Pediatric Hearing Loss and Cochlear Implant Update

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Disclosure

• Nothing to disclose

Learning Objectives

1. Review etiologies and various presentations of pediatric hearing loss.

2. Select appropriate workup and recognize findings that lead to a decision for cochlear implant.

3. Discuss surgery, plan of care, and the PA/NP role in followup for pediatric CI patients.
Why is early detection and treatment of sensorineural hearing loss so important?

- Hearing loss is the most frequent birth condition.

Incidence per 10,000 of Congenital Defects/Diseases

Epidemiology

- 1-3 of 1,000 live births with moderate to severe hearing loss
- Approximately 12,000 infants born annually in the U.S. with SNHL
  - 33 babies / day
- 90% of deaf genetic kids / hearing parents
Why is early detection and treatment of sensorineural hearing loss so important?

- Hearing loss is the most frequent birth condition
- Undetected hearing loss has important negative consequences.

Reading Comprehension Scores of Hearing and Deaf Students

- Deaf
- Hearing

Age in Years


Why is early detection and treatment of sensorineural hearing loss so important?

- Hearing loss is the most frequent birth condition
- Undetected hearing loss has important negative consequences.
- Early intervention has significant benefits.
Benefits of intervention

- Yoshinaga-Itano (1998)

<table>
<thead>
<tr>
<th>72 kids</th>
<th>Diagnosis birth–6 months</th>
<th>vs</th>
<th>78 kids</th>
<th>Diagnosis after 6 months</th>
</tr>
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<tbody>
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<td></td>
<td>Same intervention</td>
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Conclusion

Children diagnosed by 6 mths:
Better receptive, expressive language skills
Independent of age, gender, SES, ethnicity

Universal newborn hearing screen

- States with newborn hearing screen
  - Goal is: 1-3-6
  - Screen by 1 MONTH
  - Audiological diagnosis by 3 MONTHS
  - Early intervention by 6 MONTHS

Etiology

- Acquired: 25%
- Genetic: 50%
- Unknown: 25%
Syndromic Etiologies

- More than 500 syndromes

Pendred

- Autosomal recessive
- Described by Pendred in 1896
  - Irish family with 2/10 kids deaf and with goiter
- Goiter, not always present
- Associated with Mondini and LVA

Pendred

- Chromosome 7q21-34
- Mutation in SLC26A4 (or PDS gene)
- Encodes protein, pendrin
  - Transports chloride and iodide
- Diagnosis: Perchlorate discharge test
**Pendred**

- **Phenotype**
  - Bilateral, prelingual
  - More severe high frequency
- **Phelps, 1998**
  - 31 of 40 with LVA
  - 8 of 40 with Mondini
- **Recommend:** PDS or SLC26A4 testing in patients with LVA or Mondini on CT

**Jervell and Lange-Nielson**

- Meinsner (1856): “Patient was a deaf-mute girl in the Leipzig Institute for the deaf, who collapsed and died while being publicly admonished by the director for a misdemeanor.”
- Prolonged QT interval: syncope and sudden death- Jervell and Lange-Nielson, 1957
- Chromosome 11
- Once identified, mortality rate <6%

QTc: >470 ms, asymptomatic or >460 ms with hx
Atrophic stria, degenerated organ of Corti
SNHL with blindness

Usher Syndrome

- Four types
- Retinitis pigmentosa
- Dx: electronretinography or electronystagmography

<table>
<thead>
<tr>
<th>Type</th>
<th>Gene location</th>
<th>Hearing loss</th>
<th>Vestibular</th>
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<tbody>
<tr>
<td>1A</td>
<td>14q</td>
<td>Profound congenital</td>
<td>Absent</td>
</tr>
<tr>
<td>C</td>
<td>11p13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1q41</td>
<td>Mod-Severe congenital</td>
<td>Nil or dec</td>
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<tr>
<td>3</td>
<td>3q</td>
<td>Progressive</td>
<td>Absent</td>
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<tr>
<td>4</td>
<td>X-linked</td>
<td>Mod-severe congenital</td>
<td>Nil or dec</td>
</tr>
</tbody>
</table>
- MYO7A: implicated in type 1A

RP with Usher

- Onset is not at birth
- Affects Rods and Cones
  - Rods: night vision
    - First affected, therefore have poor night vision
  - Cones: bright light and fine details/color
    - Affected second
Waardenburg Syndrome

- Dystopia canthorum
- Flat nasal root
- Confluent eyebrow
- Heterochromic irides
- White Forelock
- Pigmentary changes
- Diminished vestibular function
- Cleft lip and palate

Waardenburg Syndrome

- Autosomal dominant
- Type I: with dystopia canthorum, 2p
- Type 2: without dystopia, 3p
- Type 3: with dystopia/ upper limb abnormalities
- Type 4: No dystopia/ Hirschprung disease
- 2-5% of infants with congenital deafness
- SNHL in 20% cases

What is dystopia canthorum???
Alport Syndrome

- X-linked (80%) or autosomal recessive and dominant
- Progressive glomerulonephritis and SNHL
- Dx: (3 of 4)
  - Family hx: hematuria +/- RF
  - EM evidence of glomerulonephritis
  - High frequency SNHL
  - Ophthalmologic signs: eg. retinal flecks
- Associated with COL4A3, COL4A4, COL4A5
  - Collagen genes

Branchio-Otorenal Syndrome

- Autosomal dominant, 8q
- Features
  - Branchial cleft fistula or cysts
  - Malformed pinnae
  - Preauricular pits/sinuses
  - Hearing loss
    - 32% CHL
    - 20% SNHL
    - 50% mixed
  - Renal abnormalities
- EYA1: gene for development of kidneys and inner ear

<table>
<thead>
<tr>
<th>Syndromes</th>
<th>Renal</th>
<th>Aur</th>
<th>Lateral</th>
<th>Renal-Ano</th>
<th>SLC26A4 (PDS)</th>
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<tbody>
<tr>
<td>Pendred Aut Recessive Goiter</td>
<td>LVA/M</td>
<td>Recessive</td>
<td>Syncope</td>
<td>EKG prolonged QT</td>
<td>KCN1, KCN20</td>
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<tr>
<td>Syndromes</td>
<td>Branchio-Otorenal</td>
<td>Recessive</td>
<td>Blindness Retinosis Pigmentosa</td>
<td>Electrocochleography</td>
<td>MHOYA, 8 others</td>
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<td>Branchio-Otorenal</td>
<td>Aur Dominant</td>
<td>Branchial anomalies</td>
<td>Auricular cupping</td>
<td>pits</td>
<td>Renal anomalies</td>
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<td>Beardenburg</td>
<td>Aur Dominant</td>
<td>White forelock</td>
<td>Syndactyly camptodactyly</td>
<td>Retina anomalies</td>
<td>Clinical</td>
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<tr>
<td>Alport</td>
<td>Aur Dominant</td>
<td>X-linked</td>
<td>Hematuria Glomerulonephritis</td>
<td>Clinical</td>
<td>COL4A3, COL4A4, COL4A5</td>
</tr>
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</table>
Etiology: Non syndromic
What is the most common inheritance?

1. Autosomal recessive
2. Autosomal dominant
3. X-linked
4. mitochondrial

Etiology: Non syndromic

- Autosomal recessive 60-80%
- Autosomal dominant 15-20%
- X-linked 2-3%
- mitochondrial <0.5%

Autosomal dominant

- One parent usually has hearing loss
- Parent with 50% risk of transmitting to child
- In general, milder hearing loss
- Starts in 2nd-3rd decades of life
  - Allows for normal speech development
Autosomal dominant

- DFNA loci
  - DFN = deafness
  - A = dominant
- > 54 loci
  - www.uia.ac.be/dnalab/hh

Autosomal recessive

- Require inheritance from each parent
- Parent usually does not have hearing loss
  - Parents are carriers
- 25% offspring of these parents will be affected

Autosomal recessive

- DFNB loci
  - DFN: deafness
  - B = recessive
- > 67 loci identified
Connexin 26

- DFNB1 mapped to chromosome 13q12-13
- Mutation of gene GJB2
- GJB2 encodes for connexin protein Cx26
- Mutation associated with 50% of autosomal recessive hearing loss
  - Carrier rate in midwest US: 2.5%

Connexin

- Transmembrane protein that oligomerizes
  - 6 connexin = connexon
- Gap junction protein stria vascularis, basement membrane, limbus, spiral prominence of cochlea
- Inability to recirculate potassium in the inner ear
  - Resultant decrease of the endocochlear potential and deafness

Connexin 26

- 35delG mutation predominates
- One Base-pair deletion: Frame shift and premature protein truncation
- Over 60 other non-35 del G mutations
Other mutations in GJB2

- **35 delG**
  - 68.7%
- **167 del T**
  - most common in Ashkenazi Jews, 4% carrier
- **235 del C**
  - in Asians, 1%
- **V37I Missense mutation**
- **De342 kB**

Phenotype of GJB2 hearing loss

- Typically, prelingual bilateral nonprogressive loss
- Varies from mild to profound
  - Severe to profound most common (80%)
  - Small fraction only mild (<2%)
- Cryns K et al, March 2004
  - Homozygote 35delG had more impairment than 35delG/non-35delG mutation

Connexin 26 Phenotype

- Usually congenital
  - Reports of homozygote 35 delG passed newborn screen, later developed profound SNHL
- Usually symmetric, > 20 dB in less than ¼
- Nonfluctuating, nonprogressive
- No comorbidities
- Normal vestibular function
- Normal CT, but....
X-linked Recessive

- DFN
- Prevalence: <2%
- 5 mapped loci
- Hallmark: No male to male transmission
- 50% of her sons: express the trait
- 50% of her daughters: carriers for the trait

X linked recessive mixed deafness with perilymphatic gusher

- Mixed HL
- Risk of gusher with stapes
- CT: lateral aspect of IAC may be bulbous
- POU3F4

Mitochondrial

- 2 to 10 copies of a small ring-shaped piece of nonnuclear DNA, each with 16 kb
- Inherited maternally
- Mutations impact energy production, tissues with high energy requirements (e.g., muscle, cochlea) are particularly vulnerable
Mitochondrial Hearing loss

- Usually associated with syndromes
- With aminoglycoside ototoxic hearing loss
  - A1555G mutation in the 12S ribosomal RNA gene
  - Maternally transmitted predisposition to aminoglycoside ototoxicity

Acquired Hearing Loss

- Infection
- Ototoxins
- Prematurity
- Kernicterus
- Birth Anoxia

Infection

- CMV
  - Most common intrauterine infection associated with SNHL
    - CMV+ in 1/100-200 newborns
  - 10-15% of babies with congenital CMV asymptomatic
    - 5-10% develop SNHL
  - DX:
    - Infant’s urine and saliva : PCR test
    - PCR on cord blood

25% Acquired
Ototoxins

- Aminoglycoside
- Loop diuretics
- Cisplatin: dose dependent
- Salicylates: High dose, reversible
- Ethyl Alcohol
- Cocaine

Prematurity

- Most significant perinatal factor
- 20 fold increase in SNHL
- 5% of NICU grads have SNHL
- Risk factors of preemies
  - Anoxia
  - Low birth weight
  - Acidosis
  - Hyperbilirubinemia
  - Meds
  - Meningitis

What is the appropriate workup for hearing loss?

- Previous to genetic tests:
  - History and Physical
    - 22-35% of cases, may identify cause
  - Shotgun approach
    - Laboratories
    - CT scans
History

• Prenatal
  – environmental teratogens
  – maternal infections
  – drugs
  – metabolic and nutritional disturbances

• Perinatal
  • Intrauterine hypoxia secondary to placental insufficiency
  • Placenta previa or abruptio placenta
  • Prolonged labor with evidence of fetal distress
  • Prematurity
  • Low Apgar scores at birth
  • Birth trauma
  • Neonatal jaundice
  • Neonatal infection

• Postnatal
  • Infections
  • Speech and language problems

• Family history
  – Hearing aid before age 30
  – Stigmata of syndromes
  – Consanguinity
Physical exam

- Ears: shape, location, EAC
- Eyes: Synophrys, Dystopia canthorum, Color of eyes, retinal pigmentation
  - ½ of children with severe-profound HL with ocular abnormalities (Leguire LE, 1992)
  - 20% of children with ophthalmologic abnormality
    - Sharma, et al Archives 2009
- Face: shape, symmetry
- Skin: texture, pigmentation, cafe au lait
- Extremities: shape of toes, fingers

Diagnostic Tests

- Laboratories
- Genetic screen
- EKG
- CT/MRI

Laboratory tests

- CBC
- Chemistries
- TSH
- ESR
- FTA/ MHA-TP
- TORCH
Results of Laboratory Tests and CT scans

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Lab Tests</th>
<th>CT</th>
<th>Dx test</th>
<th>Dx CT</th>
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<tbody>
<tr>
<td>Ohlms</td>
<td>86</td>
<td>N/A</td>
<td>70</td>
<td>0</td>
<td>14</td>
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<tr>
<td>Billings</td>
<td>301</td>
<td>N/A</td>
<td>156</td>
<td>N/A</td>
<td>23</td>
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<tr>
<td>Lalwani</td>
<td>114</td>
<td>789</td>
<td>97</td>
<td>0</td>
<td>38</td>
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<tr>
<td>Preciado</td>
<td>650</td>
<td>2676</td>
<td>616</td>
<td>2</td>
<td>169</td>
</tr>
<tr>
<td>Totals</td>
<td>1151</td>
<td>3465</td>
<td>939</td>
<td>2(0.06%)</td>
<td>244(26%)</td>
</tr>
</tbody>
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Recommend: 1) laboratory tests (eg. UA, TSH, ESR) based on history  
2) Imaging every child with SNHL.

Radiographic anomalies

• Incidence of CT anomalies with hearing loss: 6.8-39%
• Most common is LVA

Inner ear abnormalities

• Michel’s
• Mondini’s
• Scheibe’s
• Alexander’s

More dysplasia
Less dysplasia
Large Vestibular Aqueduct Syndrome

- Inheritance not defined
- Usually bilateral
- Risk of hearing loss progression with head trauma
  - Transmission of intracranial pressure to inner ear?
- Counselling of avoiding contact sports

>1.5 mm in middle third
>2 mm anywhere

Michel aplasia

- Autosomal dominant
- Complete aplasia of inner ear
- Etio: arrests of development of the inner ear at 4th week
- Contraindication for cochlear implant

Mondini aplasia

- Described in 1791
  - Cochlea 1.5 turns
  - Large vestibule
  - Large vestibular aqueduct
- Insult during 6th week
- Variable severity
- May be implantable
Narrowed IAC

- May signal absent 8th nerve
- Relative contraindication for implant

CT or MR

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
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<tbody>
<tr>
<td><strong>CT</strong></td>
<td>Easier to obtain</td>
</tr>
<tr>
<td></td>
<td>Less sedation need</td>
</tr>
<tr>
<td></td>
<td>Cheaper</td>
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<tr>
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<td>Great bony detail: trauma</td>
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<td></td>
<td>Most ENT more familiar with CT</td>
</tr>
<tr>
<td></td>
<td>Limited information of cochleovestibular nerve</td>
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<tr>
<td><strong>MR</strong></td>
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Should we use CT’s in Children?

- Cumulative dose of 50-60 mGy
  - 3 fold increased risk of Brain tumor
  - 3 fold increased risk of leukemia

- 50-60 mGy reached with
  - 3-5 head CT: Brain
  - 5-10 head CT: marrow

Algorithm for work up

- Shotgun
  - Order all tests all the time
- Staged
  - Connexin first
    - If negative, then CT
      - Preciado, et al

What is everyone else doing?

  - Questionnaire 63 of 250 ASPO members

  - 70% use connexin testing
  - 70% use CT/ MRI
  - 45% answered correctly recurrence risk
10 year old girl with severe hearing loss

Spring is my favorite season. The sun shines bright. The flowers begin to grow. I like spring.
Normal hearing

Degrees of hearing loss

- May range from mild to profound
- Hearing aids are an option
- Severe to profound loss:
  - Children may not benefit from hearing aids alone

Early experience with electrical stimulation

- In 1790 Volta experienced “a boom in the head” followed by the sound of “boiling soup” when running current through metal rods held to his ears
- “The disagreeable sensation, which I apprehended might be dangerous, prevented me from repeating the experiment.”
Electrical stimulation of the ear

- Quack electrogadgetry
  - 19th century
  - Electro-magnetic head cap
    - “revive the nerves of the ear”

- Duchenne, 1855
  - Electrode in warm saline in ear canal
  - Sounds like crackling parchment paper
  - When current strength was increased, loudness increased

First implant

- Djourno and Eyries, 1957
  - Implanted induction coil into stump of cochlear nerve in temporal bone resection patient
  - Transcutaneous stimulus via external induction coil
First experiments

- Djourno and Eyries, 1957
  - Implanted induction coil into stump of cochlear nerve in temporal bone resection patient
  - Transcutaneous stimulus via external induction coil

- Pt perceived environmental sounds; could distinguish high and low frequencies and several words
- Could not understand speech
- Paper had limited recognition because written in French

- House, Los Angeles 1960’s
  - Work of Djourno and Eyries brought to William House by a patient
  - Collaborated with neurosurgeon John Doyle and engineer James Doyle to create single-channel device
  - Short-lived due to lack of biocompatible materials
Pioneers

- Simmons, Stanford 1960's
  - Implanted patients with a six channel device
  - Demonstrated that separate electrodes could stimulate tonotopically

- Michelson 1970's
  - Implanted a 2 channel device
  - Congenitally deaf patient able to hum a melody after presentation of synthesized sound
  - Reports of outcomes a watershed for the scientific community

Blair Simmons

Robin Michelson

First experiments

- House, 1970's
  - House continued work with engineer Jack Urban
  - Collaborated with 3M to create House/3M unit, FDA approved for adults in 1984

- Clarke, Melbourne 1970's
  - Multichannel device (eventually Cochlear Corp. Nucleus 22)

William House

Graeme Clark

1990s to current

- Miniaturization of components
- Multichannel Nucleus 22 device FDA approved
- 1990- FDA lowered approved age to 2
- 1998: FDA approved for children 18 months
- 2002: FDA approves for babies of 12 months
How does a cochlear implant work?

• Replace the hair cell function of the cochlea
  – Acoustic signal
  – Electric signal
  – Processed
  – Signal delivered to auditory nerve

Components of CI

• External component (outside the body)
  – Small microphone
  – Speech processor
  – Decoding unit
  – Coil
• Internal component
  – AKA Receiver-Stimulator
  – Signal is transmitted via electrodes the cochlea
What is it like to hear with a CI?

- Initially robotic or mechanical
- Over time, the sound perception is “natural”

Who are the Candidates?

Selection Criteria

- Age 24 months to 17 years
  - Severe to profound bilateral hearing loss
  - Lack of auditory development and minimal benefit from hearing aid
  - No medical contraindications
  - High motivation and realistic expectations
Selection Criteria for Kids

• Age 12 to 24 months
  – Profound bilateral sensorineural hearing loss
  – Minimal hearing aid benefit
  – No medical contraindications
  – High motivation and realistic expectations

Who are the non candidates?

• No cochlea
  • No auditory nerve
Non-Candidates:
Those that don’t desire hearing

• “deafness” = hearing impairment, usually profound
  -- includes all persons with hearing loss
• “D”eaf = a member of Deaf World
  – Separate culture from mainstream hearing society
  – Minority culture with unique customs, values, language

Deaf culture

• Deaf World
  – In the US, ASL is defining language
  – Deafness as disability rejected
  – Deafness is a culturally defining characteristic
  – Deafness is highly valuable to the Deaf Culture

Deaf culture

• Deaf World
  – Deaf World has a moral claim to the well-being of deaf children born to hearing parents
    • A child born deaf is a member of the Deaf world
  – Cochlear implantation is antithetical to the principles of Deaf culture
    – www.cochlearwar.com
How about younger than 12 months?

- Becoming possible because of UNHS
- Considered based on extrapolated data from Hearing Aids
  - Goal of amplification by 6 months
- Feasible because cochlea adult size by birth

Typical scenario

- A 3 month old girl diagnosed with newborn screen
- Bilateral profound loss
- No response to Hearing aids
- Connexin positive
- Parents read on-line that implants are done before 12 months

Is it safe to implant at less than 12 months?

- Roland JT (Laryngoscope, Nov 2009)
  - 50 infants, ages 5-11 months
  - No anesthesia problems
- Blood volume: 80 ml/kg in infants <12 months
  - 10% loss can lead to hypovolemia
Is there a benefit to implant before 12 months?

- Schauwers (Otol and Neurotol, 2004)
  - 5 children
  - Ages 5-10 months
  - Approach normal for babbling and CAP scores
- Colletti (Laryngoscope, 2005)
  - 10 children
  - Age 4 – 11 months
  - Approached normal age for babbling (6-11 mths)

Follow up data

- Colletti (Acta Otolaryngologica, 2009)
  - 4-9 year follow up of initial group
  - Compared group implanted 4-11 months to those implanted 12-23 months and 24-36 months.
  - Children implanted early had quicker outcomes to reach normal
  - At 5 years,
    - 0 children in special schools
    - 30% implanted age 12-23 months
    - 60% implanted age 24-36 months

Expanding Indications

- Hybrid cochlear implants
Bilateral Cochlear Implants

Drawbacks of Bilateral Cochlear Implantation

• Future Technology
  – The bilateral implant may prevent the use of other technologies in the future
    • Hair Cell Regeneration
    • Stem cells
    • Drug delivery systems
    • Better cochlear implant

Hair Cell Regeneration

• Gene Atoh1 injected
Despite these risks...

- New technologies are not likely to be available for 20 years.
- Benefits
  - Sound localization
  - Hearing in noise
- While waiting, there may be negative consequences...

Changes in the contralateral unstimulated ear

- Leake, 1999
  - Deafened kittens
  - Measured SGC survival
  - Ipsilateral stimulated ear: 50%
  - Contralateral unstimulated ear: 30%

What about for unilateral hearing loss?

- Questions
  - How does brain adapt to acoustic signal in one ear and electric signal in another?
  - Benefits?
  - Risk?
  - Cost?
Unilateral hearing loss

- Adults (primarily European studies)
  - Improved speech recognition scores
  - Suppression of tinnitus
  - Improved balance
  - Improved sound localization
- Better than compared with BAHA or CROS aid

Costs of CI

- K-12 education per hearing child- $9000
- K-12 education per mainstreamed deaf child- $44,000
- K-12 education per child in residential school for the deaf- $429,000
  (Johnson et. al. Seminars in Hearing 1996)
- $60,228 lifetime cost for medical care and associated services
- $113,426 lifetime reduction in expenses from decreased educational costs and increased expected earnings
- Net expected lifetime savings of $53,198 for CI vs. no CI
  (Cheng et. al. 2000)

A Look to the Future

- Totally implanted CI
Role of PA/NP in Hearing Center

- Jennifer Hanselman, PA-C
- Coordinate visits
- Manage database of Hearing Center patients
- Participate in the evaluation of patients

Conclusion

- Hearing loss is the most common birth condition, occurring in 12,000 US births per year
- Cochlear implants stimulate the auditory nerve directly
- Cochlear implants allow children with severe to profound hearing loss to develop speech and language