-CI).

Results:

The children with isolated AN performed equally well to the children with SNHL on auditory and speech recognition tests in both quiet and noise.

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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 of children with ANSD have normal hearing sensitivity
- Results of behavioral testing are necessary before specific recommendations can be made (imaging and genetics may also help guide decision)
- 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

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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

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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


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Resources


BRITISH COLUMBIA UNIVERSITY OF NEUROSCIENCE
 BC Early Hearing Program Video for Families
 Auditory Neuropathy Spectrum Disorder




<https://youtu.be/ZZFERUP15wE>


BRITISH COLUMBIA UNIVERSITY OF NEUROSCIENCE
 British Columbia Early Hearing Program
 Brochure for Families




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2016
 Version 2016.02
 PROTOCOL FOR AUDITORY BRAINSTEM RESPONSE – BASED AUDIOLOGICAL ASSESSMENT (ABRA)



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BRITISH COLUMBIA UNIVERSITY OF NEUROSCIENCE
 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.
 - Important not to delay decision regarding cochlear implant if child is not making speech and language progress
- 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.
- Collaboration among speech/language pathologists, teachers of the deaf, audiologists and family members essential for optimal outcomes.

Harrison et al 2014:

- *It is reasonable to conclude that a reliable prediction of functional outcomes for children with ANSD is presently not possible.*
- *It is clear that ANSD is a disease category with many different etiologies and includes patients with wide range of functional severity. In addition to the range of functional impairments from the neuropathy per se, there is the added heterogeneity caused by anatomical abnormality (particularly nerve hypoplasia) as well as developmental and behavioral comorbidities.*
- *Until the ANSD group is subdivided down into more discrete disease entities, it is unlikely that outcome measure studies will be definitive enough to offer prognostic information.*

Thank you! Questions?

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