

**Fanconi Anemia Research Fund  
Annual Family Meeting 2010**



**Ear & Hearing Problems in FA**

***H. Jeffrey Kim, M.D. FACS***  
*Georgetown University Hospital*  
*Email: [HK7@gunet.georgetown.edu](mailto:HK7@gunet.georgetown.edu)*

2010 Fanconi Anemia Family Summer Camp

## Ear and Hearing Problems in Fanconi Anemia

H. Jeffrey Kim, MD  
 National Institute on Deafness & Other Communication Disorders  
 National Institutes of Health  
 Bethesda, MD  
 Dept of Otolaryngology-Head & Neck Surgery  
 Georgetown University Medical Center  
 Washington, DC

## 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
Eye (Microphthalmia)	38
Renal & Urinary tract	34
Male genitalia	20
Mentally challenged	16
GI (duodenal, anorectal atresia)	14
Cardiac	13
Central nervous system	8
No Abnormalities	30

(David, 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": 276 articles
  - "Fanconi anemia and ears": 14 since 1970
- Reasons:
  - Non-life threatening problem
  - Not commonly recognized by 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 of 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

(Santus et al, 2002)

## Fanconi Anemia

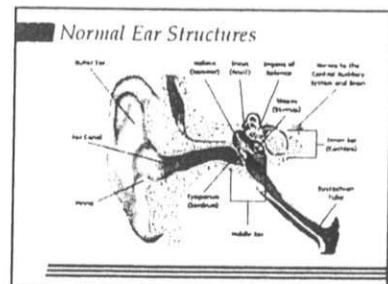
- Previous studies were limited because
  - They were either a brief single case report or a retrospective review
- Hearing loss is one of major factors correlated with a risk of bone marrow failure in FA
  - Rosenberg et al, 2004
- Description of typical ear findings & their prevalence in FA patients 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



### 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

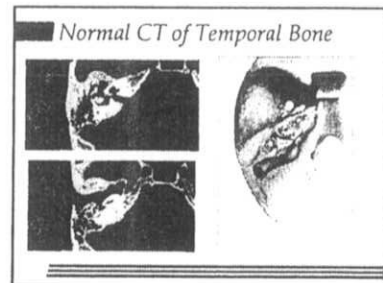
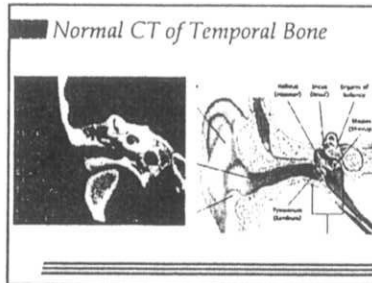
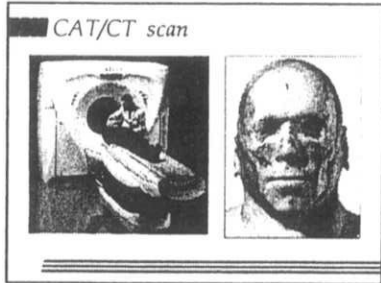
Conductive HL

### 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

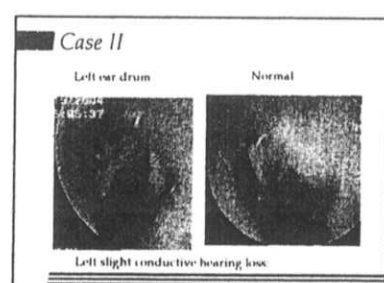
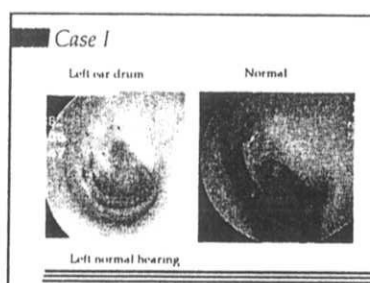
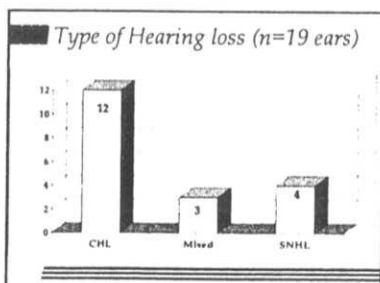
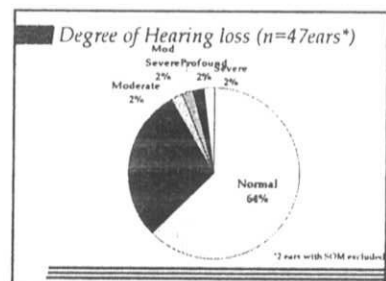


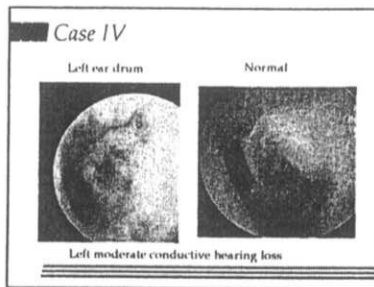
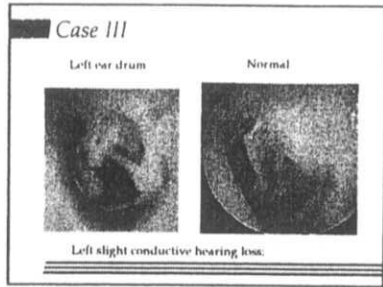
**Magnetic Resonance Imaging (MRI) of internal auditory canal**

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

**NIH Experience:**

- 32 pts
  - Age range: 5 - 56 yrs (Mean age=22, SD 12.6)
  - 4 pts excluded due to inadequate information
- Total of 56 ears in 28 pts
  - 4 pts with 5 major ear surgeries
  - Ear surgeries for conductive hearing loss (Ossicular chain reconstruction) and enlarging ear canal (Canalplasty)
- Examined non-operated 51 ears in 28 pts
  - 2 ears with middle ear fluid

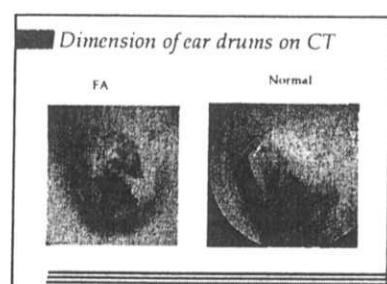
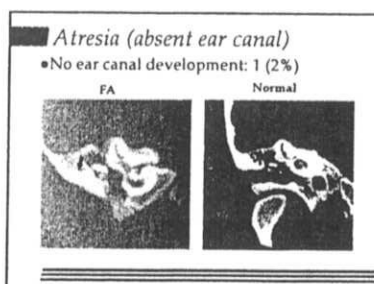
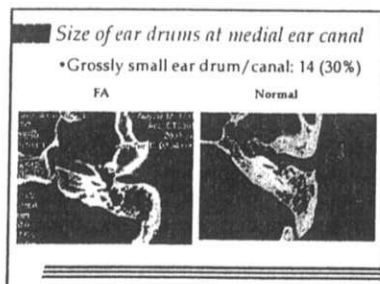
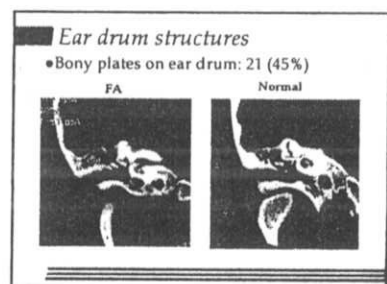
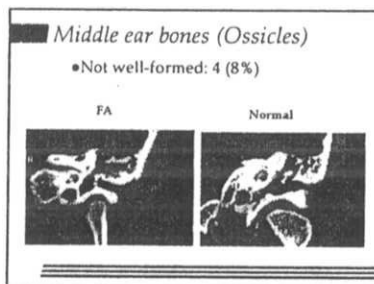


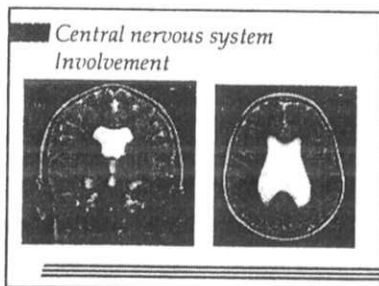
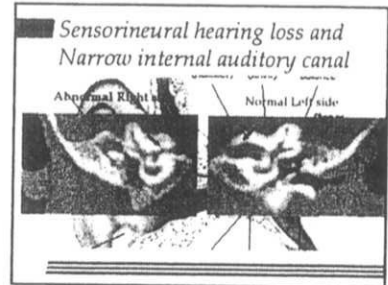
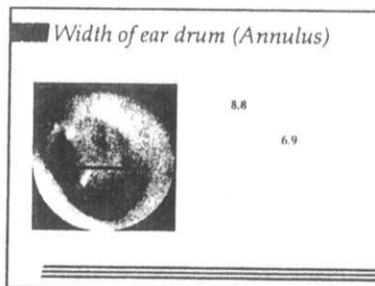
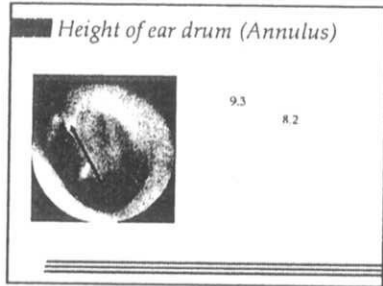


**TM/Middle ear abnormalities**

Ears (n=51)	# ears	%
Normal	20	39%
Scar	2	4%
Abnormal	28	55%
Atresia (No ear canal)	1	2%

- CT scans**
- N = 47 ears when
    - Excluded 5 ears with prior surgery; no CT in 2 patients
  - Middle ear bones
  - Bony plates on ear drum
  - Dimension of ear drum



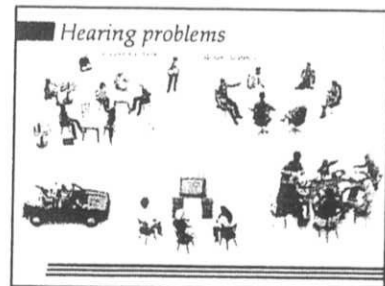


- ### Common Ear manifestations
- Small ear drum with bony island and usually malformed middle ear bones
    - Rarely aural atresia (complete closure of EAC)
  - Conductive hearing loss
  - Rarely associated with sensorineural hearing loss and narrow ear nerve canal
    - Perhaps associated with brain structural problems

- ### 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

- ### Why Ear Problems in FA?
- 
- Shark and gills
- No one knows why
  - Congenital problem
  - Auricle, ear canal and middle ear bones are derived from 1<sup>st</sup> and 2<sup>nd</sup> branchial apparatus
  - Prob due abnormal embryologic development

- ### FA on ear development
- 
- Knockout (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
- 



### 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", "z", and "v")
    - 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 OITME 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

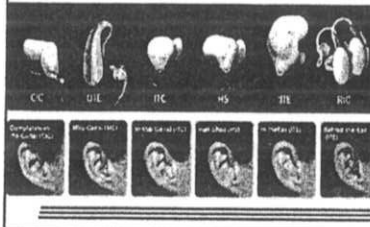
### Management for hearing loss

- Early detection
  - Newborn hearing screening program-very helpful
    - Mandated in >47 states and District of Columbia
  - May not detect slight to mild hearing loss
  - Need formal audiological evaluation by audiologists for all FA cases
- Early Intervention
  - Auditory rehabilitation
    - Good language skills if intervened prior first 6 months of age
  - Speech therapy

### Management options

- Auditory amplification
  - hearing aids
  - Assistive listening device (FM system)
- Surgical correction to widen ear canal and middle ear bone problems
- Implantation hearing device (BAHA<sup>®</sup>)

### Conventional hearing aids

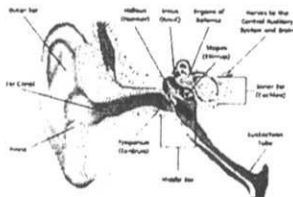


### FM auditory trainer

FM-based system



### Surgical Treatment

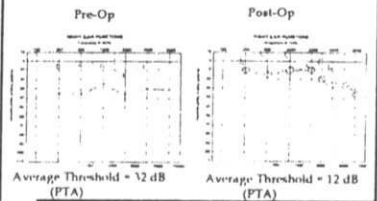


### Middle ear exploration

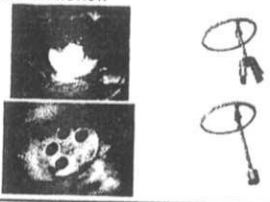


- Surgery through ear canal or behind the ear
- Usually after age of 7 yrs
- Laser technique is less traumatic
  - Argon laser
  - CO<sub>2</sub> laser


### Audiograms



**Middle ear bone (Ossicular Chain) Reconstruction**




**Absent or narrowed ear canal**




**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® (Bone Anchoring Hearing Aid)**



**BAHA® (Bone Anchoring Hearing Aid)**



**BAHA® (Bone Anchoring Hearing Aid)**



**Risks of BAHA®**

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

**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.

**Ear and hearing evaluation**

- For individual with FA
  - Audition only 2 to 3 yrs
  - CHI prob do not change; NHI may change
  - More frequently, if exposed to medications that can cause hearing loss or ototoxic (OTMs)
    - Deferoxamine (Iron-chelating agents)
    - Aminoglycosides (Antibiotics)
    - Cisplatin (Chemotherapy agents)
- For siblings of FA
  - Comprehensive ear exam and hearing test
  - If abnormal, further genetic evaluation to rule out FA
    - Blood chromosome breakage test
    - 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
  - Macroscopic 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 Disorders (NIDCD)

Carmen Brewer, Ph.D. Christopher Zakewski, M.A.  
Susan Rudy, BS, NP Andrew Griffith, M.D., Ph.D.

#### National Cancer Institute (NCI)

Blanche Alter, M.D., MPH Neelam Giri, M.D.  
Lisa Leathwood, RN, RSN

#### Radiology Dept of Clinical Center, National Institutes of Health

John A. Butman, MD PhD

All the Fanconi Anemia patients at NIH