Menière’s Disease

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Tripler Army Medical Center

Overview

- Clinical Presentation
- Pathology
- Intratympanic therapy
Clinical Manifestations

- Classical type (1861)
  Vertigo, hearing loss, tinnitus, aural fullness

- Atypical forms
  Lermoyez syndrome (1919)
  Tumarkin’s drop attack (1936)

- Delayed vertigo syndrome
  Nadol et al 1975; Wolfson & Leiberman 1975

Diagnosis

- History
- Physical
- Audiogram
- Vestibular Studies
  - Normal
  - Reduced Function
- Imaging

New Techniques
- Stacked ABR
- VEMP
- Refined Imaging

<table>
<thead>
<tr>
<th>Certain Meniere’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Define disease with histopathological confirmation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Definite Meniere’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two or more definitive episodes of vertigo with hearing loss, plus tinnitus, aural fullness, or both</td>
</tr>
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<table>
<thead>
<tr>
<th>Probable Meniere’s disease</th>
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<tbody>
<tr>
<td>Only one definitive episode of vertigo and the other symptoms and signs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Possible Meniere’s disease</th>
</tr>
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<tbody>
<tr>
<td>Definitive vertigo with no associated hearing loss or hearing loss with non-definitive disequilibrium</td>
</tr>
</tbody>
</table>

### 1. Recurrent spontaneous and episodic vertigo.
A definitive spell of vertigo lasting at least 20 min, often prostrating, accompanied by disequilibrium that can last several days; usually nausea or vomiting, or both; no loss of consciousness. Horizontal rotary nystagmus is always present

### 2. Hearing loss (not necessarily fluctuating)

### 3. Either aural fullness or tinnitus, or both

### Pathophysiology

- Fluctuating SNHL → Flat loss & poor discrim
- Episodic Vertigo → Chronic dysequilibrium
- Positive Hennebert’s sign
- Drop attacks of Tumarkin
- Aural Fullness
Episodic Vertigo & Fluctuating Sensorineural Loss

- Implies reversible process
- Endolymphatic hydrops
- No loss of sensory or neural elements in cochlea and vestibular organs

Rupture Hypothesis:
Lawrence and McCabe 1959
Schuknecht et al 1962

Rupture of Membranous Labyrinth
### Irreversible Sensorineural Loss

- Flat audiometric pattern
- Progressive loss of speech discrimination

At light microscopy, there is poor correlation between histopathology and hearing loss.

#### Electron Microscopy

(Kimura et al, 1976; Nadol & Thornton, 1987)

<table>
<thead>
<tr>
<th>OHC</th>
<th>OHC &amp; IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Fusion of cilia</td>
<td>• afferent nerve endings</td>
</tr>
<tr>
<td>• Disruption of cuticular bodies</td>
<td>• afferent synapses</td>
</tr>
<tr>
<td>• Basalward displacement of cell body</td>
<td></td>
</tr>
</tbody>
</table>
Chronic Dysequilibrium

- \( \downarrow \) in type II hair cells in cristae & maculae (Tsuji et al, 2000)
- \( \downarrow \) in Scarpa’s ganglion cells (Tsuji et al, 2000)
- Distortions of ampullary & utricular walls (Rizvi, 1986; Wall 1989)

Light Microscopy Findings

- Hydrops of Saccule
- IAC
- Middle Ear
- Scale: 2.0 mm
Hennebert’s Sign (Nadol, 1977)

- “Positive fistula sign” without a fistula
- Positive in 30%
- Most effective stimulus is negative pressure
- Mechanism - vestibular fibrosis

Tumarkin’s Drop Attack

Proposed mechanism -
Sudden momentary stimulation of an otolithic organ due to shifting or collapsing membranes
**Classical Concept**

**After Kiang 1988**

- Genetic
- Infection
- Vascular
- Dietary
- Allergy
- Autonomic
- Endocrine
- Autoimmune

**Endolymphatic Sac or Duct**

- Episodic vertigo
- Fluctuating hearing loss
- Tinnitus
- Fullness
- Normal Flow
- ELS

**Obstruction of Endolymphatic Duct → Hydrops**

*(Kimura & Schuknecht 1965)*

- Mechanism thought to be blockage of longitudinal flow, based on Guild (1927)

- Measured rate of longitudinal flow is too low to support this theory (Salt 1989)
Discrepancies

- Hydrops can be asymptomatic (Rauch et al 1989; Sperling et al 1993)
- Menière’s during life but no hydrops on histology (Belal & Ylikoski 1980)
- Animals with hydrops do not exhibit vestibular symptoms

Spiral Ligament

Fibrocytes contain numerous enzymes & proteins that are critical to maintaining metabolic & ionic homeostasis of the cochlea

Ichimiya et al 1994; Kikuchi et al 1995; Adams 2002
Obstruction of endolymphatic duct in guinea pig results in change in immunostaining within type I fibrocytes of spiral ligament before development of hydrops:

Taurine (Osmolyte), Na K 2 Cl cotransporter (regulates cellular volume), c-Jun-N-terminal kinase (JNK) (Cellular Stress Marker)

Alteration transmitted through perilymph result in cellular stress and dysfunction of SL. Hydrops is a result rather than a cause of the disorder and cellular mechanisms rather than flow obstructions are pathologic.
Treatment Options

- Relieving Hydrops
  - Altering Fluid & Flow (Diet & Diuretics)
  - Enhancing Flow (Meniette)
  - Endolymphatic Sac Surgery (1927)

- Ablate Function
  - Vestibular Nerve Section (1928)
  - Physical Labyrinthectomy
  - Chemical Labyrinthectomy (1957)

Aminoglycosides

- Streptomycin 1943
- Antibiotic
  - Gram negative infections
  - Tuberculosis
- Side effects
  - Imbalance & hearing loss
- Fowler 1948
  - IM Streptomycin in Menière's Disease
Intratympanic Therapy
Streptomycin → Gentamicin

- 1st proposed by Lange 80’s
- Popular in 90’s
- Shotgun approach (Nedzelski)
- Low-dose (Magnusson)

Gent IT Trials

<table>
<thead>
<tr>
<th>Author</th>
<th>Dosing</th>
<th>Control</th>
<th>Hearing loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beck</td>
<td>QOD 30mg/ml</td>
<td>92%</td>
<td>15%</td>
</tr>
<tr>
<td>Nedzelski 93</td>
<td>Daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parnes</td>
<td>Weekly 26mg/ml</td>
<td>90%</td>
<td>8%</td>
</tr>
<tr>
<td>Driscoll</td>
<td>1x repeat prn 30d</td>
<td>82%</td>
<td>1%</td>
</tr>
<tr>
<td>Hoffer</td>
<td>Microcatheter</td>
<td>92%</td>
<td>0</td>
</tr>
</tbody>
</table>
**Diamond et al**  
**Gent IT Meta-analysis**

<table>
<thead>
<tr>
<th>Studies</th>
<th>Control</th>
<th>Hearing loss</th>
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<tbody>
<tr>
<td>N=35</td>
<td>Overall</td>
<td>89%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(73-100%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>26%</td>
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<tr>
<td></td>
<td></td>
<td>(0-90%)</td>
</tr>
<tr>
<td>Dosing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mult Daily</td>
<td>94%</td>
<td>26%</td>
</tr>
<tr>
<td>Daily</td>
<td>84%</td>
<td>32%</td>
</tr>
<tr>
<td>Weekly</td>
<td>87%</td>
<td>21%</td>
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**Cohen-Kerem et al**  
**Gent IT Meta-analysis**

<table>
<thead>
<tr>
<th>Studies</th>
<th>Control</th>
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<tbody>
<tr>
<td>N=15 (627)</td>
<td>Overall</td>
</tr>
<tr>
<td></td>
<td>Class A</td>
</tr>
<tr>
<td></td>
<td>74.7%</td>
</tr>
<tr>
<td></td>
<td>Class B</td>
</tr>
<tr>
<td></td>
<td>92.7%</td>
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Success not affected by dosing regimen (fixed or titration)

Hearing and word recognition not adversely affected
IT Steroids

- Sakata 1982 Tinnitus
- Sakata 1986 MD
- Silverstein 1999
  - No difference
- Garduno-Anaya 2005
  - RCT
  - 82% vs 57%

Which Medication?

<table>
<thead>
<tr>
<th>Aminoglycoside</th>
<th>vs</th>
<th>Steroid</th>
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<tbody>
<tr>
<td>↓ Function</td>
<td></td>
<td>↑ Function</td>
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<tr>
<td>Suggested Protocol</td>
<td></td>
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<td>-------------------</td>
<td></td>
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<tr>
<td>IT Steroid</td>
<td></td>
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</tr>
<tr>
<td>Decadron 10mg/ml or 4mg/ml</td>
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<tr>
<td>Series of Weekly Injections</td>
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<tr>
<td>Assess response</td>
<td></td>
<td></td>
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<tr>
<td>Repeat or consider IT Gentamicin</td>
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<td></td>
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<tr>
<td>IT Gentamicin</td>
<td></td>
<td></td>
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<tr>
<td>One Dose</td>
<td></td>
<td></td>
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<tr>
<td>30mg/ml</td>
<td></td>
<td></td>
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<tr>
<td>Assess response</td>
<td></td>
<td></td>
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<tr>
<td>Subjective or Objective Vestibular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Audiogram</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repeat as necessary</td>
<td></td>
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<th>Technique</th>
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<tr>
<td>Patient reclined head turned</td>
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<tr>
<td>Anesthetize with phenol Anterior/Superiorly</td>
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<tr>
<td>27 g needle TB syringe</td>
</tr>
<tr>
<td>Inject and observe for meniscus</td>
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<tr>
<td>Supine for 30 minutes</td>
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Conclusions & Remaining Questions

- Menière's Remains a complex disorder
- Pathology suggests a complex impairment of cellular mechanisms and paradigm shift
- IT therapy effective treatment
  - indications?
  - best medication?
  - concentration?
  - dosing frequency?
  - endpoints?

Acknowledgements

Dave Healy, MD
Saumil Merchant, M.D.
MEEI & Temporal Bone Consortium
Joseph B. Nadol, Jr., M.D.
Joe C. Adams, Ph.D.
Steven D. Rauch, M.D.
Nelson Y.S. Kiang, Ph.D.
Robert S. Kimura, Ph.D.
Harold F. Schuknecht, M.D.
- Low frequency nature of hearing loss
- Simultaneous ruptures
- Cochleosaccucotomy in patients
- Ruptures may be asymptomatic

Endolymphatic compartment is defined as the lumen of the epithelium that is sealed by tight junctions.
Pathogenesis of Sensorineural Hearing Loss

- Dysfunction of fibrocytes within spiral ligament
- Dysfunction of hair cells
- Dysfunction of afferent neurons

Ichimiya et al 1994; Nadol et al 1995; Adams 2002
Fibrocytes contain numerous enzymes & proteins that are critical to maintaining metabolic & ionic homeostasis of the cochlea

Adams 2002