





2012 Fanconi Anemia Family Summer Camp

Ear and Hearing Problems in Fanconi Anemia

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Fanconi Anemia

- Autosomal recessive disorder
 - FANCB: X-linked
- Incidence: 3 per 1,000,000
- Very heterogeneous condition
- A wide variety of clinical manifestations
 - Especially multi-organ congenital anomalies

Fanconi Anemia

Nonhematologic Presentations	Frequency(%)
Skeletal (radial ray, hip, vertebra)	71
Skin Pigmentation (Café-au-lait)	64
Short Stature	63
Eyes (Microphthalmia)	38
Renal & Urinary tract	34
Male genitalia	20
Mentally challenged	16
GI (duodenal, anorectal atresia)	14
Cardiac	13
Hearing	11
Central nervous system	8
No Abnormalities	30

(Dokal, 2000)

Ear problems in FA

- Not much information in medical literature
 - Fanconi (1927)-Auricular deformity
 - Uehlinger (1929)-Ear canal narrowing
 - Emile-Weil (1938)-hearing loss
- Pubmed Medical literature search:
 - » “Fanconi anemia”: 3194 articles
 - » “Fanconi anemia and ears”: 14 since 1970
- Reasons:
 - Non-life threatening problem
 - Unawareness of healthcare providers
 - » More common than we think



Dr. G Fanconi

Hearing loss in FA

- A chart review study of 69 subjects from NYC
- Incidence:
 - Only 26 out 69 pts had audiograms
 - 12/69 (17%) with either subjective or documented hearing loss
 - » Only 8 of 12 hearing loss had audiograms
- Type and degree of hearing loss
 - Primarily mild conductive hearing loss

(Santos et al, 2002)

Recent ear study on FA

- Vale et al, 2008
 - From Portugal
 - 8 subjects (age 3 to 13 years)
 - 4/8 (50%) hearing loss
 - Bilateral conductive hearing loss
 - 2 subjects with small ear canal

Fanconi Anemia


- Previous studies were limited because
 - Many were either a brief single case report or a retrospective review
- Hearing loss is one of major factors correlated with a risk of bone marrow failure in FA
 - Rosenberg et al, 2004
- Description of typical ear findings & their prevalence in FA patients would be important
- May lead to early diagnosis of FA
 - Especially in absence of low blood counts or other typical physical features.

Fanconi Anemia Study at NIH

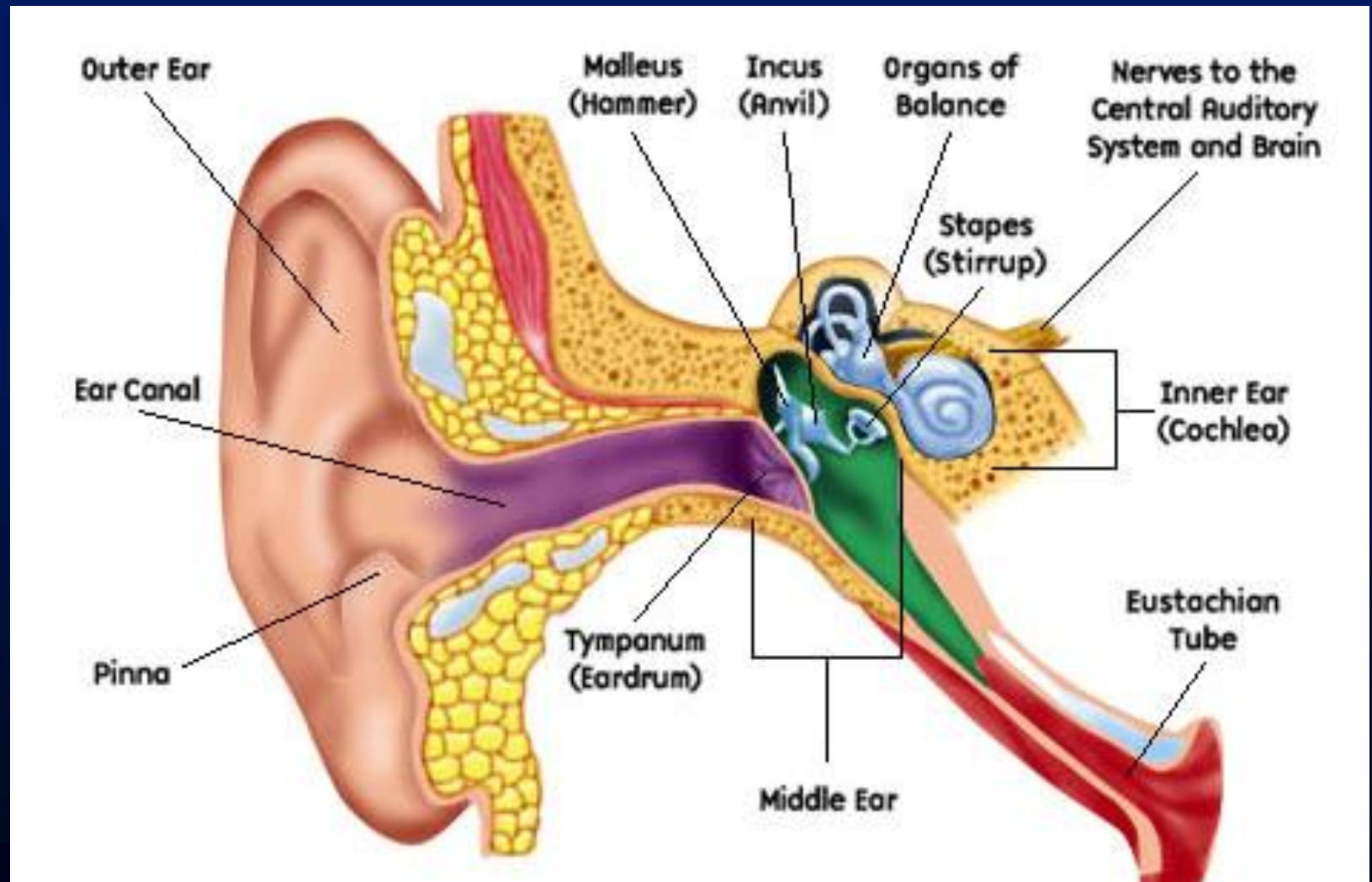
- Inheritable bone marrow failure disease protocol at NIH
 - Multi-disciplinary protocol
 - Systematically look at ear and hearing manifestations in FA
 - Comprehensive ENT evaluation, audiogram and CT of Temporal Bone



Outline of this talk

- Anatomy and physiology of our auditory system
 - Routine hearing & imaging tests
 - Common ear findings in FA
 - Consequences of FA ear problems
 - Treatment options
- 

Normal Ear Structures



Examination of ears



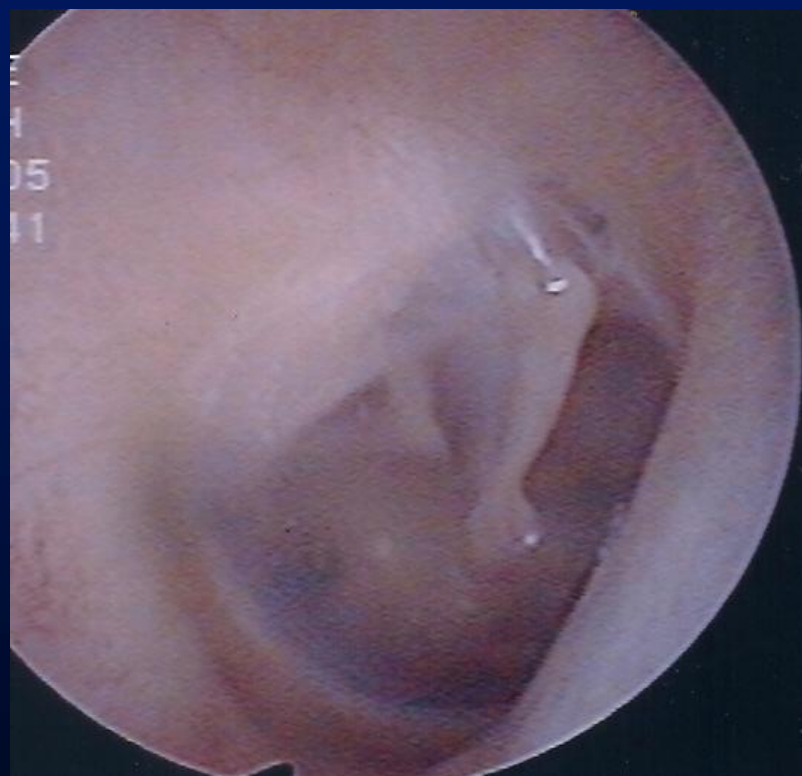
Otoscope



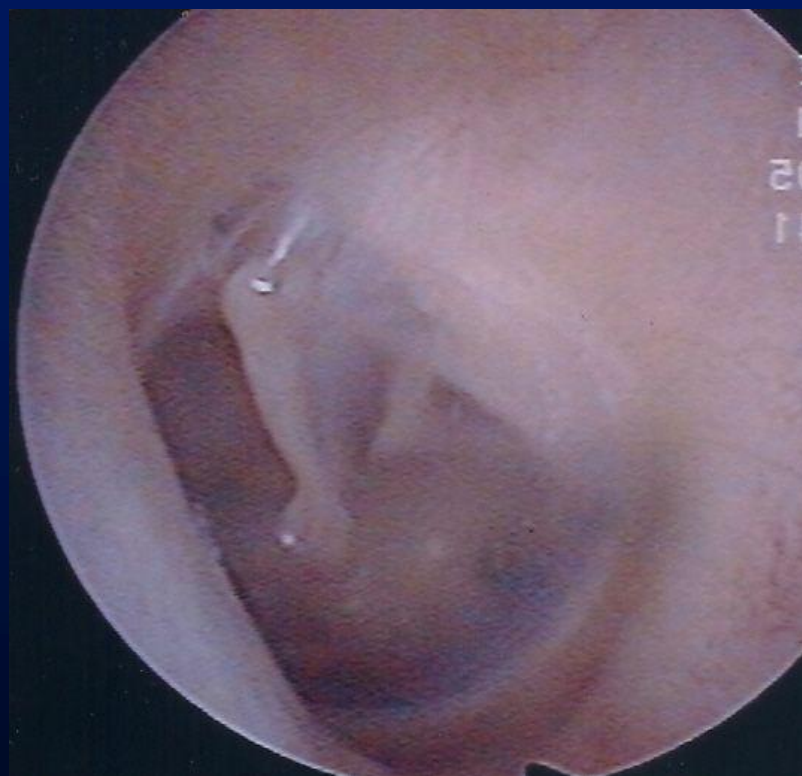
Microscope

Normal tympanic membranes

Right

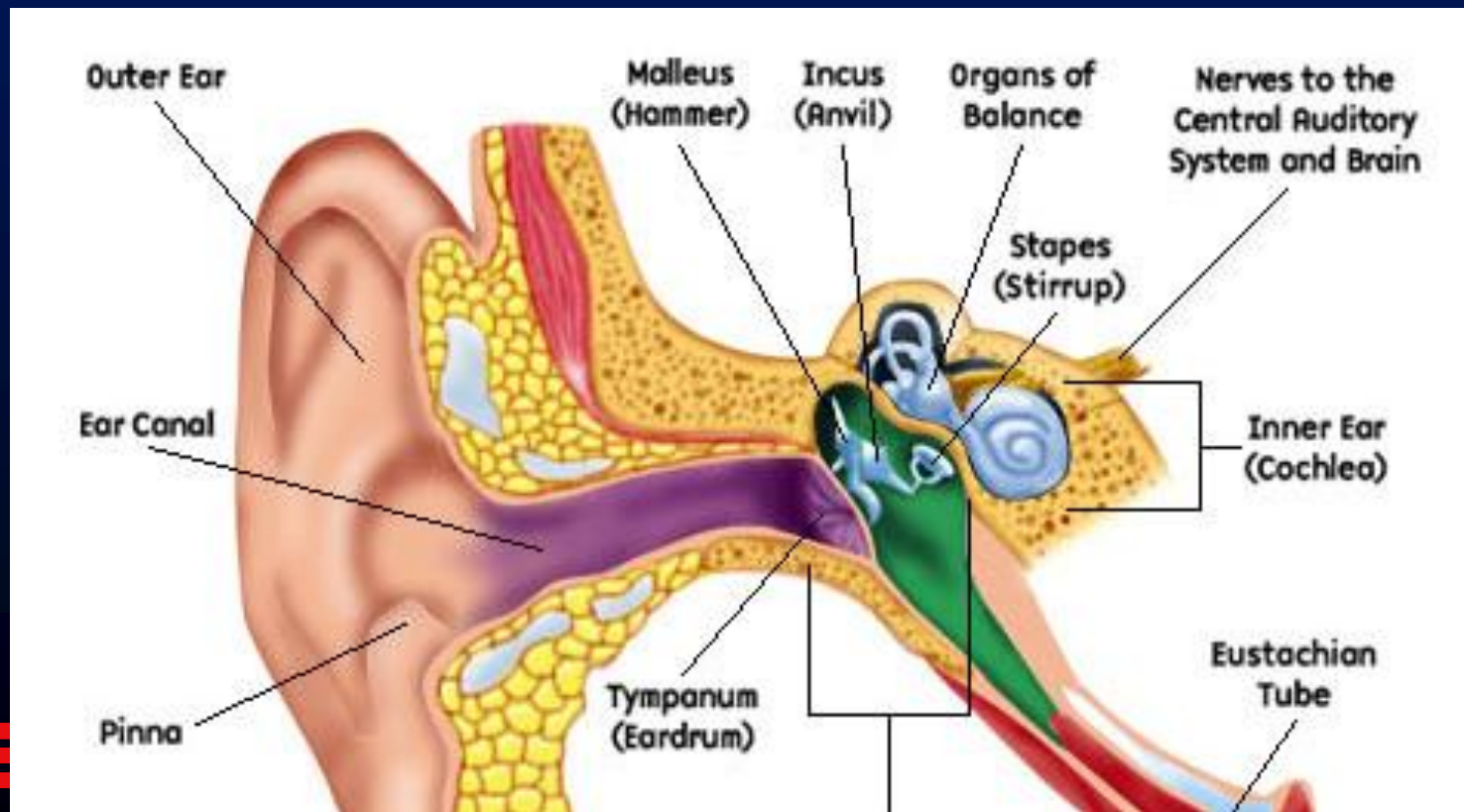


Left



Types of hearing loss

- 3 types of hearing loss
 - Conductive hearing loss (CHL)
 - Sensorineural hearing loss (SNHL)
 - Mixed hearing loss (MHL)



Audiologic evaluation

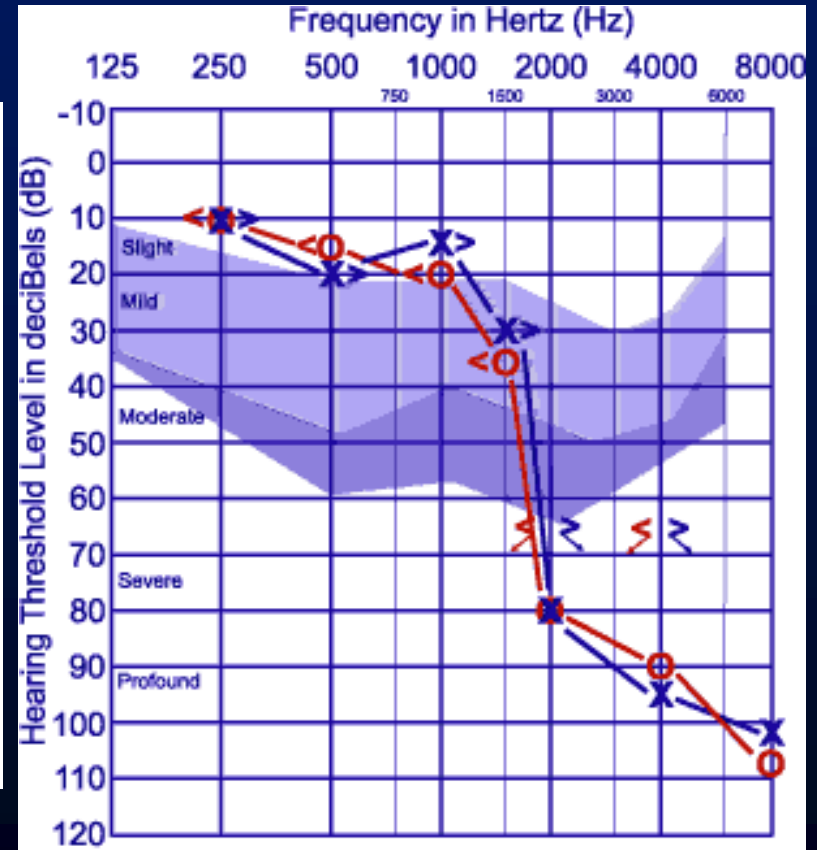
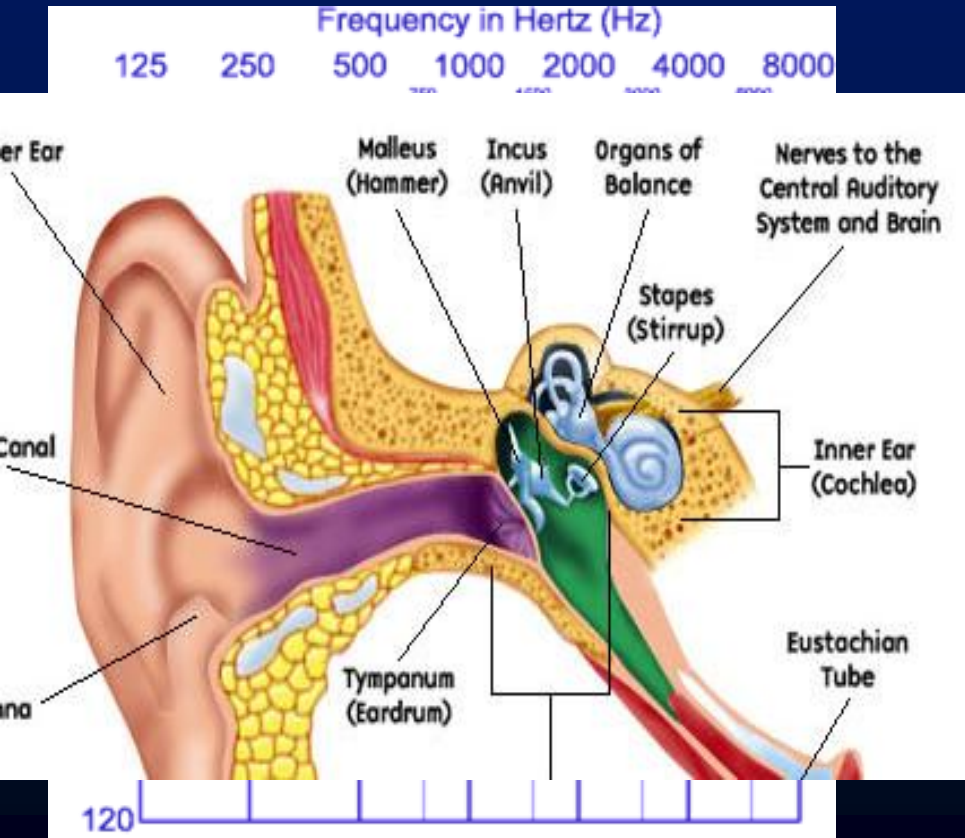
- Behavioral audiologic test
 - Pure tone audiometry
 - Speech audiometry
- For children
 - Play audiometry
 - Visual-reinforced audiometry



Typical audiograms

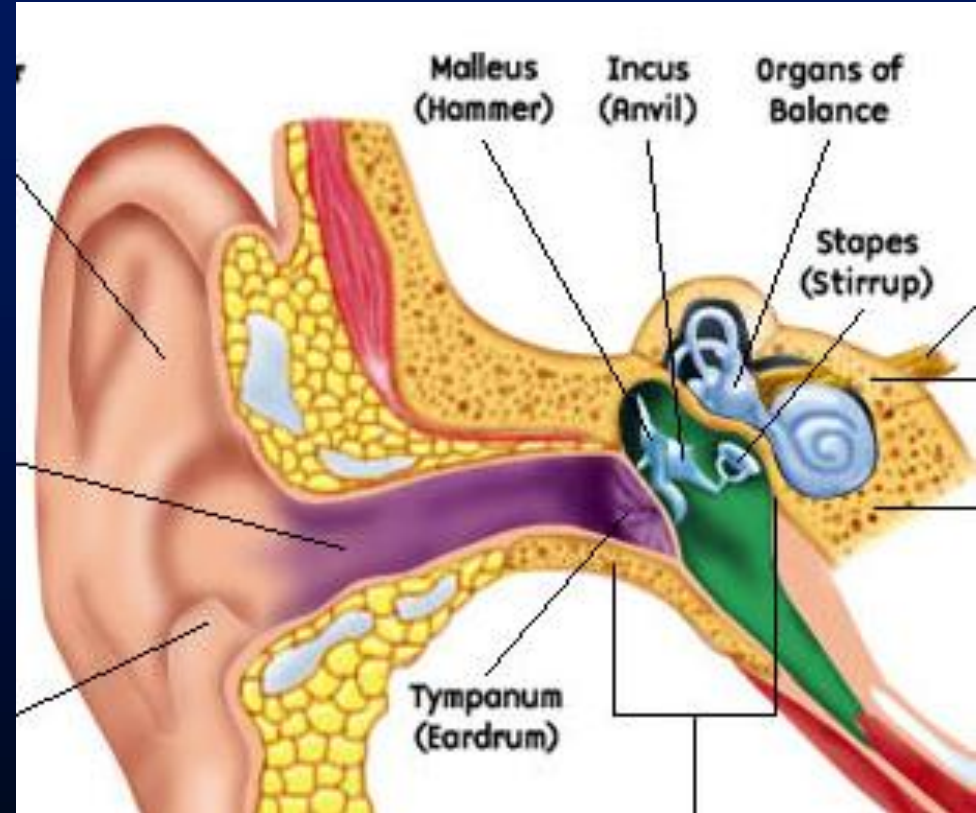
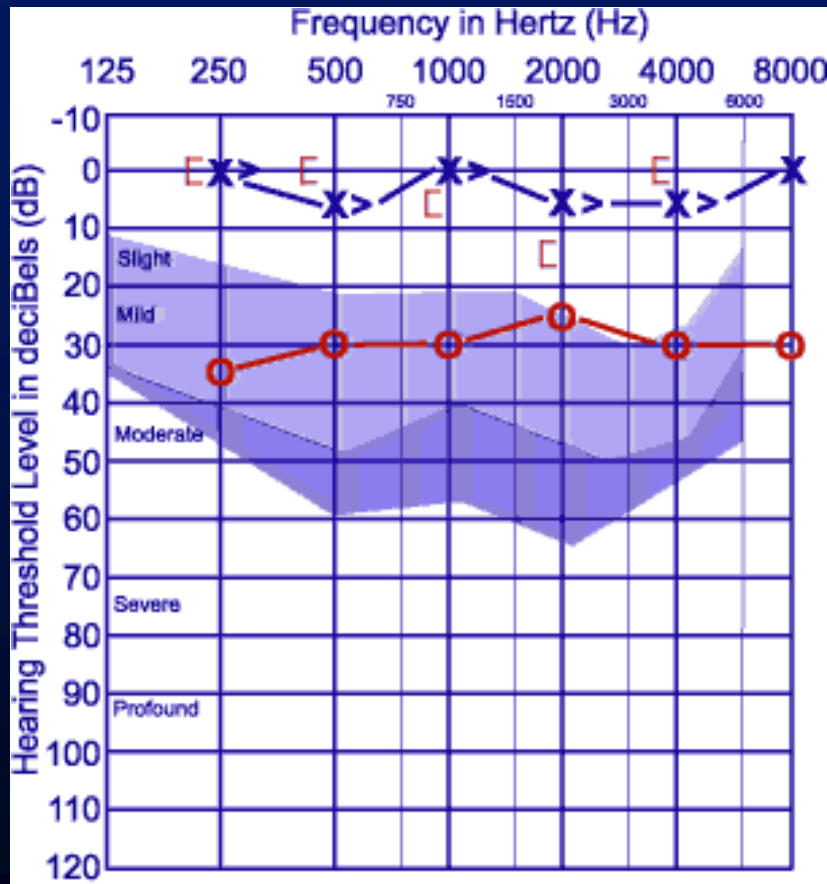
Normal Hearing

Sensorineural HL



Conductive hearing loss

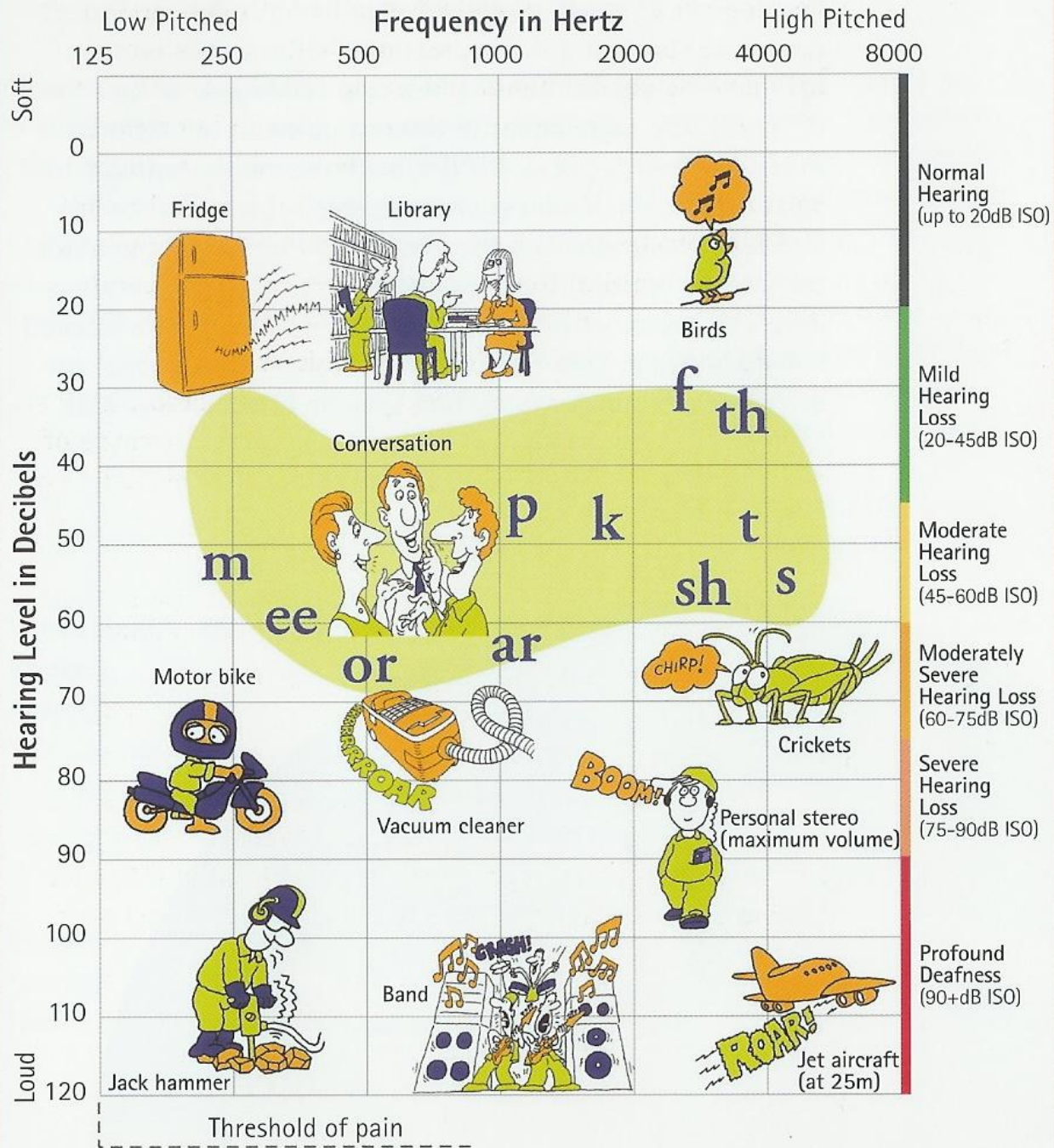
Conductive HL



Audiologic evaluation

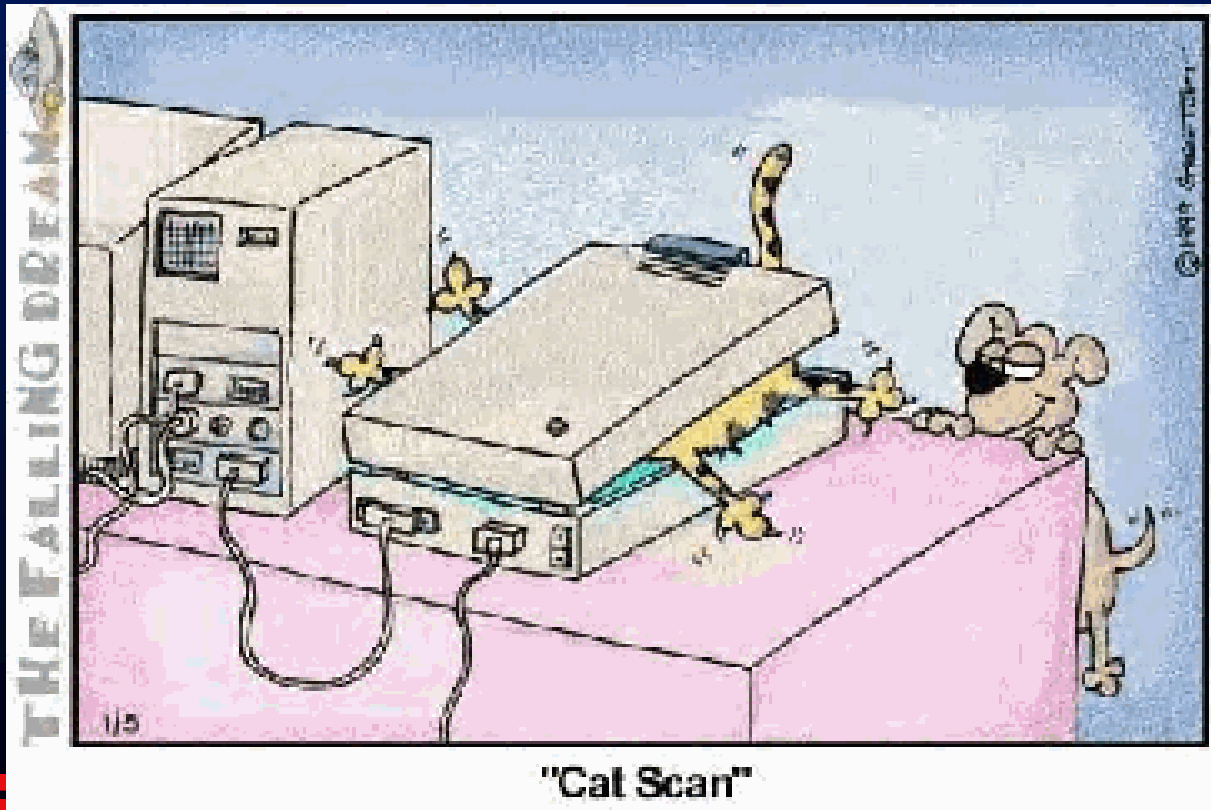
- For younger pts
 - Otoacoustic emission (OAE)
 - ABER (Auditory brainstem evoked response)
 - ASSR (Auditory steady-state response)
 - Do not need patient's cooperation
 - May require sedation



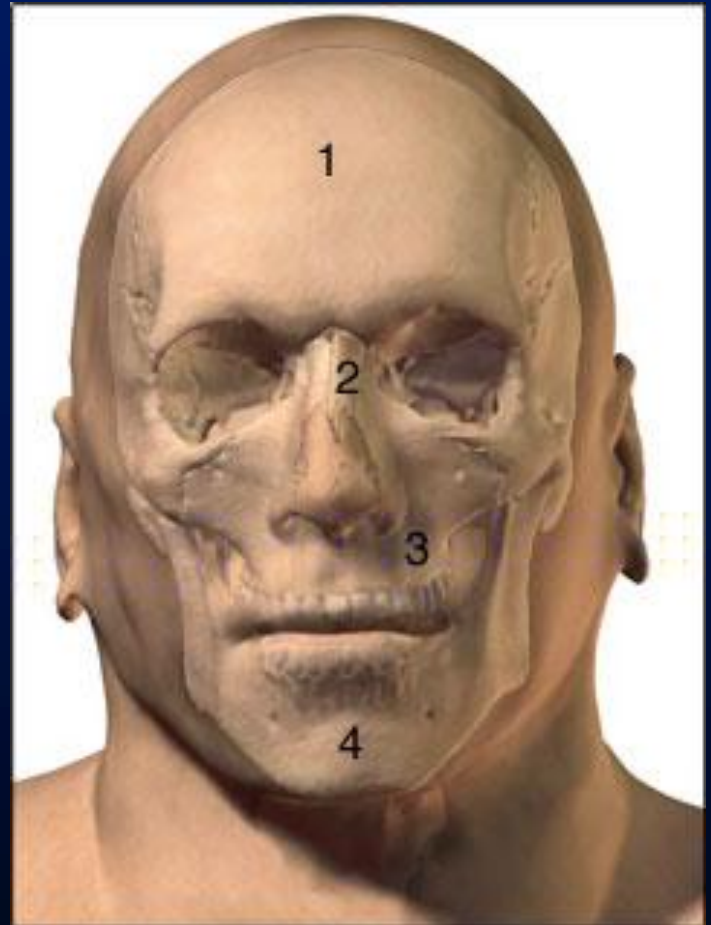


Imaging study

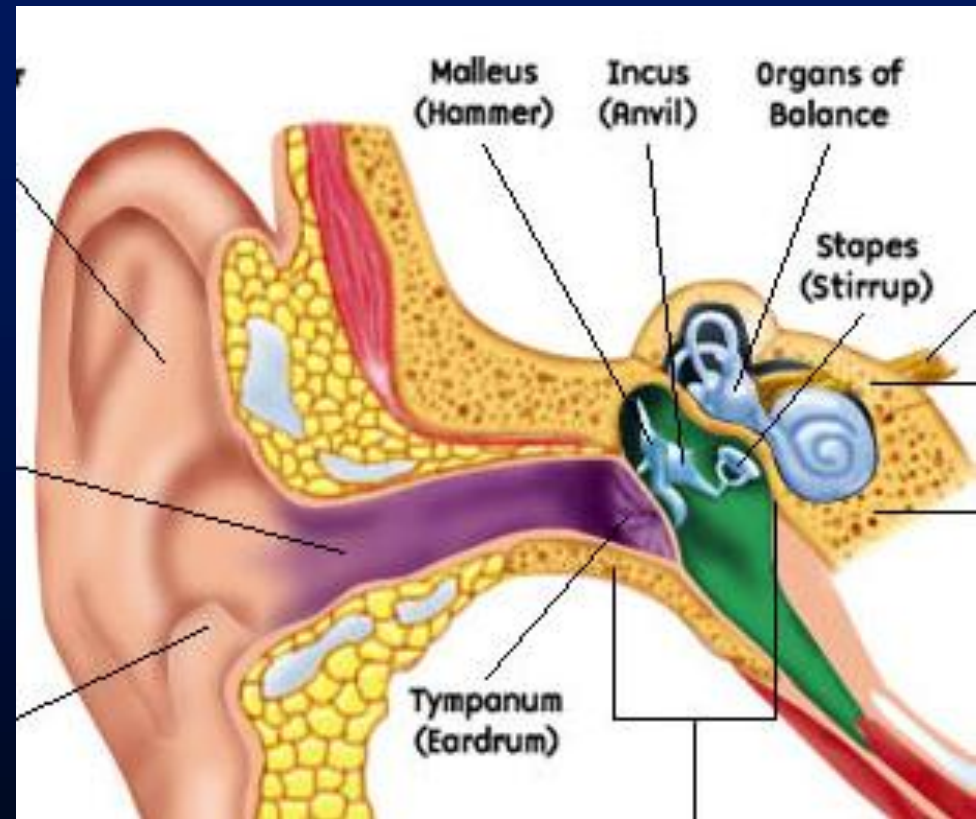
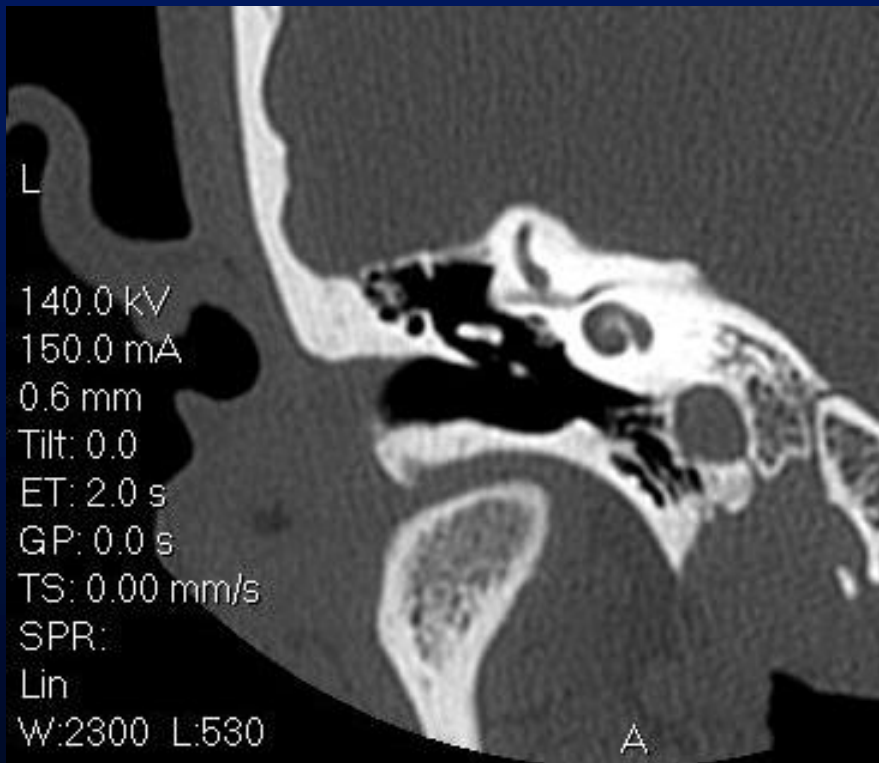
- CT/CAT (Computerized Axial Tomography) scans help to evaluate bony ear and middle ear bones



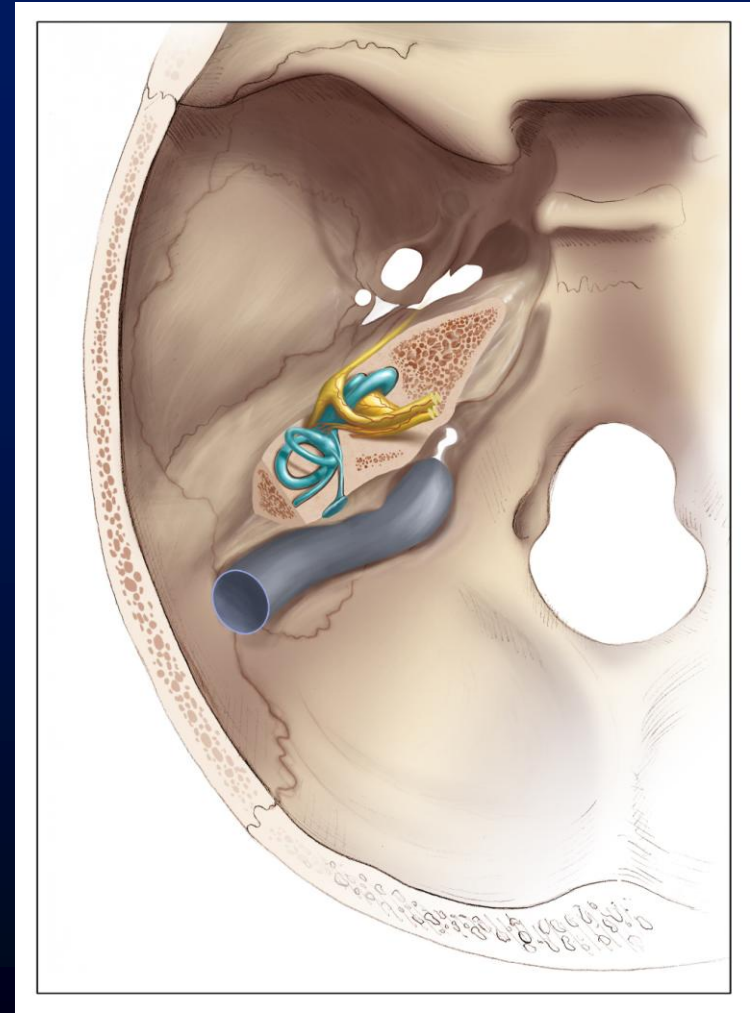
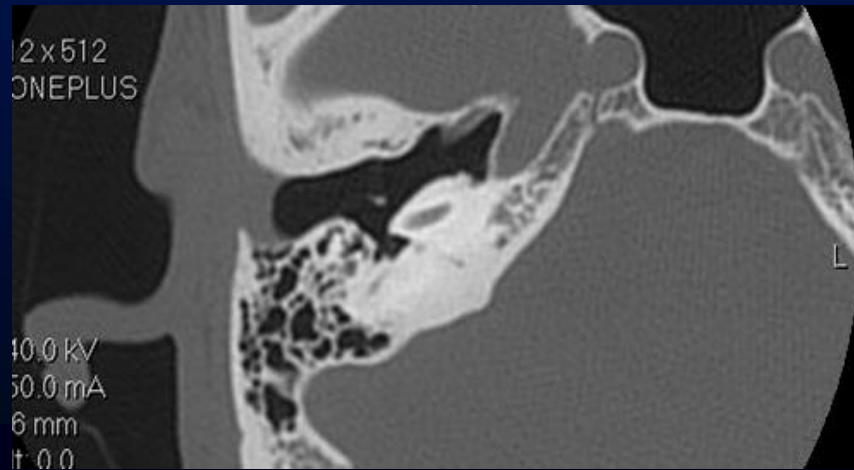
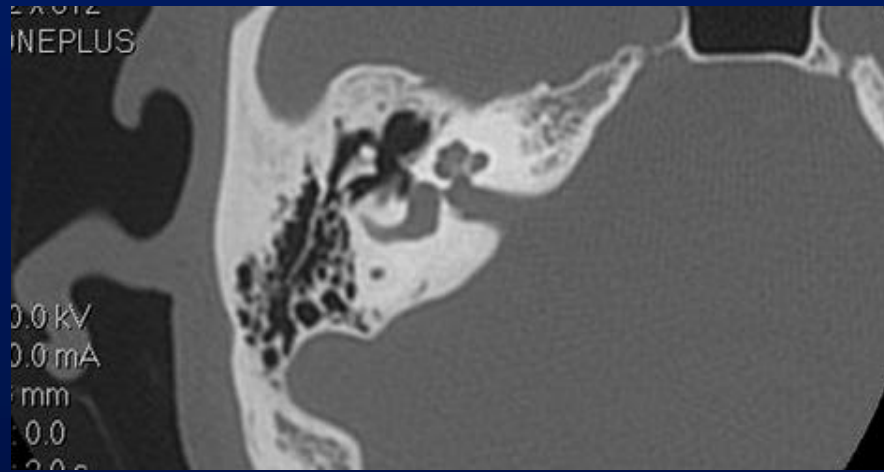
CAT/CT scan



Normal CT of Temporal Bone



Normal CT of Temporal Bone





Magnetic Resonance Imaging (MRI) of brain and ear

- Not necessary unless sensorineural hearing is present
- Look for inner ear malformation, auditory nerve, and brain changes

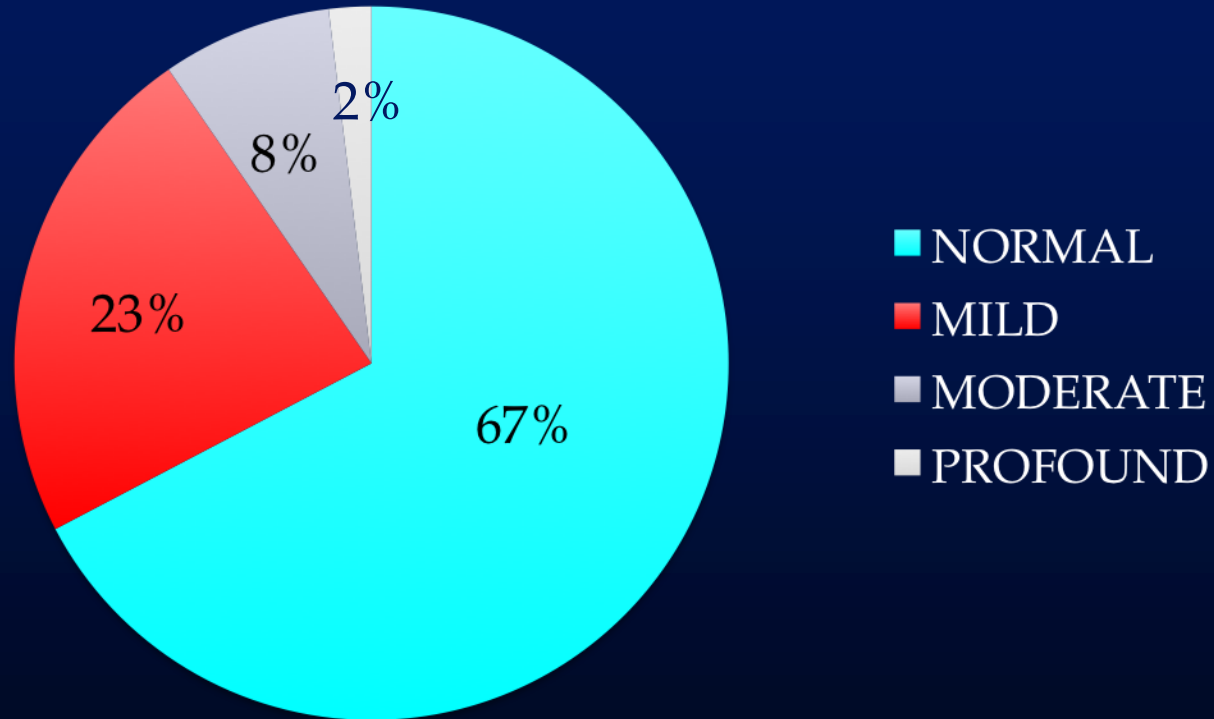


NIH Experience:

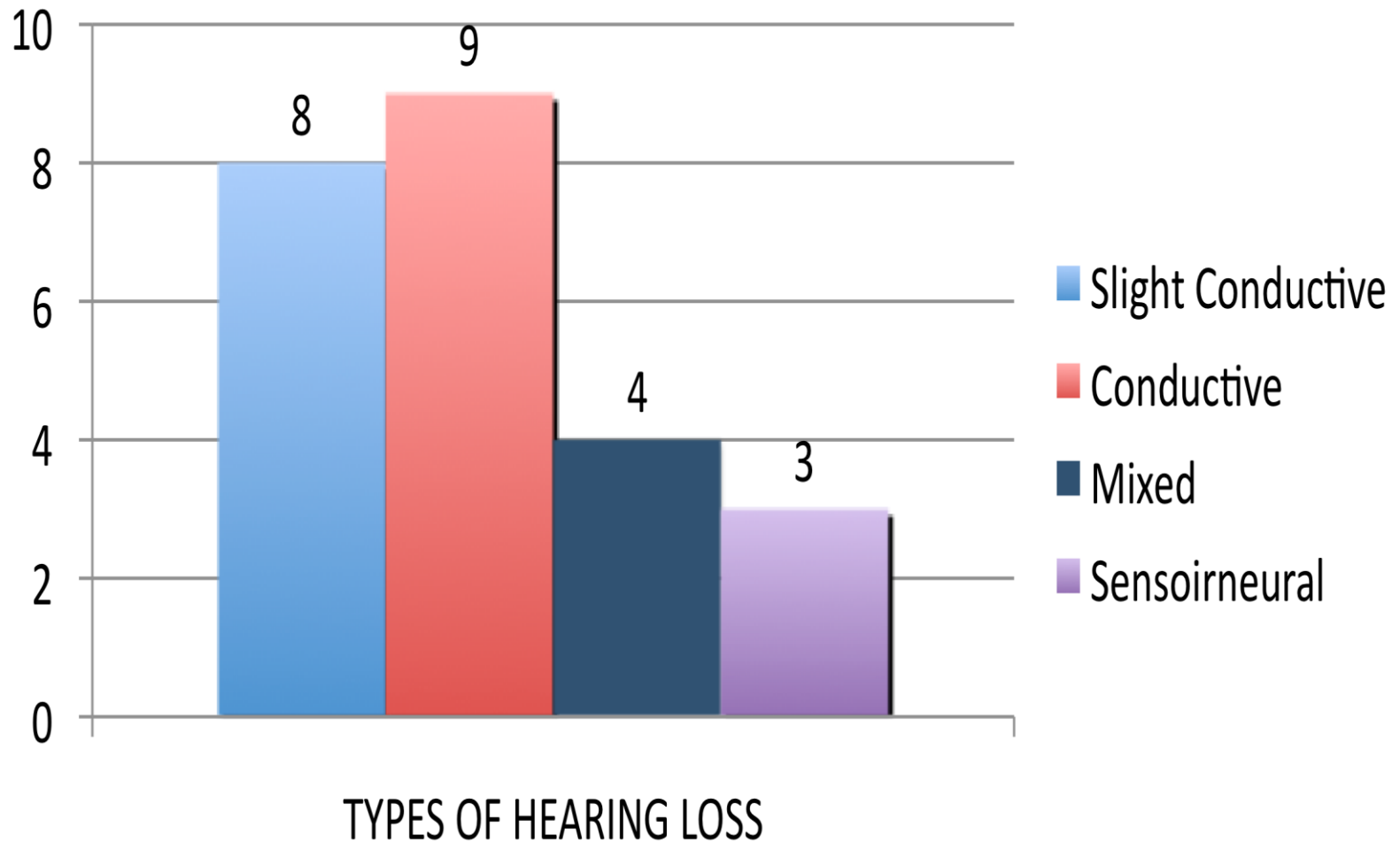
- 31 pts
 - Age range: 3 – 56 yrs (Mean age=20)
- Total of 62 ears in 31 pts
 - Ear surgeries for conductive hearing loss (Ossicular chain reconstruction) and enlarging ear canal (Canalplasty)
 - pts excluded due to unavailable audio or CTs
 - No sufficient information
 - For audio data->58 ears (4 excluded)
 - For CT scan data->52 ears (10 ears excluded)

Degree of Hearing loss (n=58 ears)

Degree of Hearing Loss



Types of hearing loss (n=24)



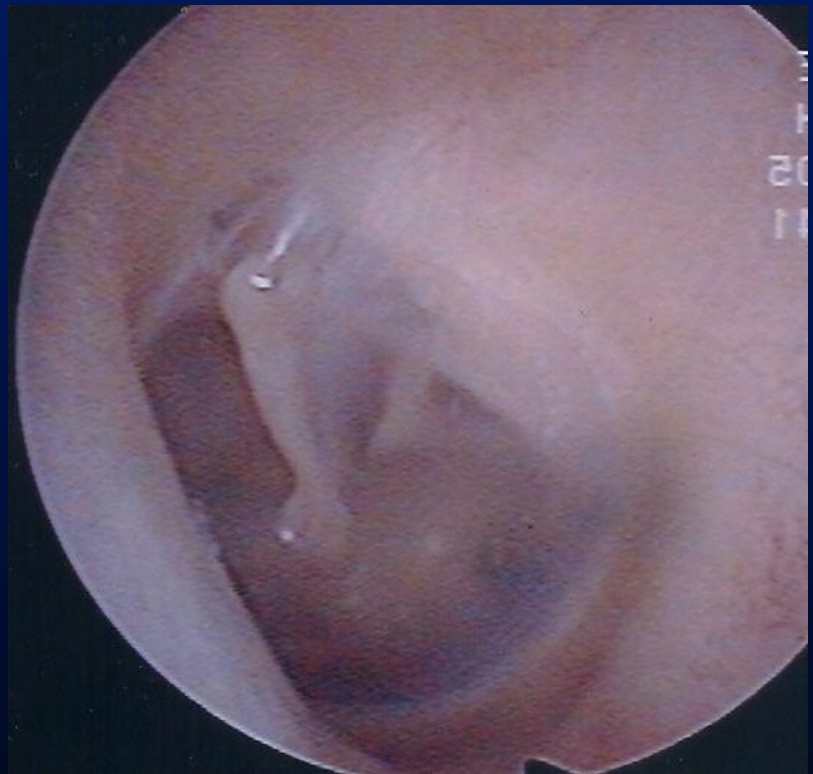


Case I

Left ear drum



Normal



Left normal hearing

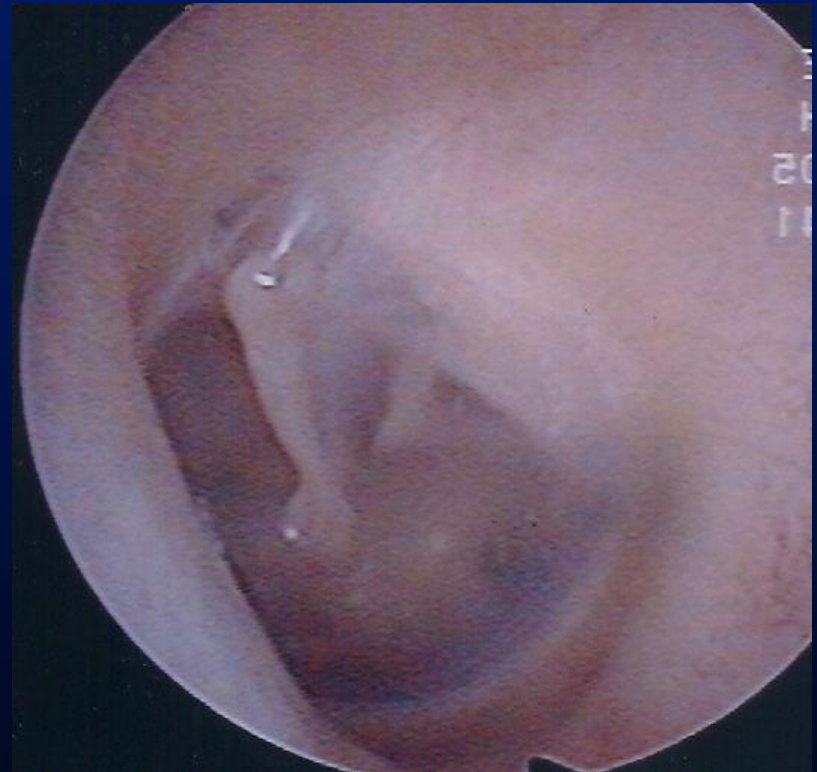


Case II

Left ear drum



Normal



Left slight conductive hearing loss:

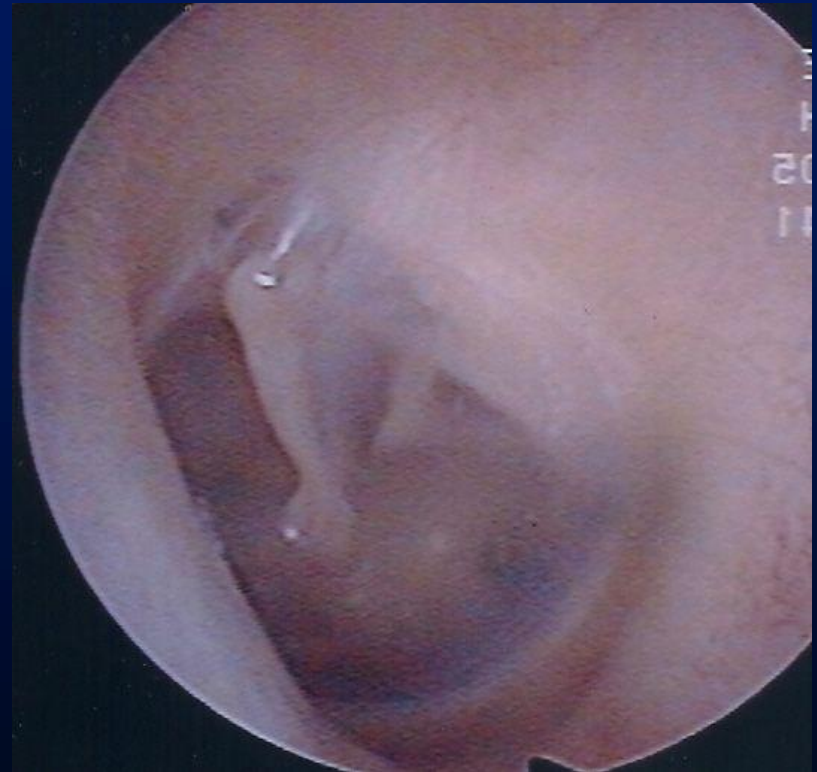




Case III

Left ear drum

Normal

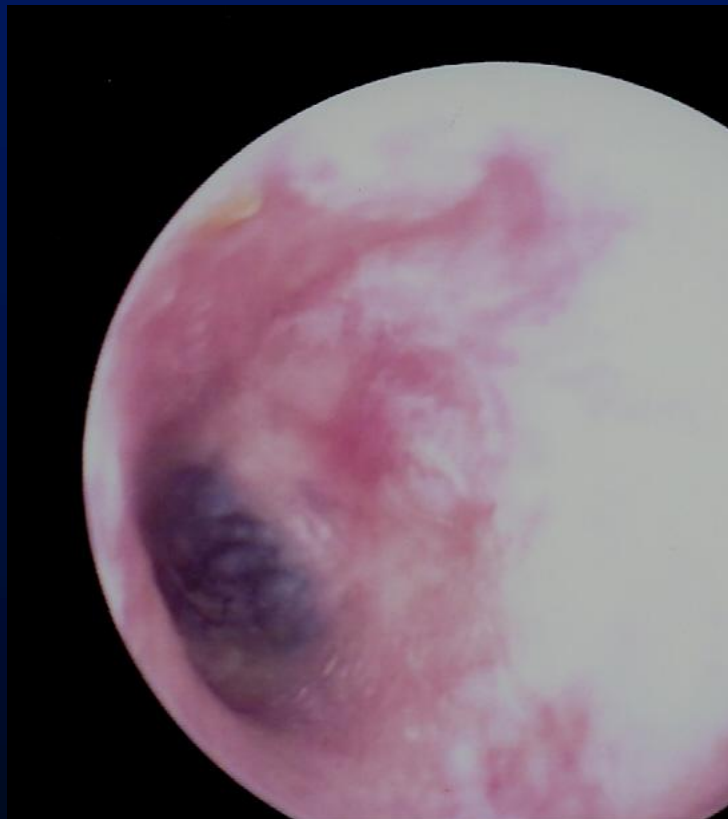


Left slight conductive hearing loss:

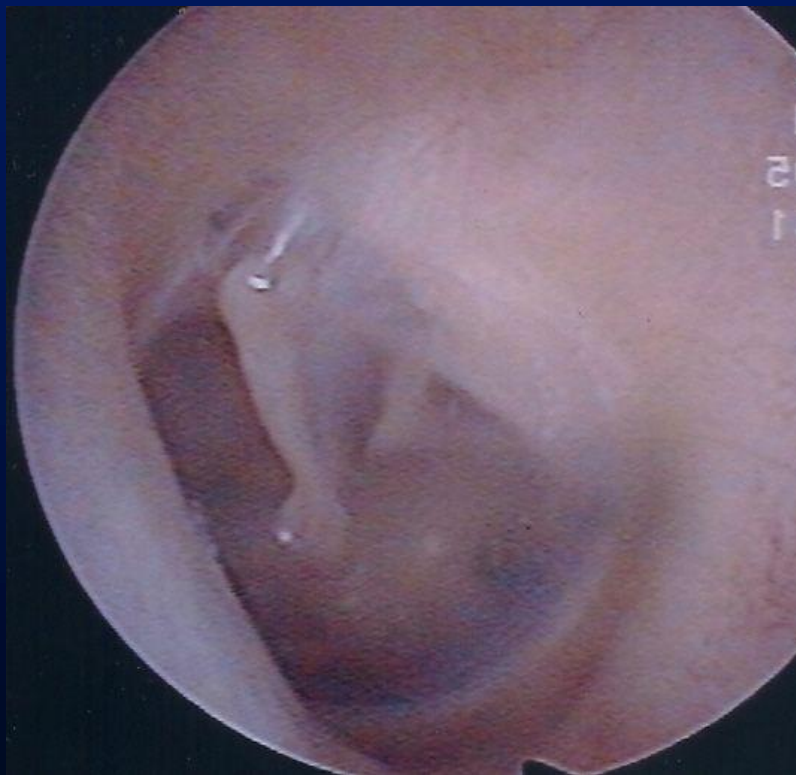


Case IV

Left ear drum



Normal



Left moderate conductive hearing loss



Ear drum and middle ear abnormalities

Ears(n=54)	# ears	%
Normal	22	41%
Scar	1	2%
Abnormal	30	56%
Atresia (No ear canal)	1	2%

CT scans

- N = 52 ears when
 - Excluded due a prior surgery; no or inadequate CT
- Middle ear bones
- Bony plates on ear drum
- Dimension of ear drum



Middle ear bones (Ossicles)

- Not well-formed: 6 (11%)

FA



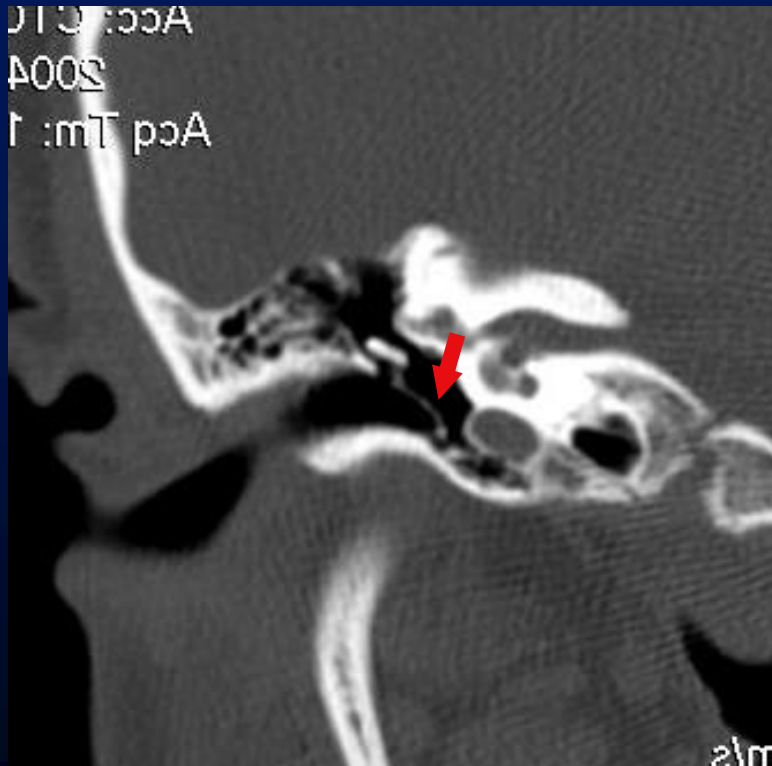
Normal



Ear drum structures

- Bony plates on ear drum: 24 (44%)

FA



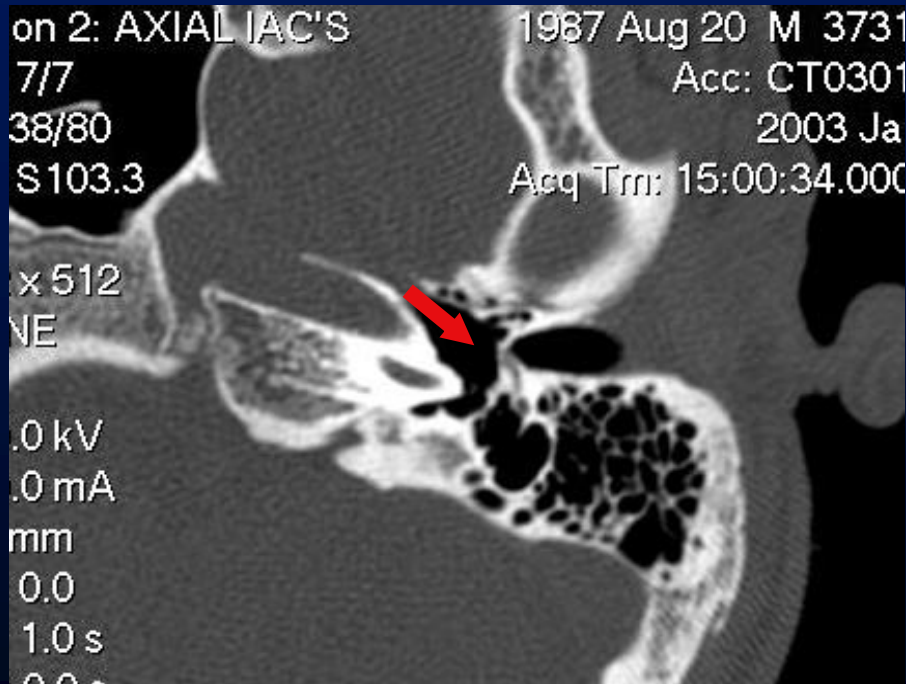
Normal



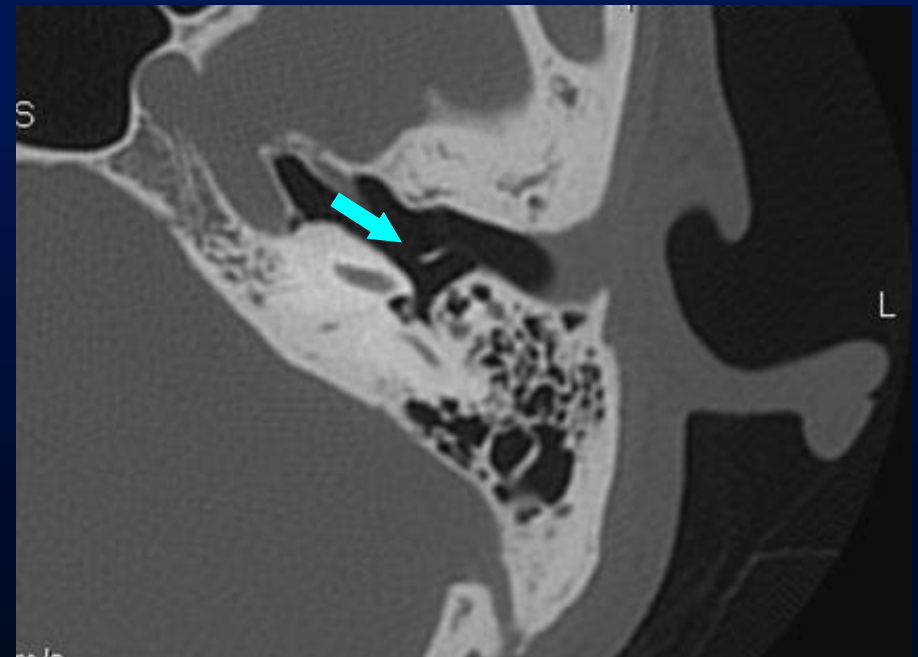
Size of ear drums at medial ear canal

- Grossly small ear drum/canal: 12 (23%)

FA



Normal



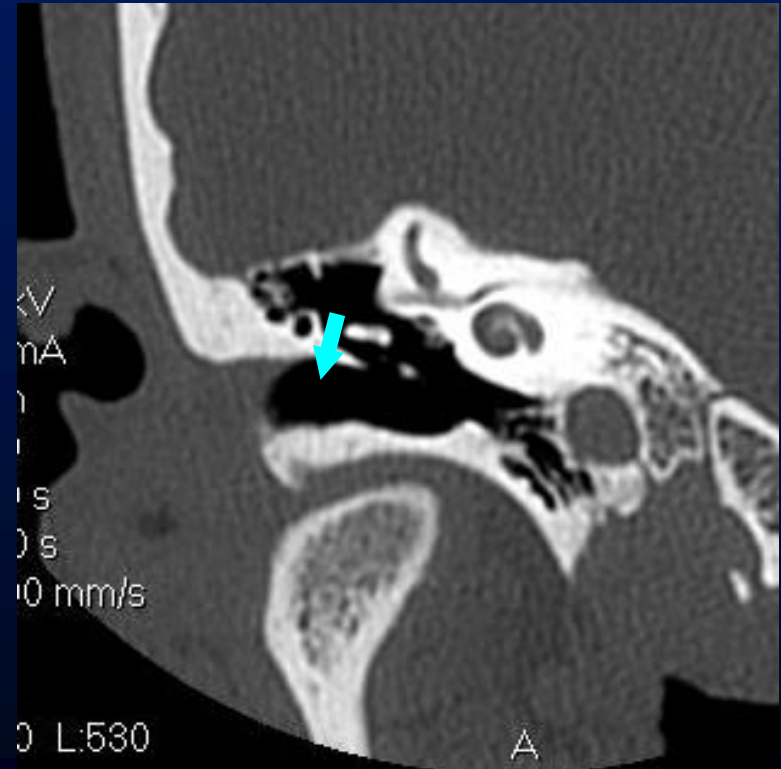
Ear Atresia (absent ear canal)

- No ear canal development: 1 (2%)

FA



Normal

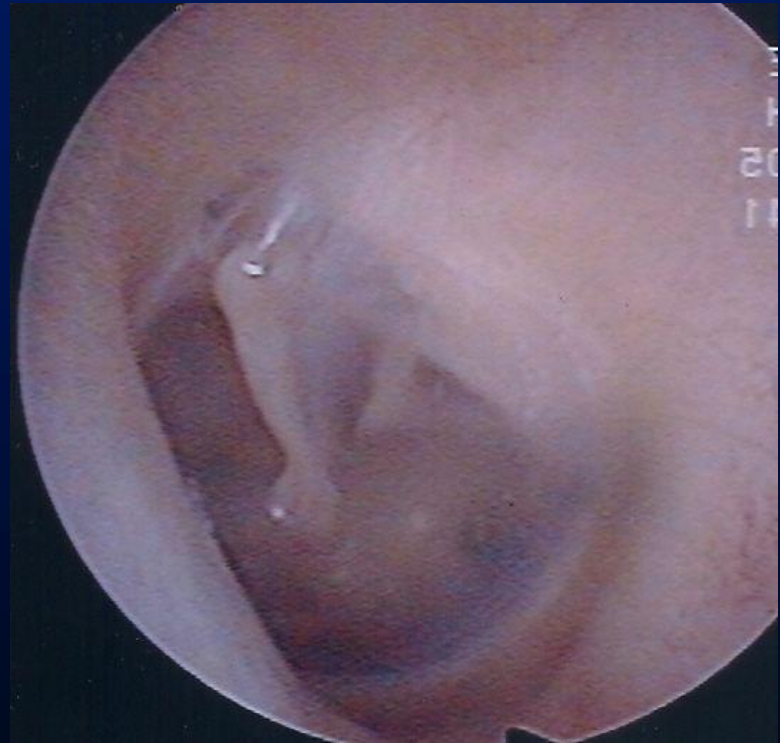


Dimension of ear drums on CT

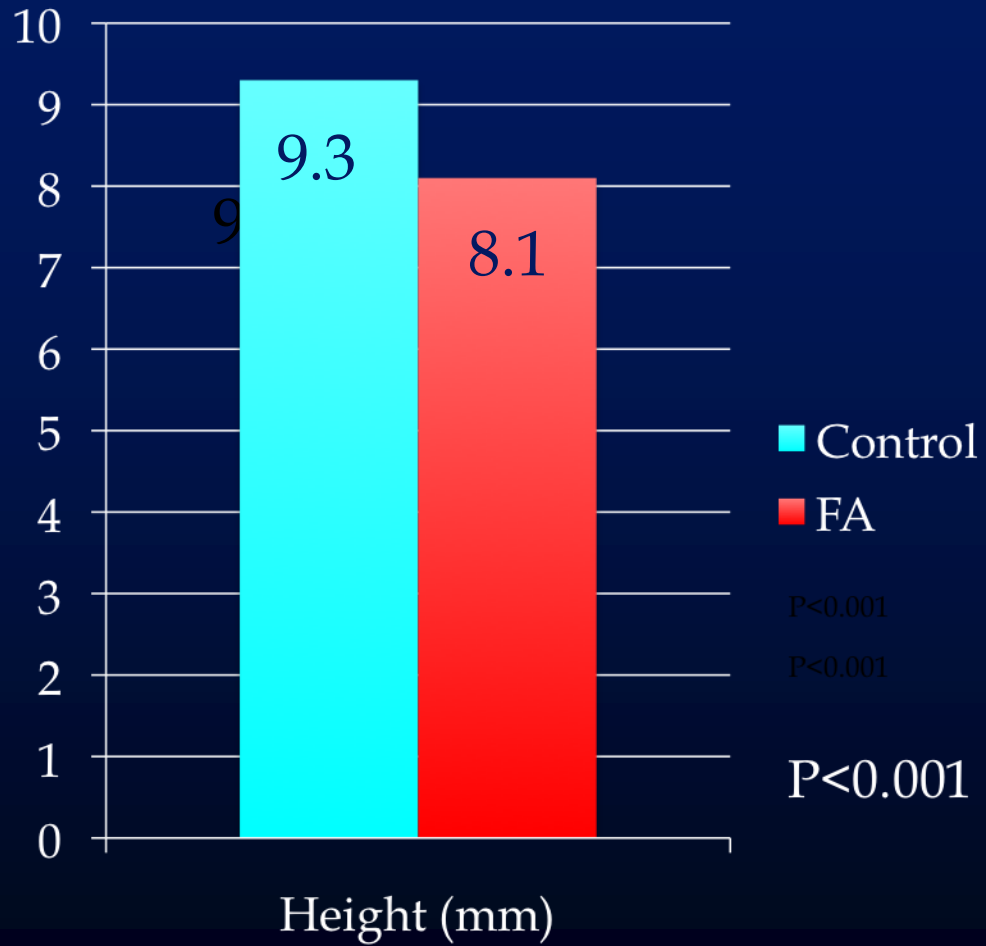
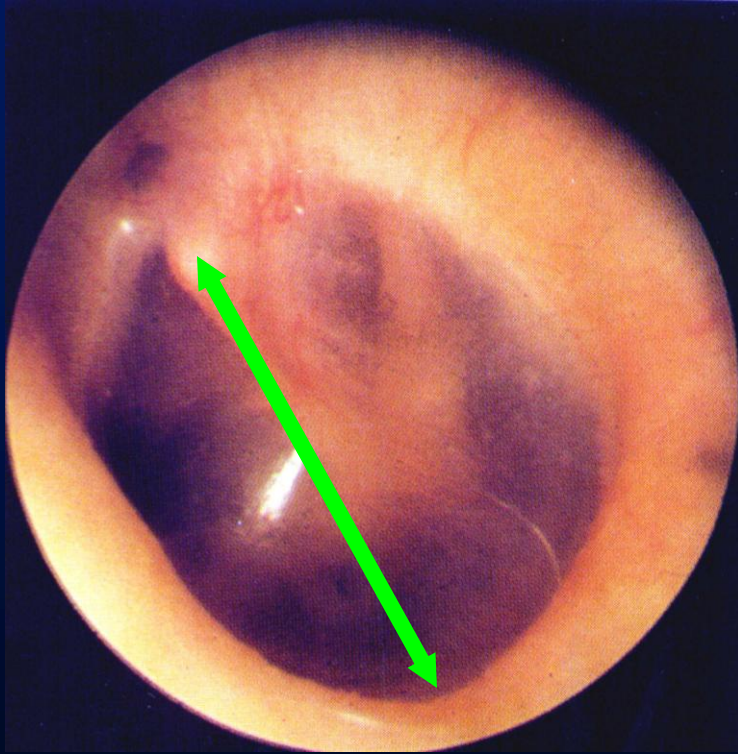
FA



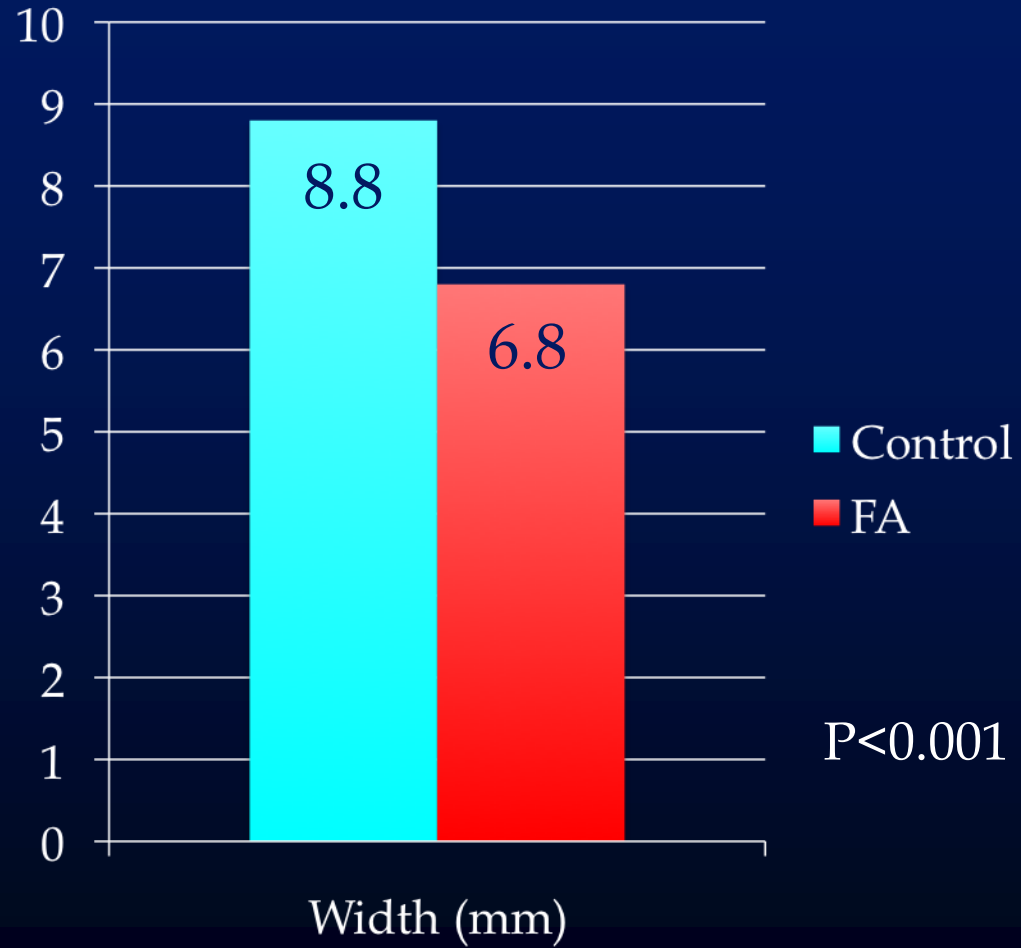
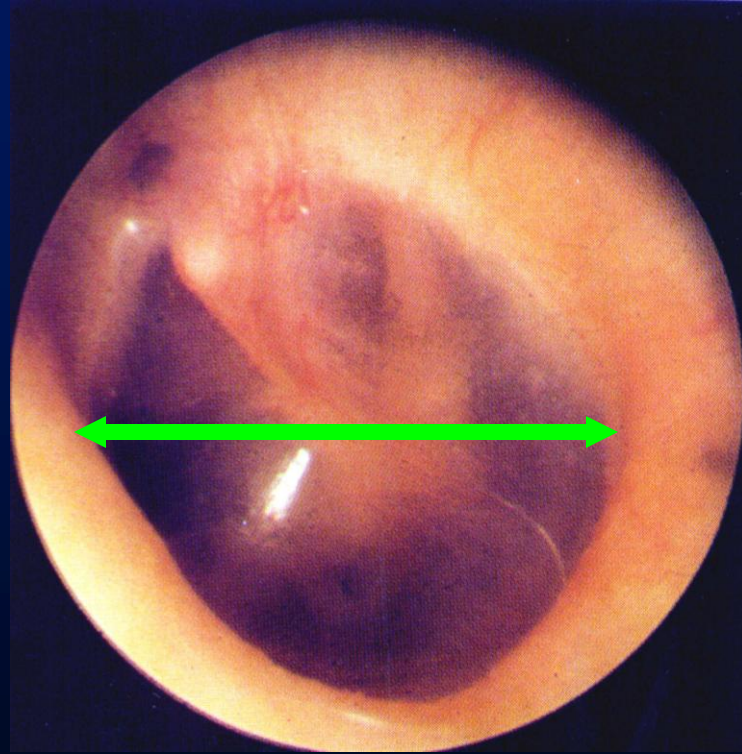
Normal



Height of ear drum (Annulus)

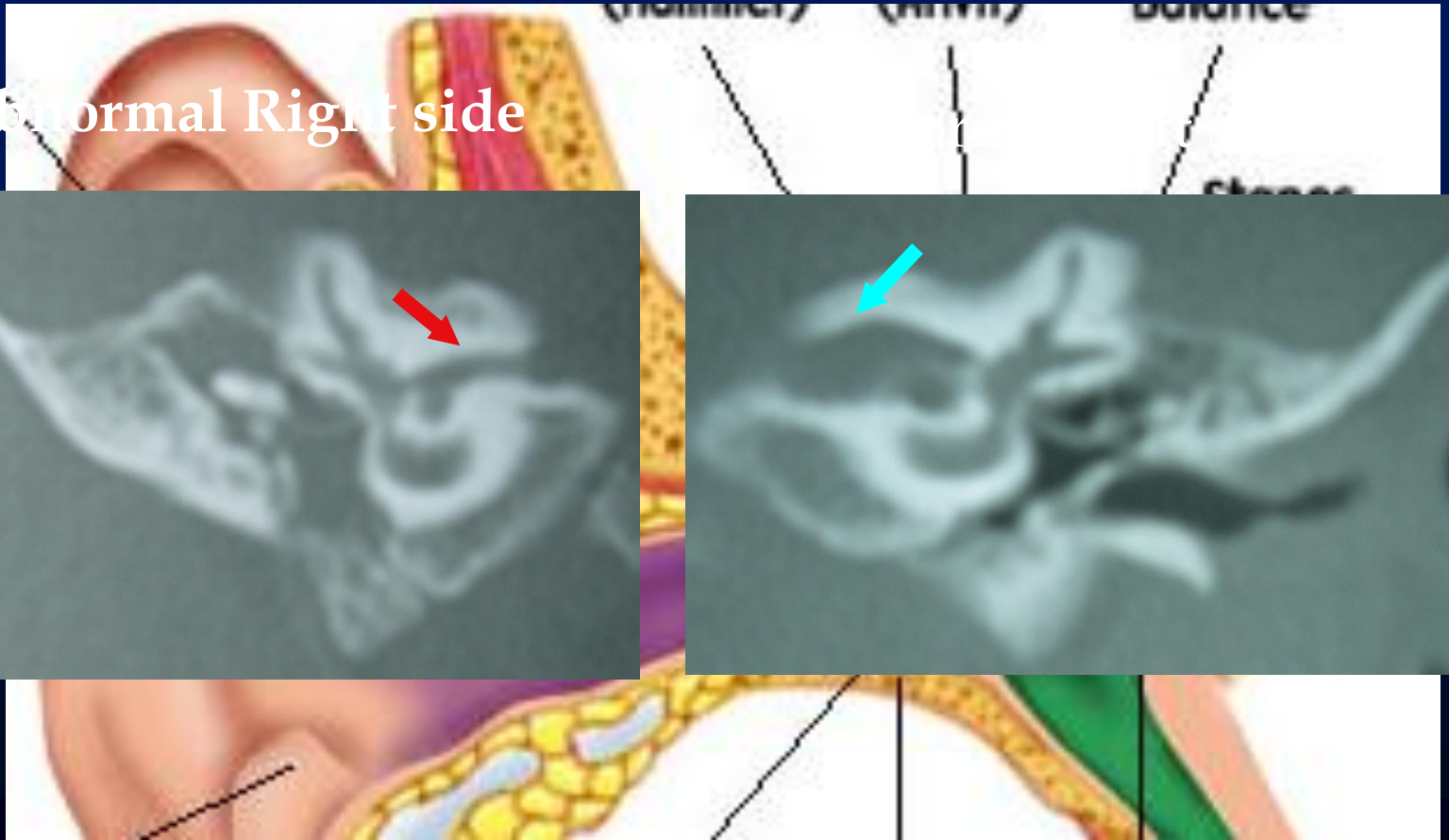
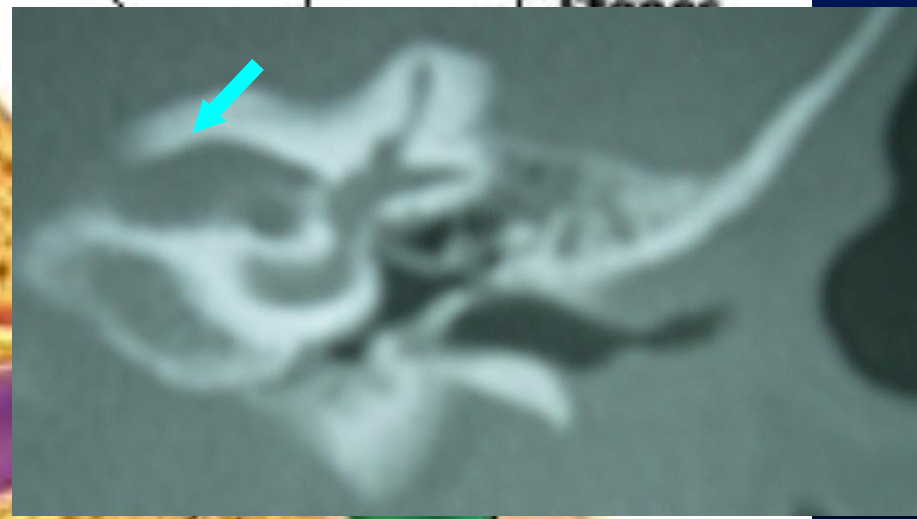


Width of ear drum (Annulus)

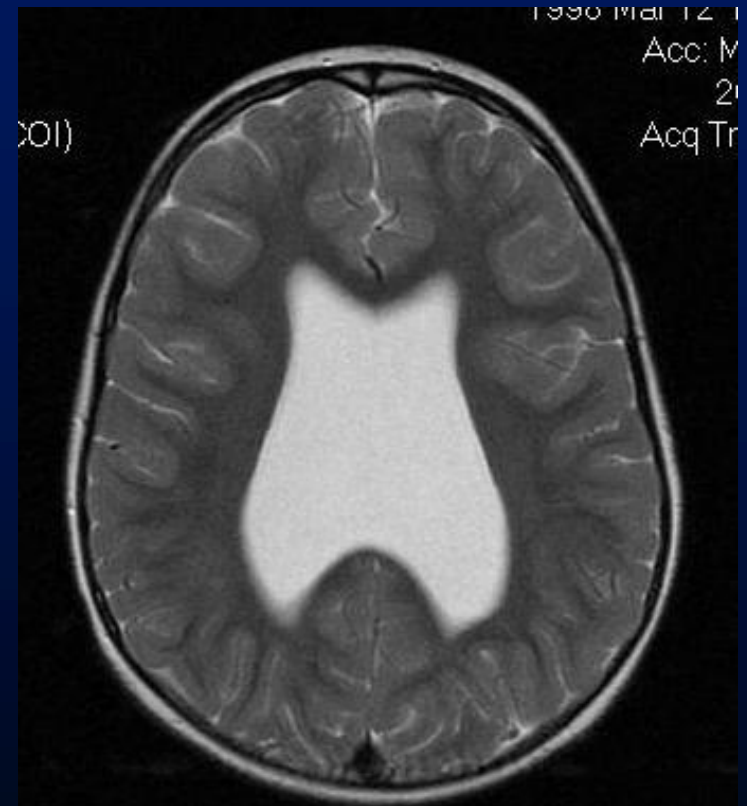
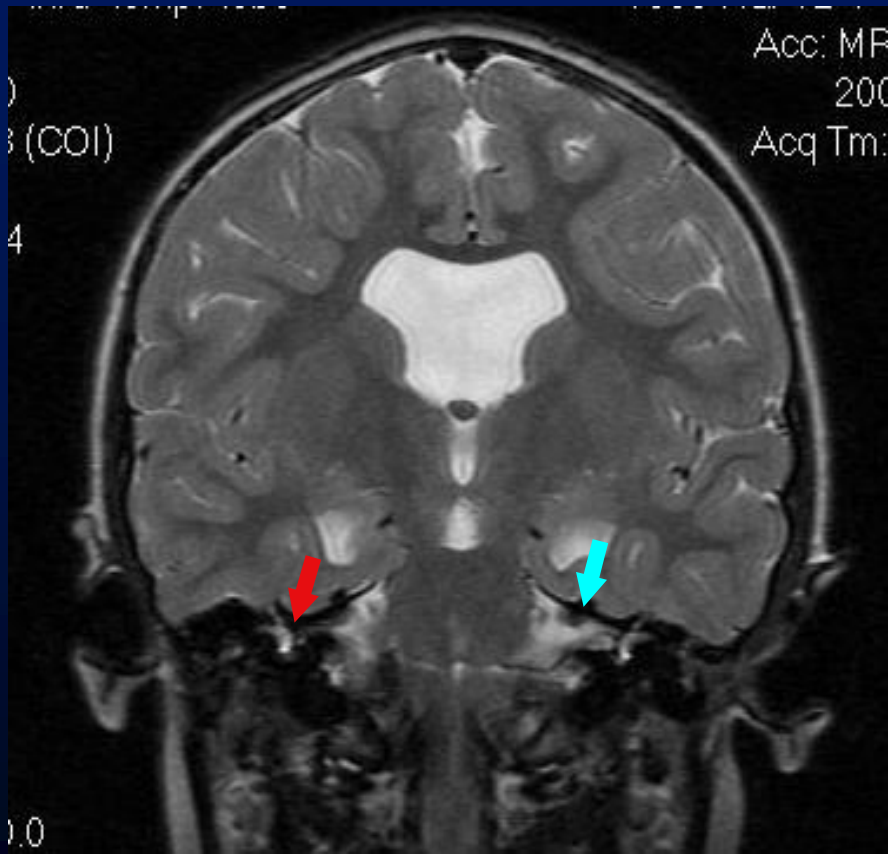


Sensorineural hearing loss & Narrow internal auditory canal n=2

Abnormal Right side



Central nervous system Involvement

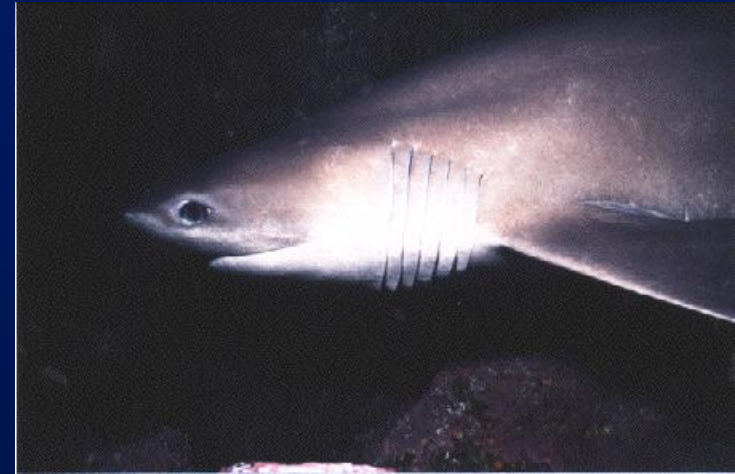


Common Ear manifestations

- Small ear drum with bony island and usually malformed middle ear bones (58 %)
 - Rarely aural atresia (Absent ear canal)
- Hearing loss (33%)
- Conductive hearing loss
- Rarely associated with sensorineural hearing loss and narrow ear nerve canal
 - Perhaps associated with brain structural problems

Why Ear Problems in FA?

- No one knows why
- Congenital problem
- Auricle, ear canal and middle ear bones are derived from 1st and 2nd branchial apparatus
- Prob due abnormal embryologic development

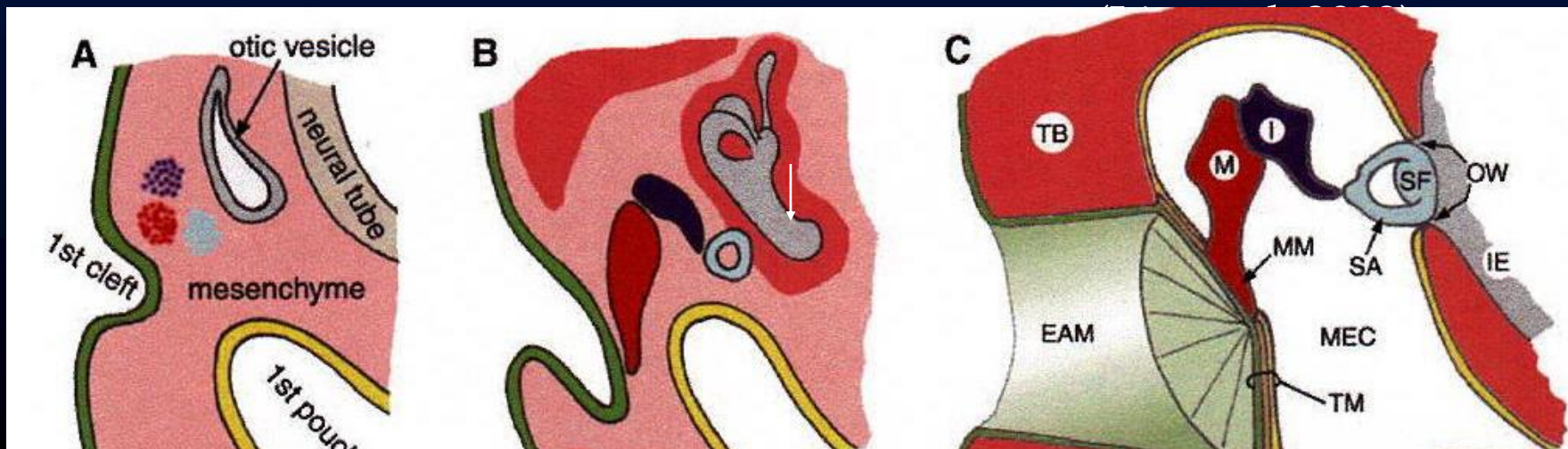


Shark and gills

FA on ear development



- Knockdown (Removal) of *Fancd2* in Zebrafish
 - Physical features include short body, small eyes and head
 - During fetus development, many cells divide and proliferate. But without *Fancd2*, cells inappropriately die
 - This results in congenital malformations

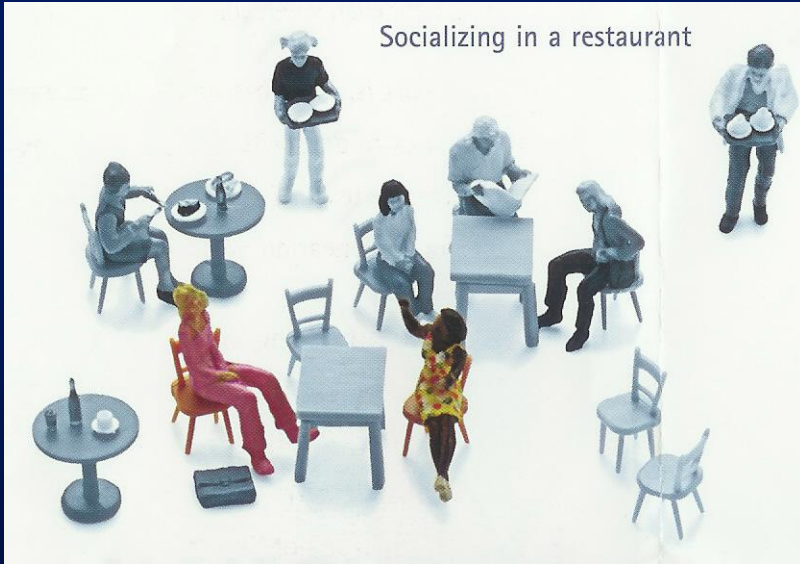


3 Types of hearing loss situations in FA

- The most common type of hearing loss is mild & moderate conductive hearing loss
- Rarely, absent ear canal and maximum conductive hearing loss
- Rarely, complete nerve hearing loss due to absent hearing/auditory nerve

Hearing problems

Socializing in a restaurant



Group situations



Mild to Moderate Hearing Loss

- Mild to moderate hearing loss
 - Difficult to detect sounds with background noises
 - Decreased interactions with and responsiveness to environment (eg school, work)
 - Difficulty to hear certain sounds (“f”, “s”, “th”, “v”, and “z”)
 - » Can affect language development, especially when mentally challenged

Mild to Moderate Hearing Loss

- Mild hearing loss effects from chronic ear infection cases:
 - A study of 207 children with prolonged ear infections from Boston
 - » Followed from birth to age of 7 years
 - » Time spent with OTME especially during first three years of life was associated with lower scores on tests of cognitive ability, speech and language, and school performance at age of 7

Management options

- Auditory amplification (hearing aids)
 - Conventional hearing aids
 - FM assistive listening device
- Traditional ear surgery to widen ear canal and correct middle ear bone problems
- Other hearing devices (BAHA[®] and SoundBite[®])

Conventional hearing aids



Completely-in-the-Canal (CIC)

Mini-Canal (MC)

In-the-Canal (ITC)

Half-Shell (HS)

In-the-Ear (ITE)

Behind-the-Ear (BTE)

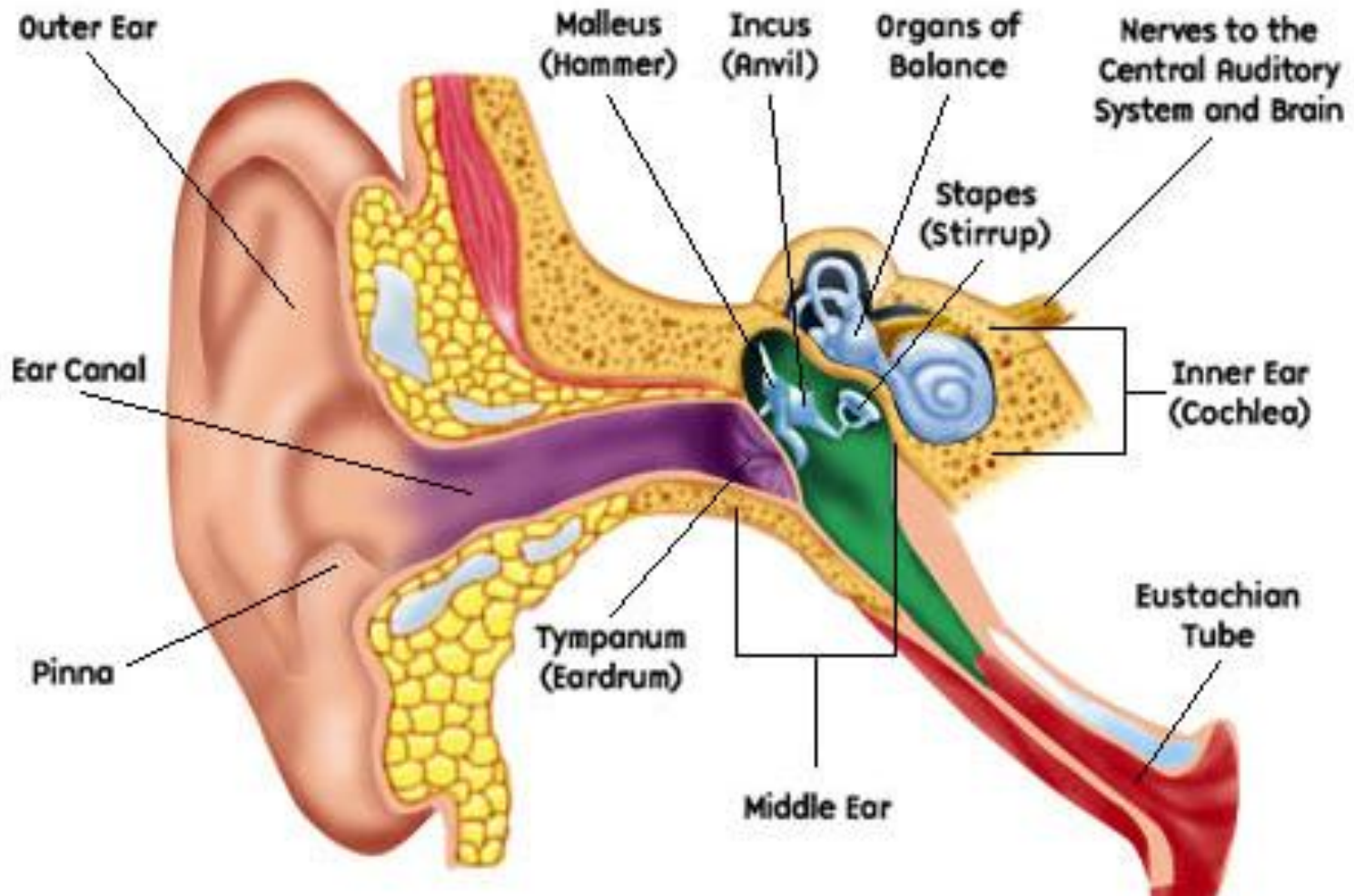


FM auditory trainer

FM-based system



Surgical Treatment



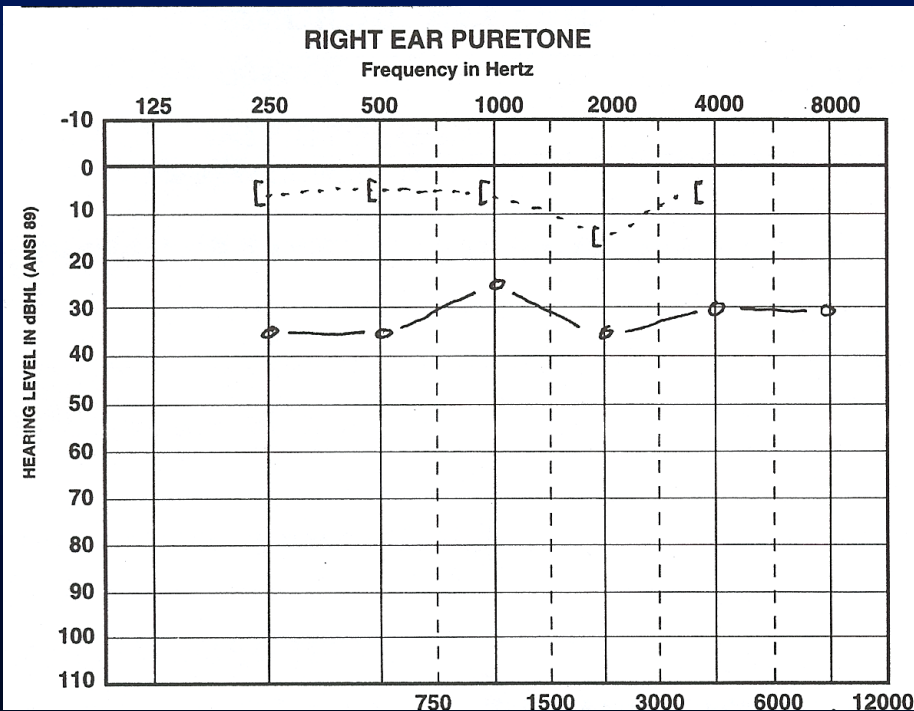
Middle ear exploration



- Surgery through ear canal or behind the ear
- Usually after age of 7 yrs
- Laser technique is less traumatic
 - Argon laser
 - CO2 laser

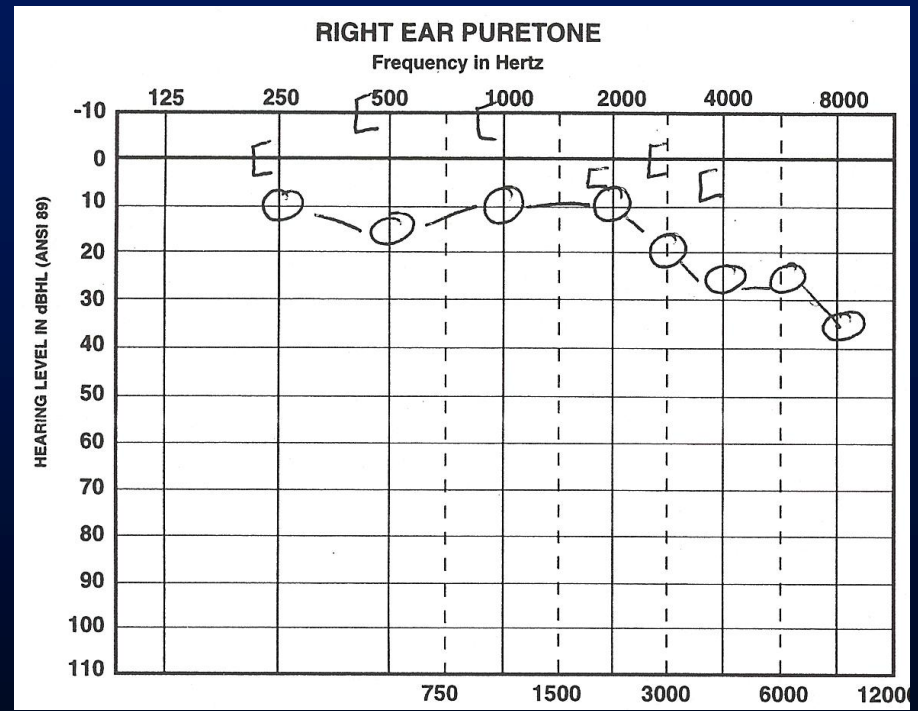
Audiograms

Pre-Op



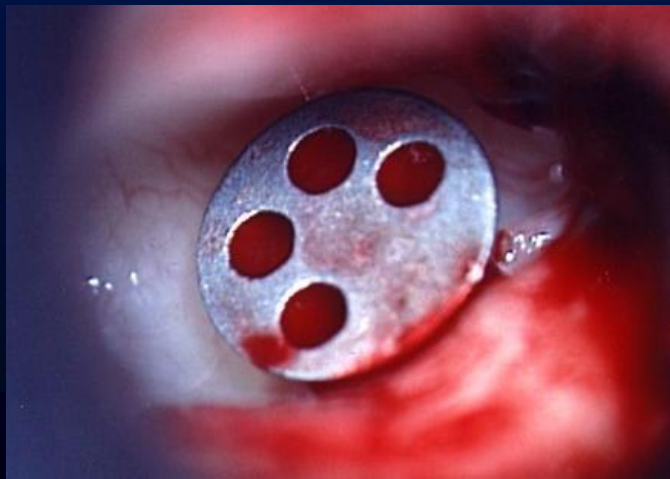
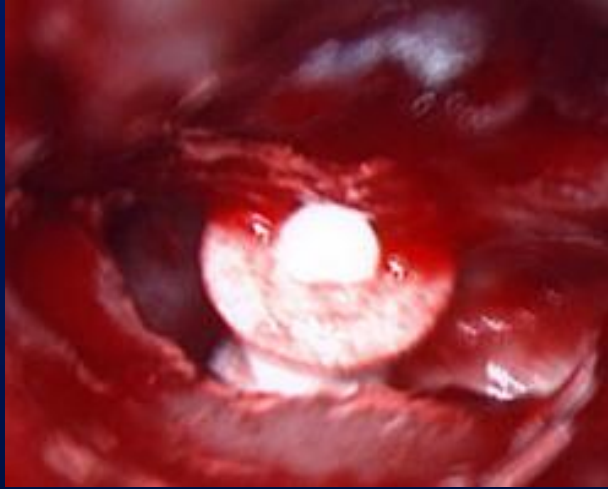
Average Threshold = 32 dB
(PTA)

Post-Op



Average Threshold = 12 dB
(PTA)

Middle ear bone (Ossicular Chain) Reconstruction



Risks of Operation

- Minor complications (<5%)
 - Infection
 - Bleeding
 - Ear drum perforation
 - Metallic taste in tongue-only transient
- Major complications (<1%)
 - Profound hearing loss
 - Imbalance/vertigo
 - Facial nerve injury
 - » Uncommon unless congenital facial nerve anomaly present
 - » Intraoperative facial nerve monitoring and CT scan helps
- No improvement in hearing
 - Usually can still wear hearing aids

BAHA[®] (Implantable Bone Anchoring Hearing Device)





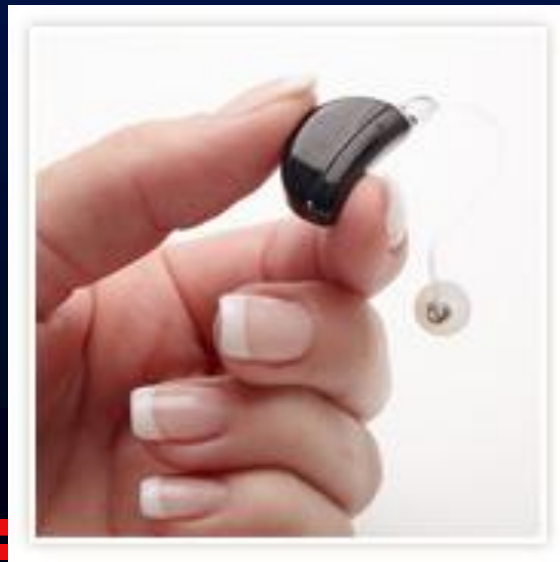


Risks of BAHA®

- Infection
- Bleeding
- Extrusion of the implant
- Daily care of implant site




SoundBite[®] Hearing System



Absent Ear Canal

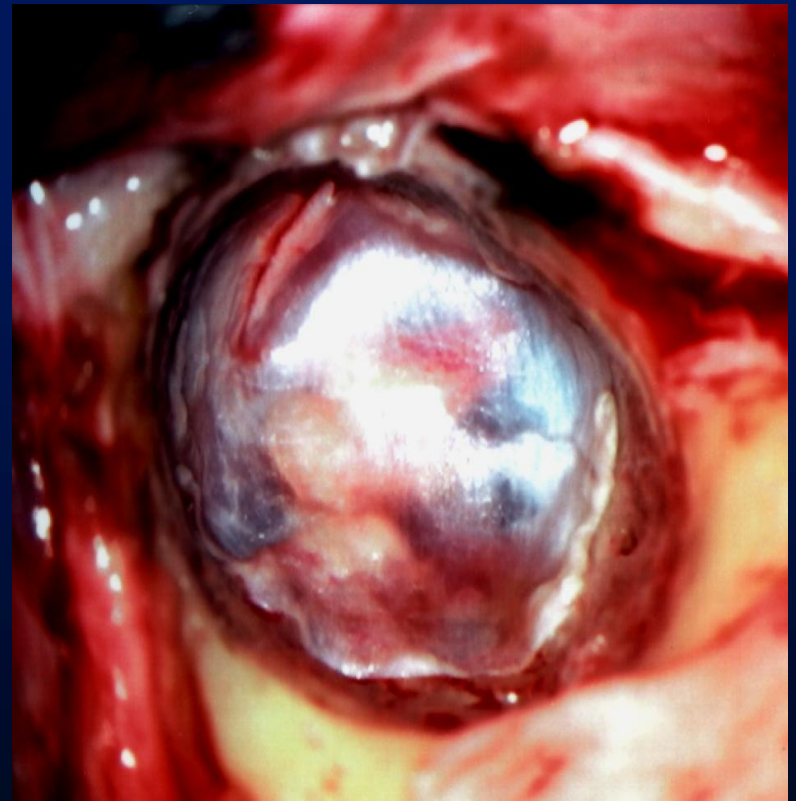
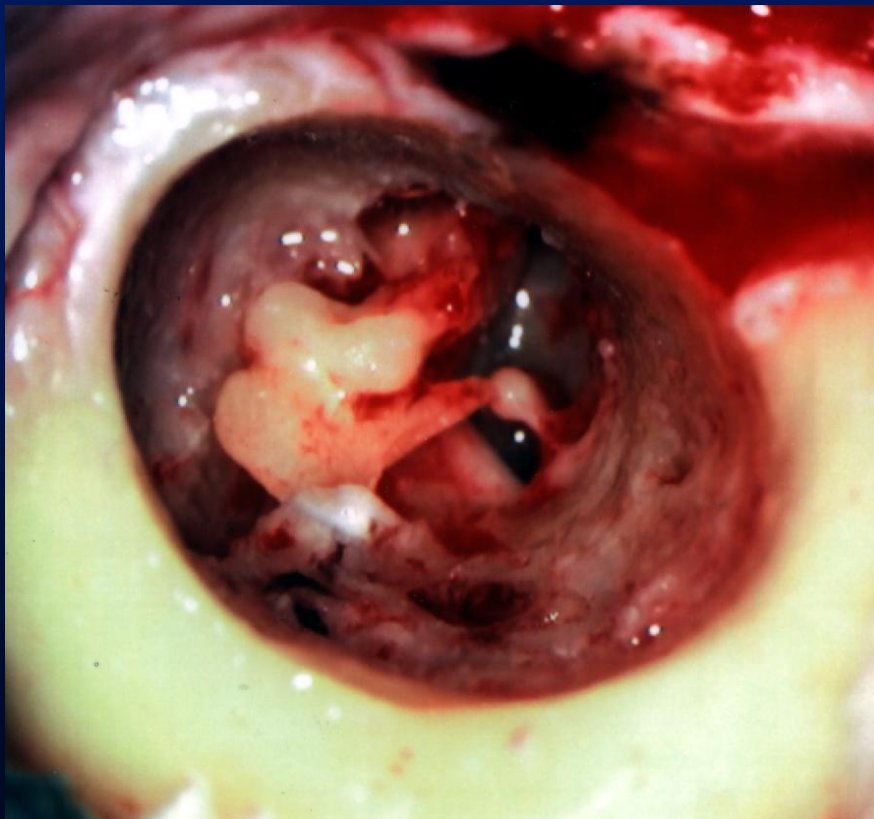


Absent Ear Canal

- Maximum conductive hearing loss
 - Difficult with localization of sound
 - May or may not need an intervention
 - Usually can not wear traditional hearing aids
 - Surgical ear canal reconstruction
 - BAHA[®]
 - SoundBite[®]
- 



Absent or narrowed ear canal



BAHA[®] and SoundBite[®]



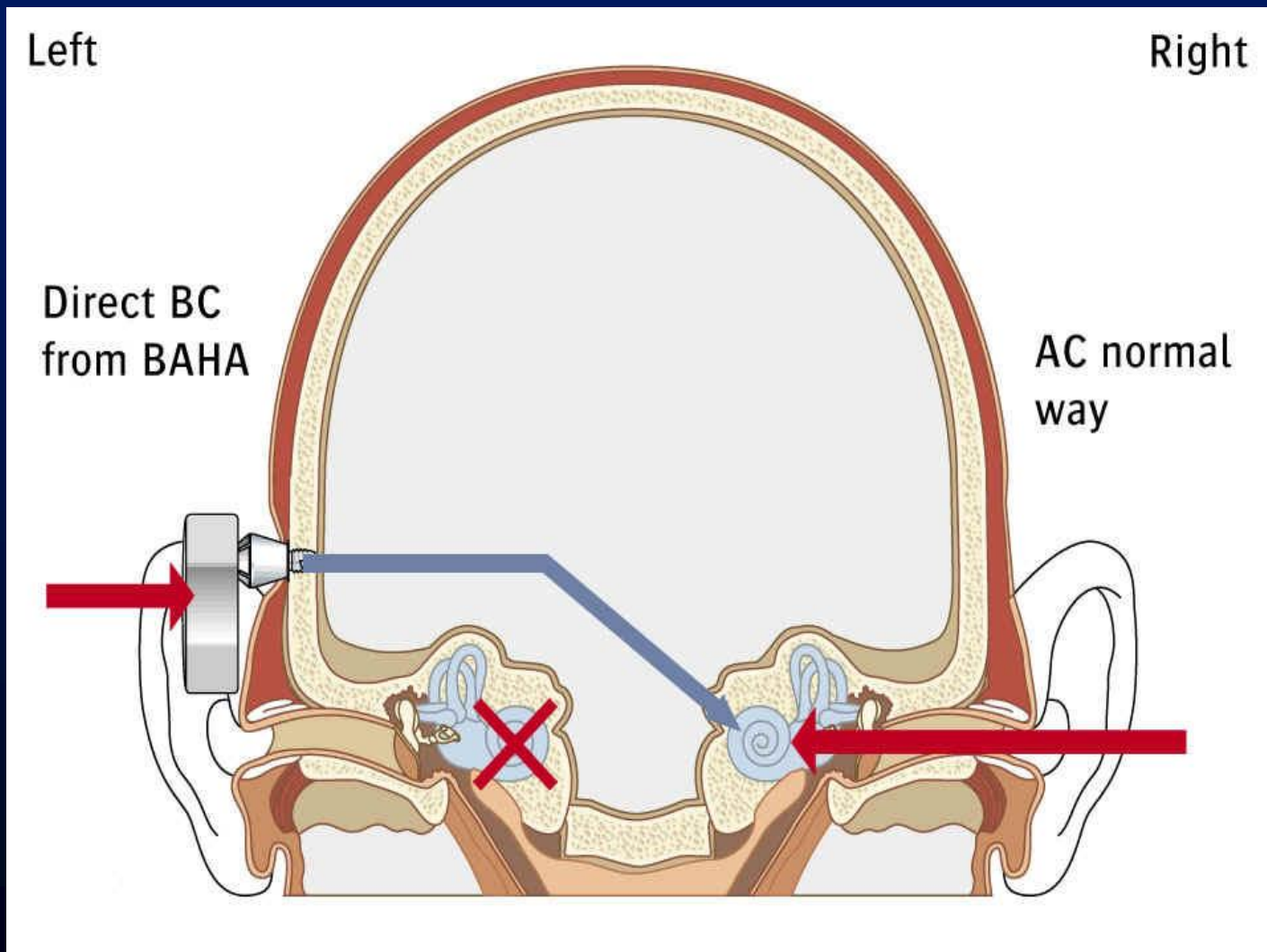
Absent Hearing/Auditory Nerve

- No hearing->Unilateral profound sensorineural hearing loss
- A problem with localizing sound
- Traditional hearing aids are not helpful
- CROS hearing aids
- BAHA[®]
- SoundBite[®]

CROS/BiCROS hearing aids



BAHA[®] and SoundBite[®]



Practical communication tips

- Help your child to make a habit to watch the speaker
- Instruct your child to let the speaker know when he/she is aware something that was said was missed, and to ask for it to be repeated
- Reduce or move away from background noises. Help to manipulate the environment to allow communication in as noise-free an atmosphere as possible.
- Do not over-articulate and speak clearly and slowly.

Recommendations

- For individual with FA
 - Comprehensive ENT and audiologic evaluation
 - Audiogram every 2 to 3 yrs ?
 - More frequently, if exposed to medications that can cause hearing loss
 - » Deferoxamine (Iron-chelating agents)
 - » Aminoglycosides (Antibiotics)
 - » Cisplatin (Chemotherapy agents)
- For siblings of FA
 - Comprehensive ear exam and hearing test
 - Further genetic evaluation to rule out FA
 - » Look for somatic mosaicism in fibroblast culture

Conclusion

- Hearing loss and congenital ear anomalies are more common than previously reported
- Ear drum and middle ear bone problems
- Commonly mild and moderate conductive hearing loss
- Good ENT evaluation
 - Microscopic ear examination
 - Audiologic evaluation
 - Imaging study-helpful for moderate HL or SNHL
- If significant hearing loss, can be easily treated with assistive-listening devices, amplification, and/or surgery



Collaborators at NIH

National Institute on Deafness and Communication Disorder (NIDCD)

Carmen Brewer, Ph.D.

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Georgetown University Medical Center

Adediyun O Kalejaiye, MD

National Cancer Institute (NCI)

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Lisa Leathwood, RN, BSN

Neelam Giri, M.D.

Radiology Dept of Clinical Center, National Institutes of Health

John A Butman, MD PhD

All the Fanconi Anemia patients at NIH



