

Summary - Hearing Loss in Mitochondrial Disease

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Ear Anatomy (slides 3-5)

- External Ear - visible part of the ear.
- Inner Ear - internal part of the ear, lying deep inside the bones of the skull, which houses the cochlea, the main area when mitochondrial disease affects hearing. The ear drum is the structure commonly visualized by practitioners with an otoscope.

How Hearing Works (slides 6-7)

- Conversion of sound waves into electrical, nerve signals occurs within the cochlea in the inner part of the ear. Within the cochlea, sensory conduction causes sound waves to move tiny hair cells, creating nerve impulses in a very complex mechanism. Nerve cells lie at the base of the hair cells, detecting movement by sound waves.
- Understanding why mitochondrial disease leads to hearing impairment is the focus of Dr. Kullar's research, including examining the variation of the degree of hearing loss within the same mutation or genotype. Mitochondria, the powerhouse of the cell, is important in energy production, cellular respiration, and other functions that all impact the sense of hearing.

Hearing Loss (slide 8)

- Can be *sensorineural* or *conductive*.
 - Sensorineural hearing loss - defined as changes within the cochlea or within the nerves that lead to the brain. All mitochondrial hearing loss is sensorineural in origin.
 - Conductive hearing loss - involves anything that stops sound waves, originating at the external ear, from traveling to the cochlea in the inner ear. Conductive losses are commonly seen with glue ear or otitis media with effusions as the sound waves are blocked from reaching the inner ear. Conductive hearing loss is not found with mitochondrial disease at a higher rate than the general population. Mitochondrial disease does not cause conductive hearing losses for most individuals.
 - Mitochondrial problems also play a part in age related hearing loss. Research on mitochondrial disease related hearing loss, therefore, has broad implications for the large percentage of the general population with age related hearing loss.

Mitochondrial Disease (slides 9-12)

- Many different diseases result from mitochondrial dysfunction.
- Disease results from:
 - changes in the mitochondrial DNA (mtDNA).
 - changes in the cell's nuclear DNA, which makes many mitochondrial proteins and complements.

- These DNA changes or mutations have a complex relationship with disease presentation, with great variation in disease presentation between patients and even within family members with the same defect. There is often not an obvious relationship between the genotype (individual collection of genes, including mutations) and the phenotype (observable symptoms or presentation of the individual) causing that great deal of variation in disease common with mitochondrial disease. Variation can range from very severe symptoms, in this case, severe hearing loss, to no symptoms at all, or no hearing loss at all despite having the gene for hearing loss.
- Hearing loss can be the sole symptom of mitochondrial disease or can be just one symptom among many other symptoms.
- Up to one-third of individuals with mitochondrial disease have normal hearing for their age, leaving approximately two-thirds of Mito patients falling on the broad spectrum of hearing loss, from very mild to profound deafness.
- Hearing loss results from dysfunctional mitochondrial energy production, causing dysfunction within the hair cells of the cochlea and changes of the cochlea's ability to change sound waves into nerve impulses to be sent off to the brain for interpretation. Although some debate persists, most believe that hearing loss is caused by the cochlear changes (hair cells) rather than changes in the nerves carrying the impulses to the brain.

Hearing Assessment (slides 13-14)

- In the UK, patients need a referral from their general practitioner to an ENT (Ear, Nose, and Throat) doctor/clinic or to an audiology clinic. Those with insurance requiring a referral would follow the same path in the USA as well.
- Most use pure tone audiometry, requiring the patient to press a button when a sound is heard over a range of sounds or frequencies and volumes.
- In mitochondrial disease, both ears tend to lose high frequencies in comparison to low frequencies.
- Auto Acoustic Emissions test - directly measure hair cell function in the cochlea. This test is not routinely performed in most clinics.
- Brain stem electrode test - measure nerve signal generation to determine cause of hearing loss. Again, this test is not routinely performed in most clinics.

Treatment

- **Hearing Aids** - primary treatment for hearing loss (slides 14-24), but need intact hair cells, as sound is simply boosted. Hearing aids still require the hair cells to send stimulate the nerve cells.
 - Electronic, battery operated device that acoustically amplifies and changes sound to allow for improved communication.
 - **Components**
 1. Microphone - receives and converts sound into electrical impulses.
 2. Amplifier - intensifies electrical impulses.
 3. Receiver - translates electrical impulses into louder sounds.
 4. Battery - power source for device.
- **Types of Hearing Aids**
 - Conventional - increases volume of all incoming sound with some minor adjustments possible over all frequencies.

- Programmable Analog - able to make more adjustments to improve hearing.
- Digital - more advanced, automatically adapts to multiple listening and sound environments with more tailored frequency boosting and a much better clinical outcome.
- Many styles - all styles may not be covered by all insurance policies
 - 1) Behind the Ear (BTE) - Most commonly used with mitochondrial disease patients. Worn behind the ear with a plastic ear mold that sits inside the outer ear. All the important components sit exposed behind the ear, but has the advantage of being able to boost sounds significantly. Used for mild to profound losses. May need more frequent re-calibration with initial use. All styles of hearing aids carry some stigma, but Dr. Kullar describes this problem as a societal issue as wearing glasses does not carry the same stigma as glasses are accepted in all social circles around the world.
 - 2) In the Ear (ITE) - more aesthetically pleasing as the aid is less noticeable but lack the same ability to boost sounds. Only effective for those with mild losses. May cause ear irritation and infections. Recalibration may be needed.
 - 3) In the Canal (ITC) - more aesthetically pleasing but, again, lack the same ability to boost sounds. Only effective for those with mild losses. May cause ear irritation and infections. Recalibration may be needed.
 - 4) Completely in the Canal (CIC) - smaller, but again, provide less signal boosting. May cause ear irritation and infections. Recalibration may be needed.
- **Cochlear Implantation (CI)** - (slides 25 - 28)
- Replacing the defective cochlea directly with an implant can have great benefit, even with severe hearing loss because the CI bypasses damaged hair cells. Unlike traditional hearing aids, the CI functions well even if cochlear hair cells are damaged or non-functional.
- A microprocessor sits directly on the skull, converting acoustic sound into electrical impulses, and via electrodes implanted in the scalp, directly stimulates the nerve fibers in the cochlea. The resulting electrical sound information is sent through the auditory system to the brain for interpretation.
- Requires surgery that destroys any remaining cochlear function, rendering the decision for a CI a serious one.
- **Criterion** for CI
 - Bilateral (both ears) severe to profound sensorineural hearing loss.
 - Limited benefit from appropriate hearing aids.
 - Patients with limited communication due to hearing loss, relying heavily on speech reading, sign language, or note writing to understand speech.
 - Other medical issues and/or handicaps such as mitochondrial disease (for example: anesthesia is difficult for the 3-4 hour surgery).
 - Age
 - Duration of deafness
 - Mode of communication
 - Motivation of patient to change life style and use the device. A length post operative period of learning to adjust to the device is required. Counseling regarding types of implants and expectations is needed.

- Audiological assessment - Audiogram and specialized hearing tests, speech perception tests with appropriate amplification.
- **Surgical Risks and/or Adverse Effects**
 - Loss of any remaining natural hearing in the operated ear. If the CI fails for any reason, the patient may be left with worse hearing than prior to the surgery.
 - Facial nerve injury (small risk).
 - Infection.
 - Pain and numbness.
 - Temporary dizziness, tinnitus (ringing in the ear), or taste disturbances.
 - MRI precautions after surgery, due to metal inside the skull.
- **Recovery Period**
 - The journey begins after the surgery as the adjustment to the hearing world brings both joy and challenges.
 - Initial stimulation occurs after the 4-6 week healing period.
 - Rehabilitation to meet specific patient needs
 - Regular appointments to fine tune the implant are necessary, based on feedback from patient, therapists and educators.
- **CI in the Mitochondrial Disease Patient**
 - The first recorded mitochondrial disease patient (KSS - Kearns-Sayre Syndrome) received a CI in 1997 in Japan.
 - Mitochondrial disease patients can be ideal CI candidates, especially if have lost hearing post-lingually (after the development of language and speech).
 - Results vary, but development of more sophisticated technologies are improving results. For example, discovering that an increase in the number of electrodes used to stimulate the nerves improves results has advanced the field

Dr. Kullar's Research

- Hearing tests in patients with different mitochondrial diseases to determine how mitochondrial disease causes different types and degrees of hearing loss.
- Specific interest in the A1555G mutation, a mutation in a mitochondrial gene that causes antibiotic associated deafness, particularly with Gentamicin. Dr. Kullar is interested in why individuals with this specific mutation causing non syndromic hearing loss (this mitochondrial mutation only affects the ears) have such a variability in hearing loss. Dr. Kullar would like to find the set of cell signaling molecules (proteins) that are responsible for the loss or preservation of hearing with this mutation, hoping that, in time, a treatment could be developed to prevent or even restore this hearing loss.
- For more information about Dr. Kullar's research, or if you have the A1555G mutation and would like to be involved in this non-invasive research, contact: **peter.kullar@newcastle.ac.uk**.

Additional Reading:

[Understanding the Mechanisms of Mitochondrial Deafness](#)

[Adults with Mito-related Hearing Loss](#)

[Audiology](#)

[Caption Call](#)

[Issues Affecting the Hearing](#)