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- Email customerservice@AudiologyOnline.com

Sudden Sensorineural Hearing Loss: Diagnosis and Treatment

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Background

- First *described* in 1944 by De Kleyn
- Wilson et al. 1980 – *defined* as ≧ 30 dB sensorineural loss in at least 3 contiguous frequencies over 72 hours
- Between 7-15% have identifiable cause – allows for specific treatment
- Majority “idiopathic”
- Despite research, controversy in etiology, work-up, and care

Background

- > 1200 articles on PubMed
- For practitioners, difficult to reconcile 'correct' treatment paradigm

Goal: to summarize the literature and propose guidelines and management pearls for the practicing audiologist

Epidemiology

- Incidence 5-20/100,000
- Up to 60,000 cases annually in US
- Many affected individuals who recover never present
- 1.5-1.7/100 new patients in a busy otology practice
- Peak incidence 5th-6th decade
- Men = women
- < 2% bilateral, typically sequential

Byl, 1984
Fetterman et al., 1996

Epidemiology, cont.

- Accompanying symptoms:
  - Tinnitus ("roaring") 40-90%
  - Dizziness 30-56%
  - Aural fullness 40-50%
  - Ear 'popping'
- Often noted upon awakening

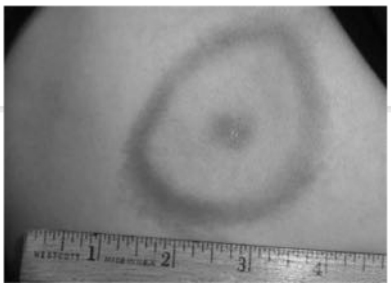
Xenellis et al., 2006
Chau et al., 2010

Identifiable Causes of SSNHL

- 7-15% have identifiable cause
- > 100 possible etiologies
- Broad categories:
  - Infectious (13%)
  - Autoimmune
  - Traumatic (4%)
  - Neurologic
  - Vascular (3%)
  - Neoplastic (2%)
  - Otologic (5%)
  - Functional

Fetterman et al., 1996
Nosrati-Zarenoe et al., 2007
Chau et al., 2010

Infectious

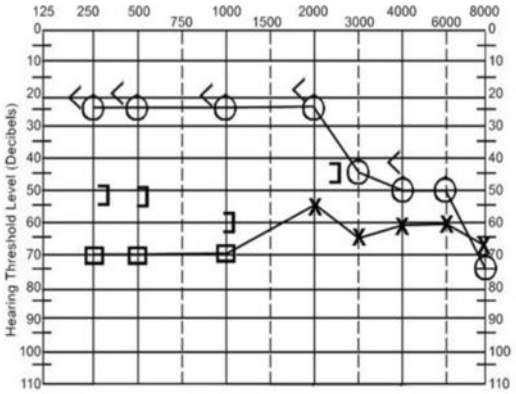


- Lyme Disease (Borrelia burgdorferi)
  - Early– erythema migrans
  - Up to 20% SSNHL with positive Lyme titers, as low as 0%
  - Rash often absent (90%), 40% without risk factors
  - *Hearing recovery similar between Lyme- and Lyme+ pts*
- Syphilis (Treponema pallidum)
  - Neurosyphilis: usually late stage, can be early
  - Consider in immunosuppressed or high-risk patients
  - Consider in bilateral SNHL

Lorenzi et al., 2003
Heman-Ackah et al., 2010
Mishra et al., 2008
Marra et al., 2009

Otologic Disorders

- Up to 5% with SSNHL with otologic disorder
- Meniere's Disease
  - 15/100,000
  - Typically low frequency hearing loss
  - Recurrent
- Autoimmune inner ear disease
  - 5/100,000
  - Bilateral SNHL over weeks to months



Otologic Disorders

- Vestibular Schwannoma (acoustic neuroma)
  - Incidence 1/100,000
  - Incidence in SSNHL 1/100
- Neoplastic causes 2.3%
  - Includes rare metastatic and benign tumors
- Spontaneous or treated return of hearing *does not* rule out vestibular schwannoma

Systemic disease

- Autoimmune Disease
  - Cogan's Syndrome – nonsyphilitic interstitial keratitis and audiovestibular disease/hearing loss
  - SLE
  - Wegener's granulomatosis
  - AIED
- Thyroid Disease
  - 1-15% with SSNHL
  - TSH as routine part of work-up?

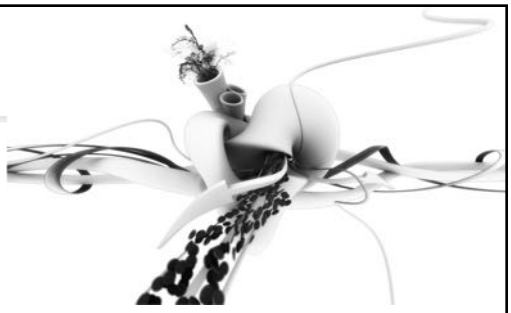
Narozny et al., 2006
Heman-Ackah et al., 2010

Etiologies: Vascular

- Cochlea blood flow – 2 end arteries, lack collateral flow = high risk
- Sudden onset of SNHL similar to ischemic events (i.e. TIA)
- Vascular risk factors (tobacco, HTN, hyperlipidemia) may be related to increased incidence of SSNHL
- Perlman (1959) – loss of cochlear microphonic 60 seconds after occlusion of labyrinthine artery in guinea pig
- Schweinfurth (2000) – 12-37 dB drop after embolizing artery

Ballesteros et al., 2009
Capaccio et al., 2007

Etiologies: Vascular



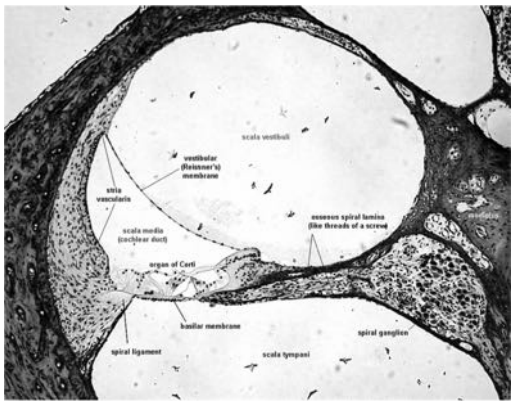
Arguments against vascular etiology

1. Hearing loss in many cases is reversible
2. Histologic changes of the cochlea in animals with experimental vascular compromise not seen in humans
3. Young patients with no risk factors

Mattox et al., 1977
Schuknecht et al., 1986
Stokroos et al., 1996

Etiologies: Intracochlear

- Rupture of intracochlear membranes (? Reissner's)
- Increased ICP, Valsalva
- "Popping" prior to hearing loss
- Several small studies showing histologic changes with rupture
- Relevant in barotrauma, fractures?



Simmons, 1968

Etiologies: Viral

- Infection/reactivation causes inner ear inflammation or damage
- Antibodies to CMV, HSV, HZV, influenza B, mumps, enterovirus, rubeola all isolated from SSNHL patients
- Temporal bones in patients with SSNHL show similar findings to viral labyrinthitis
- Cochlear/labyrinthine enhancement on MRI in 4-9%
- Inoculation of animals with HSV induced SNHL

Mentel et al., 2004
Wilson et al., 1983
Chon et al., 2003

Natural History

- Discoverable causes often cause permanent hearing loss
- Some with SSNHL regain hearing
  - Recovery without treatment = 32-65%
  - Typically recovery within 2 weeks of onset
  - Complete recovery = 36%

Xenelis et al., 2003
Byl, 1984

Evaluation of SSNHL

Guideline

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery
146(1S) S1–S35

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Clinical Practice Guideline: Sudden Hearing Loss

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Evidence Quality	BENEFITS-HARMS ASSESSMENT: Preponderance of Benefit or Harm	BENEFITS-HARMS ASSESSMENT: Balance of Benefit and Harm
A. Well-designed, randomized controlled trials or diagnostic studies on relevant populations	Strong Recommendation	Option
B. RCTs or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies	Recommendation	
C. Observational studies (case control and cohort design)		
D. Expert opinion, case reports, reasoning from first principles	Option	No Recommendation

Evaluation

- STATEMENT 1. EXCLUSION OF CONDUCTIVE HEARING LOSS: Clinicians should distinguish SNHL from CHL in a patient presenting with sudden hearing loss.

Strong recommendation based on evidence showing a preponderance of benefit over harm

- STATEMENT 4. AUDIOMETRIC CONFIRMATION

Recommendation based on observational studies with a preponderance of benefit over harm.

Evaluation

- STATEMENT 2. MODIFYING FACTORS: Clinicians should assess patients with presumptive sudden sensorineural hearing loss for bilateral sudden hearing loss, recurrent episodes of sudden hearing loss, or focal neurologic findings.

Recommendation based on observational studies with a preponderance of benefit over harm.

Evaluation: Office Assessment

- Thorough history
- Detailed H&N physical exam
- LOOK IN THE EARS
- Pneumatic otoscopy

Evaluation: Laboratory Testing

- STATEMENT 5. LABORATORY TESTING: Clinicians should not obtain routine laboratory tests in patients with SSNHL

Strong Recommendation based on large cross sectional studies showing a preponderance of benefit over harm.

- Specific tests may be useful for specific patients (vascular risk factors, Lyme titers, TFTs, Immune markers, FTA/VDRL
- Multiple studies questioning cost-effectiveness

Rupa et al., 2003
Murphy et al., 2002
Wilson et al., 2010

Evaluation

- Number and type of tests for SSNHL varies by location
- Sweden (400 patients)
  - 100% audiology, 65% laboratory testing, 40% imaging
- US (128 patients)
  - 100% audiology, 85% MRI
- Lab testing in endemic areas (i.e. Lyme)

Nosrati-Zarenoe et al., 2010
Fortnum et al., 2009

Evaluation: Imaging

- **STATEMENT 3. COMPUTED TOMOGRAPHY: Clinicians should not order CT of the head/brain in the initial evaluation of a patient with presumptive SSNHL**

Strong recommendation

- Patients who cannot get MRI (CT t-bones + contrast)
- Sensitivity decreases for tumors < 1cm

Cueva et al., 2004

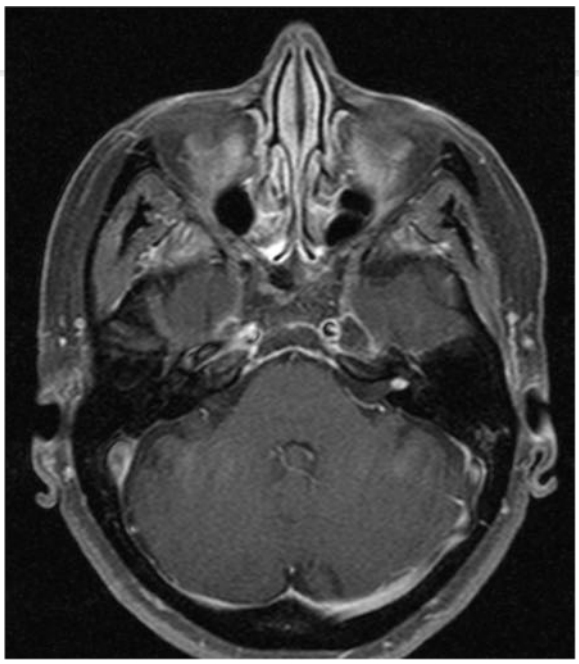
Evaluation: Retrocochlear Pathology

- **STATEMENT 6. RETROCOCHLEAR PATHOLOGY: Clinicians should evaluate patients with SSNHL for retrocochlear pathology by obtaining an MRI or auditory brainstem response testing (ABR)**

Recommendation based on benefit over harm

- SN and SP of MRI + gad nearly 100% for tumors > 3mm
- High incidence of vestibular schwannoma in patients with SSNHL (1-10% vs. 1/10,000)

Cueva et al., 2004
Fortnum et al., 2009



Patient Education

- STATEMENT 7. PATIENT EDUCATION: Clinicians should educate patients with SSNHL about the natural history of the condition, the benefits and risks of medical interventions, and the limitations of existing evidence regarding efficacy.

Strong recommendation based on systematic reviews with a preponderance of benefit over harm

Treatment for SSNHL: Steroids

Treatment

- Initiate disease-specific treatment when appropriate
- Even with identifiable etiology hearing recovery no better then for SSNHL
- Numerous treatments tried: anti-inflammatory, steroids, antimicrobials, vitamins, calcium antagonists, vasodilators, volume expansion, diuretics, chelation, hyperbaric oxygen
- Studies small, poorly designed, heterogeneous
- Incidence is low, etiology unknown

Nosrati-Zarenoe et al., 2010
Yimtae et al., 2007

Steroids and SSNHL

- Wilson WR, *Arch Otolaryngol*, 1980
- "Prospective, double-blind RCT"
- Steroids: 61% partial or complete recovery
- Placebo: 32% partial or complete recovery
- *Untreated control: 58% partial or complete recovery*
- Problems:
  1. Treatment protocol not standardized
  2. Poor statistical methodology
  3. Non-randomized sample

BUT…

This study is what we use to define our practice patterns in the 21st century

Steroids and SSNHL

- STATEMENT 8. INITIAL CORTICOSTEROIDS: Clinicians may offer corticosteroids as initial therapy to patients with SSNHL

Option based on systematic reviews of RCTs with a balance between benefit and harm

- EVEN IN 2018 – CLINICAL EQUIPOISE EXISTS

Not-so Evidence Based Medicine

- 98% of US Otolaryngologists treat SSNHL with oral steroids
- Does the OTO-HNS literature support the use of steroids for SSNHL?
  - Pub med search: 1980-2014: 491
  - 43 RCT and 5 meta-analysis
  - 16 RCT and 3 meta-analysis selected

Shemirani et al., 2010

Level	Type of evidence
1A	Systematic review (with homogeneity) of RCTs
1B	Individual RCT (with narrow confidence intervals)
1C	All or none study
2A	Systematic review (with homogeneity) of cohort studies
2B	Individual Cohort study (including low quality RCT, e.g. <80% follow-up)
2C	"Outcomes" research; Ecological studies
3A	Systematic review (with homogeneity) of case-control studies
3B	Individual Case-control study
4	Case series (and poor quality cohort and case-control study
5	Expert opinion without explicit critical appraisal

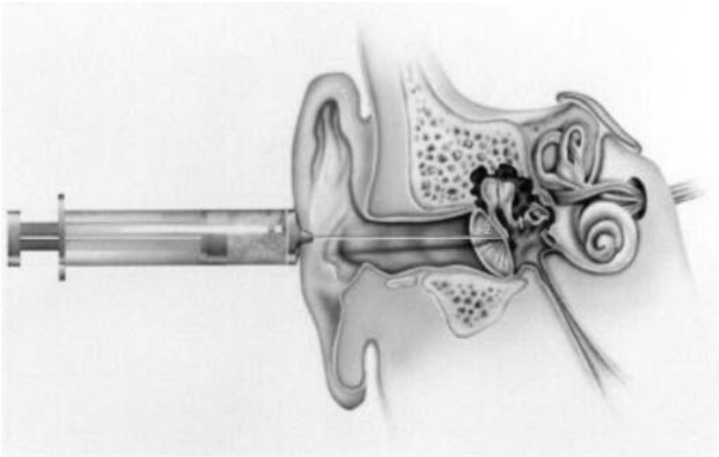
Meta-analysis of RCT

	Location	Journal	Articles	Conclusion
Conlin & Parnes, 2007	Ontario, Canada	*Arch Otolaryngol Head Neck Surg*	2	Unclear benefit of steroid vs. placebo
Labus et al. 2010	Brussels, Belguim	*Laryngoscope*	6	Medical therapy > placebo but not significant
Wei et al. 2013	Melbourne, Australia	*Coch Database Sys Rev*	3	Unclear benefit of steroid vs. placebo

How much steroid to give?

- Slattery et al., *Otolaryngol Head Neck Surg*, 2005
  - 75 patients
  - High dose course over 14 days
  - Smaller dose (i.e. Medrol dose pack)
  - Two courses of any amount
- 35% of patients with at least 50% improvement
- No difference between steroid groups

Intratympanic (IT) Steroids



Why are IT steroids better than oral?

- Little to no systemic absorption (side effects)
- Patients in whom systemic steroids are contraindicated
- Higher concentration to the end organ (cochlea)
- Salvage oral steroid "non-responders"

TABLE VI.
Intratympanic Dexamethasone Dosing.

Hours After Injection	Scala Tympani Perilymph	Scala Vestibuli Perilymph	Endolymph
1	1.553 ± 1.047	1.540 ± 1.311	9.062 ± 5.527
2	1.320 ± 0.864	1.390 ± 1.121	1.702 ± 1.401
4	0.283 ± 0.278	0.400 ± 0.348	0.323 ± 0.443
6	0.073 ± 0.070	0.103 ± 0.059	0

Concentrations (mean ± SD, mg/L) in scala tympani perilymph, scala vestibuli perilymph, and endolymph.

TABLE V.
Intravenous Dexamethasone Dosing.

1	0.220 ± 0.053	0.187 ± 0.006	2.123 ± 0.470
2	0.160 ± 0.026	0.123 ± 0.031	1.487 ± 0.486
4	0.063 ± 0.015	0.050 ± 0.010	0.377 ± 0.318
6	0.020 ± 0.035	0	0.050 ± 0.078

Parnes et al., 1999

IT Steroids: Systematic Reviews/Meta-analyses

- Spear & Schwartz, 2011
  - IT steroids were superior to placebo
  - 40-50% had improvement
  - Mean gain was 13 dB in treatment group
  - Clinical significance is unknown
- Crane et al., 2015
  - OR of improvement with IT steroids 6.04
  - Studies limited quality and considerable heterogeneity

Oral Steroids vs. IT Steroids

- 3 RCT's
- *Hong et al., 2009; Dispenza et al., 2011; Rauch et al., 2012*

- All showed oral steroids were equivalent to IT (**non-inferiority demonstrated in Rauch study)

Combined (Oral + IT) vs. Oral Alone

- 6 RCTs
- 3 no difference; 3 combination therapy > oral therapy
  - 88% v 44% improvement (Battaglia et al.)
  - 46% v 21% improvement (Zhou et al.)
  - 89% v 61% improvement (Gundogan et al.)

Main problem: Does statistical significance = clinical significance?

Combined Therapy vs. IT Therapy

- 2 RCT's
- **Battaglia et al, 2008** – significant benefit for combined therapy (87.5 v 70.5%)
- **Lim et al, 2012** – no difference

IT Steroids for Salvage Treatment

- 5 RCTs
- All 5 studies showed significant benefit of IT therapy after failed initial therapy
- Study protocols varied tremendously
- Groups heterogeneous

Ho et al., 2004
Xenelis et al., 2006
Lee et al., 2011
Wu et al., 2011
Peng et al., 2011

IT Steroids for Salvage Therapy

- **STATEMENT 11. SALVAGE THERAPY: Clinicians should offer IT steroids when patients have incomplete recovery from SSNHL, after failure of initial management**

Recommendation based on RCTs with a preponderance of benefit over harm

So, do I give steroids or not?

1. No clear benefit of steroids over placebo
2. Initial high dose prednisone therapy equivalent to IT
3. Combination therapy does not seem to be significantly better than either therapy alone
4. Salvage treatment with IT steroids seems to have a beneficial effect, but does statistical significance = clinical significance?

Treatment for SSNHL: Hyperbaric Oxygen

HBOT and SSNHL

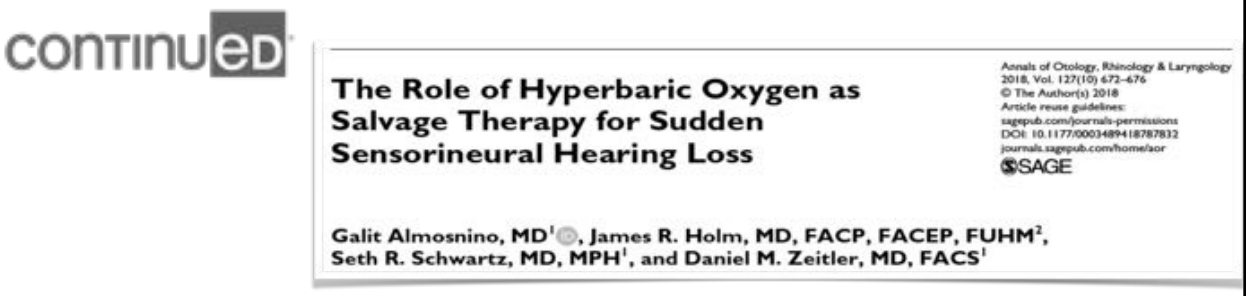
- Hypothesis: vascular compromise and secondary cochlear ischemia
- 100% oxygen at pressure > 1 atm
- Increased pO2 to cochlea
- Complex effects on immunity, oxygen transport, hemodynamics
- Reducing edema and potentiating normal host responses

Lamm K. *Adv Otorhinolaryngol*, 1998
Gill AL. *QJM*, 2004

HBOT and SSNHL

- Bennett MH. *Cochrane Database Syst Rev, 2012*
  - *7 RCT (N = 392)*
  - *PTA > 20 dB not significant*
  - *> 50% return not significant*
  - *> 25% return significant (NNT = 5)*
- Greater improvement with less severe initial loss
- Results better if performed in 2 weeks

THE COCHRANE COLLABORATION®



The Role of Hyperbaric Oxygen as Salvage Therapy for Sudden Sensorineural Hearing Loss

Annals of Otology, Rhinology & Laryngology
2018, Vol. 127(10) 672–676

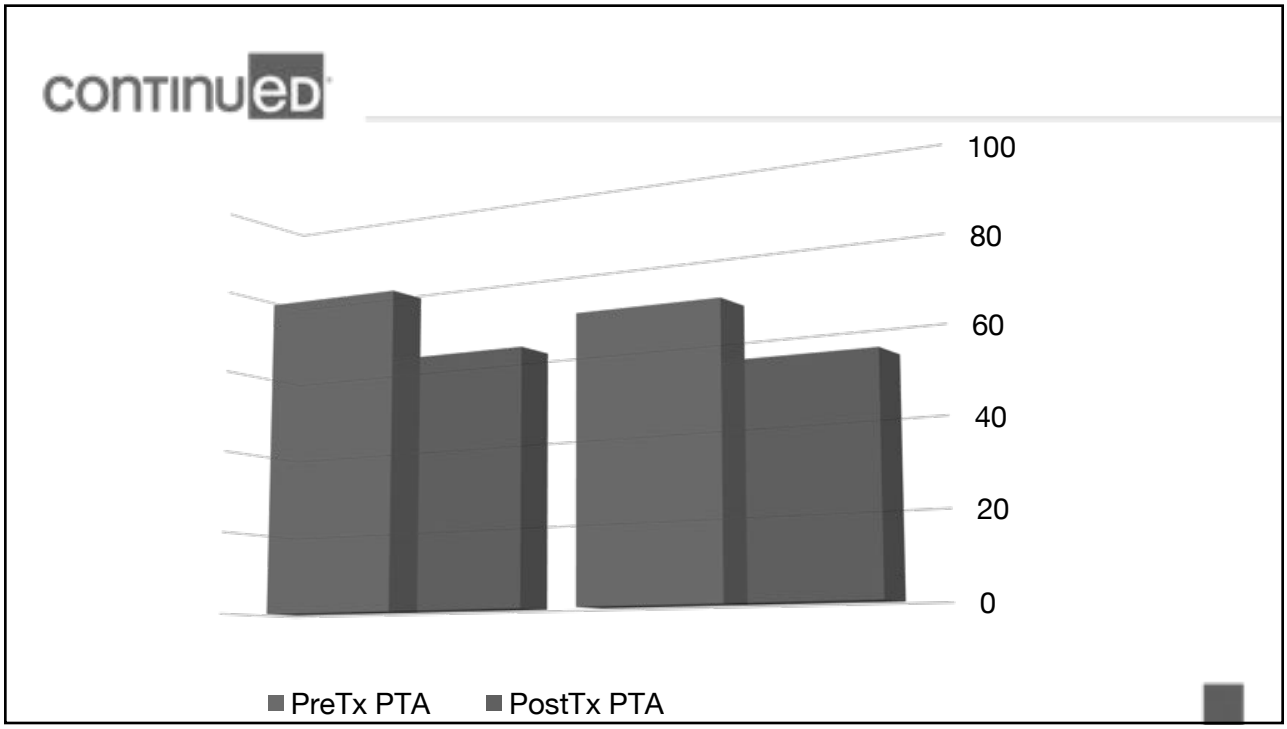
DOI: 10.1177/0003489418787832
journals.sagepub.com/home/aor
SAGE

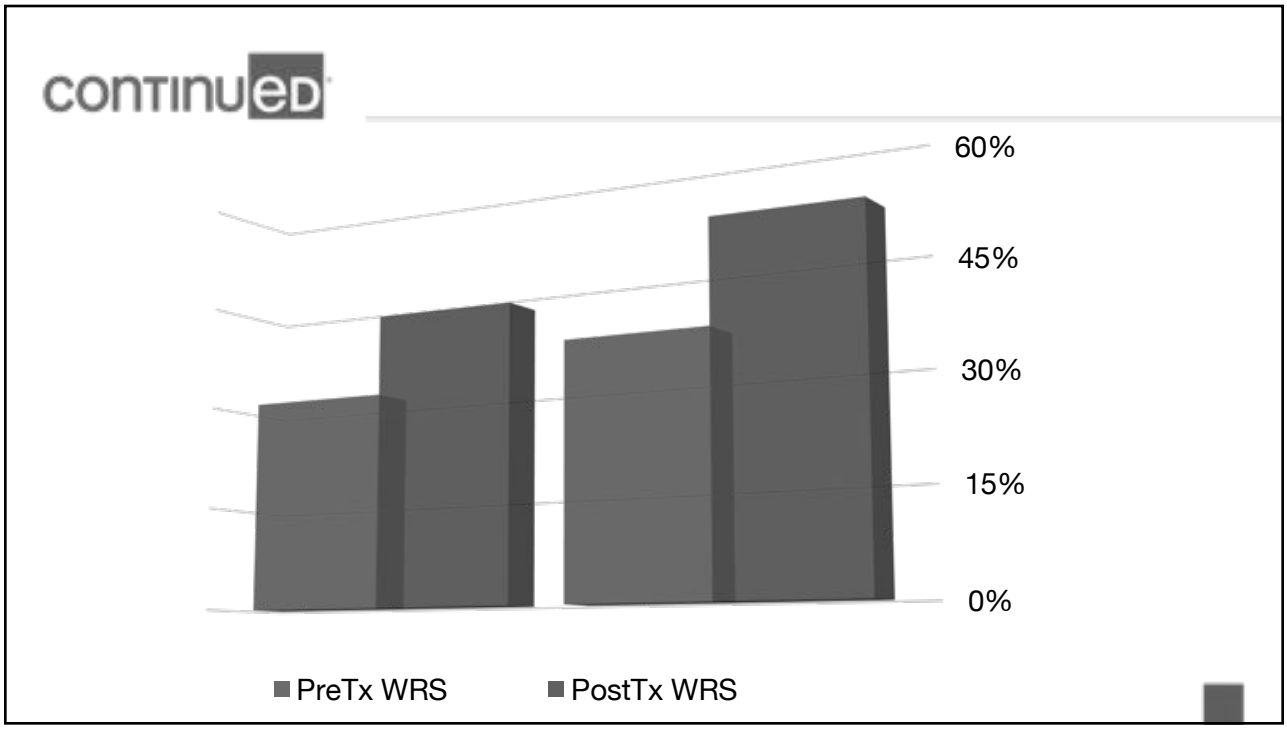
Galit Almosnino, MD[1], James R. Holm, MD, FACP, FACEP, FUHM[2], Seth R. Schwartz, MD, MPH[1], and Daniel M. Zeitler, MD, FACS[1]

- Case controlled, matched retrospective review
- Adult patients > 18 years treated for SSNHL of unknown etiology between 2014-2017
- 20 consecutive subjects undergoing HBO2 vs. 20 matched controls
- All patients received steroids (PO +/- IT)

Demographics

	Group 1 (N = 20)	Group 2 (N = 20)
Age (yrs)	54.7	58.2
Gender	9 Females	12 females
Pre-treatment PTA (dB)	77.4	66.9
Pre-treatment WRS (%)	30.8	36.2


100
80
60
40
20
0
PreTx PTA
PostTx PTA


60%
45%
30%
15%
0%
PreTx WRS
PostTx WRS

HBOT and SSNHL

- STATEMENT 9. HYPERBARIC OXYGEN THERAPY: Clinicians may offer hyperbaric oxygen therapy within 3 months of diagnosis of ISSNHL

Option based on systematic reviews of RCTs with a balance of benefit and harm

- *2012: HBOT approved by the Undersea and Hyperbaric Medicine Society for treatment of ISSNHL*

Treatment for SSNHL: Alternative Therapy

Antivirals

Stokroos 1998: RCT = Prednisolone +/- Acyclovir

- PTA improvement 68% (drug) v 43% (placebo)
- p>0.05 (n=44)

Tucci 2002: RCT = Prednisone +/- Valacyclovir

- PTA improved 30 dB (drug) v 43 dB (placebo)
- n=84

Westerlaken 2003: RCT = Prednisolone +/- Acyclovir

- Average PTA recovery 35 dB and WRS 49-75%
- No treatment effect (n=91)

Antiviral Therapy and SSNHL

- Awad Z, et al. *Cochrane Database of Reviews*, 2012
  - 4 RCTs, 257 patients
  - Steroid alone vs. steroid + antiviral (acyclovir, valcyclovir)
  - No difference between groups
  - No effect on tinnitus, aural fullness, or vertigo

- 1 systematic review and 1 meta-analysis (Conlin & Parnes)
  - No significant benefit of antivirals

Conlin & Parnes, 2007

Other Pharmacologic Therapies

- NO DATA SUPPORTING ANY…
  - Carbogen
  - Vasodilators
  - Rheophoreis
  - Antioxidents
  - Vitamin E**

Vitamin E

- Joachims HZ, Israel, 2003
  - RCT = Steroids and carbogen +/- Vitamin E
  - 75% or more improvement significantly higher in Rx group
- Hatano 2008
  - Retrospective review (n = 87)
  - Steroids +/- vitamin C and E
  - Hearing gain and recovery rate in anti-oxidant group better

Joachims et al., 2003
Hatano et al., 2008

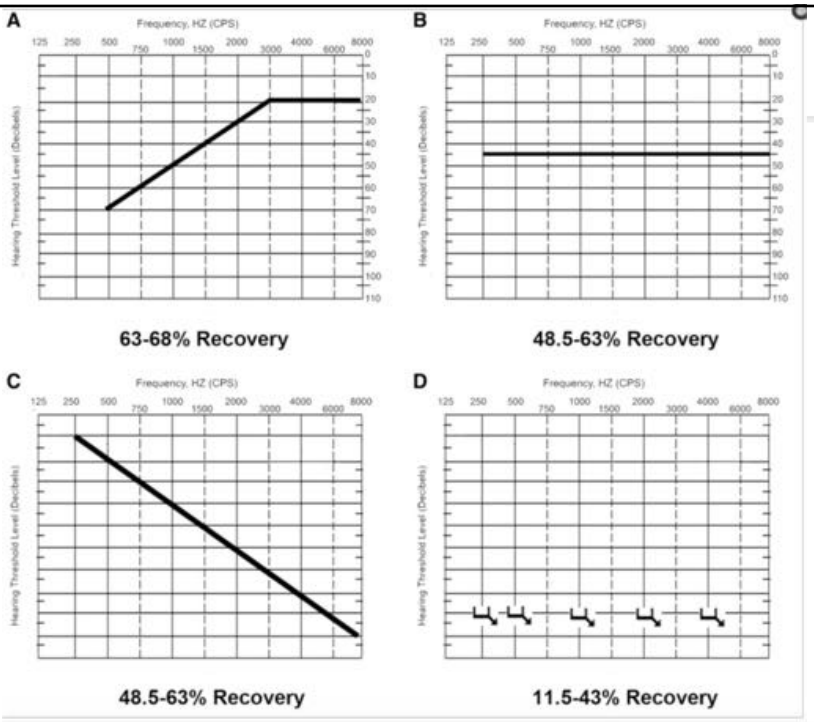
Other Pharmacologic Therapy

- STATEMENT 10. OTHER PHARMACOLOGIC THERAPY: Clinicians should not routinely prescribe antivirals, thrombolytics, vasodilators, vasoactive substances, or antioxidants to patients with SSNHL

Recommendation against based on systematic reviews of RCTs with a preponderance of harm over benefit

Prognosis

- SSNHL due to discernable etiology depends heavily on that disease, its duration, and treatment options
- SSNHL – 45-65% regain hearing even without therapy with average gains of 35 dB
- Of all demographic factors, *advanced age (>60 years)* universally correlated with poor prognosis
- Factors affecting recovery rates: severity, duration, audiogram 'shape', presence of vertigo, time to treatment



Prognosis

- Time to presentation correlates with hearing recovery
  - Within 7 days = 87%
  - Within 2 weeks = 52%
  - Longer than 3 months = < 10%
- May represent a bias towards natural history of disease
- Still…considered an otologic "emergency"

So…what should you do for a patient with possible SSNHL?

- ***Determine if CHL or SNHL***
- Evaluate with urgent audiogram
  - Treat with PO steroids 1 mg/kg/day up to 70 mg/day (shared decision making, risks, etc.)
  - Treatment up to 4 weeks (controversial)
- If audiogram unavailable and SNHL – treat and refer
- Refer to Otolaryngology for consideration of HBOT +/- IT steroids
- Use the clinical practice guidelines to determine treatment

CONTINUED

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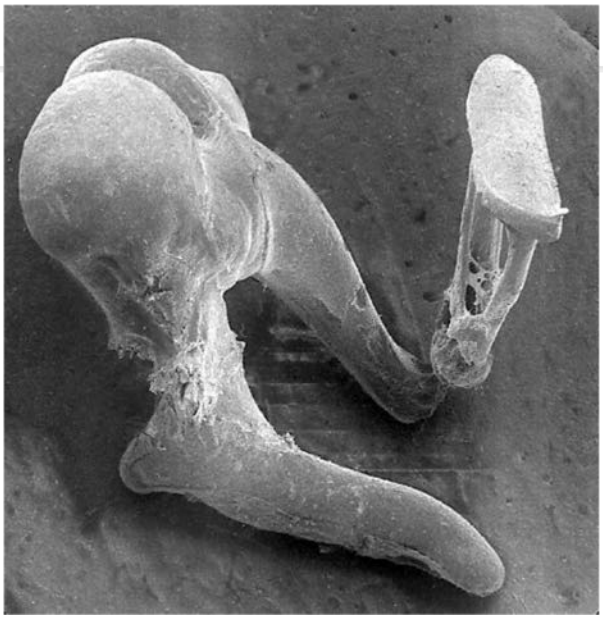

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