

Management of Hearing Loss in Children

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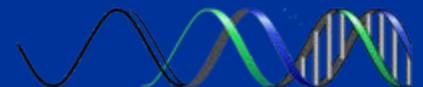


Harvard
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School



Children's
Hospital
Boston

Harvard Medical School
Center for Hereditary Deafness



Incidence of congenital disorders detected by newborn screening in Massachusetts

Congenital hypothyroidism	1 in	3,800
Toxoplasmosis	1 in	8,000
PKU	1 in	12,000
Congenital adrenal hyperplasia	1 in	14,000
Biotinidase deficiency	1 in	32,000
Galactosemia	1 in	55,000
Maple syrup urine disease	1 in	157,000
Homocysteinuria	1 in	200,000

HEARING LOSS

1-2/1000 bilateral severe to profound

1-2/1000 milder bilateral or unilateral

What Do You Do next?

- Try to figure out what kind of hearing loss it is
- Try to figure out what caused it
- Try to figure out how to manage it

Better Definition of Types and Distribution of Hearing Loss

- Conductive hearing loss
- Sensorineural hearing loss
- Mixed hearing loss
- Auditory Dyssynchrony

Auditory Dyssynchrony

- Auditory neuropathy
- Auditory dyssynchrony spectrum disorder
- Otoacoustic emissions present
- Absent/very abnormal ABR
- About 10% get better, many do well with CI
- Only occasionally helped by HA
- May be missed in newborn screening program using otoacoustic emissions
- Multiple etiologies

Causes of Auditory Dys-synchrony

- Hyperbilirubinemia
- Extreme prematurity
- Associated with other neurological findings
- Abnormal temporal bone anatomy
- Genetics
 - Otoferlin, including a temperature sensitive variant
 - Cx32 (CMT syndrome)
 - Autosomal dominant form

Why Figure Out the Cause of Hearing Loss?

- Treatable
 - Toxoplasmosis
 - Cytomegalovirus
 - Syphilis
 - Autoimmune
- Dangerous if missed: other organ systems involved
 - Long QT syndromes (cardiac)
 - BOR (renal)
 - Alport's (renal)
 - CMV, toxoplasmosis, Usher's (vision)
- Prognosis of HL; choice of habilitation, communication mode

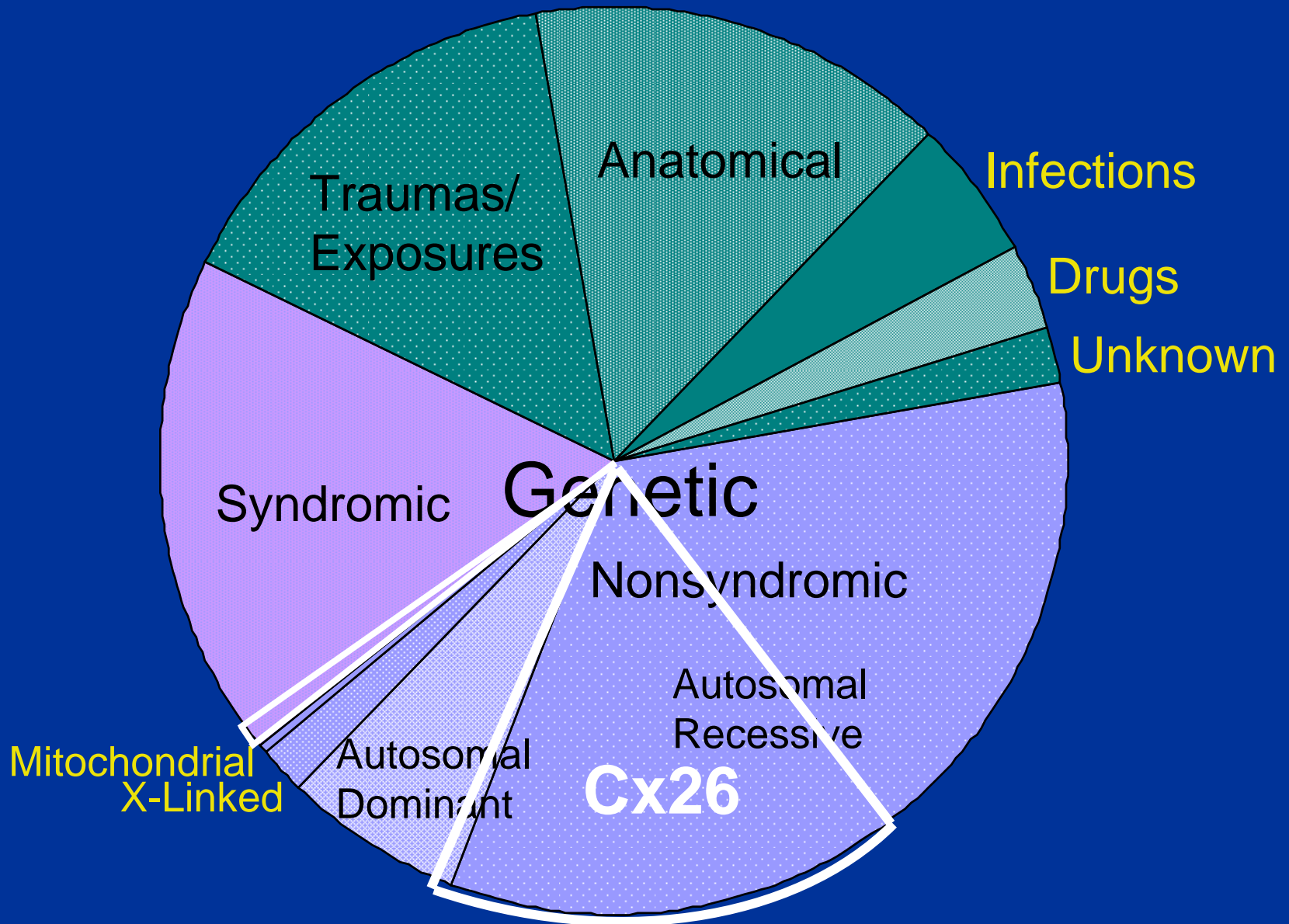
Hearing Loss: “Olden Days”

- Missed diagnoses all the time
 - No routine newborn hearing screening
 - Poor imaging of the temporal bone
 - No genetic testing
 - CMV not recognized as a major cause of SNHL
- Rarely identified a definite cause of the hearing loss
- Higher incidence of bacterial meningitis
- Less opportunity to intervene in a timely fashion
 - Consequences for S&L, academics, social skills

Hearing Loss: “Modern Times”

- Nearly universal NHS in US and many other countries
- High resolution MRI and CT
- Genetics: A1555G, Cx26, PDS, Usher
- CMV most common viral cause of congenital SNHL
- HIB and Prevnar® have reduced meningitis dramatically
- More opportunities to intervene, better interventions
 - Cochlear implants FDA approved for adults in 1984 and for children in 1990
 - Hearing aids that are small, actually work, and connect to phones, MP3 players, FM systems
- But new causes of SNHL identified (and created)
 - NICU, ECMO and other medical interventions
 - Noise (MP3, etc)
 - HIV, Lyme

Major Causes of Hearing Loss



SNHL: Anatomic Inner Ear Anomalies

- 20-40% of children with SNHL have abnormalities on CT/MRI of the TB
- Higher incidence for unilateral
- Association of EVA with Pendred Syndrome
- Over 400 other syndromes with SNHL, many with TB abnormalities
 - CHARGE
 - Branchio-oto-renal
 - Hemifacial microsomia
 - Waardenburg's

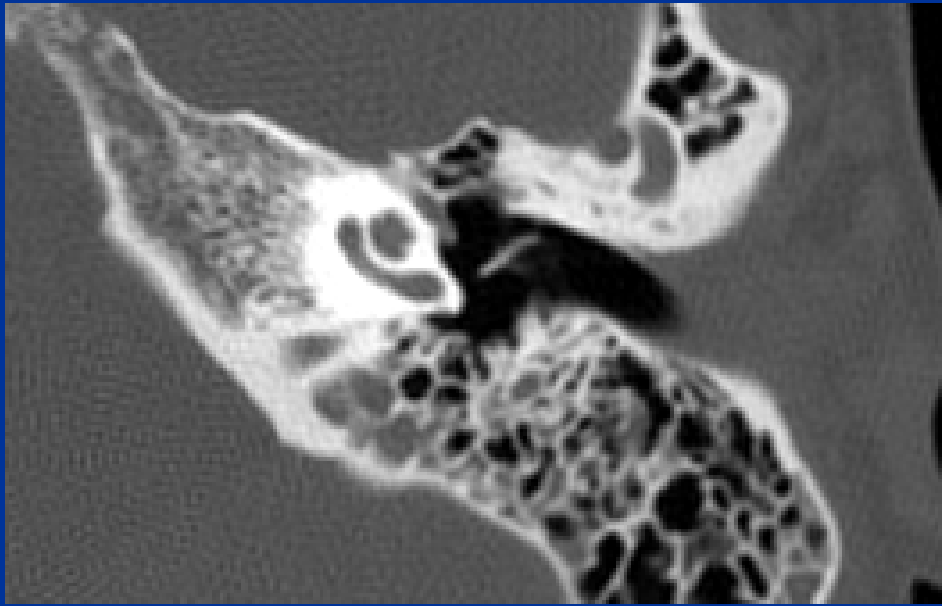
Diagnostic Imaging

- **Computed tomography (CT)**
 - Enlarged vestibular aqueduct
 - Cochlear or vestibular dysplasia
 - Internal auditory canal narrowing (IAC)
 - Cochlear stenosis
 - Calcifications of brain (congenital infections)
- **Magnetic resonance imaging (MR)**
 - Presence/absence of VIIIth nerve
 - Presence of ossification of cochlea/SCC
 - Neurofibromatosis type 2
 - Brain abnormalities
 - Functional MR (fMRI)

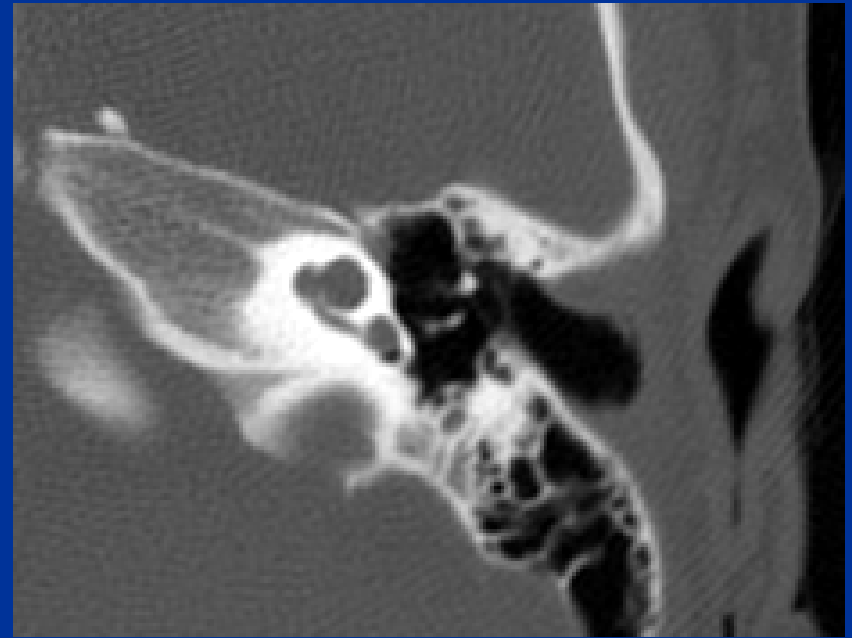
Enlarged Vestibular Aqueduct

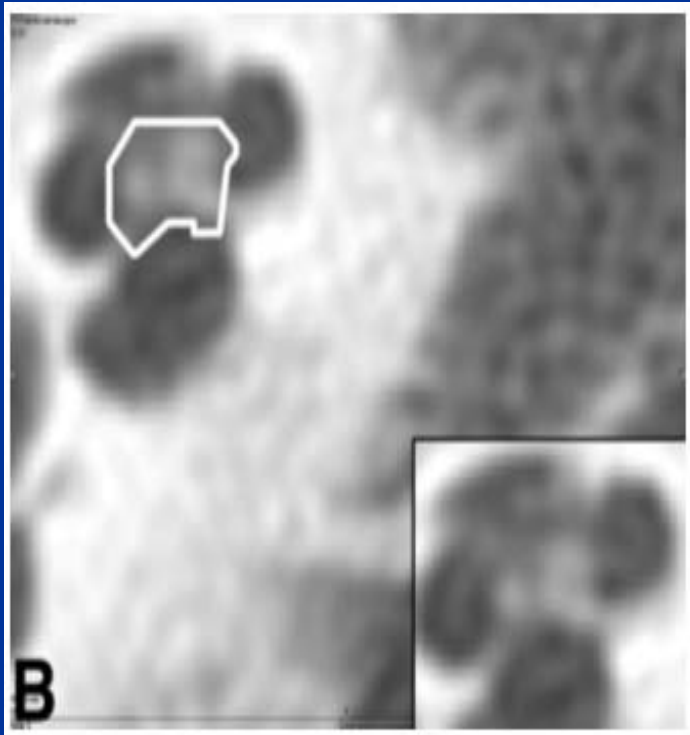
- Most common radiographic abnormality with SNHL
- Associated with fluctuating/progressive hearing loss
- HL often mixed
- About 10% of AU EVA associated with full Pendred syndrome



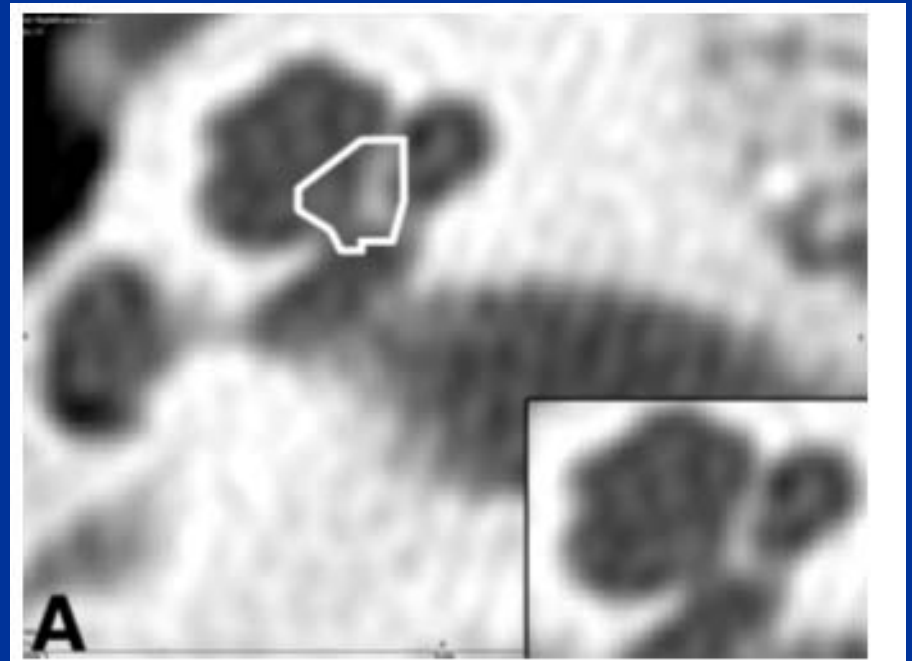


- Incomplete partition
- Modiolar deficiency
- “Mondini”



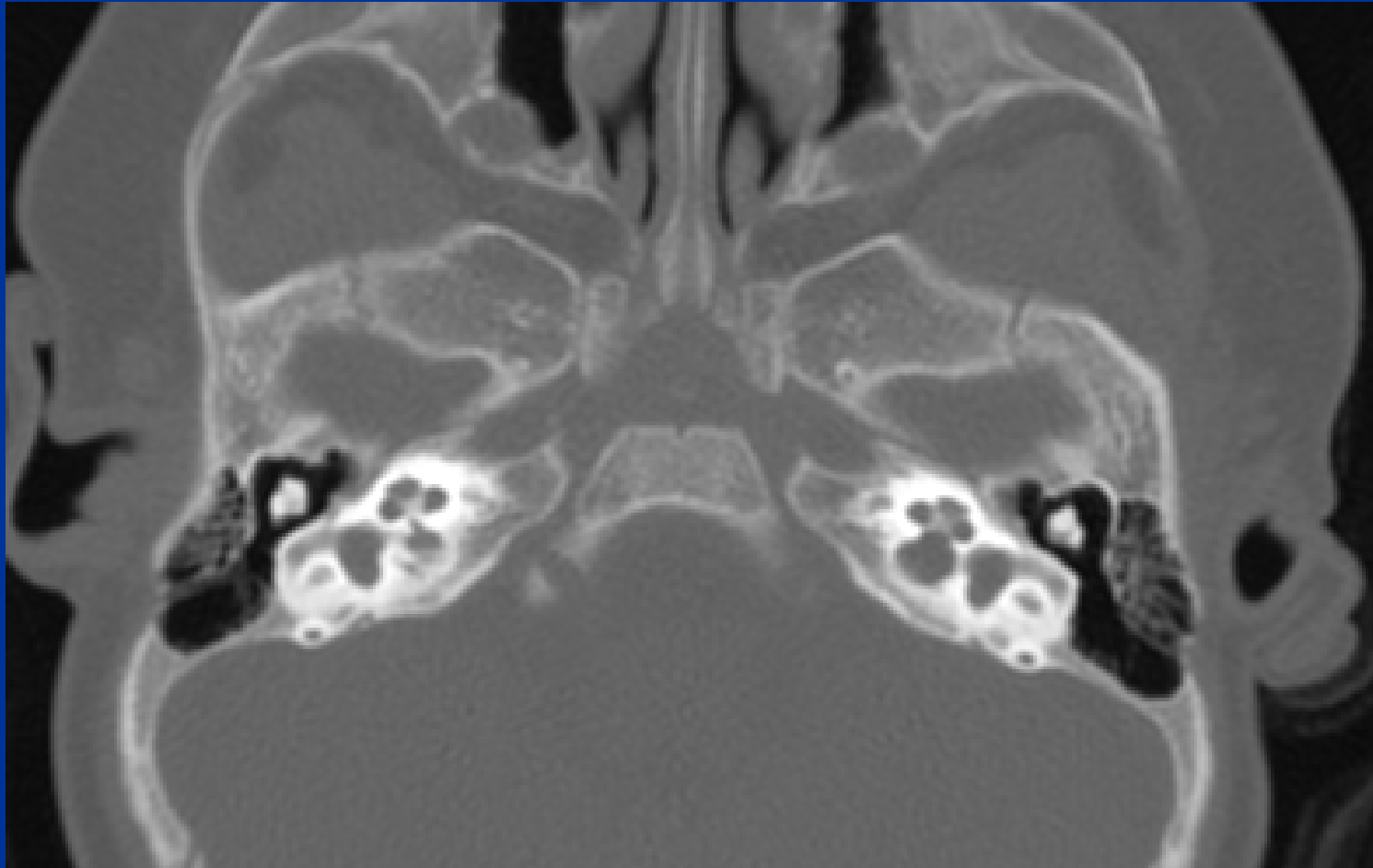


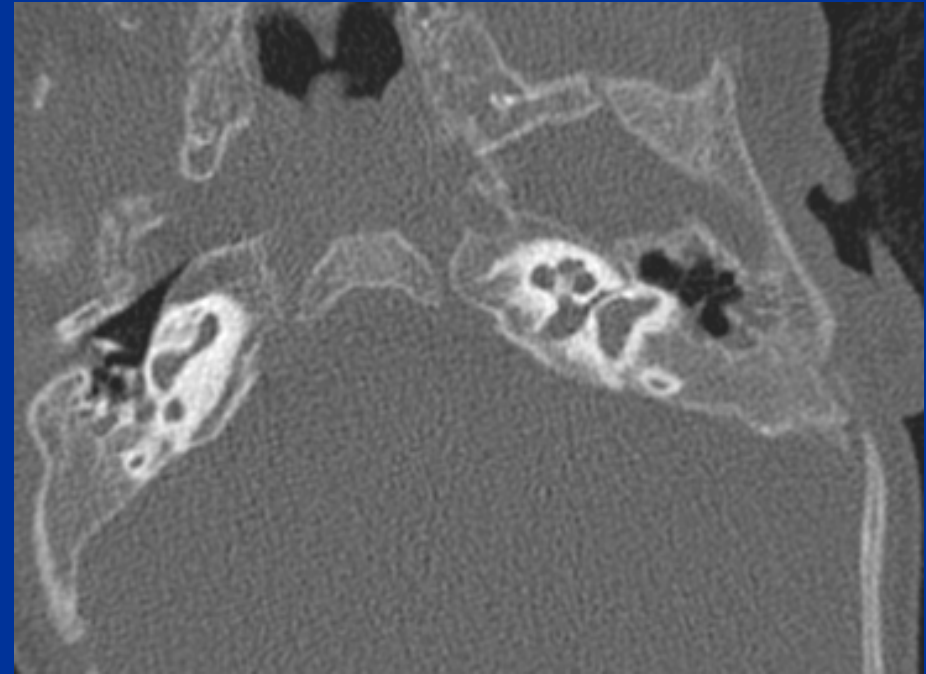
Normal modiolus



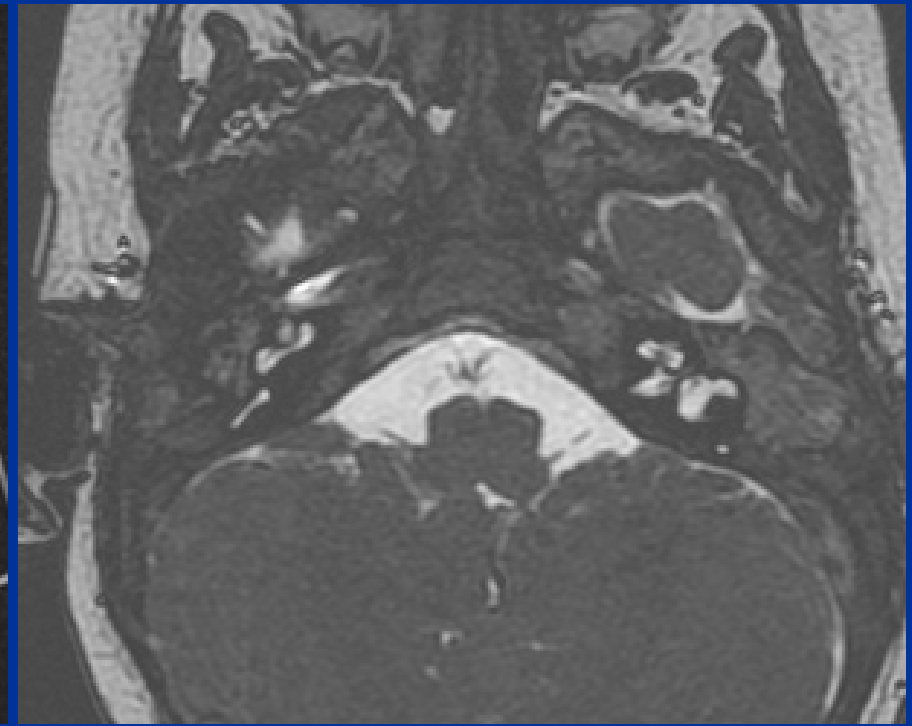
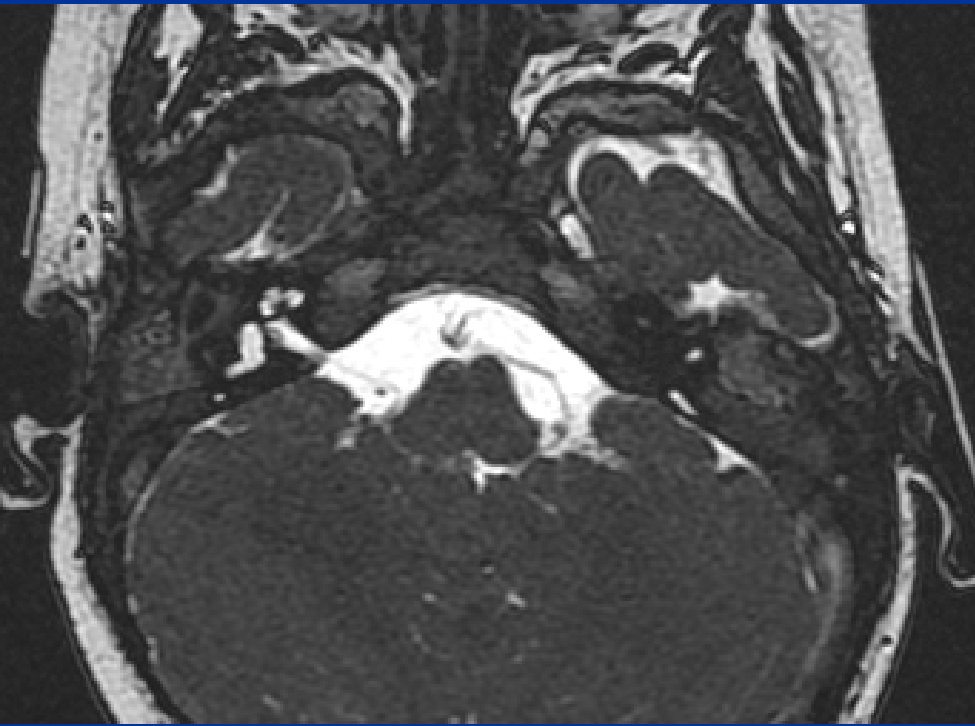
Deficient modiolus

Right cochlear stenosis and thickened modiolus

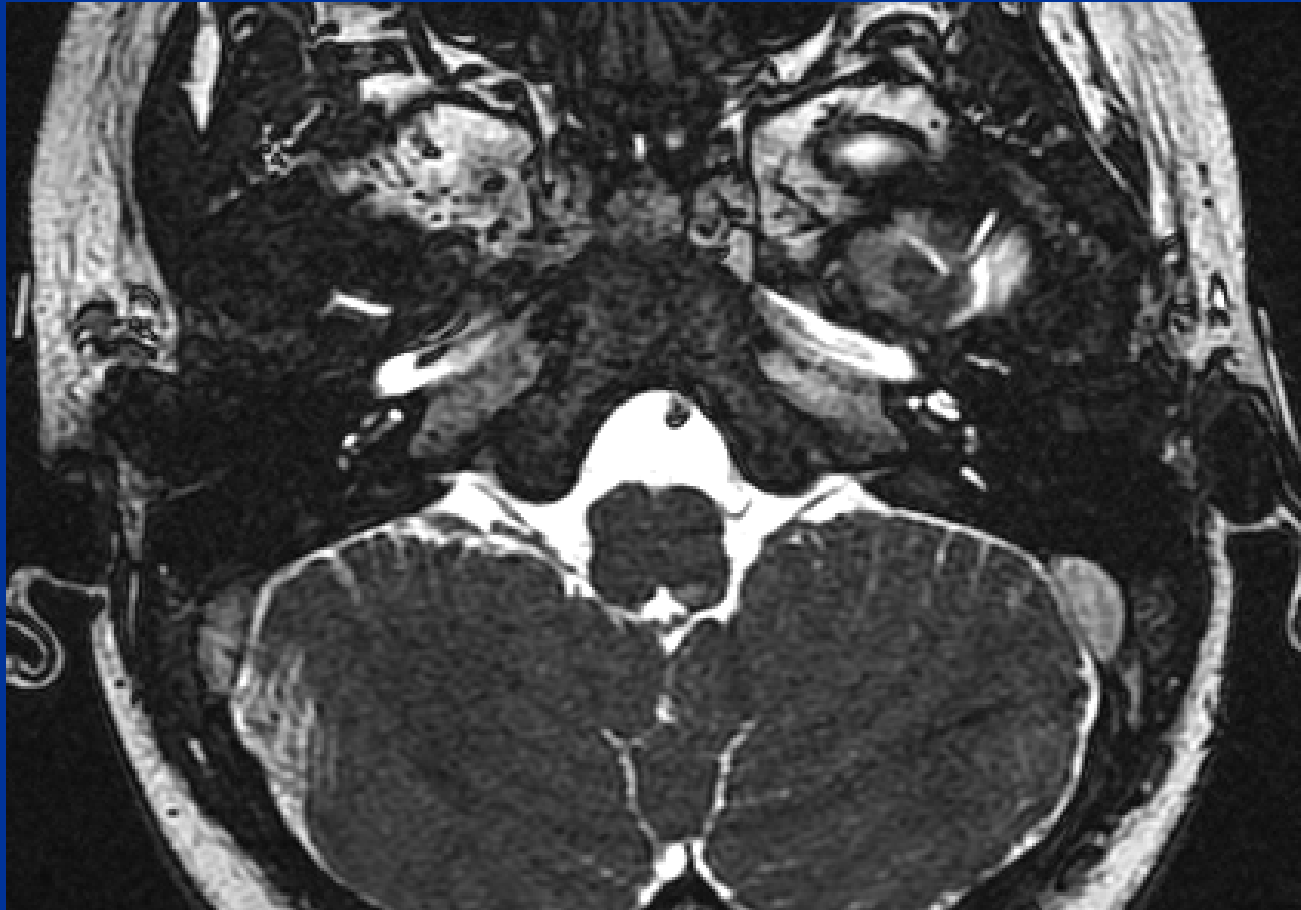




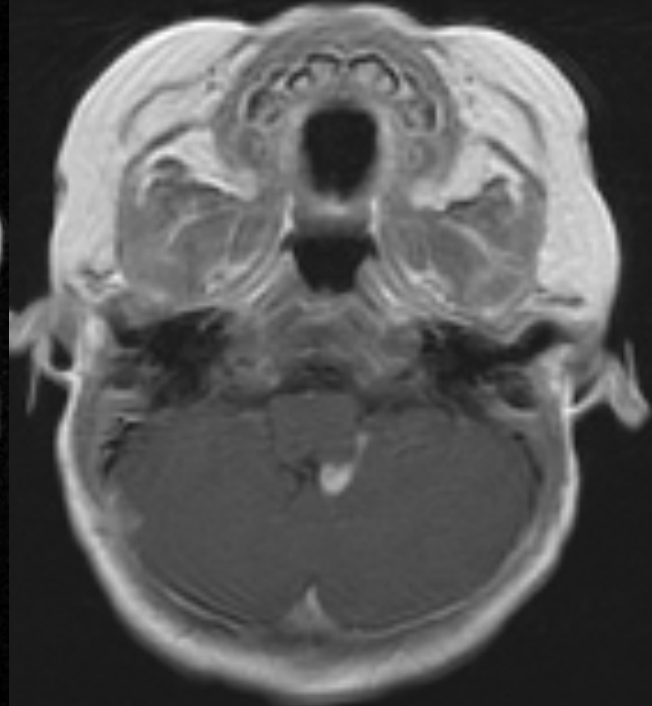
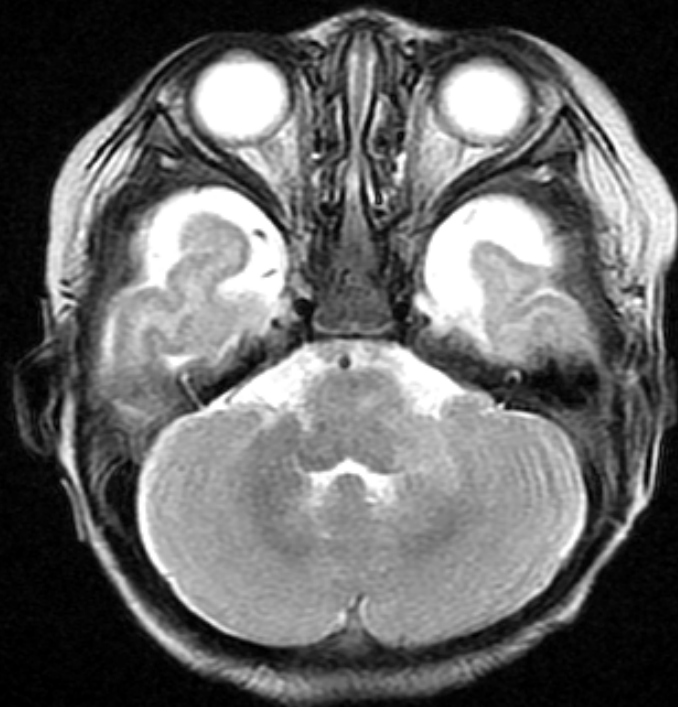
-CT absent eighth nerve AU
-Infant failed UNHS



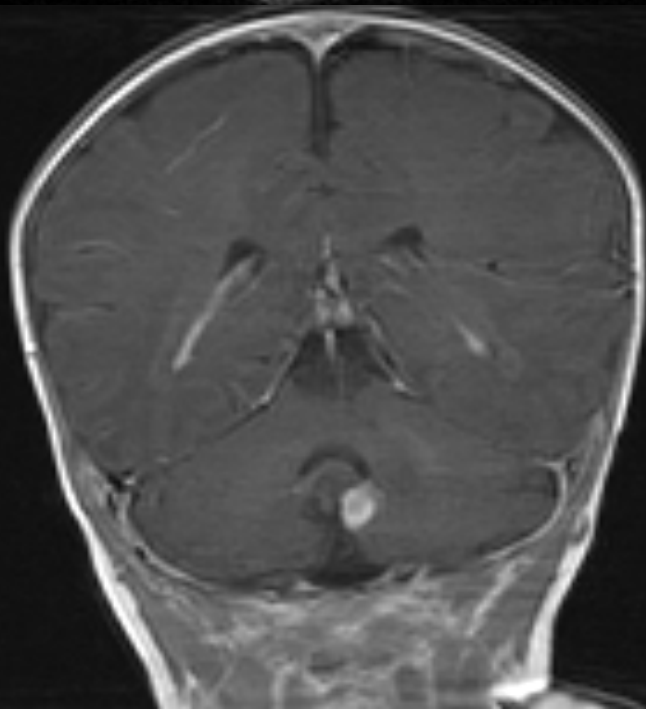
MRI absent eighth nerve AU



Loss of fluid signal in basal turn of cochleae AU
and left posterior semicircular canal



Newborn
with
abnormal
ABR AS



What can be treated?

Congenital Infections

- TORCHES
- Toxoplasmosis 1:8000; tested at birth in MA
- Rubella (one reported case in 2006)
- CMV 1/100-200 births; not tested at birth
- Herpes 1:2500-10,000, but HL very rare unless the baby has obvious systemic infection
- Syphilis 1/100,000
- Inflammatory mediators pre/peri natal

Epidemiology of CMV

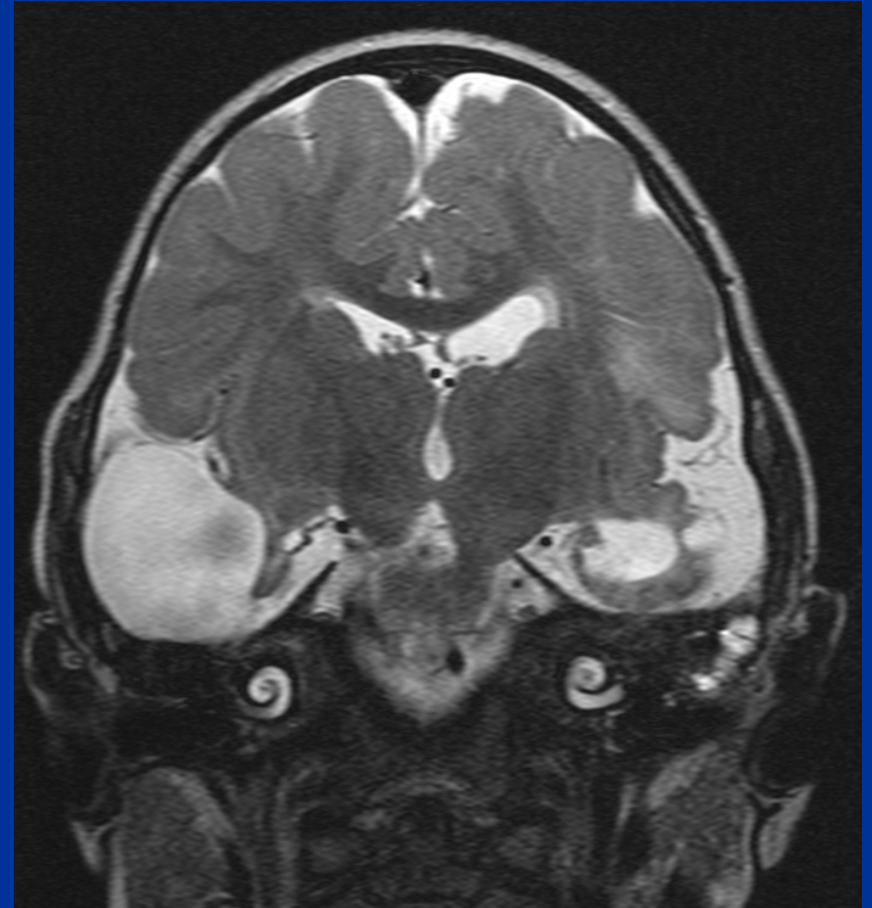
- 1% of all live births
- 10-15% of babies with congenital CMV are symptomatic
 - 75% of these will have CNS symptoms
 - 65% of these will have SNHL
- Of asymptomatic babies 5-10% develop SNHL
- Challenge: how to diagnose and who to treat

CMV: Hearing Loss

- 50% bilateral
- Up to 40% of all unknown causes of SNHL
- 25% develops or progresses after age 1 year
- Higher likelihood if pt has periventricular calcifications
- High percentage with SNHL >70dB

Radiological features

- Polymicrogyria
- Cerebral calcifications
- White matter loss
- Ventricular dilatation
- Cystic changes
- Overall, abnormal in 54% if symptomatic



Ganciclovir Trials

- Kimberlin et al, J Peds 2003
- 42 patients with ABR at baseline, 6, 12 months
- 6 weeks intravenous ganciclovir
- Stable or improved hearing at 6 months (P=.06)
 - 21/25 (84%) treated patients
 - 10/17 (59%) control patients
- Worsening hearing at 6 months
 - 0% of ganciclovir patients
 - 41% of controls patients
- Stable or improved hearing at 12 months (P=.08)
 - 79% treated patients
 - 59% control patients
- Worsening hearing at 12 months (P=.002)
 - 21% of ganciclovir patients
 - 61% of controls patients

Prevention of CMV

- Epidemiologic modification
- Testing of mothers
 - Distant prenatal CMV infection can still transmit the virus
 - Distance between pregnancies affects CMV transmission rate
 - Not clear how immune status alters transmission rate to fetus
 - Testing intrapartum to know about seroconversion
- Avoidance
 - Day care centers
 - Young children
 - Known CMV shedders
 - ??Breast milk??
- Vaccines
 - Women of childbearing age exposed to kids
 - Women before they become childbearing

Postnatally Acquired Infections

- Bacterial meningitis
 - Marked decrease since HIB, Prevnar®
 - *N. meningitidis* vaccination
 - Other pathogenic pneumococcal serotypes emerging
- Parvovirus B-19 (Fifth's disease)
- Mumps (2007, 800/100,000 US)
- Measles (2005, < 6/1,000,000 US)
- Lyme
 - Facial nerve dysfunction more common than hearing loss
- HIV
- Other viruses

Autoimmune Inner Ear Disease (AIED)

- Prevalence unknown
- Isolated vs. part of systemic disorder
- Systemic disorders include
 - Cogan's
 - JRA
 - Crohn's disease
 - Sjogren's
 - Lupus
- Treatment
 - Steroids
 - Cyclophosphamide
 - MTX

Dangerous if missed

Genetics

- Long QT (Jervell and Lange-Nielsen; JLN)
 - 1.6-6/1,000,000 (1:200,000 in Denmark)
 - KCNQ1, KCNE1 (recessive)
 - Dominant form causes Romano-Ward; HL not profound
 - Symptoms include syncope, sudden death, torsades de points
- Branchio-oto-renal syndrome (BOR, autosomal dominant)
 - Incidence: 1:40,000
 - EYA1, SIX5, SIX1
 - Variable renal anomalies; incidence of renal failure unclear
- Alport Syndrome
 - 1:50,000
 - AR, X-linked, possibly AD
 - Most develop renal failure

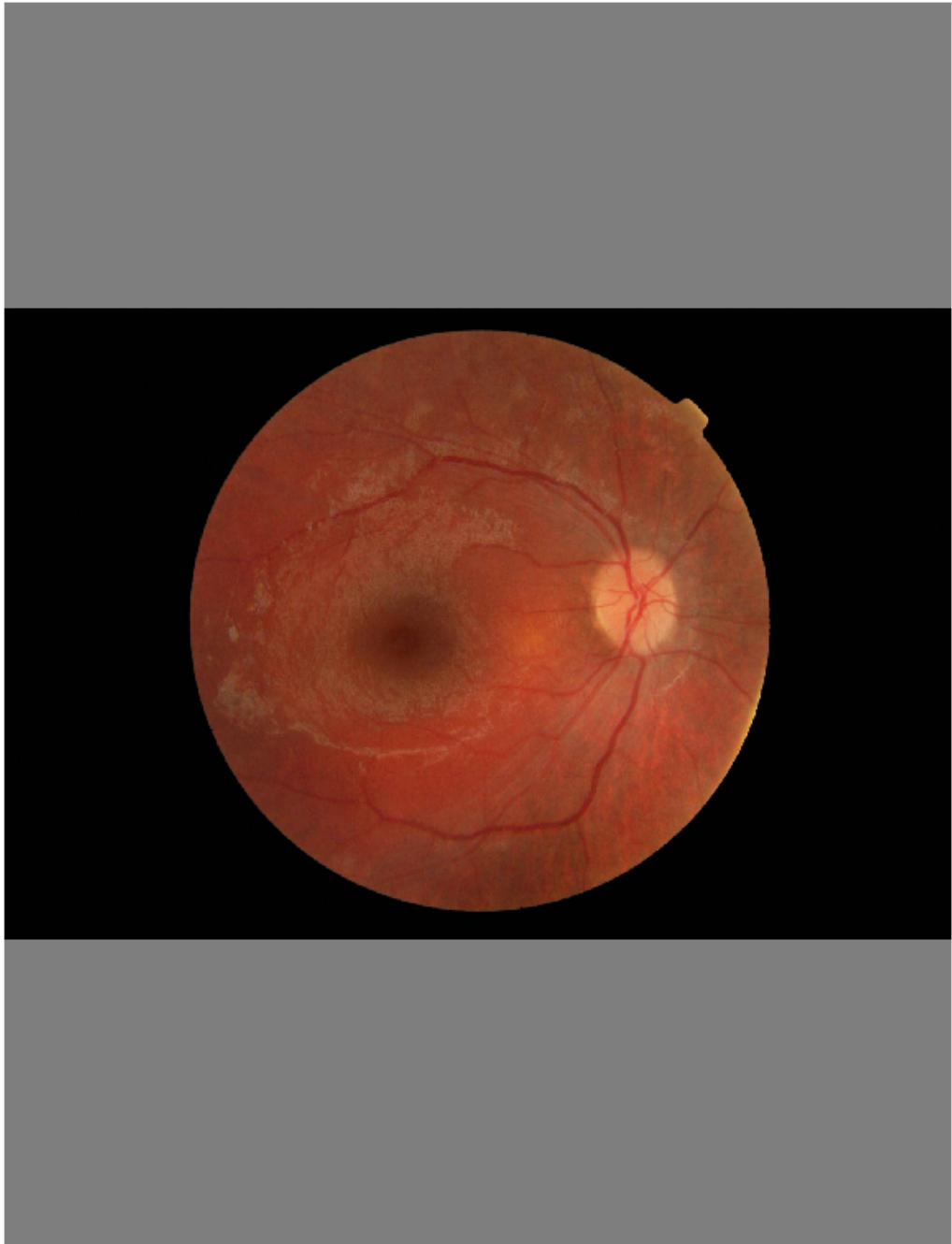
Usher Syndrome

(3-6% of childhood deafness)

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

Usher Syndrome Loci and Genes

Locus name	Genome Location	Gene name	Gene Protein Product
USH1B	11q13.5	MYO7A	Myosin 7A
USH1C	11p15.1-p14	USH1C	Harmonin
USH1D	10q22-q22	CDH23	Cadherin 23
USH1E	21q21.1	Unknown	Unknown
USH1F	10q21.1	PCDH15	Protocadherin 15
USH1G	17q25.1	USH1G	Usher Syndrome Type 1G protein
USH1H	15q22-23	USH1H	Unknown
USH2A	1q41	USH2A	Usherin
USH2C	5q13	GRP98	G protein-coupled Receptor 98
USH2D	9q32-34	DFNB31	Cask-interacting protein
USH3	3q21-q25	CLRN1	Clarin-1

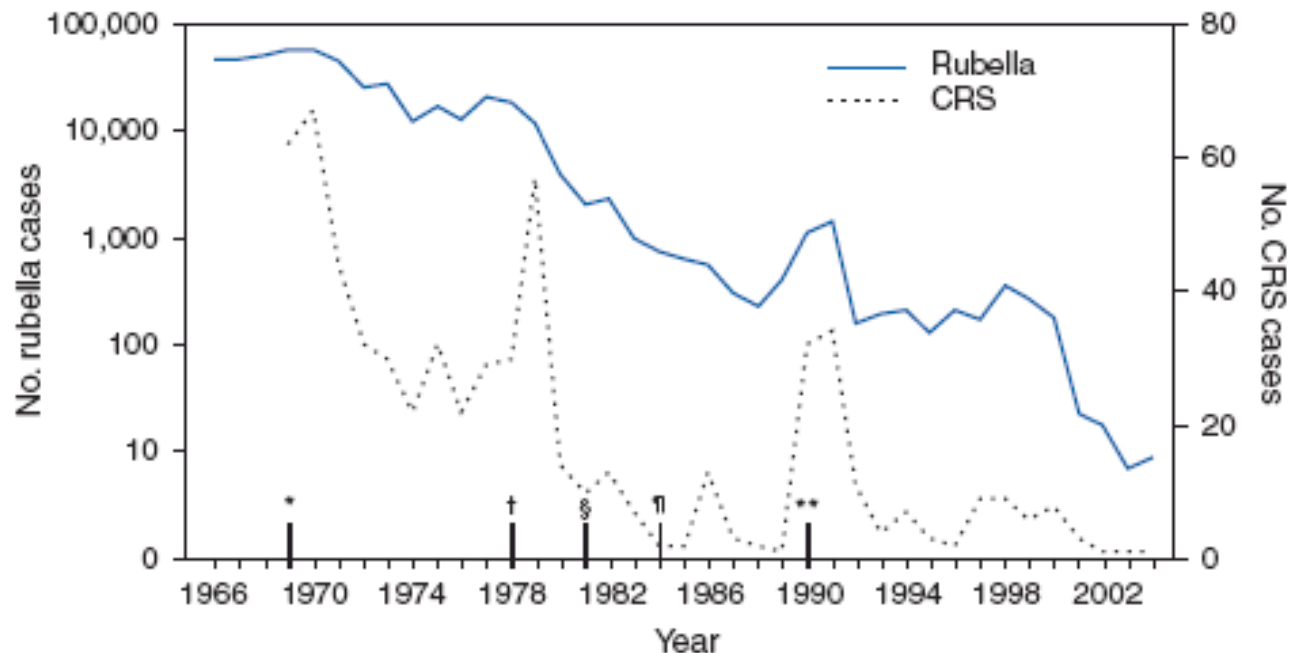


May be able to prevent occurrence
or progression

Postnatally Acquired Infections that are preventable

- Bacterial meningitis
 - Marked decrease since Hib (1980), Prevnar® (2000)
 - N. meningitidis vaccination
 - Other pathogenic pneumococcal serotypes emerging
- Mumps (2007, 800/100,000 US)
- Measles (2005, < 6/1,000,000 US)
- Rubella (since 2001, <1 CRS case/yr)
- Lyme
 - Facial nerve dysfunction more common than hearing loss
- HIV
- Other viruses

FIGURE. Number of reported cases of rubella and congenital rubella syndrome (CRS), by year, and chronology of rubella vaccination recommendations by the Advisory Committee on Immunization Practices — United States, 1966–2004



* 1969 — First official recommendations are published for the use of rubella vaccine. Vaccination is recommended for children aged 1 year to puberty.

† 1978 — Recommendations for vaccination are expanded to include adolescents and certain adults, particularly females. Vaccination is recommended for adolescent or adult females and males in populations in colleges, certain places of employment (e.g., hospitals), and military bases.

§ 1981 — Recommendations place increased emphasis on vaccination of susceptible persons in training and educational settings (e.g., universities or colleges) and military settings, and vaccination of workers in health-care settings.

¶ 1984 — Recommendations are published for vaccination of workers in daycare centers, schools, colleges, companies, government offices, and industrial sites. Providers are encouraged to conduct prenatal testing and postpartum vaccination of susceptible women. Recommendations for vaccination are expanded to include susceptible persons who travel abroad.

** 1990 — Recommendations include implementation of a new 2-dose schedule for measles-mumps-rubella vaccine.

Enlarged Vestibular Aqueduct

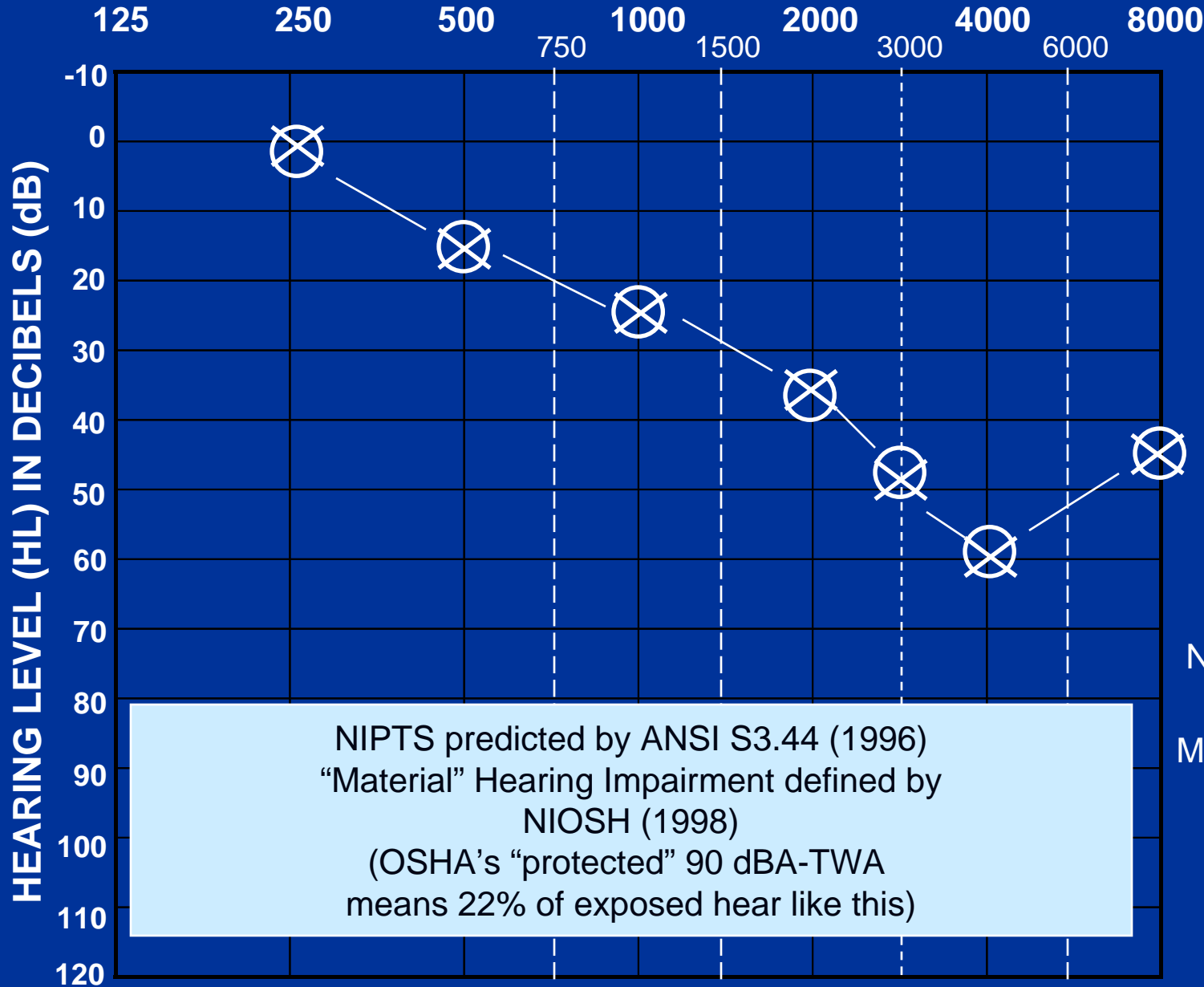
- Head trauma
- Flying
- ??steroids for sudden change??



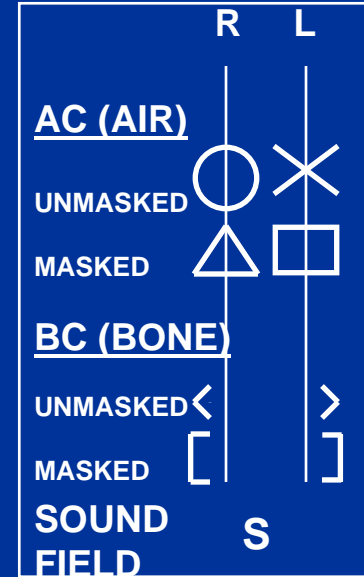
“Modern” acquired causes of HL

- NICU
 - 5-15/1000 NICU babies
 - Ototoxicity, prolonged ventilation, sepsis, low birth weight, hyperbilirubinemia
- ECMO
 - 20-30 % with SNHL
 - Prolonged ECMO runs
 - Prolonged courses of aminoglycosides
 - Diaphragmatic hernia
 - HL delayed onset and progressive
- NOISE
 - MP3 players
 - Loud music
 - Genetic predisposition
 - May be able to prevent
 - Auralon™ ®

FREQUENCY IN HERTZ (Hz)



KEY



Normal 

Material NIHL 

How to manage the hearing loss

- Medical intervention if possible
 - Autoimmune
 - Infectious
 - Antioxidants?
 - Vitamin A?
 - DHA?
- Hearing aids
- FM systems
- Preferential seating
- Cochlear implants

Thank you