Diagnosis And Management Of Auditory Neuropathy Spectrum Disorder (ANSD)

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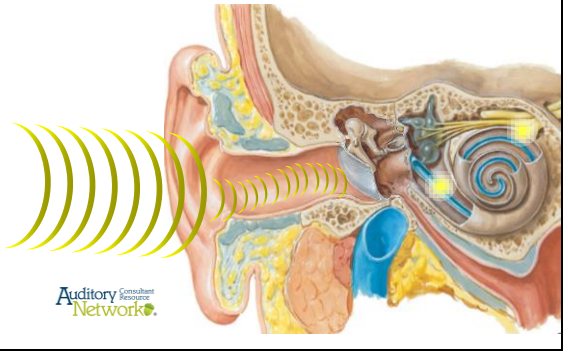
Physiology of Normal Hearing



The Cochlea

- Contains the organ of hearing
- Encased in the temporal bone of the skull
- "Snail-shaped"

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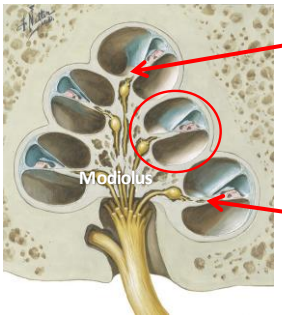
Physiology Of Normal Hearing



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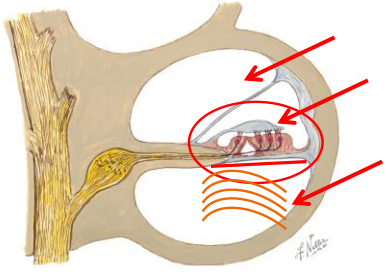
Physiology Of Normal Hearing



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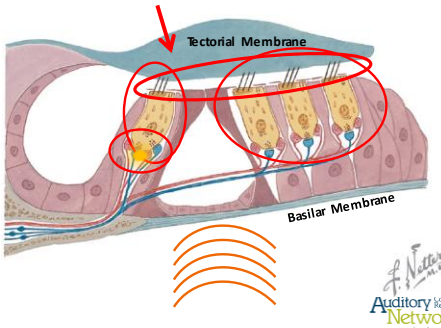

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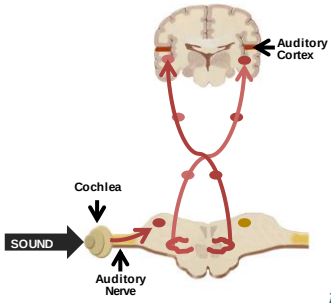
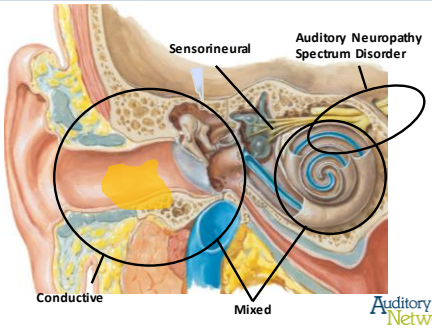
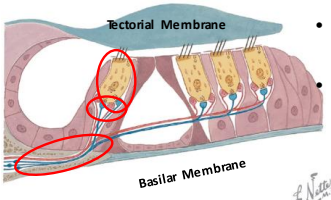


Auditory Pathway Interrupted



What's The Site Of Lesion (SOL)?



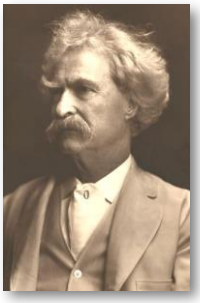
- Inner hair cells
- Synapse/neurotransmitters
- Auditory nerve- can involve myelin, spiral ganglion, and/or axons)

- *Routine clinical test findings do not readily identify the specific SOL*

"Conventional Wisdom" re: ANSD

- Audiogram is not really useful in planning remediation/management
- Hearing aids are rarely, if ever, effective
- Cochlear implants are the "go to" treatment
- Label of ANSD characterizes a patient's auditory performance

About Conventional Wisdom…



"What gets us into trouble is not what we don't know, it's what we know for sure that just ain't so"…Mark Twain

Heterogeneity & Complexity

- **Auditory Neuropathy *SPECTRUM* Disorder**
- **Avoid generalizations from single case examples**
- **Are conclusions based on systematic studies?**
- **View every case individually and comprehensively**

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ANSD: Different From SNHL?

- **Impaired auditory function**
  - **May** have elevated auditory thresholds
  - **May** have poorer than expected speech perception, especially in noise
- **Impaired auditory neural function**
  - Abnormal/absent ABR (not reliable predictor)
  - Absent /elevated middle ear muscle reflex (MEMR)
- **Evidence of normal OHC function**
  - Normal otoacoustic emissions (OAEs)
  - Present cochlear microphonic

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A Brief History

- **Newly identified, but not a newly emergent**
- **"Paradoxical" cases in early ABR literature**
- **Advent of OAEs helped clarify new diagnostic category**
- **First labeled auditory neuropathy in mid 1990's (Sinninger et al., 1995; Starr et al., 1996)**

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Incorrectly Named?

- **Is "Auditory Neuropathy" inaccurate?**
  - Only 30% - 40% of reported cases have additional neural abnormalities
  - Berlin (2001) proposed name change to auditory dys-synchrony
- **Auditory neuropathy/auditory dys-synchrony (AN/AD)**
- **Auditory Neuropathy Spectrum Disorder (International NHS Conference, 2008)**

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ANSD: It's Settled Then…

- **Auditory Neuropathy Spectrum Disorder**
  - Reflects the heterogeneity of individuals with the same clinical findings
  - Recognizes the limitations of current tests to readily identify site of lesion
- **Still seems to routinely be shortened to "Auditory Neuropathy"**

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What Causes ANSD?

- **Hyperbilirubinemia**
- **Hypoxia/anoxia**

} >50% of pediatric ANSD cases have one of these factors in the birth history

- **Infectious disease**
- **Genetic**
  - Syndromic
  - Nonsyndromic
  - Recessive
  - Dominant

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Etiology: Genetic Causes

- **Syndromic "non-isolated" forms w/ peripheral neuropathy (more than 20)**
  - Charcot-Marie-Tooth
  - Mohr-Tranebjaerg syndrome
  - Friedreich Ataxia
  - Poorer outcomes???
- **Non-syndromic forms**
  - Mostly in families identified with NSRA
  - Several genetic mutations being associated with "isolated" ANSD

Prevalence/Incidence?

- **Estimates have ranged from .5% to 15+% of all hearing loss**
- **Accuracy confounded by populations studied (NICU, all HL, at risk, deaf schools)**
- **7% to 10% (Rance, 2005)**
- **10% would mean:**
  - 1 to 2 per 10,000 births
  - .01 to .02% of all births

Accurate Diagnosis of ANSD

- **Impaired auditory function**
  - Behavioral audiometry
  - Speech perception
- **Abnormal auditory nerve function**
  - Absent or significantly abnormal ABR
  - Absent acoustic reflexes

One test for auditory nerve function (at least)

- **Normal cochlear outer hair cells (OHC)**
  - Present otoacoustic emissions (OAEs)
  - Cochlear microphonic on ABR

One test for OHC function (at least)

Diagnostic Test Battery

- **Tympanometry**
- **Otoacoustic emissions (OAEs) for OHCs**
- **Auditory Brainstem Response (ABR)**
  - Information about neural function
  - Information about OHCs
- **Acoustic Stapedial Reflexes (MEMR)**
- **Behavioral Audiometry**

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Tympanometry

- **ANSD may have normal or abnormal tympanometry**
- **Presence of middle ear fluid or negative pressure or TM perforation will influence:**
  - OAE / Cochlear microphonic (CM)
  - Ability to measure acoustic reflexes
- **Should be the first test in the battery**

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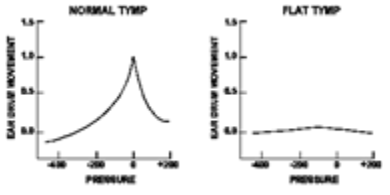
Tympanogram ("Tymps")



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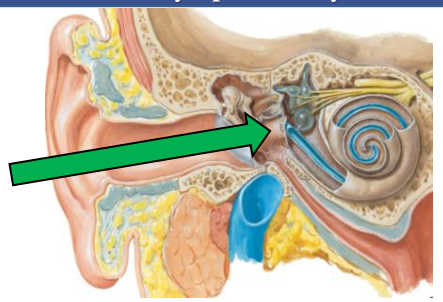
Tympanometry



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Otoacoustic Emissions (OAE)

- Acoustic response from outer hair cells (OHC), reflective of normal function
- Typically present in patients with ANSD, at least in early childhood
- Sometimes reported as very robust

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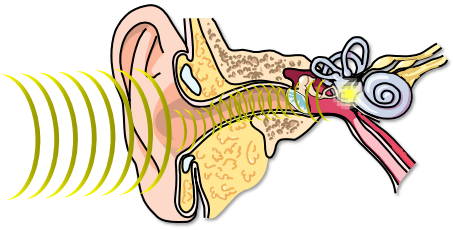
Otoacoustic Emissions (OAE)



***What* does it test?**

The function of the sensory hair cells in the cochlea

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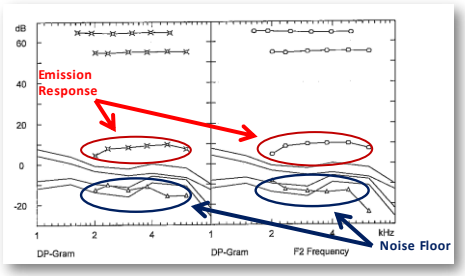
Otoacoustic Emissions (OAE)



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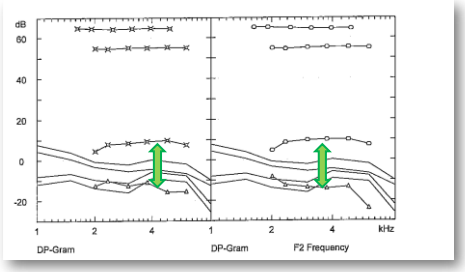
Otoacoustic Emissions (OAE)



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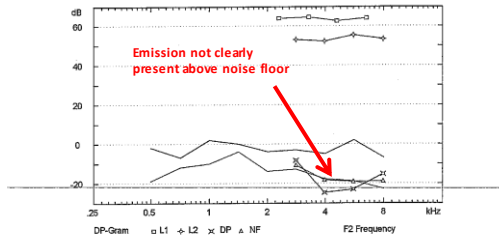
Otoacoustic Emissions



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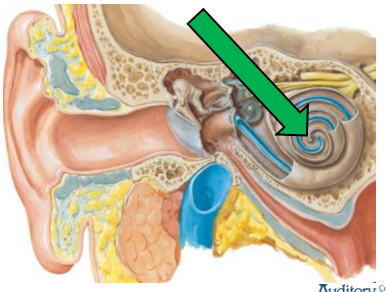
OAEs Test Outer Hair Cells



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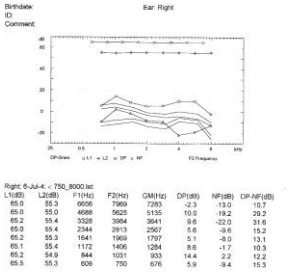
Oaes: Keep In Mind…

- **OAEs may over time:**
  - Decrease in level
  - Disappear
- **Sensitive to changes in middle ear status**
- **Absent OAEs are not enough to eliminate ANSD as a potential diagnosis**



Right: 6-Jul-4: < 750_8000.lst:

L1(dB)	L2(dB)	F1(Hz)	F2(Hz)	GM(Hz)	DP(dB)	NF(dB)	DP-NF(dB)
65.0	55.3	6656	7969	7283	-2.3	-13.0	10.7
65.0	55.0	4688	5625	5135	10.0	-19.2	29.2
65.2	55.4	3328	3984	3641	9.6	-22.0	31.6
65.0	55.4	2344	2813	2567	5.6	-9.6	15.2
65.2	55.3	1641	1969	1797	5.1	-8.0	13.1
65.1	55.4	1172	1406	1284	8.6	-1.7	10.3
65.2	54.9	844	1031	933	14.4	2.2	12.2
65.5	55.3	609	750	676	5.9	-9.4	15.3

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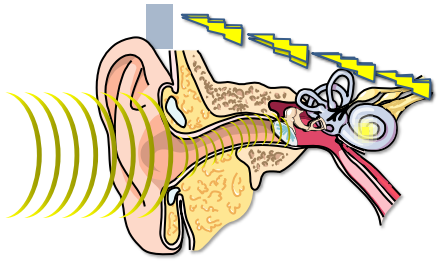
Auditory Brainstem Response (ABR)



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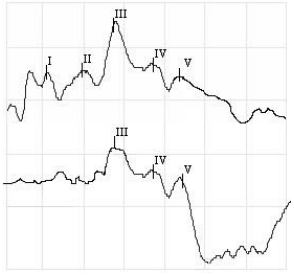
Example – ABR Waveform



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ABR In ANSD

- **ANSD – Absent or abnormal**
  - Absent is obvious
  - What is "abnormal"?
- **ABR thresholds not predictive of behavioral sensitivity threshold, i.e. poor correlation between the two**

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Cochlear Microphonic

- **Considered OHC response**
- **Bio-electric analog of the stimulus signal**
- **Reverses polarity with changes in stimulus polarity (rare/cond)**
- **Finding in ANSD is present CM with absent/abnormal ABR**

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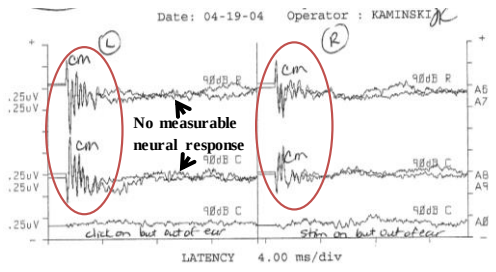
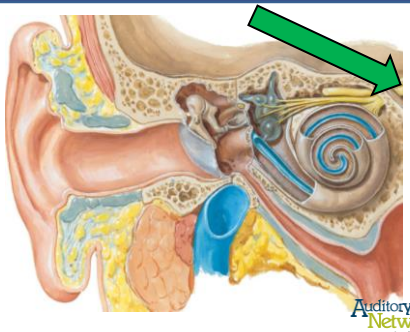
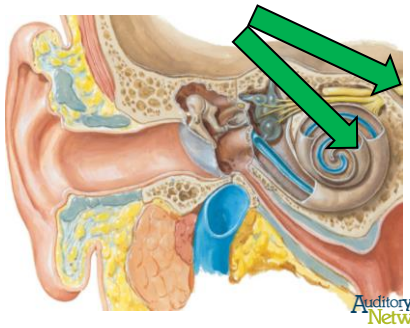
Cochlear Microphonic (CM)



ABR Tests Auditory Nerve Function



Can ALSO Tell About OHC Function



Middle Ear Muscle Reflexes

- a.k.a. Acoustic reflex or stapedial reflex
- Absent or elevated in cases of ANSD
- Berlin et al. (2005)
  - None had normal AR pattern
  - None had reflexes at both 1000 and 2000 Hz

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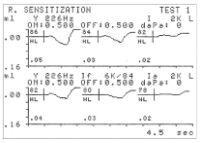
Acoustic Reflexes: Keep In Mind

- Abnormal acoustic reflexes can result from a number of causes
- By itself not sufficient to make a diagnosis of ANSD
- Results abnormal or inconsistent with what is expected = consider referral for ABR



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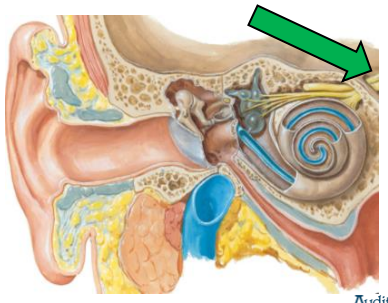
Acoustic Reflex Tests Nerve Function



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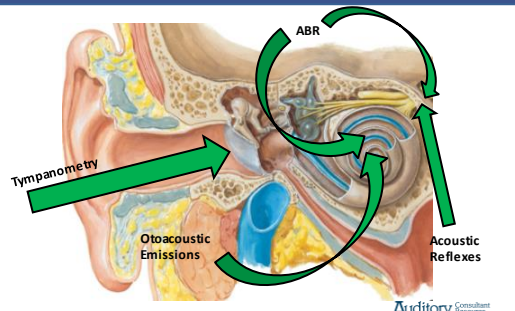
Audiogram

- Can vary from normal to profound
- Rising configuration in some cases
- May be progressive/fluctuating
- Not a reliable indicator of speech perception ability
  - May be poorer than similar degree of SNHL
  - May be the comparable to similar degree of SNHL
- "Audiogram tells you nothing…"?

Test Battery For ANSD



Classic Battery Findings For ANSD

- Normal middle ear function
- Normal OAEs
- Abnormal ABR
  - Absent waveform
  - Presence of cochlear microphonics for high amplitude test stimuli
- Absent acoustic reflex thresholds

ANSD Or Not?

- Flat tympanograms/abnormal middle ear function
- OAEs absent
- ABR abnormal
  - Absent waveform
  - Absent cochlear microphonics

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AN 15 Background

- Male, 4 years of age, speech-lang. Concerns
- Clinic contacted with inquiries about testing for CAPD
- No particular concerns for hearing
- Scheduled for speech-lang. evaluation and hearing screening

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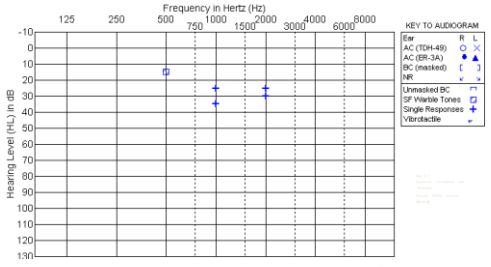
Previous Findings (Age 2)



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Audiological Testing

- No particular concerns for hearing
- Very active and difficult to condition to testing task
- Proceeded with SLE, but rescheduled audio testing

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Risk Factor History

- Premature: 27 weeks G.A., 1 lb. 3 oz.
- Ventilator dependent for 2 ½ months
- Ototoxic medications
  - Gentamycin
  - Vancomycin
- Numerous bradycardic and apnic episodes
- Passed newborn hearing screen at discharge
- Language concerns from an early age

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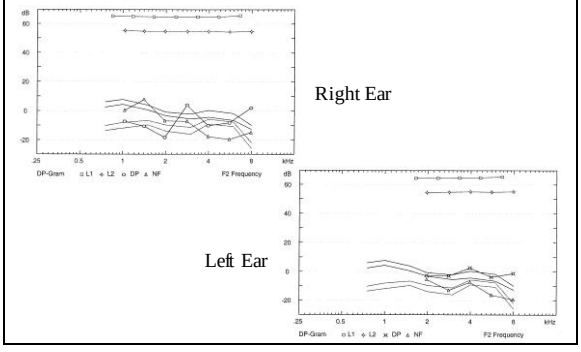
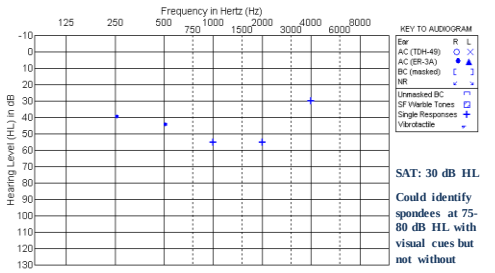
Distortion Product OAEs (Age 4)



Pre-ABR Audiogram (Age 4)



SAT: 30 dB HL

Could identify spondees at 75-80 dB HL with visual cues but not without

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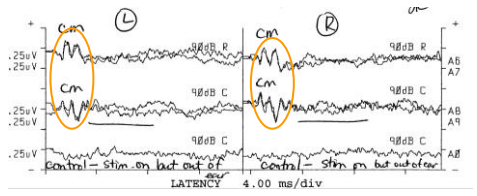
ABR results



No neural responses at 90 dB HL, AU, but cochlear microphonic present

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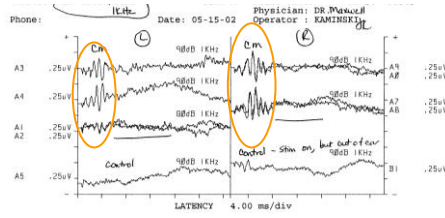
ABR Results



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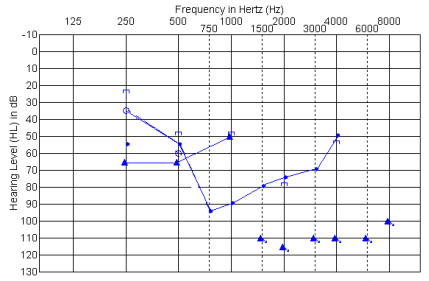
Complete Audiogram (2 mos. later)



Following diagnosis

- Enrolled in auditory/oral school program
- Consistent use of binaural BTEs and wireless FM system
- Aided results: 88% correct at 55 dB HL for NU-CHIPS (closed set)
- Recommendation to supplement auditory input with sign language

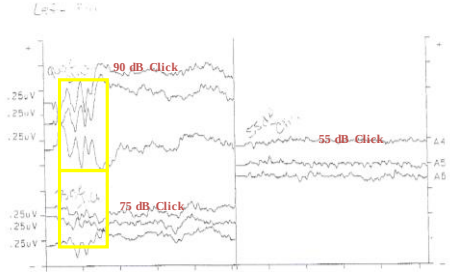
Recovery From ANSD

- "Growing out" of the disorder
- Neuromaturation?
- Association with hyperbilirubinemia
- Seems to occur within age 12-16 months
  - Not likely after 24 months
- Implications for cochlear implantation?

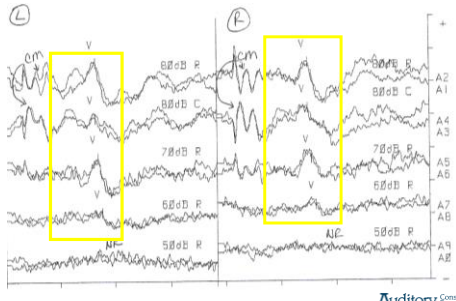
Recovery From ANSD?

- Madden et al., 2002: 9/18 improved
- Psarommatis et al., 2006: 13/20 from NICU
- Raveh et al., 2007: 4/19 improved
- Attias & Raveh, 2007: Case reports for 5 children with partial or full recovery

Recovery Example 1 : Initial ABR



Recovery Example 1: ABR 1 Yr. Later



Remediation Options For ANSD

- Amplification/ hearing aids
- Cochlear Implantation

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Big Assumptions In ANSD?

- Audiogram is not useful in treatment
- Label of ANSD means poor speech perception skills
- Hearing aids are not effective remediation
- Cochlear implants are the best treatment option

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Management And Intervention

- Heterogeneity
  - Audiometry
  - Speech recognition
  - Etiology/S.O.L.
- One management approach is unlikely to be successful for all patients with ANSD

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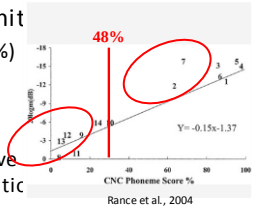
Mean Scores Can Be Mean

- **Children with ANSD**
  - Mean speech recognit
    - Normal hearing (96%)
    - SNHL (84%)
- **Conclusion?**
  - Children with ANSD have expected word recognitic



Rance et al., 2004

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Hearing Aids With ANSD

- **Controversial topic**
- **Assumption of poor speech perception abilities**
- **Several studies report limited or no hearing aid benefit**
  - Few studies have evaluated this issue systematically
  - Adult patients with ANSD tend to not perform well with amplification.

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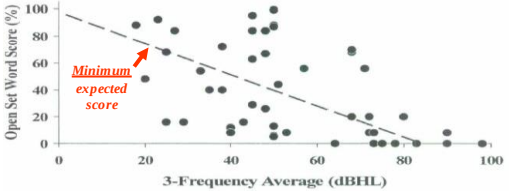
Low Speech Perception? (Rance, 2005)



- **Word Rec. scores from 10 studies of ANSD**
- **Compared to minimum expected score from Yellin et al., 1989**

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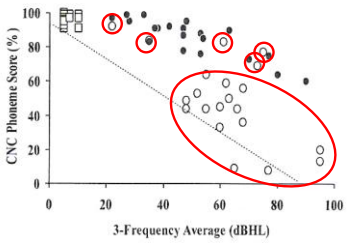
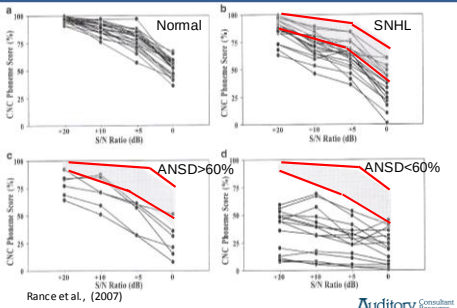
CNC Scores In Quiet



Rance, Barker, Mok, Dowell, Rincon, & Garratt (2007)

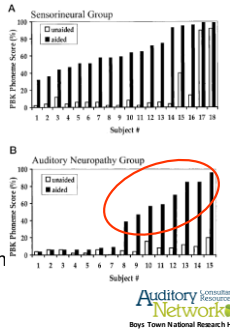
Poorer Speech Perception In Noise?



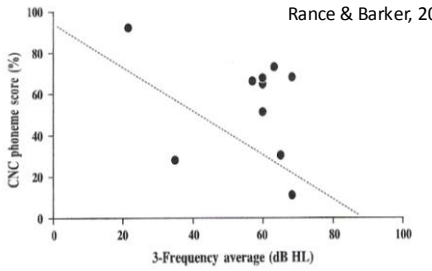
Rance et al., (2007)

Does Amplification Seldom Help?

- **Rance et al. (2002)**
  - aided vs. unaided scores
    - 7 subjects - no improvement
    - 8 subjects - mean difference score of 56.8%
    - Not correlated with the audiogram.

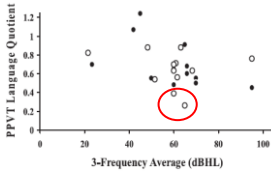


Aided CNC Scores



Rance & Barker, 2007

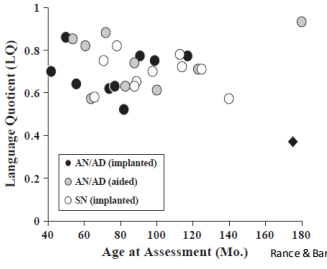
Language Quotient & Articulation



Rance, Barker, Sarant, & Ching (2007)

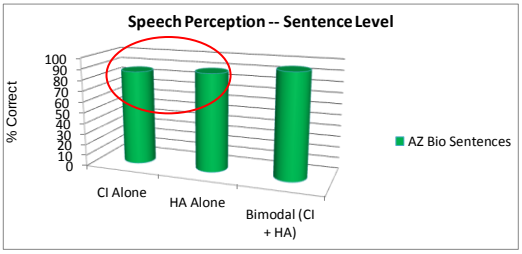
Hearing aid users with ANSD compared to matched SNHL

Language Quotient



Rance & Barker, 2009

Data from BTNRH Patient



Arguments Supporting HA Trial

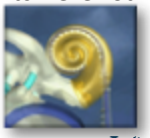
- **Sensitivity loss not explained by dys-synchrony alone**
- **Some studies show benefit with amplification**
  - Particularly with early intervention
  - Difficult to predict who will benefit
- **"Treat the patient, but don't ignore the audiogram"**
  - Audibility, audibility, audibility…
  - Consider "limited" benefit vs. no benefit/decrement

Summary: Amplification In ANSD

- **Data show mixed results**
- **Assumption of poor aided speech perception is overgeneralization**
- **Physiological results and detection thresholds alone do not predict who will benefit**
- **Further research is needed to determine if the means exist to help predict benefit**

Cochlear Implants And ANSD

- **Initially assumed to be poor candidates**
  - Site of lesion = auditory (VIIIth) nerve
  - CI directly stimulates VIIIth nerve
- **Earliest published reports were not promising**
  - Miyamoto et al. (1999)
  - Rance et al. (1999)



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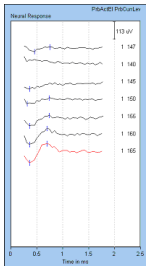
Changing Ideas About CI

- **Restored synchronous activity of VIIIth nerve**
  - Fabry, 2000
  - Trautwein et al, 2000
- **Mayo Clinic experience**
  - Shallop et al., 2001
  - Peterson et al., 2003
- **Numerous case reports and studies emerged**



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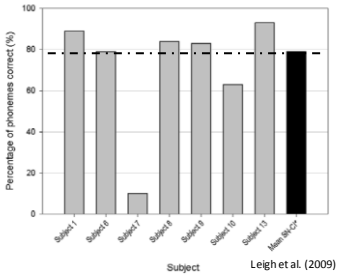
Outcomes With CI



Leigh et al. (2009)

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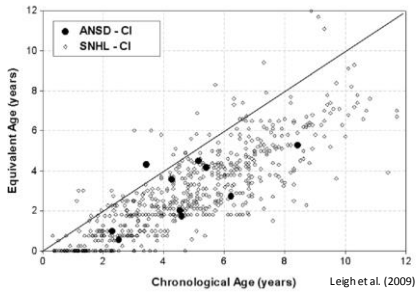
Language Development



Leigh et al. (2009)

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Why Does CI Work?

- **Bypasses site of lesion just as in recipients with SNHL**
  - Inner Hair Cell (IHC) disorder
  - IHC/VIIIth nerve synapse disorder
- **Improved neural responses due to either:**
  - Improved synchrony of neural firing
  - Increased number of neural elements recruited
- **CI can address multiple sites of lesion**

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The Silver Bullet For ANSD?

- **Some reports of limited benefit from CI**
  - Miyamoto et al, 1999; Rance et al, 1999; Gibson & Sanli, 2007; Leigh et al, 2009; Teagle et al, 2010
- **Additional neuropathies/medical complications**
  - Charcot-Marie-Tooth disease, Friedreich ataxia, Mohr-Tranebjaerg syndrome, etc.
  - May be present in as many as 30-40% of patients with ANSD

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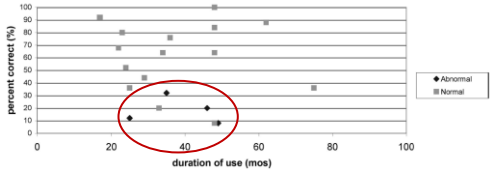
Cochlear Nerve Deficiency (CND)

- **Condition in which auditory nerve is abnormally small or even absent**
- **May only be identifiable through MRI**
- **Buchman et al., 2006; Adunka et al., 2006; Bradley et al., 2008; Walton et al., 2008**
- **Consideration for CI candidacy?**
  - Possible poor/limited CI outcomes
  - MRI for all patients with ANSD (CT may be normal)

Outcomes In Abnormal MRI



Teagle et al. (2010)

CI & ANSD Data (Gibson & Sanli, 2007)

- **60 of 435 CI recipients (13.8%) diagnosed with ANSD**
- **Abnormal EABR after CI in 15 (25%)**
  - Significantly poorer speech perception than SNHL with CI controls
  - Significantly poorer than other ANSD with CI
  - Assumed to have true "auditory neuropathy" (AN) or "brainstem auditory neuropathy" (BAN)

Recent Data (Teagle et al. 2010)

- **52 CI Recipients**
  - 27% have limited speech recognition
  - Significant variability
- **Predictive factors include**
  - Normal MRI
  - Normal ECAP

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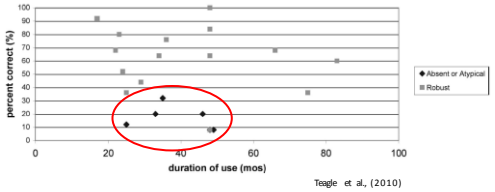
Abnormal VIIIth Nerve Potentials

ECAP – Evoked Compound Action Potential



Teagle et al., (2010)

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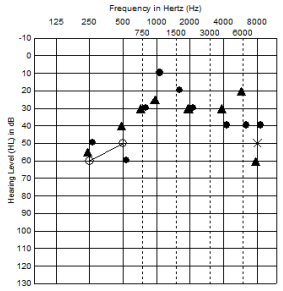
CI Candidate?



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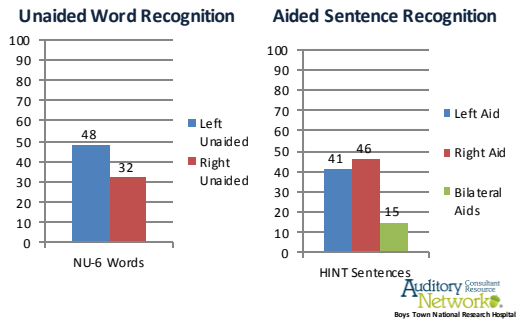
CI Candidate?



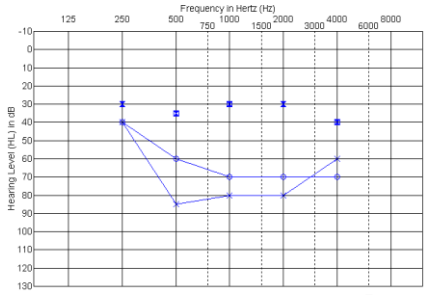
CI in ANSD With Milder Hearing Loss

- **2007 JCIH**
- **2008 Guidelines and Development Conf. on the Identification and Management of Children with Auditory Neuropathy**
- **Rationale is to restore synchronous function in the auditory nerve**
- **Few reports in the literature & more evidence is warranted**

CI In Milder Degrees Of Hearing Loss

- **Cautious and methodical approach**
  - Trial with amplification
  - Assessment of speech perception
  - Assessment of speech-language skills development
- **Delay implant beyond 12-18 month range**
- **Can child benefit from less invasive intervention than CI?**

CI In Milder Degrees Of Hearing Loss



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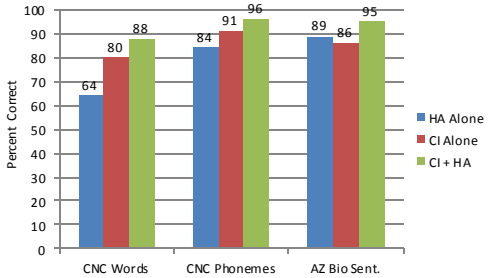
Post CI Speech Perception



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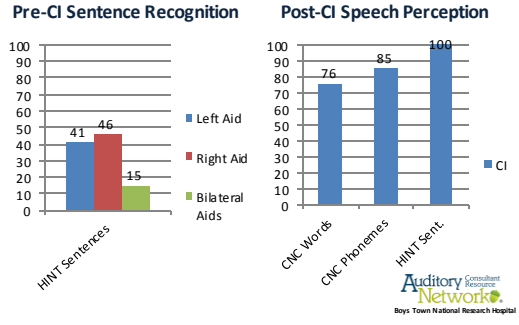
CI Candidate?



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Summary Of CI In ANSD

- **No difference compared to SNHL?**
  - Speech perception and language development
  - ECAP and EABR in normal range
- **Sometimes poorer for ANSD**
  - Related to etiology or site of lesion
    - Demyelinating or axonal disorder – true AN/BAN
    - Cochlear nerve deficiency
  - Limited speech perception benefit
- **May be appropriate in milder degrees of loss when amplification is not satisfactory**

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Key Points

- **Cochlear implantation may be an option for individuals with ANSD**
- **Hearing aids can be of benefit in some individuals with ANSD**
- **BUT, behavioral results are needed in order to appropriately fit amplification**
- **Dx of ANSD should not mean an immediate referral for CI**
- **Don't automatically discard any intervention options**

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Auditory Neuropathy Spectrum Disorder (ANSD) Case Studies

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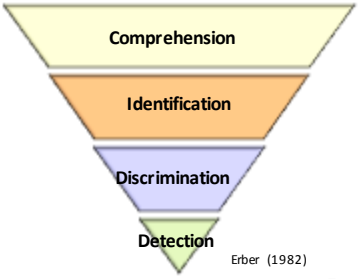
Erber's Hierarchy Of Auditory Skills



Erber (1982)

Variety Of Tests Over Time

- What is child's level of auditory development?
- Detection…presence vs. absence
- Pattern Perception
- Closed-set words
- Open-set words
- Open-set phrases
- Paragraph/narrative comprehension

Auditory Tests

- Behavioral Audiogram with Hearing Aid or Cochlear Implant
  - Detection task
  - For monitoring over time
  - Overall picture of potential for audibility and perception of speech
- Speech Perception Testing
  - Skills develop over time

Pattern Perception

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Closed-Set Words

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Closed-Set

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Open-Set Words

- From an effectively "infinite" set
- Can vary in vocabulary level
- Lexical Neighborhood Test (LNT)
- Multi-syllable Lexical Neighborhood Test (MLNT)
- PBK-50 Words
- CNC Words

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Open-Set Words

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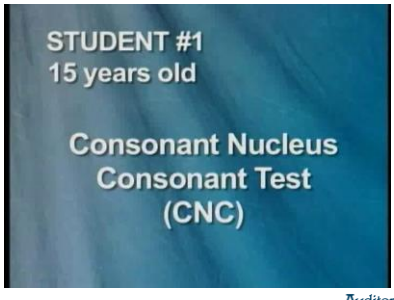
Open-Set Words



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Open-Set Phrases/Sentences

- **Levels of linguistic complexity**
- **In quiet or in varying levels of noise**
- **Commons Phrases**
- **Hearing in Noise Test (HINT)**
  - Children's version (HINT-C)
  - Standard version
- **AZ Bio Sentences**

Open-Set Sentences

Open-Set Sentences

Narrative Comprehension

- **Varying length and linguistic complexity**
- **Test of Auditory Comprehension**
- **Subtests from speech-language protocols**
  - Paragraph Comprehension (from CASL)
  - The Listening Comprehension Test-2
  - Test of Auditory Processing Skills-3 (TAPS-3)
  - Understanding Spoken Paragraphs (from CELF-4)
- **Comprehension of passages from books or of stories**

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Narrative Comprehension

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