



Sudden Sensorineural Hearing Loss and Intratympanic Steroids

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Grand Rounds Presentation

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Sudden Sensorineural Hearing Loss

- ❑ First described in 1944 by DeKleyn
- ❑ Incidence: 5-20 per 100,000
- ❑ 4,000 new cases/year in US
- ❑ Idiopathic
- ❑ Hearing loss in 3 contiguous frequencies of at least 30 dB
 - Some authors use at least 20 dB loss
- ❑ Onset of hearing loss occurs in less than 72 hours
- ❑ Recovery rate without treatment 32% - 79%
 - Usually within 2 weeks of onset
 - Only 36% with complete recovery
- ❑ No middle ear disease
- ❑ Otologic emergency!

Sudden Sensorineural Hearing Loss

- Clinical Presentation
 - Sudden onset hearing loss
 - Less than 3 days
 - Usually unilateral
 - Left side possibly more common (55%)
 - Bilateral 2%
 - Median age 40-54
 - Equal among males and females
 - Awakening from sleep
 - Hearing a “popping” prior to hearing loss
 - Aural fullness
 - Tinnitus
 - Vertigo

Sudden Sensorineural Hearing Loss

- Differential Diagnosis
 - Infectious
 - Bacterial: meningitis, labyrinthitis, syphilis
 - Viral: Mumps, CMV
 - Inflammatory
 - Autoimmune, Cogan syndrome, Lupus, MS
 - Traumatic
 - Temporal bone fracture, acoustic trauma, perilymph fistula
 - Neoplastic
 - CPA tumor, temporal bone metastasis
 - Toxic
 - Aminoglycosides, aspirin
 - Vascular
 - Thromboembolism, macroglobulinemia, sickle cell disease, cerebral infarct, TIA
 - Congenital
 - Mondini malformation, enlarged vestibular aqueduct

Sudden Sensorineural Hearing Loss

□ Theories

■ Viral infection

- Temporal association of SSNHL with viral URI in 25% - 63%
- Serology confirming active viral infection
 - HSV, VZV, CMV, influenza, parainfluenza, rubeola, mumps, rubella
 - Immunoreactivity against virus
- Histopathology of human temporal bones
 - Atrophy of organ of Corti, spiral ganglion, tectorial membrane
 - Hair cell loss
 - Unraveling of myelin
- Animal experiments confirm viral penetration of the inner ear

Sudden Sensorineural Hearing Loss

□ Theories:

■ Vascular injury

□ Sudden onset suggesting infarction

- Perlman (1959) demonstrated loss of cochlear microphonic 60 seconds after occlusion of labyrinthine artery in guinea pig
- Buerger's, macroglobulinemia, sickle cell, fat embolism

□ Histopathologic changes in cochlea caused by vascular occlusion in animal models

- In guinea pigs, labyrinthine vessel occlusion lead to loss of spiral ganglion cells, mild to moderate damage to organ of Corti, cochlear duct fibrosis

□ Controversial

Sudden Sensorineural Hearing Loss

□ Theories:

■ Intracochlear membrane rupture

- Loss of endocochlear potential due to mixing of endolymph and perilymph
- Gussen (1981) histologic evidence
- Fallen out of favor

□ Likely combination of viral cause and vascular insult

Sudden Sensorineural Hearing Loss

□ Challenges

- True incidence is not known
 - Patients with spontaneous recovery usually do not present to an otolaryngologist
- Patients may present beyond what is considered to be therapeutic window
- Etiology still unclear
- Relative paucity of studies examining treatments based on prospective, double-blind, randomized, controlled trials

Sudden Sensorineural Hearing Loss

Clinical Evaluation

- History
- Complete head and neck exam
 - Pneumatotomscopy to evaluate for fistula sign
- Audiogram including pure-tone audiometry (PTA), speech reception threshold (SRT), and speech discrimination scores (SDS)
- Tympanometry
- +/- Auditory brainstem response (ABR) and otoacoustic emission (OAE)
- ENG if vestibular symptoms and/or signs are present

Sudden Sensorineural Hearing Loss

Radiography

■ MRI with gadolinium

0.8%-2% of patients with SSNHL have been diagnosed with IAC/CPA tumors

■ Non-contrasted CT of temporal bones in younger patients

Mondini malformation

Enlarged vestibular aqueduct

Sudden Sensorineural Hearing Loss

- ❑ Laboratory Evaluation
 - CBC with diff
 - ❑ Polycythemia, leukemia, thrombocytosis
 - Electrolytes
 - Erythrocyte sedimentation rate (ESR)
 - ❑ Nonspecific, autoimmune or inflammatory marker
 - ❑ Antinuclear antibody or 68 kD antibody
 - Rheumatoid factor (RF)
 - FTA-Abs (Syphilis)
 - Coagulation profile
 - Thyroid function testing
 - Lipid profile

Sudden Sensorineural Hearing Loss

- Treatment
 - **Systemic Steroids**
 - Historical perspective: Reduce inner ear inflammation
 - Nonspecific
 - Dependent on time to therapy
 - Oral, IV
 - Variable to poor response for profound SSNHL
 - Cannot be used for all patients
 - Diabetics, ulcers, TB, glaucoma
 - Intratympanic steroids
 - Antivirals
 - Volume expanders
 - Vasodilators
 - Anticoagulants
 - Carbogen inhalation

Sudden Sensorineural Hearing Loss

- Cochrane Database of Systematic Reviews
 - Wei (2003, Updated 2006): Steroids for idiopathic sudden sensorineural hearing loss
 - Only 2 prospective, double-blind, randomized, controlled trials evaluating therapy of SSNHL

Wilson (1980)

- Prospective, double-blind, randomized, controlled study to examine the effectiveness of steroid therapy for SSNHL
- Parameters strictly defined
- Kaiser Permanente and MEEI combined
- Inclusion: 30 dB loss over at least 3 contiguous frequencies in less than 3 days and presentation within 10 days of onset with normal laboratory studies
- 33 treated with steroids
 - KP Decadron 10 days tapered
 - MEEI Medrol 12 days tapered
- 34 placebo treated controls
- 52 untreated controlled

Wilson (1980)

- Patients stratified by type of audiogram
 - Mid-frequency loss
 - Loss at 4 kHz greater/equal to loss at 8 kHz
 - Loss at 8 kHz greater than loss at 4 kHz
 - Profound loss greater than 90 dB PTA
 - Unaffected ear used as reference
- Recovery
 - Complete: within 10 dB of reference SRT or PTA if HF
 - Partial: > 50% of reference SRT or PTA if HF
 - None: < 50% recovery

Wilson (1980)

- Results
 - All with midfrequency loss had complete recovery
 - 14% had vertigo
 - 76% with profound loss had no recovery, and 24% with partial recovery
 - No improvement in steroid treated group
 - 79% had vertigo
 - 4 kHz loss and 8 kHz groups were combined
 - Recovery with steroids 78%
 - Recovery in placebo group 33%
- No adverse side effects

Wilson (1980)

Prognostic factors

- Vertigo not statistically significant
- Age less than 40 years favorable for recovery
- Type of audiogram
 - Midfrequency loss with best recovery
 - Profound loss less likely to have recovery
 - Loss between 40 dB – 85 dB more likely to respond to steroid therapy

Wilson (1980)

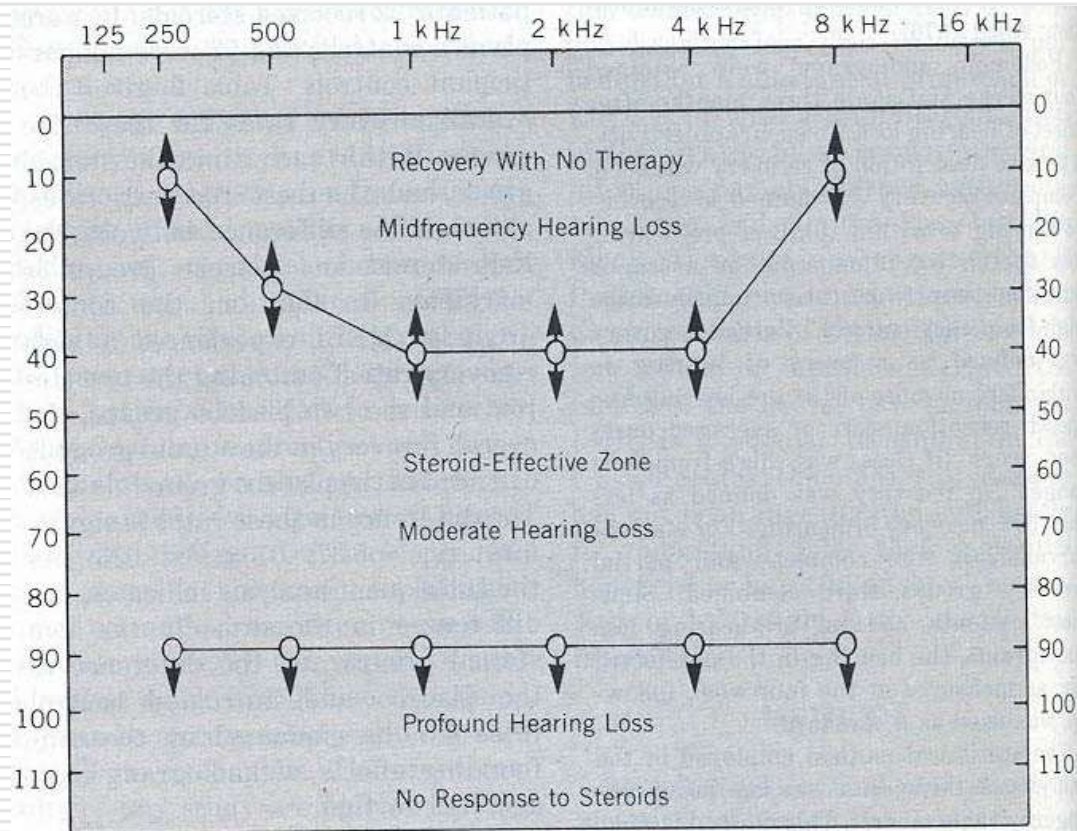


Fig 2.—Categories of sudden hearing loss as determined by spontaneous recovery rate and response to steroid therapy.

Wilson (1980)

- Relative Odds for recovery
 - Steroids vs Placebo 4.95:1
 - Steroids vs untreated controls 4.06:1
 - Untreated controls vs Placebo 1.22:1
 - Steroids vs all control 4.39:1

Cinamon (2001)

- Prospective, double-blind, randomized, controlled trial to evaluate the effectiveness of carbogen and steroids for SSNHL
- Hearing loss at least 20 dB over 3 frequencies
- 41 patients stratified by type of audiogram
 - Flat, midfrequency loss, low frequency loss, and high frequency loss
- Improvement: at least 15 dB change of PTA
- Four treatment groups for 5 days of therapy
 - Prednisone (1mg/kg/day)
 - Placebo
 - Carbogen (95% oxygen, 5% CO₂) inhalation (30 min six times daily)
 - Room air inhalation

Cinamon (2001)

□ Results

- Overall improvement in PTA at follow-up (73%)
 - Steroid 80%
 - Placebo 81%
 - Carbogen 55%
 - Placebo inhalation 77%
 - Not statistically significant

□ Trends:

- Low frequency loss improved more
- High frequency loss improved less
- Patients without vertigo have better outcome

Intratympanic therapy

- ❑ Barany (1935): used lidocaine for tinnitus
- ❑ Schuknecht (1956): used streptomycin for Meniere's disease
- ❑ Bryan (1973): used steroids for a patient with facial paralysis

Intratympanic Steroids

- ❑ Administration of steroids to middle ear round window niche/membrane directly targeting the inner ear
- ❑ Very little systemic absorption
 - May benefit patients for whom systemic steroids are contraindicated
- ❑ Higher concentration to end organ
- ❑ May salvage hearing loss when non-responsive to systemic steroids
- ❑ Only one prospective, double-blind, randomized, controlled trial of IT Dex vs placebo (for treatment of Meniere's)

Shirwany (1998)

- Examined the effects of transtympanic injection of steroids on cochlear blood flow, auditory sensitivity and histology in guinea pigs
 - Dexamethasone 4 mg/mL vs saline
 - 30 gauge needle through AI TM

Shirwany (1998)

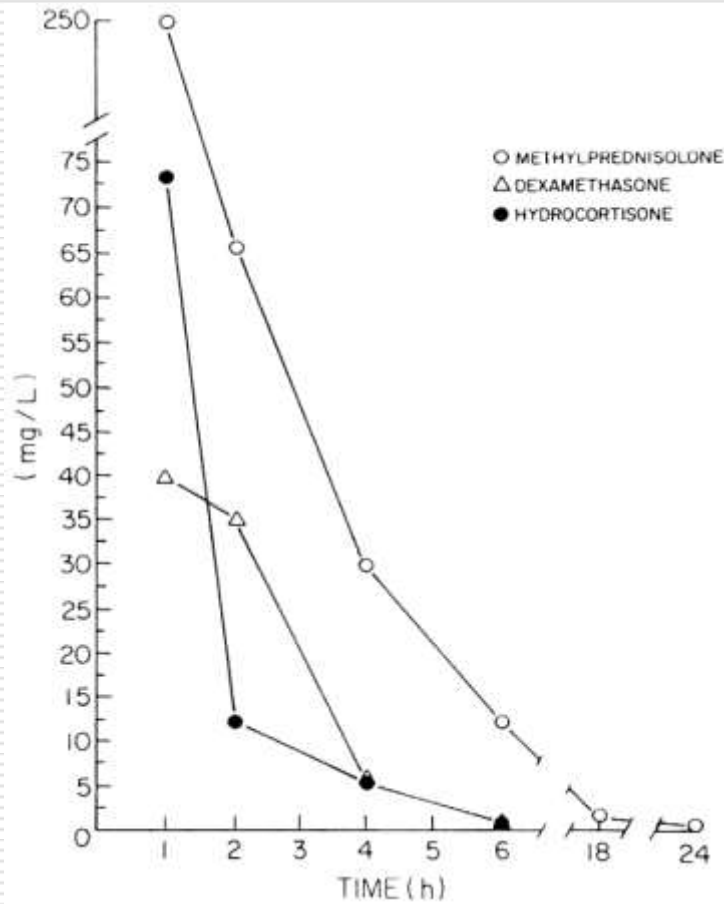
□ Results

- 29% increase in cochlear blood flow within 30 sec without change in auditory sensitivity measured by ABR
- Increase in cochlear blood flow was sustained for at least 1 hour
- No histologic changes

Parnes (1999)

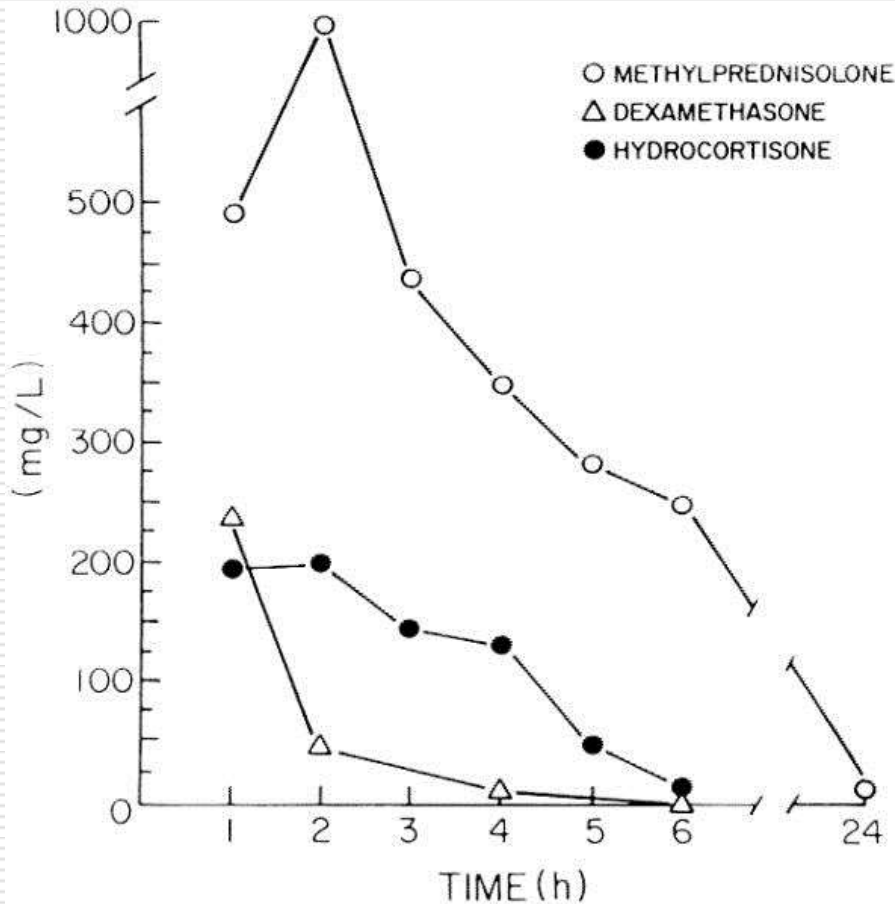
- In a guinea pig model, the concentrations of hydrocortisone, dexamethasone, and methylprednisone in plasma, endolymph, perilymph, and CSF were compared when administered orally, intravenous, and IT
 - Dexamethasone 26.7 times more potent than hydrocortisone
 - Methylprednisone 5.3 times more potent than hydrocortisone
- Also designed IT steroid treatment routines for a variety of inner ear disorders

Parnes (1999)



- Potency corrected levels in perilymph after IT administration

Parnes (1999)



- Potency corrected levels in endolymph after IT administration

Parnes (1999)

- 12 patients not previously treated for SSNHL (onset within 6 weeks of treatment) given IT methylprednisone or dexamethasone
- 27 gauge needle
- 8 with Methylprednisone 40 mg/mL
 - 1 full recovery
 - 3 partial recovery
 - 4 no recovery
- 4 with Dexamethasone 2 mg/mL
 - 2 partial recovery
 - 2 no recovery
- 50% with some recovery
 - ?
- 3 developed otitis media, which resolved with Abx

Chandrasekhar (2001)

- Guinea pig model
- Greater concentration of dexamethasone in perilymph via intratympanic route vs IV
- IT-Dex with histamine significantly increased perilymph concentration compared to hyaluronic acid, dimethylsulfoxide, or dex alone

Gianoli (2001)

- Prospective trial of intratympanic steroid therapy for patients with SSNHL when oral steroids failed or patients were unable to tolerate systemic steroids
- SSNHL: > 20 dB loss in at least 3 contiguous frequencies within 3 days
- Improvement: decrease of PTA or SRT of at least 10 dB or 10% increase in speech discrimination

Gianoli (2001)

□ Delivery:

- Posteroinferior tympanotomy and round window examined endoscopically with removal of adhesions of niche
- PET placed
- Methylprednisone (62.5 mg/mL) or dexamethasone (25 mg/mL) placed through tube
- 4 applications (0.4 – 0.6 mL) over 10 - 14 day period

Gianoli (2001)

□ Results (23 patients)

- 44% had improvement in PTA
 - 15.2 dB
- 48% had improvement in SRT
 - 15 dB
- 35% had improvement in speech discrimination
 - 21%
- 4% had worsening of speech discrim by 16%

Gianoli (2001)

- Stratified by time of onset to therapy
 - <6 weeks, >6weeks
 - Range 0-520 weeks
 - No statistical significance in improvement
- Stratified by Age (<60, >60 years)
 - No statistical significance
 - Trend: younger patients with favorable results
- Stratified by type of steroid
 - No statistical significance
 - Trend: methylprednisone group had greater improvement than dexamethasone group

Gianoli (2001)

- 1 (4%) adverse event: otitis media, resolved
- Disadvantages/Advantages
 - No control group, not blinded, not randomized
 - Small sample size
 - Not used as primary treatment for SSNHL in all
 - Improvement may not be noted by patients
 - Profound loss
 - Systematic approach
 - IT steroids may be an option for patients unable to take systemic steroids or as salvage

Kopke (2001)

- Prospective trial using round window microcatheter for delivery of methylprednisone in patients with SSNHL refractory to oral prednisone therapy
- Patients stratified by time of onset to catheter placement
 - 6 patients in six week or less group
 - 4 with SSNHL
 - 1 with hearing loss after stapedotomy
 - 1 with Meniere's with hearing loss while undergoing aminoglycoside therapy
 - 3 in late group
 - 1 with SSNHL
 - 1 following acoustic trauma
 - 1 following closed head injury
 - Improvement: decrease in PTA of 10 dB or increase in SDS by 15%

Kopke (2001)

- IT Delivery via Microcatheter
 - GETA
 - Tympanomeatal flap elevated
 - Round window niche cleared of adhesions
 - 1.5 mm to 2.0 mm microcatheter placed into niche
 - Methylprednisolone (62.5 mg/mL) delivered continuously for 14 days at rate of 10 μ L/hour using pump

Kopke (2001)

□ Results

- 100% in group treated in 6 weeks had improved PTA scores
- 83% with improved SDS
- 66% to normal hearing
- No improvement in late group

□ Lefebvre (2002)

- Similar results in 6 patients using continuous infusion with round window microcatheter

□ Microcatheter removed from market by FDA

Silverstein (2002)

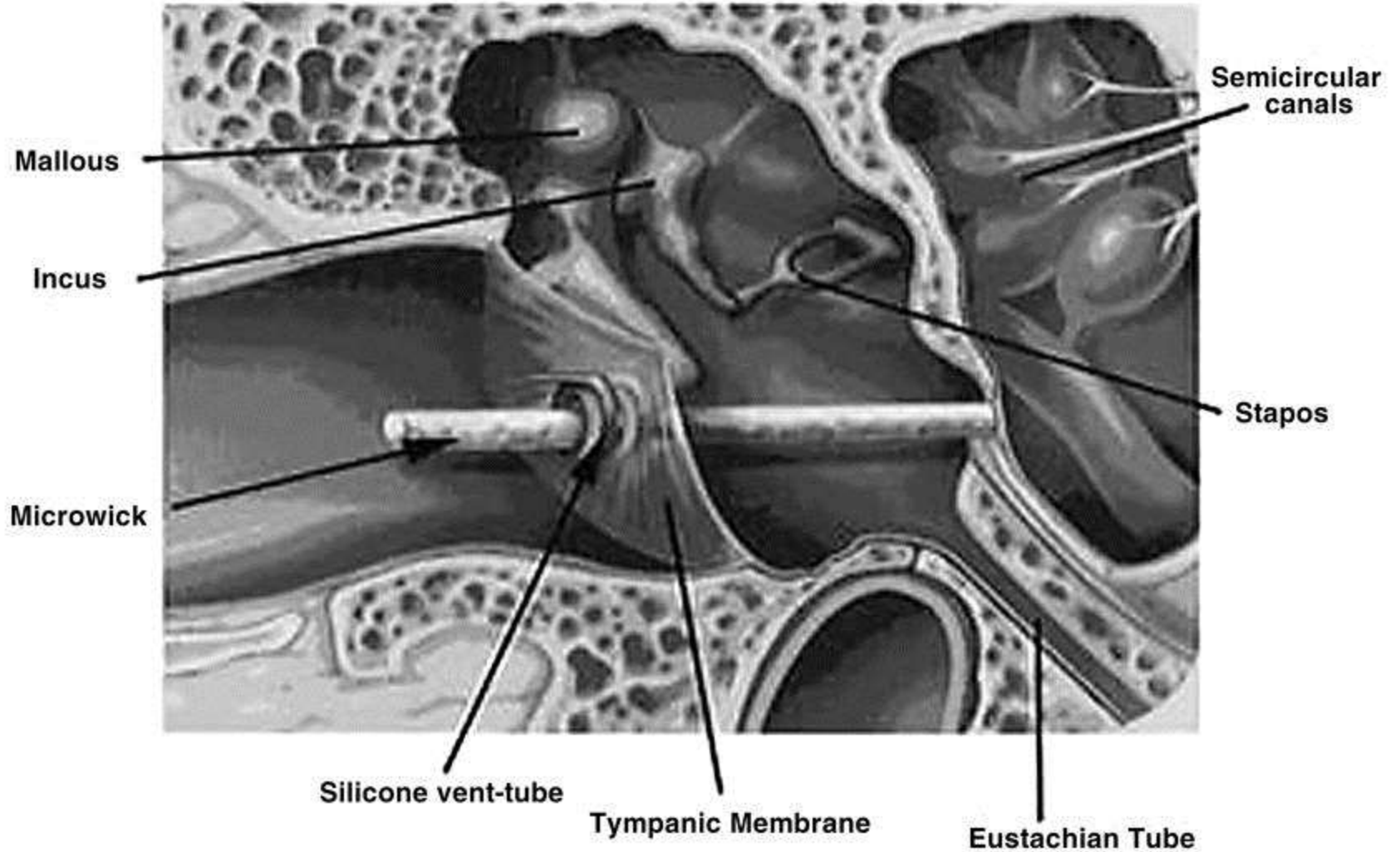
- Examined patients (48) with refractory hearing loss after systemic steroids for SSNHL using inner ear perfusion of dexamethasone 4-24 mg/mL with MicroWick
- 23% had improvement of PTA of at least 10 dB
- 35% had improved SDS of at least 15%

Silverstein (2002)



- MicroWick
 - Topical anesthetic
 - Posteroinferior myringotomy
 - Round window niche identified and adhesions removed
 - MicroWick (1 mm by 9 mm) placed
 - PET placed into myringotomy with Microwick through lumen
 - Drops instilled into ear
-

SILVERSTEIN MICROWICK



Guan-Min (2004)

- Prospective, randomized, controlled trial to study the effectiveness of IT Dex in patients with severe to profound SSNHL
 - PTA, SRT, ABR, OAE, tympanometry, viral serology, MRI/CT if indicated
 - 39 patients initially treated (18 severe, 21 profound)
 - Methylprednisolone for 10 days (except 3 with DM)
 - Nicametate (vasodilator), Vitamin B-complex, Benzodiazepine for 10 days
 - Carbogen for 5 days
 - Patients divided by response
 - Normal hearing or improvement > 30 dB (10, 8 severe, 2 profound)
 - Improvement < 30 dB, no improvement, and worsening (29)
 - Control group (14) treated with above except steroids and carbogen
 - Treatment group (15)
 - IT Dex applied 10 days after initial therapy if there was no or only partial response
 - Myringotomy with 22 gauge needle at posterior TM and 0.4 – 0.7 mL of Dex (4 mg/mL)
 - Once weekly for 3 weeks
-

Guan-Min (2004)

□ Results

- 53% (8/15) in IT-Dex group with improvement
 - 50% (4/8) with normal hearing
 - 1 with DM
 - 50% with > 30 dB improvement
 - 7% (1/14) improvement in control
 - Recovery for Severe SSNHL 44%
 - Recovery for Profound SSNHL 9.5%
 - No statistical significance:
 - Age (<50, >50 years)
 - Sex
 - Treatment delay time (<7 days, ≥7 days)
 - Side effects of IT-Dex: acne (1), vertigo (1)
-

Battista (2005)

- Prospective study examining IT dex concurrent with oral steroids for profound SSNHL
 - 25 adult patients
 - SSNHL within 24 hours
 - Range of time to presentation/treatment: 2-180 days
 - Initial PTA at least 90 dB
 - No otologic history
 - Negative MRI
 - Treatment
 - Methylprednisolone (64 mg/day, tapered over 11 days)
 - Dexamethasone injections (24 mg/mL)
 - 27 gauge needle
 - 4 injections of 0.3 cc
 - 14 days
-

Battista (2005)

□ Results

- 8% with complete hearing recovery
- 12% with partial recovery
- Those with some recovery had treatment within 14 days of onset
- 1 TM perforation repaired with paper patch

□ Oral or IT steroids?

Xenellis (2006)

- Examined effectiveness of IT steroids for SSNHL patients who failed to improve with initial therapy
 - Prednisolone IV (1 mg/kg/day, tapered)
 - Acyclovir (4 g/day, 5 days)
 - Buflomedil (300 mg/day, 10 days)
 - Ranitidine
 - Days to admission: 1-20
 - Complete workup
 - IT Methylprednisolone (40 mg/cc) vs no IT
 - Injection with 21 gauge needle
 - 4 times in 15 days
-

Xenellis (2006)

□ Results

- 47% treated with IT steroids improved > 10 dB
 - No controls improved
 - No adverse outcomes
-

Group	Study	Steroid	Delivery	Improvement
Xenelis (2006)	Prospective, controlled	Methylprednisolone	Injection	47% (PTA)
Batista (2005)	Prospective, PSSNHL	Dexamethasone	Injection	20% (PTA)
Slattery (2005)	Prospective	Methylprednisolone	Injection	55% (PTA/SDS)
Banerjee (2005)	<i>Retrospective review</i>	Methylprednisolone Dexamethasone	Via PET	69%, ≤10 days (PTA) 31%, >10 days
Herr (2005)	<i>Retrospective review</i>	Dexamethasone	MicroWick Microcatheter	53% (PTA/SDS)
Guan-Min (2004)	Prospective, randomized, controlled	Dexamethasone	Injection	53% Treatment (PTA) 7% Control
Silverstein (2002)	Academy Presentation	Dexamethasone	MicroWick	23% (PTA) 35% (SDS)
Gianoli (2001)	Prospective	Dexamethasone	Via PET	44% (PTA)
Kopke (2001)	Prospective	Methylprednisone	Microcatheter	100%, ≤6wk (PTA/SDS) 0% >6wk

Sudden Sensorineural Hearing Loss

□ Advantages to IT steroids

- May be used when systemic steroids are contraindicated or refused
- Greater concentration achieved at target end organ
- May be performed in outpatient setting
- Possible use for salvage of hearing
- Relatively low complication rate

Sudden Sensorineural Hearing Loss

- Challenges for IT steroids
 - Not well established as primary treatment strategy
 - Dosing?
 - Best delivery technique?
 - Long term effects?
 - Why does it work? Sometimes

Sudden Sensorineural Hearing Loss

□ Take Home Messages:

- SSNHL is an otologic emergency
- Systemic steroids are mainstay of therapy
 - Prednisone 60 mg/day for 3-5 days, tapered 5-7 days
- Better prognosis if treatment started early (within 4 weeks of onset)
- IT steroids may be an alternative when systemic steroids are contraindicated
- IT steroids is another option when oral steroids fail to restore hearing