Aging and the Auditory Periphery

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Aging and the Auditory System

- Review of what we've learned from animal models (gerbil, Guinea pig, cat, chinchilla and mouse)
- How the animal data can be applied to clinical studies of presbyacusis.

Human temporal bone with membranous labyrinth left intact.

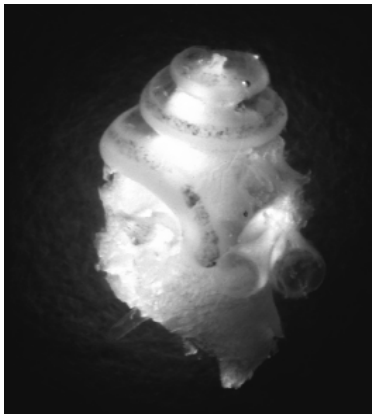
Body mass ~ 80kg
Length of BM ~ 33mm

Joe Adams

Gerbil temporal bone with membranous labyrinth left intact

Body mass ~ 0.08kg
Length of BM ~ 12mm

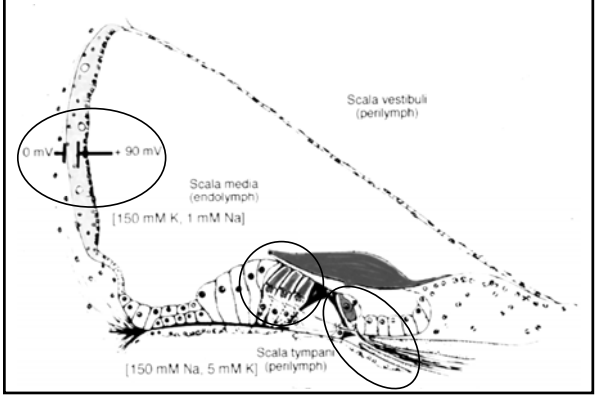
Joe Adams



The Three Main Cochlear Systems

- Inner hair cells & primary auditory neurons (transduction)
- Outer hair cells & micromechanics (OHC or cochlear amplifier)
- Lateral wall and stria vascularis (power supply)

Single Turn of the Cochlea



Cross section of a gerbil temporal bone.

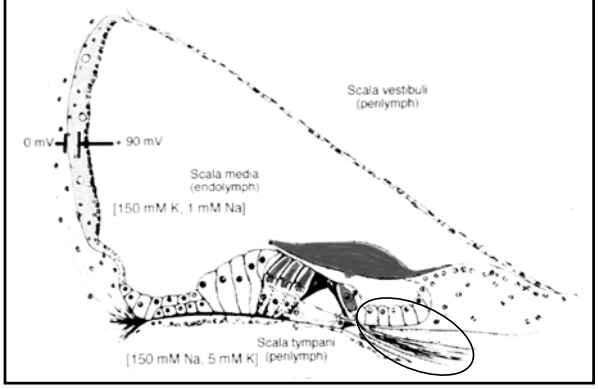
Arrows show different experimental approaches

Steve Chamberlain

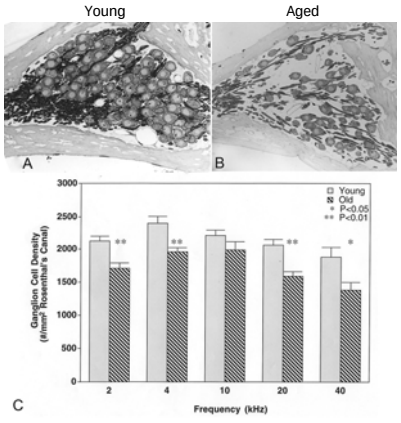
Neural Presbyacusis

?

Single Turn of the Cochlea



Spiral ganglion cells are reduced in size and number along the entire cochlear duct in aged ears.



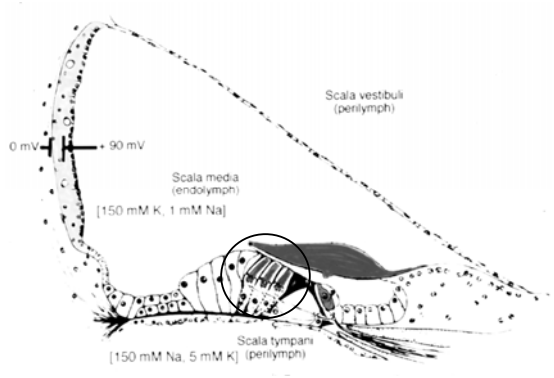
Mills et al. (2006)

Neural Presbyacusis

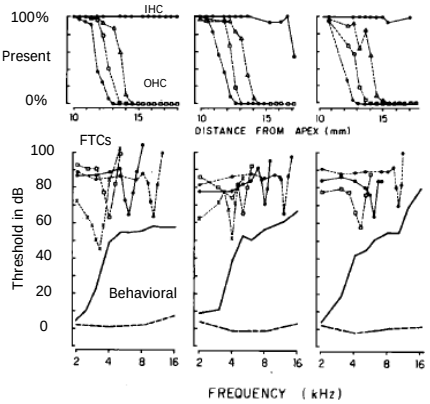
- Least understood of all types of HL
- No good animal model at present (ouabain model; early noise trauma; mouse mutants).
- Causes of neural shrinkage and loss with age? (Trophic factors?)
- Can we measure it? (Latency, Synchrony?)
- Clinical significance?

Sensory Cell Pathology and Presbyacusis

Single Turn of the Cochlea



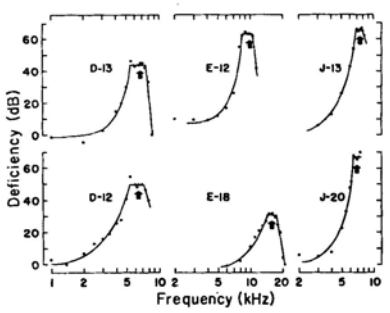
Effects of Pure OHC Loss on Single Fiber & Behavioral Thresholds (Chinchilla)



Ryan et al. (1978)

Maximum HL with no Basal OHCs Present

Single auditory nerve fiber threshold shifts in individual chinchillas with complete OHC loss. "Deficiency" in dB can be interpreted as the OHC gain now associated with the cochlear amplifier.



Dallos and Harris 1978

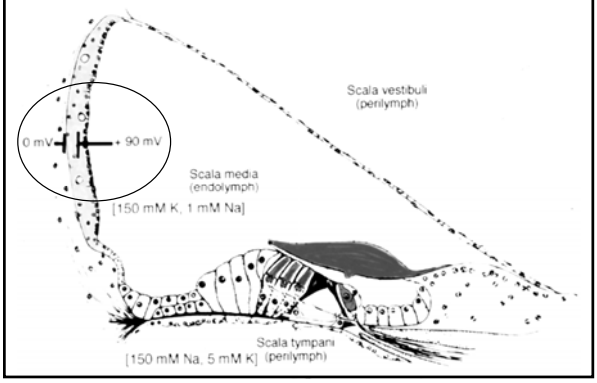
Animal Models of Sensory Pathology

- IHC loss = profound deafness
- Complete OHC loss at mid and basal regions = 50-70 dB HL (IHCs intact)
- Concept of the "Cochlear Amplifier"
- Loss of two-tone suppression
- Loss of other nonlinearities including otoacoustic emissions

Animal models of lateral wall, stria vascularis, & vascular atrophy

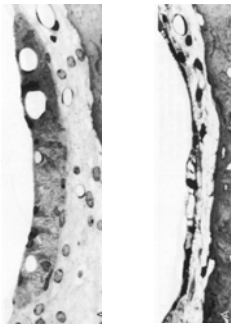
•Quiet-aged gerbils
•Chronic furosemide treatement

Single Turn of the Cochlea



Strial Atrophy with Age in Gerbil

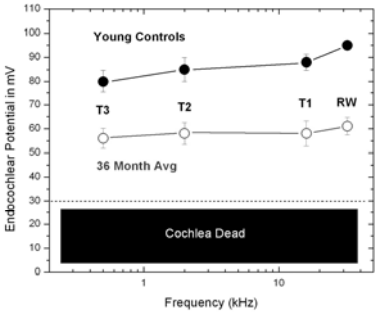
Young Control | Quiet Aged



(Toluidine blue 500 Hz region)

(Schmiedt and Schulte, 1992)

Average EP from Young and Old Gerbils



Neural thresholds in quiet-aged gerbils were elevated with age with little associated OHC loss.

Instead,
threshold shifts were correlated to EP reduction.

So,
how can we prove EP reduction caused the neural threshold shifts we found in the quiet-aged gerbils?

Furosemide Model of Presbyacusis

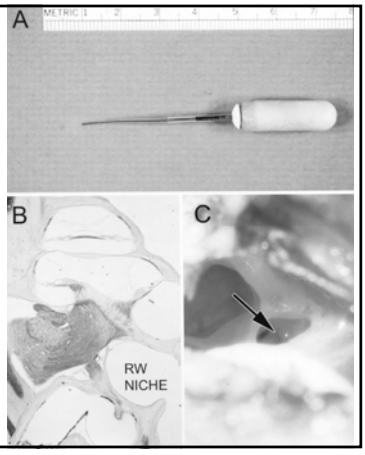
Modeling EP loss in a young ear

Furosemide Model of Presbyacusis

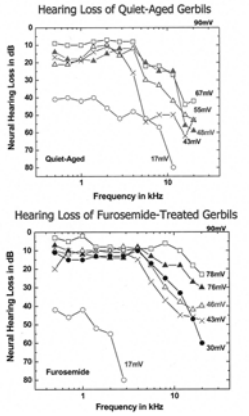
- Chronic application of furosemide to the round window in a young ear.
- Hair cell and neural systems intact and functioning
- Chronic decrease of EP can be controlled by dose and duration

Osmotic Pump with round window (RW) cannula. Pump holds 200 µl and lasts for 28 days.

Cannula is placed in RW niche without puncturing the RW membrane

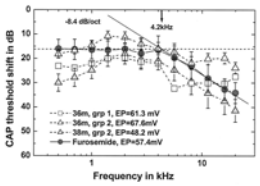


Neural audiograms obtained from the Compound Action Potential (CAP) thresholds (equivalent to Wave I in the ABR)



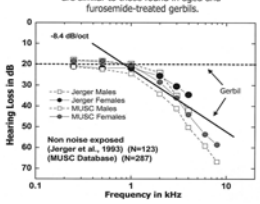
Schmiedt (2009)

CAP threshold shifts in quiet-aged and furosemide-treated gerbils



Hearing loss profiles in non-noise exposed humans are similar to those found in aged and furosemide-treated gerbils.

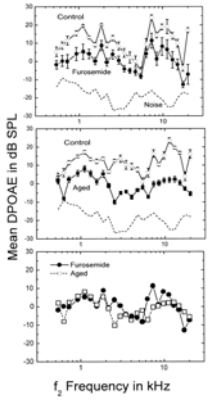
Human HL profiles compared to the CAP profile of quiet-aged gerbils



Schmiedt et al. (2002)

DPOAEs from control, furosemide, and aged ears.

Aged and furosemide ears have reduced emissions across frequency; but are not absent as with total OHC loss.



Schmiedt et al. (2002)

From Animal Models: Metabolic Loss

- EP reduction is fairly constant along entire cochlear duct in aged cochleas.
- Threshold shift from EP reduction is a function of frequency: <1kHz~20dB coupled with a shallow sloped HL at higher frequencies.
- Maximum amplitudes of evoked potentials (CAP) are greatly reduced.
- Two-tone suppression and otoacoustic emissions reduced but present.
- Seems to be the predominant “pure-aging” loss in non-mutant animals.

Overall Conclusions from Animal Models

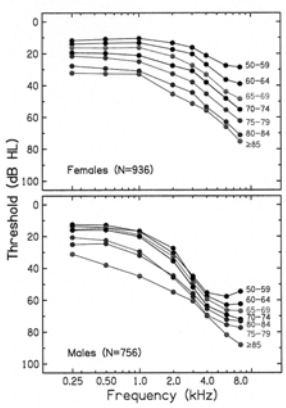
- Neural Presbyacusis
  - Neural atrophy is always present but difficult to define physiologically and clinically.
- Sensory Presbyacusis
  - Kills the OHC amplifier preferentially.
  - Nonlinearities (sharpness of tuning, suppression, OAEs) greatly reduced or absent.
  - Pure losses of basal OHCs yield steep audiogram configurations with 50-70 dB HL plateau.
  - Most often associated with environmental noise or drug exposures.

Overall Conclusions from Animal Models (continued)

- Metabolic Presbyacusis
  - Results from strial degeneration, the power supply to the cochlear amplifier, lowering EP.
  - Audiogram configuration = constant 20 dB HL below 1-2 kHz coupled with a shallow increasing loss at higher frequencies.
  - Nonlinearities (sharpness of tuning, suppression, OAEs) may be reduced but present.
  - The “pure” component of age-related HL.

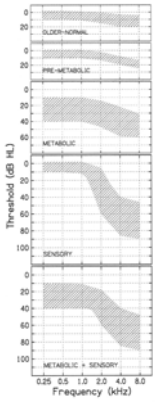
Can we apply the animal data to better understand audiogram configurations obtained from aged humans?

Mean hearing loss profiles from the MUSC study with age as the parameter

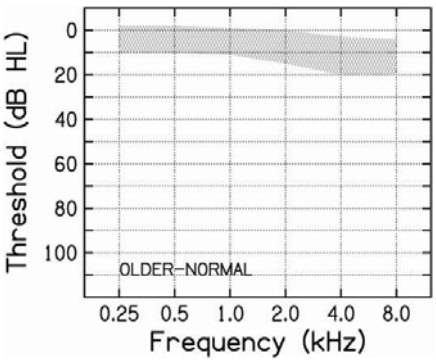


Dubno et al (2009)

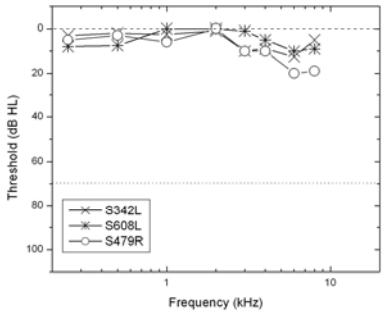
Schmiedt (2009)



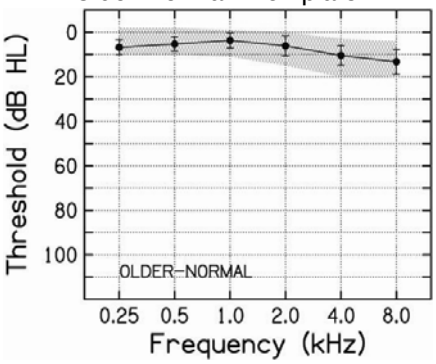
Older-Normal Schematic



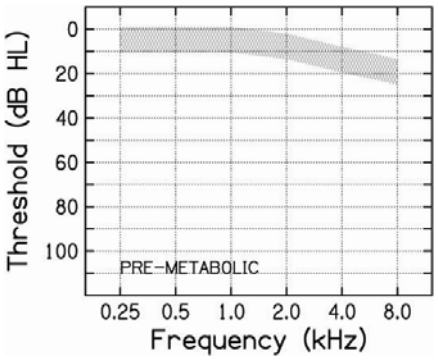
Examples of “Older-Normal” Audiograms



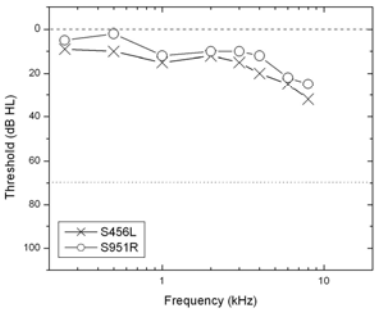
Older-Normal Exemplars



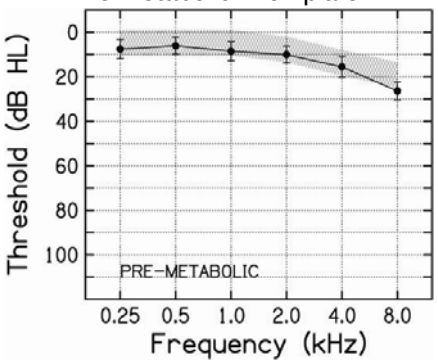
Pre-Metabolic Schematic



Examples of "Pre-Metabolic" Audiograms



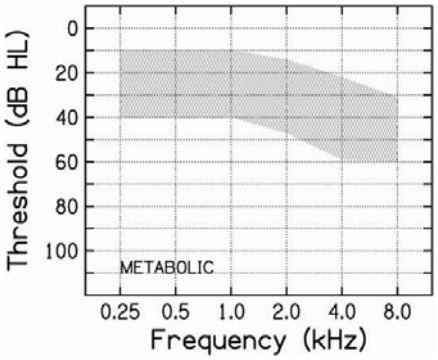
Pre-Metabolic Exemplars



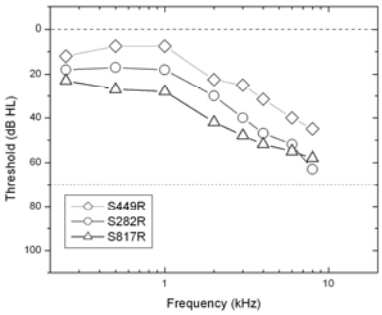
Predictions for "Older-Normal and Pre-Metabolic"

- Sharpness of tuning intact
- Suppression (compression) intact
- Nonlinearities (OAES) intact
- Subjects younger with no noise history (female?)

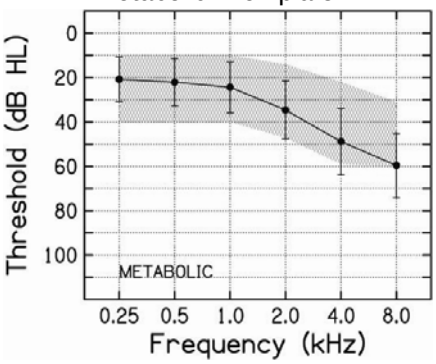
Metabolic Schematic



Examples of "Metabolic" Audiograms



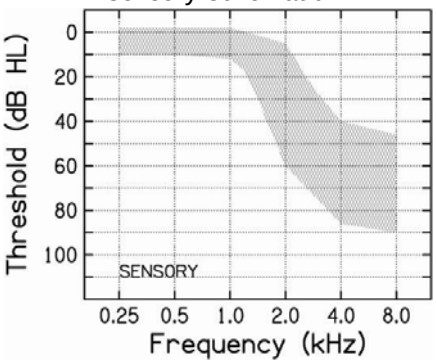
Metabolic Exemplars



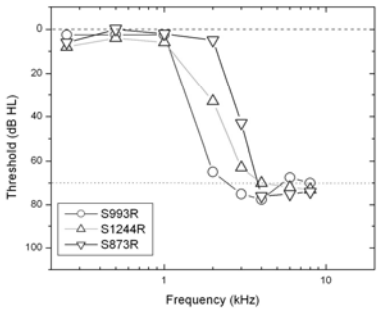
Predictions for "Metabolic"

- Sharpness of tuning intact, but with reduced thresholds
- Suppression (compression) reduced but present
- Nonlinearities (OAES) reduced but present
- Subjects older with no noise history (females?)

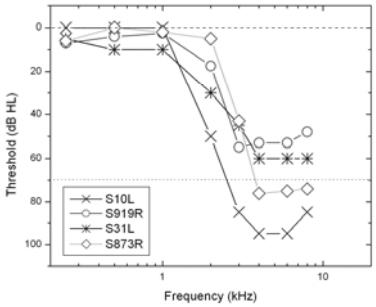
Sensory Schematic



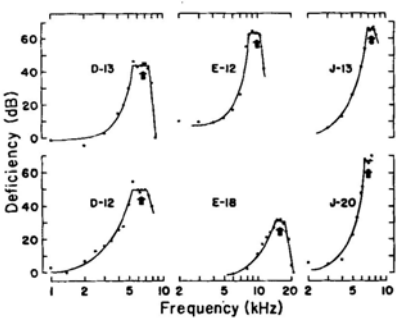
Examples of "Sensory" Audiograms



Examples of "Sensory" Audiograms with Varying Tails

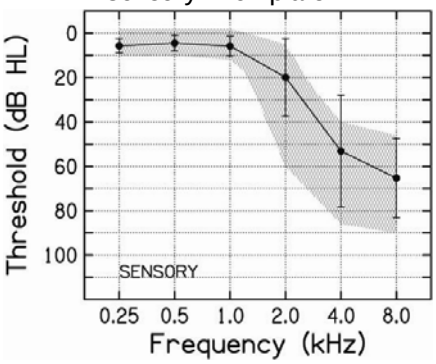


Single auditory nerve fiber threshold shifts in chinchilla with complete OHC loss.



Dallos and Harris 1978

Sensory Exemplars



Predictions for "Sensory"

In regions of OHC Loss (IHCs intact):

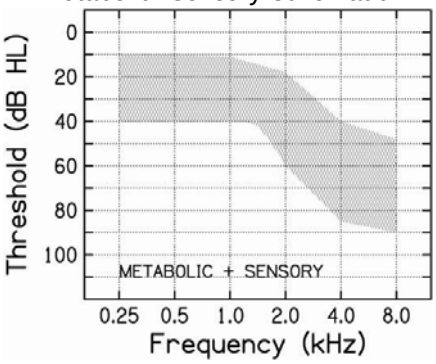
- Threshold shifts between 50 and 70 dB
- Suppression (compression) severely reduced or absent
- Nonlinearities (OAES) severely reduced or absent

In regions of no OHC Loss (IHCs intact):

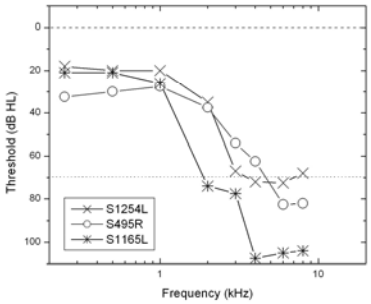
- Relatively normal thresholds
- Normal suppression (compression)
- Normal nonlinearities (OAEs)

Subjects younger with a noise history (males?)

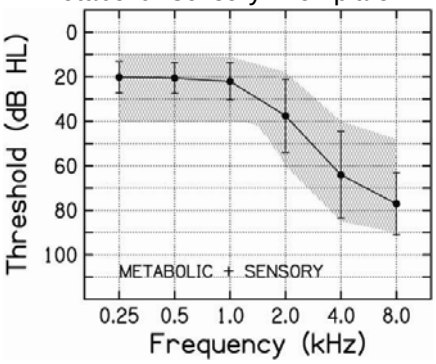
Metabolic+Sensory Schematic



Examples of "Metabolic+Sensory" Audiograms



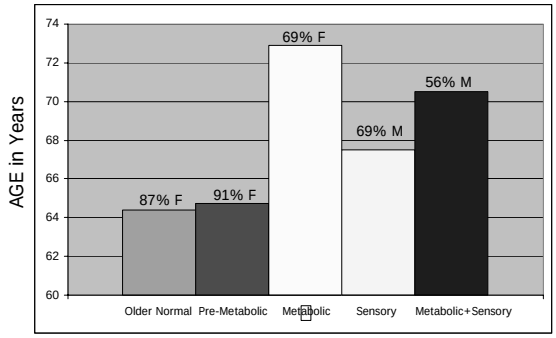
Metabolic+Sensory Exemplars



Predictions for "Metabolic + Sensory"

- Lowered EP throughout the cochlea will reduce suppression and nonlinearities but not eliminate them in regions of no OHC loss.
- At low frequencies (<1.5kHz), HL may be affected by OHC loss as well as EP.
- In areas of complete OHC loss (IHCs intact), the HL may be lower than 70 dB given the lowered EP. Nonlinearities will be absent.
- Subjects older with noise history (males?)

Mean Ages of Exemplar Groups



Conclusions

- Enough is now known from animal models to begin predicting human cochlear pathology from clinical and more advanced psychophysical tests.
- Specifically, many human audiometric profiles seem to follow what is predicted from animal data associated with OHC loss and strial pathology.
- Sensory and metabolic presbycusis should be differentiable from the audiogram and tests of compression and OAEs.
- Metabolic is the main component of true age-related hearing loss.

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- Judy Dubno
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- Jack Mills
- Judy Finkelstein

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