The Medical University of South Carolina
Department of Otolaryngology – Head & Neck Surgery

The Charleston Course at the Beach!

9th Annual Otolaryngology Literature Update

July 12 & 13, 2019
Kiawah Island Golf Resort, SC

Course Director: **Paul R. Lambert, M.D.**
Professor and Department Chair
Director, Otology - Neurotology

musc.edu/ent/cme

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July 12, 2019

Dear Colleague,

On behalf of the Department of Otolaryngology – Head and Neck Surgery at the Medical University of South Carolina, I would like to welcome you to The Charleston Course: 9th Annual Otolaryngology Literature Update. I know you will enjoy this educational program as well as the Kiawah resort. Our faculty has carefully selected articles for review, and our hope is that you will find this information valuable in your everyday practices.

We do appreciate the support received from our corporate sponsors. Without their assistance, it would be difficult to hold educational meeting such as this one.

Again, your participation is much appreciated. We also thank you in advance for your candid feedback regarding this conference. Please let me or any of our staff know if we can help with any aspect of your visit.

Sincerely,

Paul R. Lambert, MD.

Paul R. Lambert, M.D.
Professor and Chair
Course Program Director
Department of Otolaryngology – Head and Neck Surgery
Medical University of South Carolina

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Pediatric Airway & Aspiration Program
Skull Base Program
Vestibular Balance Program
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Conference Overview

The MUSC Department of Otolaryngology – Head and Neck Surgery is proud to present our 9th Annual Literature Update Course at the Kiawah Island Golf Resort, SC, on July 12 & 13, 2019.

How does a busy clinician stay current in our rapidly expanding specialty? The literature is replete with new or refined diagnostic procedures, operative interventions and treatment algorithms. It is a difficult, if not at times bewildering, task to digest this information.

This course is designed to help. Our faculty members are charged with reviewing last year's literature in their subspecialty, and then choosing the six to eight best articles for critical review. To be considered best, we are especially looking for seminal works and those with a strong evidence base. Importantly, the manuscripts must have significant applicability to every day clinical practice.

The specialty – head and neck cancer, FPRS, otology-neurotology, endocrine disease, sleep disordered breathing, allergy, rhinology-sinus disease, voice and swallowing disorders, and pediatric ENT will be covered in 15 lectures. You will receive a list of all articles reviewed and the presenters' presentations.

In two days, more than 100 manuscripts will be reviewed, and those "pearls" important to your practice will be emphasized. I believe that there may be no better way to stay current in our field than with this Literature Update Course. I hope you will join us in a beautiful location along the South Carolina coast this July.

Paul R. Lambert, M.D.
Professor and Chair
Program Director

Educational Needs

The educational content will address identified professional practice gaps in order to improve professional and/or patient outcomes. Practitioners can benefit from:

- Presentations of findings from expert critical assessment of the most relevant, current evidence-based medical literature.
- Expert lectures and discussions to evaluate best practices and strategies for how to translate the evidence into practice.

Objectives

Upon completion of this conference, participants should be able to:

- Reference the most relevant, current evidence-based medical literature to optimize treatment options for patients.
- Translate new research and best practices from evidence-based medical literature into clinical practice.
- Apply the most current diagnostic and therapeutic approaches to their patients, based on evidence-based research.

Credit Designation

The Medical University of South Carolina designates this live activity for a maximum of 12.75 AMA PRA Category I Credit(s)TM. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Accreditation Statement

The Medical University of South Carolina is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Americans with Disabilities Act

It is the policy of the Medical University of South Carolina not to discriminate against any person on the basis of disabilities. If you feel you need services or the auxiliary aids mentioned in this act in order to fully participate in this continuing medical education activity, please call the Department of Otolaryngology – Head and Neck Surgery at 843-876-0943 or attach a note to your registration.

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The Charleston Course

9th Annual Otolaryngology Literature Update 2019

Friday, July 12, 2019

6:45 to 7:10 a.m.	Registration and Breakfast with Exhibitors
7:10 to 7:15 a.m.	Welcome – **Paul R. Lambert, M.D.**
7:15 to 8 a.m.	**Paul R. Lambert, M.D.** Otology I
8 to 8:45 a.m.	**Rodney J. Schlosser, M.D.** Rhinology & Sinus I
8:45 to 9:30 a.m.	**Christopher M. Discolo, M.D., MSCR** Pediatric Otolaryngology I
9:30 to 9:45 a.m.	Q&A
9:45 to 10 a.m.	Break
10 to 10:45 a.m.	**Clarice S. Clemmens, M.D.** Pediatric Otolaryngology II
10:45 to 11:30 a.m.	**David M. Neskey, M.D., MSCR, FACS** Head & Neck Oncology I
11:30 to 11:45 p.m.	Q&A
11:45 to 12 p.m.	Break
12 to 12:45 p.m.	Lunch / Presentation **Elizabeth L. Camposeo, AuD, CCC-A** Audiology
12:45 to 1:30 p.m.	**Eric J. Lentsch, M.D., FACS** Thyroid and Parathyroid Surgery
1:30 to 1:45 p.m.	Q&A
1:45 p.m.	Submit CME forms & Adjourn

Saturday, July 13, 2019

6:45 to 7:15 a.m.	Registration and Breakfast with Exhibitors
7:15 to 8 a.m.	**Evan M. Graboyes, M. D.** Head & Neck Oncology II
8 to 8:45 a.m.	**Habib G. Rizk, M.D., MSc** Otology II
8:45 to 9:30 a.m.	**Zachary M. Soler, M.D., MSc** Rhinology & Sinus II
9:30 to 9:45 a.m.	Q&A
9:45 to 10 a.m.	Break
10 to 10:45 a.m.	**Lucinda A. Halstead, M.D.** Laryngology, Voice, & Swallowing
10:45 to 11:30 a.m.	**Samuel L. Oyer, M.D.** Facial Plastic & Reconstructive Surgery I
11:30 to 12:15 p.m.	**Krishna G. Patel, M.D., Ph.D.** Facial Plastic & Reconstructive Surgery II
12:15 to 12:30 p.m.	Q&A
12:30 to 12:45 p.m.	Break
12:45 to 1:30 p.m.	Lunch / Presentation **Judith M. Skoner, M.D.** Facial Plastic & Reconstructive Surgery III
1:30 to 2:15 p.m.	**David R. White, M.D.** Pediatric Otolaryngology III
2:15 to 2:30 p.m.	Q&A
2:30 p.m.	Submit CME forms & Adjourn

Osprey Point Clubhouse

MUSC Faculty

Course Director

Paul R. Lambert, M.D.
Professor and Chair
Director, Otology & Neurotology

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Professor, Medical Director,
Maxillofacial Prosthodontics

Terry A. Day, M.D.
Professor
Director, Head & Neck Oncology

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Auditory Neuroscience Laboratory

Jennifer K. Mulligan, Ph.D.
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Rhinology & Sinus Surgery

M. Rita Young, Ph.D.
Professor
Head & Neck Tumor Biology Laboratory

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In accordance with the ACCME Essentials and Standards,anyone involved in planning or presenting this educational activity will be required to disclose any relevant financial relationships with commercial interests in the healthcare industry. This information will be made available to participants at the beginning of the activity. Speakers who incorporate information about off-label or investigational use of drugs or devices will be asked to disclose that information at the beginning of their presentation.

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The Charleston Course, 9th Annual Otolaryngology Literature Update

July 12 & 13, 2019
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Lucinda A. Halstead, M.D.
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Eric J. Lentsch, M.D., FACS
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Habib G. Rizk, M.D., MSc
Judith M. Skoner, M.D.
David R. White, M.D.

Planning Committee members, Activity Directors, Moderators, and Presenters with financial relationships:
Evan M. Graboyes, M.D. - NIH: Head & Neck, Research Grant; NCI: Head & Neck, Research Grant; AAO-HNS: Head & Neck, Research Grant

Rodney J. Schlosser, M.D. - Arrinex: Rhinology, Consultant; AstraZeneca: Sinus/Rhinology, Research Support; GSK: Rhinology, Consultant; Healthy Humming: Sinus/Rhinology,Consultant/Research Support; Olympus: Sinus, Consultant; Optinose: Sinus/Rhinology, Consultant/Research Support; Roche: Rhinology, Research Grants; Sanofi : Rhinology, Research Grant

Zachary Soler, M.D., MSc - Olympus: Surgical Education, Consultant; Optinose: Study Design, Consultant; Novartis; Patient Journey, Consultant; Regeneron: Study Design, Consultant; Healthy Humming: Study Design, Consultant

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The Charleston Course

9th Annual Otolaryngology Literature Update 2019

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After the conclusion of the conference (3-5 business days), you will receive an email generated by Survey Monkey. The email will contain a link to the overall conference evaluation form. After the evaluation is complete, you will be further directed to the MUSC CME Tracker to claim your CME-CEU credit.

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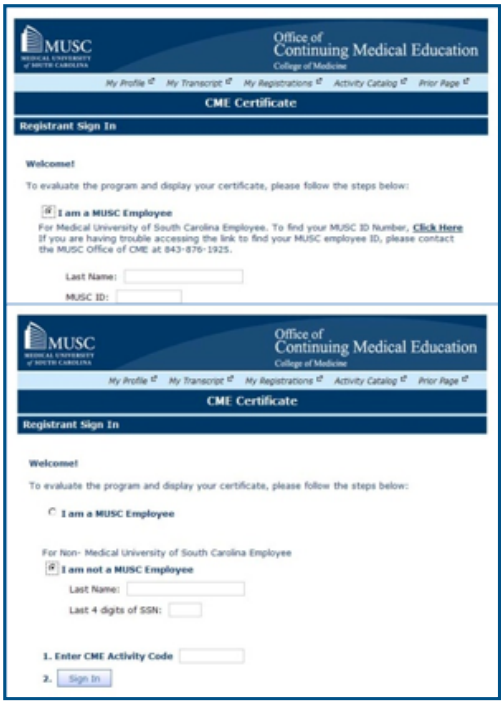
If a message displays indicating "no record has been found," it means you do not have an account in our system. Please click on "create new account" and complete the information it is requesting. Once you create an account, please refresh the login page to begin the process again of entering the activity code.



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The Medical University of South Carolina designates this educational activity for a maximum of 12.75 A*MA PRA Category I Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity. The Medical University of South Carolina is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

If you need assistance, please contact the MUSC CME Office at 843-876-1925 or cmeoffice@musc.edu. Thank you!

– Special Acknowledgements –

The MUSC Department of Otolaryngology - Head & Neck Surgery gratefully acknowledges the following companies whose support made this course possible through commercial exhibits:

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9th Annual Otolaryngology Literature Update

Otology I

-Course Director-
Paul R. Lambert, M.D.
Professor and Chair
Department of Otolaryngology - Head & Neck Surgery
Director, Otology - Neurotology
Medical University of South Carolina
lambertp@musc.edu

Paul R. Lambert, M.D. grew up in Charleston, West Virginia. He graduated from Duke University summa cum laude and Phi Beta Kappa. He then attended Duke University Medical School, graduating in 1976. His Otolaryngology-Head and Neck Surgery training was completed at UCLA Medical Center in Los Angeles. This was followed by a Fellowship in Otology-Neurotology at the House Ear Institute in Los Angeles, considered by many to be one of the world's premier centers for the treatment of ear and ear-related diseases.

Dr. Lambert began his professional career at the University of Virginia in 1982, and was on the faculty there until 1999. He was Director of Otology-Neurotology and became a Professor and Vice-Chairman of the Department. In 1999 he moved to his present position as the Professor and Chair of the Department of Otolaryngology-Head and Neck Surgery at the Medical University of South Carolina.

Dr. Lambert has been involved in hearing-related research his entire career. In 1987, he published a seminal discovery that cochlear hair cells could regenerate in birds. His subsequent work in this area was widely published in prestigious journals including Science. In 1994 he was awarded Otolaryngology's highest award for basic science research, the Edmund Prince Fowler Award, for work in this field. He has been a recipient of NIH support, including a 5-year Clinical Investigator Development Award.

Nationally, Dr. Lambert is well-recognized within the broad specialty of Otolaryngology, and especially within the subspecialty area of Otology-Neurotology. He has, for example, served on the Board of Directors and as Vice President for the American Academy of Otolaryngology-Head and Neck Surgery. He is currently one of 18 Directors for the American Board of Otolaryngology (ABOto), which is the certifying body for the specialty. For 2014-2015 he served as the President of the ABOto. He has also been President of the American Neurotology Society and the American Otological Society. Dr. Lambert has been listed in both the "Best Doctors in America" and "America's Top Doctors" continuously since 2001.

Dr. Lambert has an active clinical practice, seeing patients three days per week, and operating two days per week. In addition to these clinical responsibilities, he directs the Department of Otolaryngology-Head and Neck Surgery, is extensively involved in the training of the residents within that program, and continues his research in hearing-related diseases. Dr. Lambert has authored more than 140 manuscripts and book chapters, and several textbooks related to ear diseases and ear surgery.

9th Annual Otolaryngology Literature Update
Medical University of South Carolina

Otology I

Paul R. Lambert, M.D.

Dirain CO, Kosko B, Antonelli PJ. "Effects of Common Ear Drops on Tympanic Membrane Healing." Otolaryngology–Head and Neck Surgery. 2018 May;158(5):917-922. doi: 10.1177/0194599818757972. Epub 2018 Feb 20.

Fletcher KT, Horrell EMW, Ayugi J, Irungu C, Muthoka M, Creel LM, Lester C, Bush ML. "The Natural History and Rehabilitative Outcomes of Hearing Loss in Congenital Cytomegalovirus: A Systematic Review." Otology & Neurotology. 2018 Aug;39(7):854-864. doi: 10.1097/MAO.0000000000001861.

Liu GS, Boursiquot BC, Blevins NH, Vaisbuch Y. "Systematic Review of Temporal Bone-Resurfacing Techniques for Pulsatile Tinnitus Associated with Vascular Wall Anomalies." Otolaryngology–Head and Neck Surgery. 2019 May;160(5):749-761. doi: 10.1177/0194599818823205. Epub 2019 Jan 22.

Naples JG, Henry L, Brant JA, Eliades SJ, Ruckenstein MJ. "Intratympanic Therapies in Ménière Disease: Evaluation of Outcomes and Early Vertigo Control." Laryngoscope. 2019 Jan;129(1):216-221. doi: 10.1002/lary.27392. Epub 2018 Oct 3.

Rhee TM, Hwang D, Lee JS, Park J, Lee JM. "Addition of Hyperbaric Oxygen Therapy vs Medical Therapy Alone for Idiopathic Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-analysis." JAMA Otolaryngology–Head & Neck Surgery. 2018 Sep 27. doi: 10.1001/jamaoto.2018.2133. [Epub ahead of print].

2019

QUIZ

1. Does intratympanic gentamicin therapy cause hearing loss?

2. What are the pros & cons of intratympanic steroids versus gentamicin?

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Intratympanic Therapies in Meniere's Disease: Evaluation of Outcomes and Early Vertigo Control

Naples JG, Henry L, Brant JA, Eliades SJ, Ruckenstein MJ

University of Pennsylvania

Laryngoscope 129: 216-221, 2019

2019 Literature Review Course

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INTRATYMPANIC THERAPIES IN MENIERE'S DISEASE

Objective

- To evaluate outcomes of intratympanic (IT) dexamethasone and gentamicin in Meniere's disease (MD), especially within the first 6-12 months post injection

INTRATYMPANIC THERAPIES IN MENIERE'S DISEASE

Background

- IT steroid therapy for MD dates to the early 1990's with IT gentamicin following a few years later
- Concern with IT gentamicin was hearing loss, although more recent protocols using less frequent administrations have shown this to be minimal

INTRATYMPANIC THERAPIES IN MENIERE'S DISEASE

Background

- *LANCET* article 2016

  Double blinded - randomized, MD patients received 2 IT injections of steroid or gentamicin (injections 2 wks apart) 30 subjects in each group

  Findings: At 18-24 months post injections, recurrent vertigo in 33% of steroid pts and 37% of gentamicin pts (non-significant difference); vertigo significantly less than pre-injection in both groups

INTRATYMPANIC THERAPIES IN MENIERE'S DISEASE

Methods

- Retrospective review 103 pts receiving IT injections 2005-2017 (70 gentamicin and 33 dexamethasone)
- Inclusion criteria: definite MD, having failed diet modification and diuretics
- Exclusion criteria: bilateral MD, S-SNHL, suspected migraine, <6 months F/U

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INTRATYMPANIC THERAPIES IN MENIERE'S DISEASE

Methods

- Gentamicin (27 mg/cc; 0.3cc) protocol: IT q 2 wks, up to 3 injections until sx ceased and/or VNG showed ↓ vestibular function
- Dexamethasone (10mg/cc; 0.3cc) protocol: IT weekly X 3 unless sx ceased
- Exclusion criteria: bilateral MD, S-SNHL, suspected migraine, <6 months F/U

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INTRATYMPANIC THERAPIES IN MENIERE'S DISEASE

Results

1) Mean F/U: 23 mos dexamethasone (range 6-50 mos) and 40 mos gentamicin (range 6-151 mos)
2) Success: Overall 62% dexamethasone & 90% gentamicin; @ 12 mos 100% gentamicin & 83% dexamthasone
3) Mean time to failure: 5 mos dexamethasone & 27 mos gentamicin
4) No significant change in hearing for either group

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INTRATYMPANIC THERAPIES IN MENIERE'S DISEASE

Conclusions

- IT dexamethasone effect not as durable as gentamicin
- Hearing risk minimal with 'lower' frequency IT gentamicin

Tiered Treatment for Meniere's Disease

Personal Approach

Tiered Treatment for Meniere's Disease

Tier 1

- *Explanation and Reassurance*
  - Not something you "will just have to live with"
  - Yes hearing loss, but rarely deafness
  - Usually unilateral

Tiered Treatment for Meniere's Disease

Tier 1

- Explanation and Reassurance

Tier 2

- *Lifestyle*
  - Dietary: (only) sodium restriction < 2000mg/day
  - Common sense: minimize stress, adequate sleep and exercise, etc.
  - Treat any "triggering" components: allergies, migraine

Tiered Treatment for Meniere's Disease

Tier 1

- Explanation and Reassurance

Tier 2

- Lifestyle

Tier 3

- *Medications*
  - Diuretic (Dyazide: hydrochlorothiazide/triampterine 25/37.5mg)
  - Antivertiginous/antinausea: Antivert, Zofran, Phenegran
  - Oral steroid (10-14 days tapering Prednisone) for "flare-ups"
  - Occasionally low dose Valium 2mg;
    - Betahistine -- Serc (compounding pharmacy) ? vasodilator

Tiered Treatment for Meniere's Disease

Tier 1

- Explanation and Reassurance

Tier 2

- Lifestyle

Tier 3

- Medications

Tier 4

- *Invasive Therapies – IT Dexamethasone*

  0.3cc of 10mg/cc x3 within 7-10 days; may need to repeat q 4-6 months

Tiered Treatment for Meniere's Disease

Tier 5

- *IT Gentamicin vs. Endolymphatic Sac Decompression*

  - **E. Sac:**

    70-75% effective

    Out-patient surgery; return to work in 5-7 days

    < 1-2% SNHL

  - **IT Gentamicin**

    0.3cc of 40mg/cc x1; re-evaluate q month – may need 2nd or 3rd injection

    80-85% effective

    10-20% patients will have unsteadiness for 1 week to several months

    < 5% SNHL

    Probably not use if bilateral disease suspected

Tiered Treatment for Meniere's Disease

Tier 6

- *Ablative Surgery*
  - Vestibular nerve section (retrolabyrinthine)
  - Labyrinthectomy

QUIZ

1. What effect, if any, do ear drops have on healing post chronic ear surgery?

2019 Literature Review Course

Effects of Common Ear Drops on Tympanic Membrane Healing

Dirain CO, Kosko B, Antonelli PJ

University of Florida

Otolaryngol Head Neck Surg 158: 917-922, 2018

2019 Literature Review Course

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EAR DROPS & TM HEALING

Objective

- To evaluate TM healing in a rat model after various ototopical quinolones with and without a steroid

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EAR DROPS & TM HEALING

Background

- Ciprofloxacin and Ofloxacin are the only FDA approved drugs for ME instillation
- Potential side effects from *systemic* quinolones include damage to cartilaginous tissues and tendons

EAR DROPS & TM HEALING

Background

- Toxicity, in part, secondary to collagen disruption (upregulation of matrix metalloproteinases resulting in a reduction in the quantity and quality of collagen fibrils
- Repair of TM perforations requires synthesis of collagen by fibroblasts; could this impact TM healing?

EAR DROPS & TM HEALING

Background

- Cell culture studies: mouse TM fibroblasts exposed to quinolones have ↓viability and make less collagen
- Retrospective review in children post PET: higher rate of TM perforation after use of quinolones (hazard ratio 1.5; increases to 2.0 with quinolone and steroid)

Alrwisan A, Antonelli PJ et al. *Clin Infect Dis* 2017

EAR DROPS & TM HEALING

Methods

- Bilateral TM perforations created in rats using single CO2 laser pulse; 6 groups of 9 each compared
- Saline drops in one ear and the other ear received either:
  a) ofloxacin 0.3%
  b) ciprofloxacin 0.3%
  c) dexamethasone 0.1%
  d) cipro + dex
  e) ofloxacin + dex
  f) neomycin + polymyxin + hydrocortisone

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EAR DROPS & TM HEALING

Methods

- Ear drops administered bid X 10d (less than 1 drop instilled – 40uL; one-fifth the human dose)
- Ears followed (otomicroscopy and photography by 3 blinded observers) until TM healed or POD 40

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EAR DROPS & TM HEALING

Results

- All saline drop ears healed by day 20 (except those with cipro + dex on contralateral side); all healed by day 40
- Antibiotic drop ears healed rate at POD 10
  a) ofloxacin -- 100%
  b) ciprofloxacin -- 55% *(all healed by day 20)*
  c) dexamethasone -- 25% *(all healed by day 28)*
  d) cipro + dex -- 0% *(2 of 9 not healed by day 40)*
  e) ofloxacin + dex – 0% *(all healed by day 35)*
  f) neomyc/polymyx/hydrocort – 0% *(1 of 9 not healed by day 40)*

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EAR DROPS & TM HEALING

Results

- Cipro delayed early TM healing, but by day 14 no significant difference between ofloxacin and cipro ears
- In general, the addition of a steroid delayed healing, with cipro + dex having the most negative impact
- Cipro + dex even delayed healing (until day 40) of contralateral saline treated ear (all other contralateral ears healed by day 20)

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EAR DROPS & TM HEALING

Discussion

- Cipro causing delayed TM healing c/w tissue culture findings of ↓ collagen production with cipro vs ofloxacin
- Impaired TM healing appears to be drug specific rather than a drug class effect
- Topical steroids impair TM healing and their effect appears potentiated by cipro, c/w previously cited study of perforations post tubes in children

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EAR DROPS & TM HEALING

Discussion

- Cipro + dex may have a *systemic effect* (delayed healing of contralateral saline treated ears)
- Impaired TM healing appears to be drug specific rather than a drug class effect
- Topical steroids impair TM healing and their effect appears potentiated by cipro, c/w previously cited study of perforations post tubes in children

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EAR DROPS & TM HEALING

My Thoughts -

- Floxin OK to use in chronic ear surgery and to treat post tube otorrhea (better than cipro + dex)
- Cipro + dex best when treating granulation tissue, excessive scaring or incipient stenosis post surgery, given its effect on fibroblast proliferation and collagen deposition

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The Natural History and Rehabilitative Outcomes of Hearing Loss in Congenital Cytomegalovirus: A Systematic Review

Fletcher KT, Horrell EM, Ayugi J, Bush ML, et al.

University of Kentucky

Otol Neurol 39: 854-864, 2019

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CONGENITAL CYTOMEGALOVIRUS

Objective

- Perform a systematic review of the natural history and rehabilitative outcomes of SNHL from congenital CMV infection.

CONGENITAL CYTOMEGALOVIRUS

Background

- >40,000 new cases of cCMV infection identified in the US annually

  10% are symptomatic (CID) with hepatosplenomegaly, growth retardation microcephaly, CNS

  Approx 25% will have severe SNHL

  90% asymptomatic

  Approx 10-15% will have mild to severe SNHL

CONGENITAL CYTOMEGALOVIRUS

Background

- SNHL from cCMV is the leading cause nonhereditary cause of congenital hearing loss
- cCMV accounts for approx 20% of all pediatric hearing loss -- approx. the same as connexin 26 mutation

CONGENITAL CYTOMEGALOVIRUS

Background

- SNHL can be:

  Bilateral / unilateral (1:1)

  Delayed onset *

  Progressive / fluctuating

* Not detected newborn hearing screen

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CONGENITAL CYTOMEGALOVIRUS

Methods

- Literature Search → >1800 articles

  Duplicate data sets excluded; those meeting inclusion criteria → 36 articles (25 focusing on natural history of the hearing loss and 11 on CI outcomes)

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CONGENITAL CYTOMEGALOVIRUS

Results

- In studies examining *universally-screened newborns*, 0.2 to 1% of the infants tested positive cCMV and SNHL was present in 8 to 22%
- Mean age of late onset SNHL in asymptomatic patients was 18 months, with 75% presenting by age 2 years
- In children with symptomatic cCMV, the SNHL incidence was ⅓ to ½ of patients

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CONGENITAL CYTOMEGALOVIRUS

Results – CI Outcomes

- Significant improvement in receptive and/or expressive outcomes was unanimously observed in all 11 studies
- For asymptomatic cCMV patients, the improvement was to the same degree as non-CMV congenital hearing loss cohorts
- Children with symptomatic cCMV did less well

CONGENITAL CYTOMEGALOVIRUS

Discussion

- The lack of universal CMV screening can lead to delay in diagnosing SNHL
- Prior studies have demonstrated a potential cost saving to the health system as a whole
- Studies have demonstrated that antiviral therapy can provide protection and/or treat cCMV related SNHL

PEDIATRIC SNHL

Incidence (Births – U.S.)

- 1-2/1000 bilateral SNHL >50dB
- 3/1000 unilateral SNHL >50dB
- 10-20/1000 SNHL >25dB

PEDIATRIC SNHL

Genetic 50-60%

Acquired 40-50%

(Congenital)

PEDIATRIC SNHL

Congenital Etiologies

-
-
-

PEDIATRIC SNHL

Congenital Etiologies

- Infectious (CMV)
- Anatomic (EVA, Cochlear nerve deficiency)
- Genetic (GJB2 mutation)
  - Present at birth (congenital) or delayed
  - 70% non-syndromic

PEDIATRIC SNHL

Genetic 50-60% *

75-80% autosomal recessive
Alport's, Usher's, Jervel-Lange-Nielsen

20% autosomal dominant
Waardenburg's, OI

<2-3% X-linked

* >1000 mutations in 125 genes associated with SNHL

PEDIATRIC SNHL

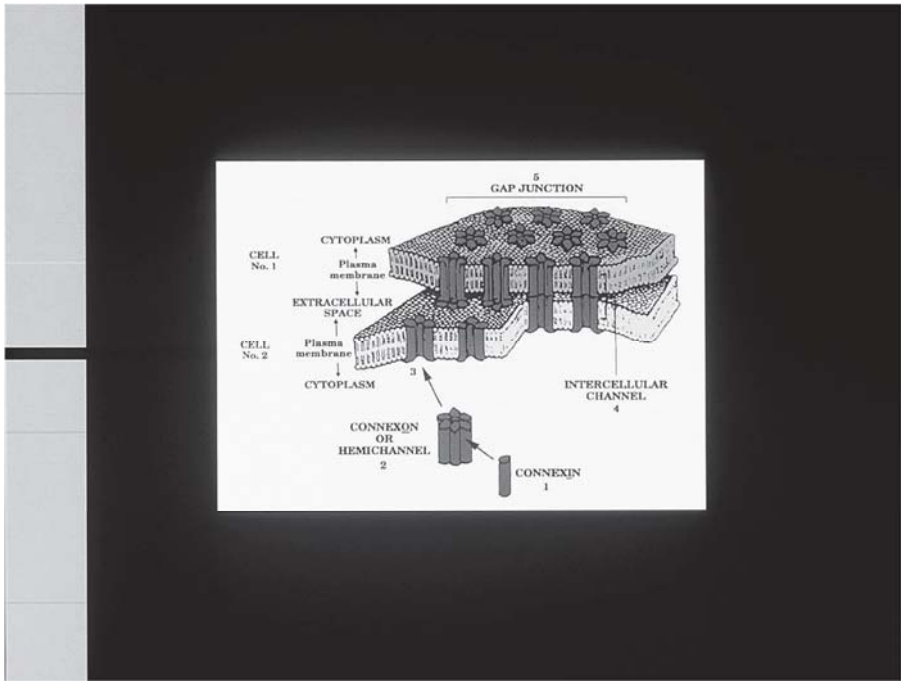
Genetic 50-60%

- ~ 1000 mutations identified with pediatric/adult SNHL occurring in 125 genes
- ~ ½ of genetic SNHL is secondary to a mutation in the gap junction beta 2 gene (*CJB2*) on chromosome 13q11 which encodes the gap junction protein *Connexin 26*
- 1st autosomal recessive gene implicated in non-syndromic SNHL (1997)

PEDIATRIC SNHL

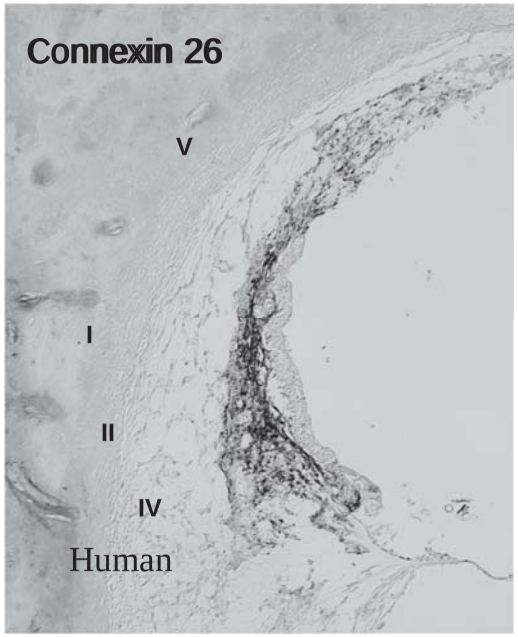
Connexin 26
Intercellular Communication

Proteins which form gap junctions – membrane connections between adjacent cells allowing exchange of small molecules, ions, messengers



Immunohistochemical staining for connexin 26.

Fibrocytes of lateral wall of human cochlea staining positive



PEDIATRIC SNHL

Connexin 26

- 600 base pair gene on 13q11
- >100 different mutations;
  majority *35delG* (deletion of one guanosine nucleotide at base pair 35 position, causing premature protein truncation)

PEDIATRIC SNHL

Connexin 26 Mutation

- Recessive
- Carrier: 2.5 - 3% population (approx. same as cystic fibrosis)
- Alters recycling potassium, affecting endocochlear potential

PEDIATRIC SNHL

Connexin 26 Mutation

Phenotype

- Prelingual onset, ? progressive
- Variable severity, but 80% bilateral severe to profound
- Audiogram: flat or sloping
- Normal vestibular function
- No syndromic features

PEDIATRIC SNHL

Connexin 26 Mutation

Temporal Bone Histopathology

- Near total degeneration of HCs
- Agenesis/degeneration of the stria vascularis
- No neural degeneration and a good population of spiral ganglion cells

Smith et al. Univ of Iowa; Laryngoscope 2000

PEDIATRIC SNHL

Connexin 26 Mutation

Cochlear Implant Outcomes

- Superior outcomes when compared to deafness from environmental etiologies (low birth weight, prematurity, intrauterine infection, meningitis, CMV infection, rubella, etc)
- Equal outcomes to other genetic causes of deafness

Abdurehim Y et al. Systemic review GJB2 CI outcomes. *Oto-H&N Surg*, 2017

PEDIATRIC SNHL

Acquired 40-50%

-
-
-
-

PEDIATRIC SNHL

Acquired 40-50%

- Cytomegalovirus - #1
- Meningitis
- Prematurity / Birth Complications
- Ototoxicity

PEDIATRIC SNHL

CMV Infection

- Herpes virus
- Transmitted – bodily secretions; transplacentally
- Adult prevalence in US > 50%

PEDIATRIC SNHL

CMV Infection

1% Newborns in US

- 10% symptomatic (CID)

  Hepatosplenomegaly, growth retardation, microcephaly, CNS

  25% severe SNHL

- 90% asymptomatic

  10-15% mild to severe SNHL

PEDIATRIC SNHL

CMV Infection

- Accounts for ~20% of pediatric SNHL

  (approx. same as connexin 26 mutation)

Nance et al., J Clin Virol, 2006

PEDIATRIC SNHL

CMV Infection

- Bilateral / unilateral (1:1)
- Delayed onset *
- Progressive / fluctuating

* not detected newborn hearing screen

PEDIATRIC SNHL

CMV Infection

Diagnosis

- Detection of virus or viral DNA in saliva (wet or dry; PCR sensitivity >95%*) or urine (may be less sensitive) within first 3-4 weeks of life
- Congenital vs. postnatal acquisition (most commonly from breast feeding or day-care centers)
- No SNHL associated with postnatal infection

*Boppana et al. *NEJM* 2011

PEDIATRIC SNHL

CMV Infection

Late Testing (>3 weeks of age)

- Newborn blood spot cards – PCR extraction of DNA to detect cCMV (years storage)
- If negative, cannot R/O cCMV (poor sensitivity)
- If positive, cCMV likely (excellent specificity)

PEDIATRIC SNHL

CMV Infection

Transplacental Transmission

- 1/3 chance of fetal infection if mother acquires CMV during pregnancy

  Maternal viremia → hematogenous spread to fetus

- 2% chance if sero(+) mother has reactivation of CMV

PEDIATRIC SNHL

CMV Infection

- Data suggests that antivirals may prevent or halt the progression of SNHL in CMV infants
- Current NIH study investigating CMV & HL that is expected to address the issue of adding CMV testing to new born hearing screening and treatment protocols

PEDIATRIC SNHL

CMV Infection

Systematic Review of Antiviral Therapy

Shin et al. *Otolaryngol HNS 144: 662, 2011*

PEDIATRIC SNHL

CMV Treatment

- 2 RCTs (42,18 patients)
- 2 prospective cohort studies
- 3 retrospective case studies

GENETIC SNHL

CMV Treatment

RCT (n=42), all neonates with CNS involvement

- IV ganciclovir before age 1 mo. X 6 weeks
- ABR at baseline, 6 mo., 12 mo.
- 41% controls showed deterioration of hearing at 6 mo.;
  0% in ganciclovir group ($p<.01$)
- Statistically significant difference maintained at 12 mo.

GENETIC SNHL

CMV Treatment

RCT (n=18), all neonates asymptomatic (IgM screening & virus isolation in urine)

- IV ganciclovir before age 10 days X 3 weeks
- 25% control group with progressive HL;
  0% in treated group (F/U 3-10 yrs, mean 7 yrs)
  did not reach statistical significance

PEDIATRIC SNHL

CMV Infection

Conclusion:

"Collective data from all studies strongly suggest that IV ganciclovir has a protective effect on hearing"

Shin et al. *Otolaryngol HNS 144: 662, 2011*

GENETIC SNHL

CMV Treatment

Persisting questions:

- How long to treat?
- Is treatment effective for HL diagnosed beyond the neonatal period?
- What is the role of oral therapy?
  Several retrospective case series have shown greater hearing stabilization with 6 mo. – 3 yrs. of oral ganciclovir vs. historical controls

GENETIC SNHL

CMV Treatment

Risk / Benefit:

- Neutropenia (in the large RCT, developed in 63%)
- Throbocytopenia, anemia
- Elevated LFTs

GENETIC SNHL

CMV Treatment

2019:

- Current NIH study investigating antiviral Rx for CMV
- CMV vaccine a high priority

QUIZ

1. Is there any benefit of using hyperbaric oxygen in the treatment of sudden SNHL?

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Addition of Hyperbaric Oxygen Therapy vs Medial Therapy Alone for Idiopathic Sudden SNHL: A Systematic Review and Meta-analysis

Rhee TM, Hwang D, Lee JS, et al.

Seoul National University Hospital

JAMA Otolaryngol Head Neck Surg 144: 1153-1161, 2018

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HYPERBARIC OXYGEN THERAPY FOR S-SNHL

Objective

- To perform a systematic review and meta-analysis to compare hyperbaric oxygen therapy (HBOT) with standard medical therapy (SMT) for S-SNHL

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HYPERBARIC OXYGEN THERAPY FOR S-SNHL

Background

- S-SNHL definition: HL occurring within 72 hours at 3 or more consecutive frequencies
- Incidence 10/100,000 per year (VS incidence 1/100,000)
- Current Rx: steroids (po, IT), antivirals, vasodilators, HBOT

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HYPERBARIC OXYGEN THERAPY FOR S-SNHL

Background

Academy Guidelines

- ► **Should**: Obtain MRI or ABR or serial audiometric F/U
- ► **Do Not**: Obtain labs or CT scan
- ► **May**: Use po steroids and/or HBO
- ► **Do Not**: Use antivirals, vasodilators, antioxidants
- ► **Should**: Use IT steroids as salvage

HYPERBARIC OXYGEN THERAPY FOR S-SNHL

Methods

- Data sources: PubMed, Embase, Cochrane; manual examination of references cited in articles
- Statistical analysis: odds ratios with 95% confidence intervals; statistical heterogeneity and publication bias quantified
- Hearing recovery (complete, partial, & as a function of initial hearing loss severity) analyzed

HYPERBARIC OXYGEN THERAPY FOR S-SNHL

Results

- 194 articles identified; 24 met criteria and fully reviewed
- 19 studies, including 2401 patients, accepted for final analysis
- Data included 3 RCTs and 2 prospective studies; the remainder were retrospective

HYPERBARIC OXYGEN THERAPY FOR S-SNHL

Results

- Mean onset to HBOT ranged from 3 days to 7 weeks
- HBOT used as salvage in ⅓ of studies
- Hearing recovery HBOT + MT vs MT alone:

  Complete recovery: 29% vs. 21% (OR favoring HBOT – 1.61)

  Any hearing recovery: 67% vs. 49% (OR favoring HBOT – 1.43)

  Absolute hearing gain also significantly greater, with all frequencies showing this trend

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HYPERBARIC OXYGEN THERAPY FOR S-SNHL

Results

- Impact of severity of initial HL on outcome

  Severe - profound ≥70dB vs. mild - moderate <70dB

  For both complete or partial hearing recovery, HBOT + MT statistically more beneficial vs MT alone for the severe to profound HL patients

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HYPERBARIC OXYGEN THERAPY FOR S-SNHL

Results

- HBOT as a salvage treatment as effective (possibly more so) vs use at onset
- Improved hearing outcomes for HBOT duration >1200 minutes
- Patient age not associated with outcome

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HYPERBARIC OXYGEN THERAPY FOR S-SNHL

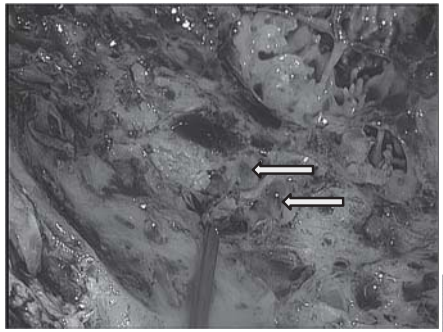
Discussion

- Mechanism HBOT – minimize ischemic damage, aid vascular recovery, promote angiogenesis
- Consider especially for patients with severe loss ≥ 70dB
- OK as salvage 1 month post steroid trial
- 14-15 90-minute sessions required
- Insurance will usually cover “indicated” procedures

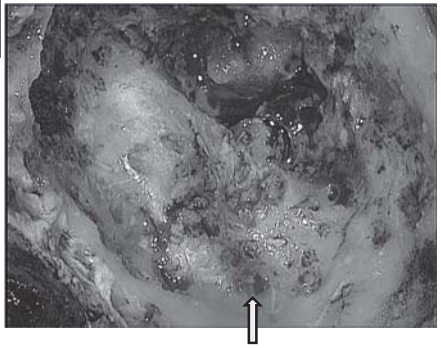
HYPERBARIC OXYGEN THERAPY FOR S-SNHL

Bottom Line

► Best evidence to date that HBOT + MT is associated with a significant improvement in complete hearing recovery and in any hearing recovery compared with MT alone



Arrows → dehiscent areas



Arrow → diverticulm

QUIZ

1. What is the most efficient work-up for pulsatile tinnitus?

2. Are there any surgeries to consider for pulsatile tinnitus?

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Systematic Review of Temporal Bone-Resurfacing Techniques for Pulsatile Tinnitus Associated with Vascular Wall Anomalies

Liu GS, Boursiquot BC, Blevins NH, Vaisbuch Y

Stanford University

Otolaryngol Head and Neck Surg 160:749-761, 2019

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BONE RESURFACING VASCULAR WALLS FOR PULSATILE TINNITUS

Objective

- To perform a systematic review of temporal bone resurfacing for pulsatile tinnitus (PT) associated with vascular wall anomalies.

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BONE RESURFACING VASCULAR WALLS FOR PULSATILE TINNITUS

Background

- PT is associated with major vascular wall anomalies involving the sigmoid sinus (SS), jugular bulb (JB), and ICA
- For the SS these anomalies include dehiscence and diverticulum and for the JB the same plus “high riding”

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BONE RESURFACING VASCULAR WALLS FOR PULSATILE TINNITUS

Background

- Resurfacing of these vascular structures is theorized to reduce PT by restoring laminar flow and creating a “sound baffle” to reduce transmission of turbulent flow sounds
- Resurfacing can be accomplished with autologous or artificial materials, both “hard” or “soft” in density

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BONE RESURFACING VASCULAR WALLS FOR PULSATILE TINNITUS

Methods

- Data sources: PubMed, Embase, Cochrane; manual examination of references cited in articles
- Intracranial vascular decompressions, endovascular procedures (such as embolization), venous ligation, and SS compression/obliteration excluded

BONE RESURFACING VASCULAR WALLS FOR PULSATILE TINNITUS

Methods

- Outcomes: complete (95-100%) resolution; partial (1-95%); or no resolution
- Outcomes stratified per materials: autologous (e.g., fascia, muscle, cartilage bone chips, bone dust) or artificial (e.g., bone cement)
- Materials classified as “hard” (e.g., cement, bone) or “soft” (e.g., cartilage, muscle, fascia); bone wax and dissolvable materials excluded from analysis

BONE RESURFACING VASCULAR WALLS FOR PULSATILE TINNITUS

Results

- 576 articles identified; 72 met criteria and fully reviewed
- 66% involved right ear and 85% were female, both statistically significant
- Resolution SS / JB: complete 75%; partial 10%; no change 15%
- Stratifying by autologous vs artificial or hard vs soft showed no differences

BONE RESURFACING VASCULAR WALLS FOR PULSATILE TINNITUS

Results

- Complications: 4% with headache, blurred vision, and/or papilledema suggesting increased intracranial pressure (secondary to compression of SS); several patients required anticoagulation or revision surgery to alieve compression
- No hearing changes

BONE RESURFACING VASCULAR WALLS FOR PULSATILE TINNITUS

Discussion

- Radiographic prevalence of SS wall abnormality is 1%
- Radiographic prevalence of SS wall abnormality in patients with PT is 23%
- Association of SS wall abnormality with female gender and obesity parallels idiopathic intracranial hypertension (another cause of PT)

Pulsatile Tinnitus

- Separate Power Point

PULSATILE TINNITUS

- **Tumors**
  - Glomus jugulare/tympanicum; middle ear adenoma
- **Vascular Abnormalities**

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PULSATILE TINNITUS

- **Tumors**
  - Glomus jugulare/tympanicum; middle ear adenoma
- **Vascular Abnormalities**
  - Venous hum (IIH)
  - Jugular bulb/Transverse-Sigmoid sinus -- diverticulum/dehiscence/stenosis
  - Extracranial venous anomaly (enlarged condylar emissary vein)
  - A-V malformation, Dural AV fistula
  - Transmitted bruit – ICA, cardiac valve
  - ICA aneurysm/aberrant course
- **Muscular Dysfunction**

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PULSATILE TINNITUS

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  - Extracranial venous anomaly (enlarged condylar emissary vein)
  - A-V malformation, Dural AV fistula
  - Transmitted bruit – ICA, cardiac valve
  - ICA aneurysm/aberrant course
- **Muscular Dysfunction**
  - Myoclonus palate
  - Myoclonus ME muscle

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PULSATILE TINNITUS

- **Tumors**
  - Glomus jugulare/tympanicum; middle ear adenoma
- **Vascular Abnormalities**
  - Venous hum (IIH)
  - Jugular bulb/Transverse-Sigmoid sinus -- diverticulum/dehiscence/stenosis
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  - ICA aneurysm/aberrant course
- **Muscular Dysfunction**
  - Myoclonus palate
  - Myoclonus ME muscle
- **SSCC Dehiscence**

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PULSATILE TINNITUS

- **Tumors**
  - Glomus jugulare/tympanicum; middle ear adenoma
- **Vascular Abnormalities**
  - Venous hum (IIH)
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  - Transmitted bruit – ICA, cardiac valve
  - ICA aneurysm/aberrant course
- **Muscular Dysfunction**
  - Myoclonus palate
  - Myoclonus ME muscle
- **SSCC Dehiscence**
- **↑ Cardiac Output -- anemia, hyperthyroid, pregnancy**

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PULSATILE TINNITUS

History

- Primary complaint vs positive ROS
- Unilateral vs bilateral (global)
- Age

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PULSATILE TINNITUS

History

- Hearing loss / dizziness / ear disease
- Cardiovascular disease
- Anemia / hyperthyroidism / pregnancy
- Headaches / blurred vision
- Trauma

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PULSATILE TINNITUS

Examination

- Otoscopy
- Auscultation - temporal area, neck
- Optic discs
- Flow alteration IJV
  - Cervical compression / neck turn
  - Valsalva

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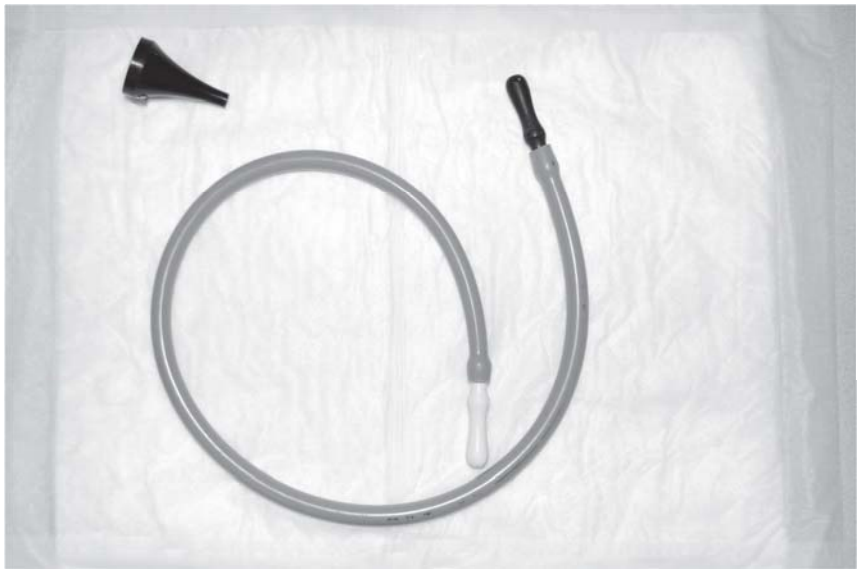


Doctors
and
Workers
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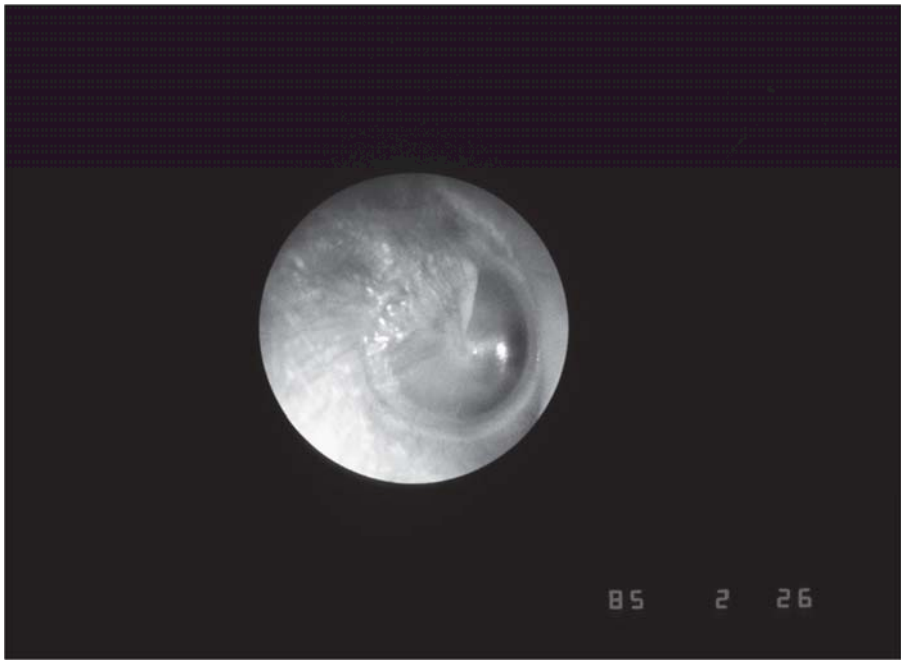
their hands
before and after
they care for you.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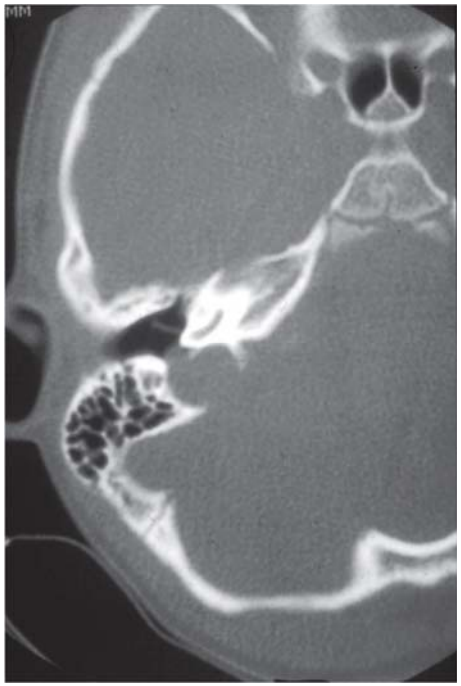

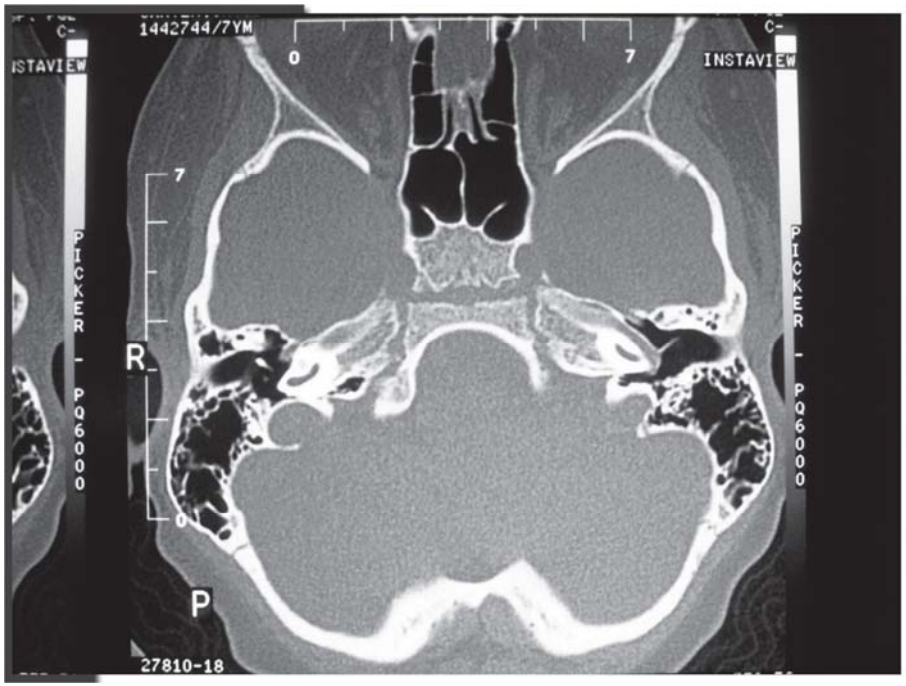
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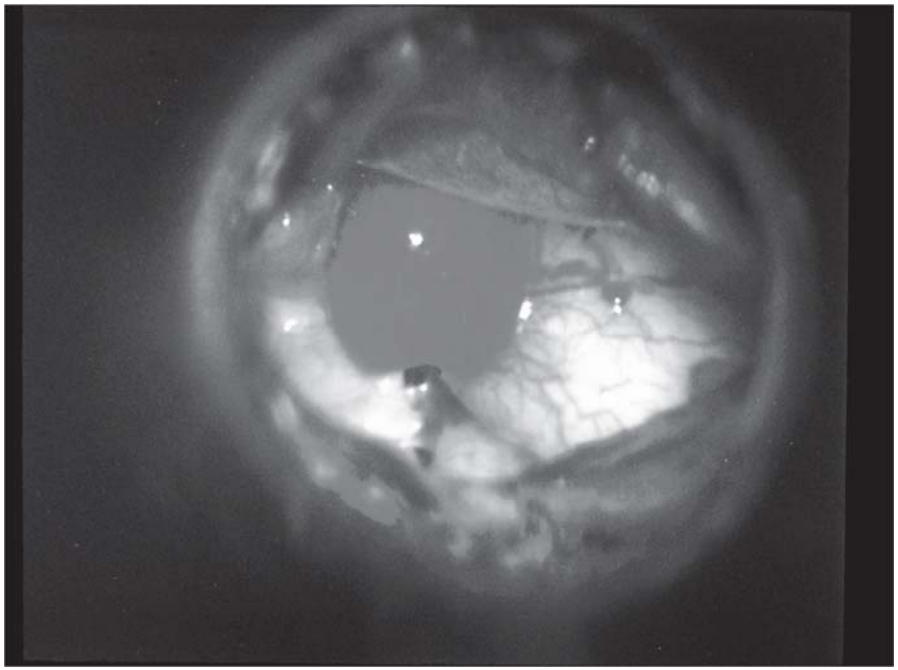

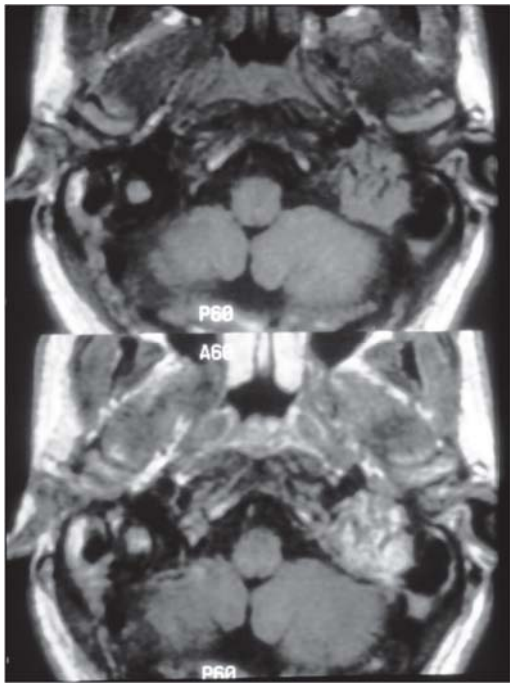

GLOMUS JUGULARE TUMORS

Treatment

- Skull base surgery
- Stereotactic radiation
- Surgery & Stereotactic radiation

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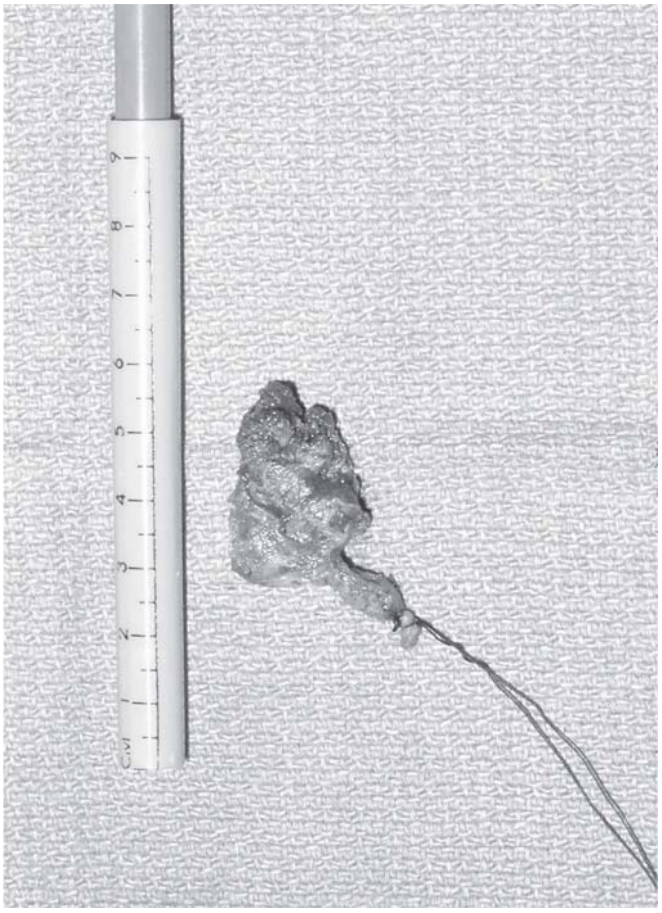

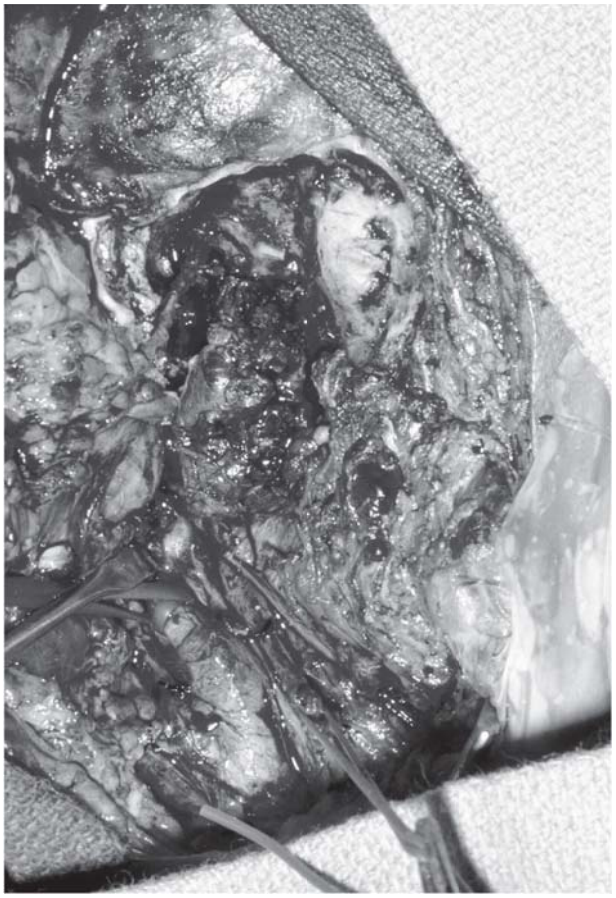

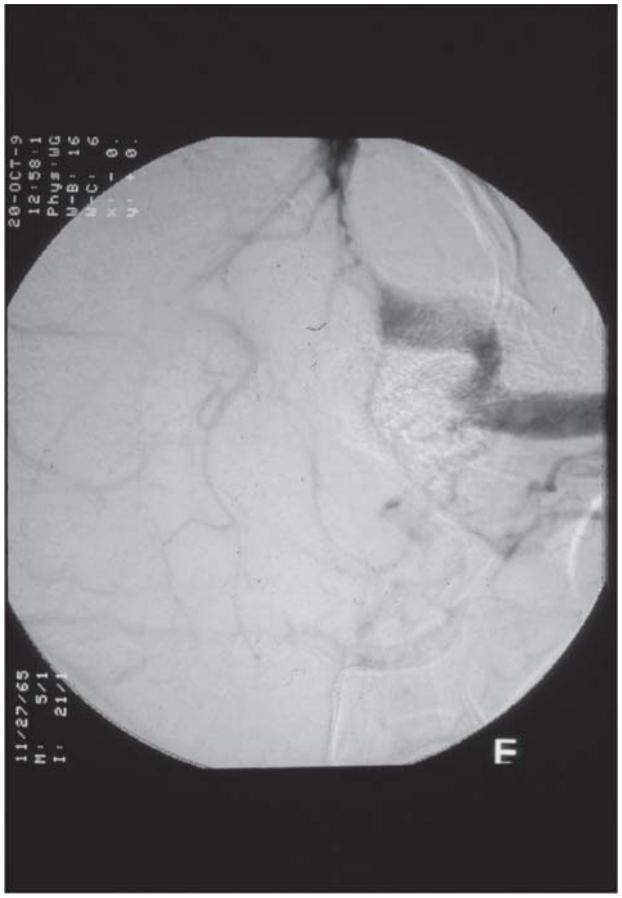
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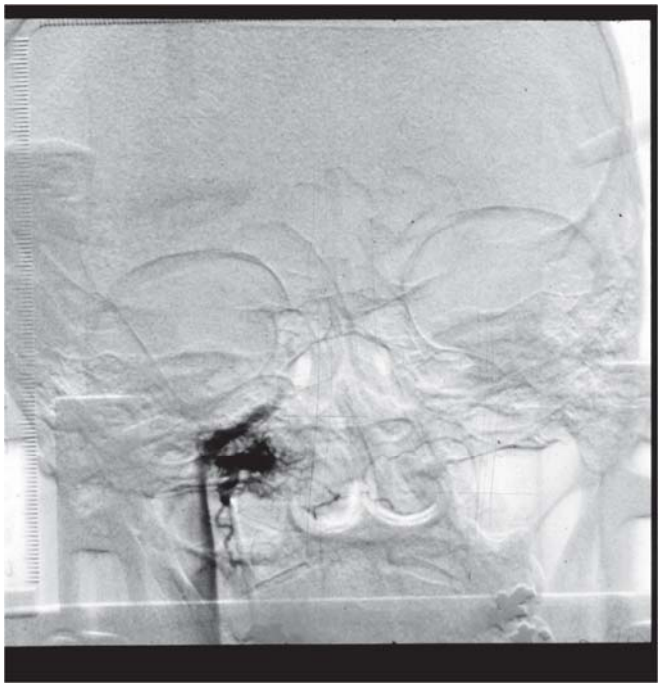

AV fistula

PULSATILE TINNITUS

Diagnostic Studies

- Audiogram, Tympanogram

  Conductive, “sensorineural” hearing loss

  Rhythmic compliance changes

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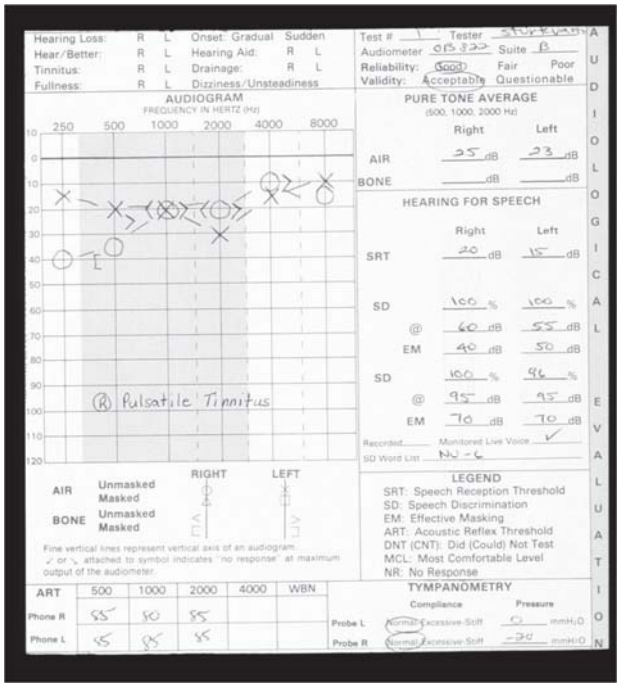

PULSATILE TINNITUS

What is the Role of Imaging in Tinnitus?

PULSATILE TINNITUS

Physical Exam: ME Mass on Otoscopy

- Glomus tympanicum/jugulare
- Aberrant or dehiscent ICA
- Jugular bulb abnormality

► **Temporal Bone CT**

PULSATILE TINNITUS

Physical Exam: Negative Otoscopy

- Radiographic Evaluation
  - ► CTA/CTV vs. MRA/MRV vs. Cerebral Angiogram

PULSATILE TINNITUS

Physical Exam: Negative Otoscopy

- CTA/CTV
  - -- Widely available and cost effective
  - -- 90% sensitivity & specificity in dx dural av fistula

PULSATILE TINNITUS

Physical Exam: Negative Otoscopy

- MRA/MRV
  - -- No radiation
  - -- May be less sensitive & specific in dx dural av fistula

PULSATILE TINNITUS

Bottom Line Best Practice

- No studies directly comparing MRA/MRV & CTA/CTV
- CTA/CTV probably best
- Cerebral angiogram gold standard, especially if high clinical suspicion for dural av fistula *
- *MRI for unilateral non-pulsatile tinnitus*

* bruit, headache

VENOUS HUM TINNITUS

- Frequently see on CT: *Large jugular bulb R>L*
- Now recognizing more: *Sigmoid sinus wall abnormality*

  Dehiscence, diverticulum

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VENOUS HUM TINNITUS

Diagnostic Studies - *Normal radiology*

- Rule out IIH

  LP for opening pressure measurement

- CBC, thyroid function tests

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PULSATILE TINNITUS

Discussion – Treatment Options

- Endovascular coiling/stenting of diverticulum

  Risks: coil migration
  ↑ ICP, especially of concern with IIH

- Transmastoid surgery

  Bipolar cautery or compression/obliteration of diverticulum; reconstruction of dehiscent sinus wall (bone pate/cement, soft tissue)

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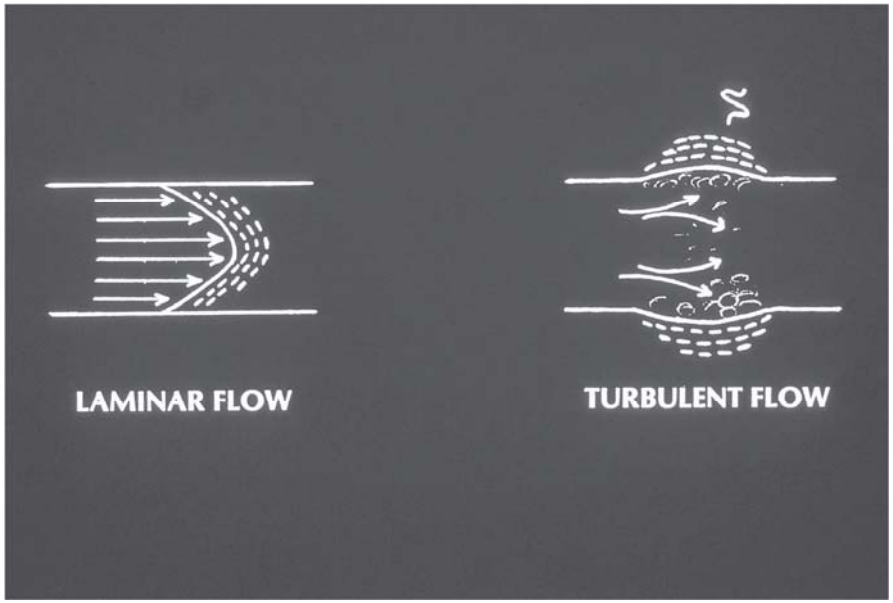

VENOUS HUM TINNITUS

Abnormal Sigmoid Sinus

Why Does It Work ?

- Sigmoid sinus “compression” may increase venous pressure in the sinus and redirect blood into other venous channels (suboccipital, deep cervical)
- Covering the sigmoid sinus with tissue, and especially cement may reduce sound transmission – i.e., both by insulating the sinus and by decreasing venous wall pulsation
- Opening the mastoid creates an air space, thus limiting bone conduction pathways

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CASE REPORT #1

- 50 year old female with bilateral pulsatile tinnitus R>L x 9 months
- Occasional headache; no vision problems
- Cervical pressure diminished the tinnitus on the right
- No bruits
- BMI 21
- Normal CBC and TFTs

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CASE REPORT #1

- Outside CT/CTA and MRI read as normal
- Our review: bilateral diverticula of sigmoid sinuses and partially empty sella

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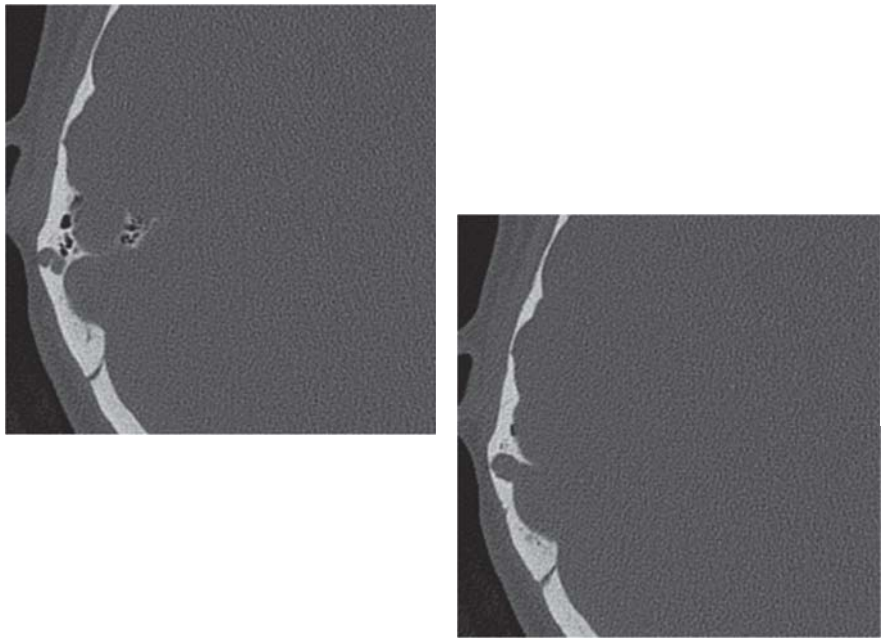

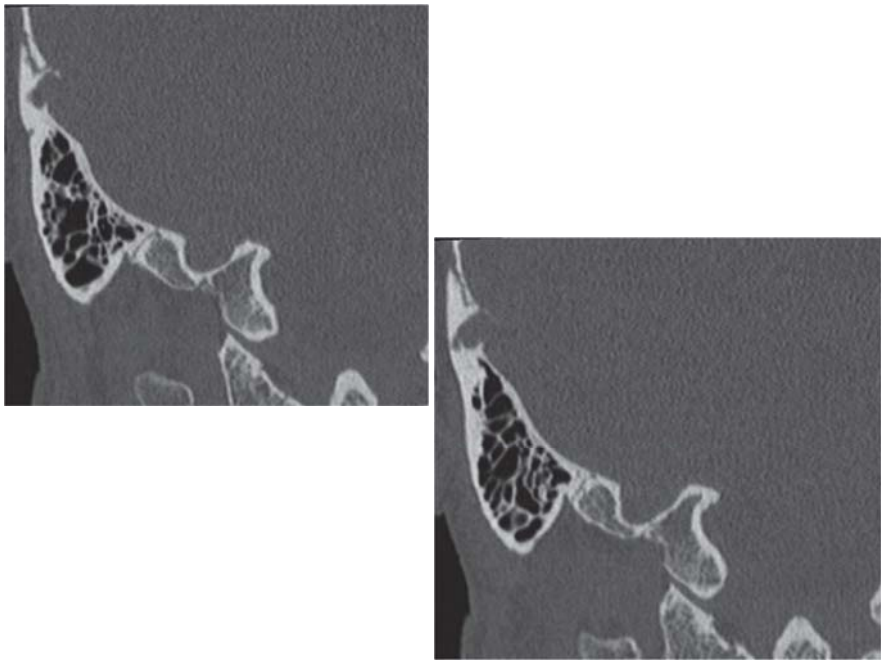

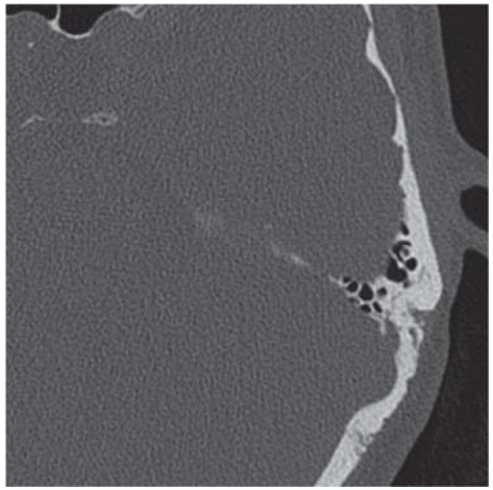

CASE REPORT #1

- Surgery (right ear):

  -- Diverticulum in SD angle exposed and obliterated with bone wax, surgicel and bone cement

  Mid sigmoid sinus appeared to have small area of dehiscence; entire sigmoid sinus exposed and slightly compressed with surgicel and covered by bone cement

  -- Right pulsatile tinnitus resolved in PACU; no recurrence x 2yrs; left present, but faint

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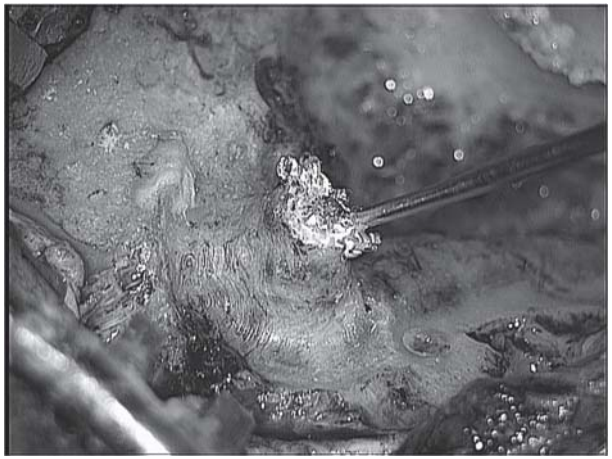
CASE REPORT #1

- Diverticulum in SD angle exposed and obliterated with bone wax, surgicel and bone cement



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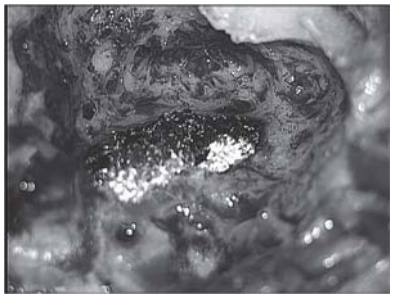


CASE REPORT #2

- 37 yo female with right pulsatile tinnitus x 6 months. She notes that pressure over right neck or turning head to right will abolish the tinnitus
- Occasional headache; no change in vision.
- BMI 39
- Rx Diamox without benefit

CASE REPORT #2

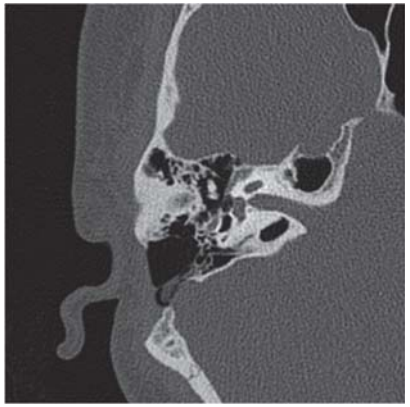
- CT/CTA and MRI/MRV all normal
- Normal CBC and TFTs
- LP – normal opening pressure (15 mm H_2O)

CASE REPORT #2

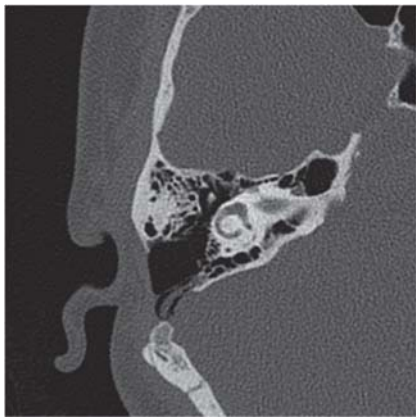
- Surgery #1:

  Skeletonized sigmoid sinus (small area dehiscence), compressed sigmoid with surgicel and bone wax

  Pulsatile tinnitus resolved in recovery room, but recurred 11 months later



1 year post-op CT
(1st surgery)



Compression of sigmoid sinus with surgicel and bone wax.

Pulsatile tinnitus immediately resolved, but recurred 11 month later.

CASE REPORT #2

- Surgery #2:

  Multiple bone chips from ledges of mastoid cavity used to compress sigmoid sinus. All covered with Otomimex cement

  Pulsatile tinnitus resolved in recovery room and no recurrence to date (4 yrs post-op)

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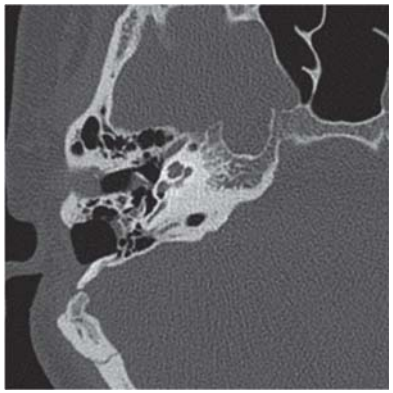
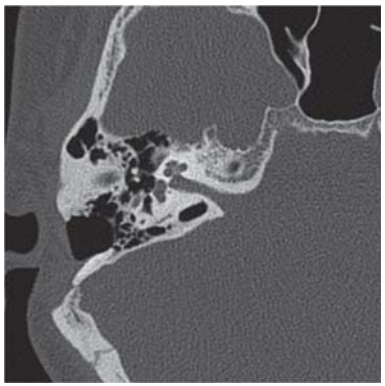


1 year post-op CT
(2nd surgery)



CASE REPORT #3

- 58 yo female with right pulsatile tinnitus and left ear fullness x 8 months
- BMI 28 (50lb weight loss in last year)
- Occasional headaches; normal vision
- Exam: amber fluid left middle ear; AC>BC bilateral
- Valsalva maneuver and cervical pressure to right neck diminished tinnitus

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CASE REPORT #3

- Audiogram showed bilateral HFSNHL only
- *Left* myringotomy – fluid aspirated; positive for Beta-2-transferrin
- CT/CTA showed prominent *right* sigmoid sinus diverticulm and dehiscence of *left* tegmen tympani

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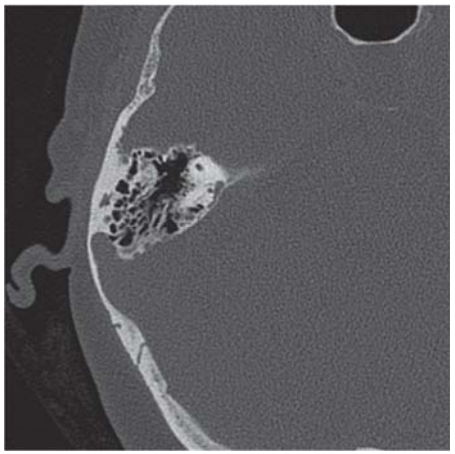
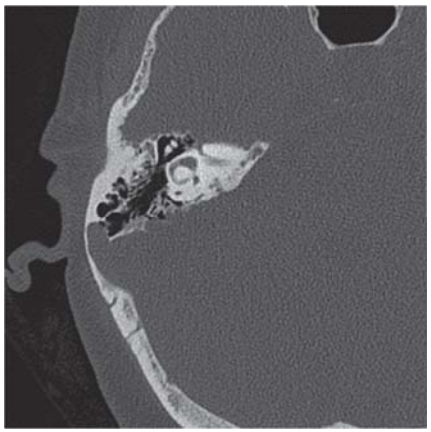
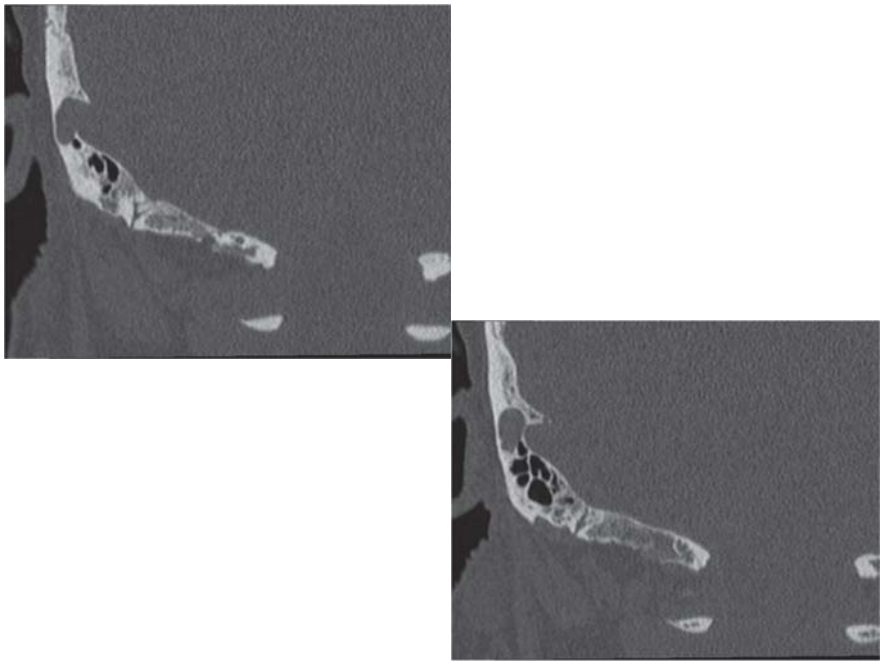
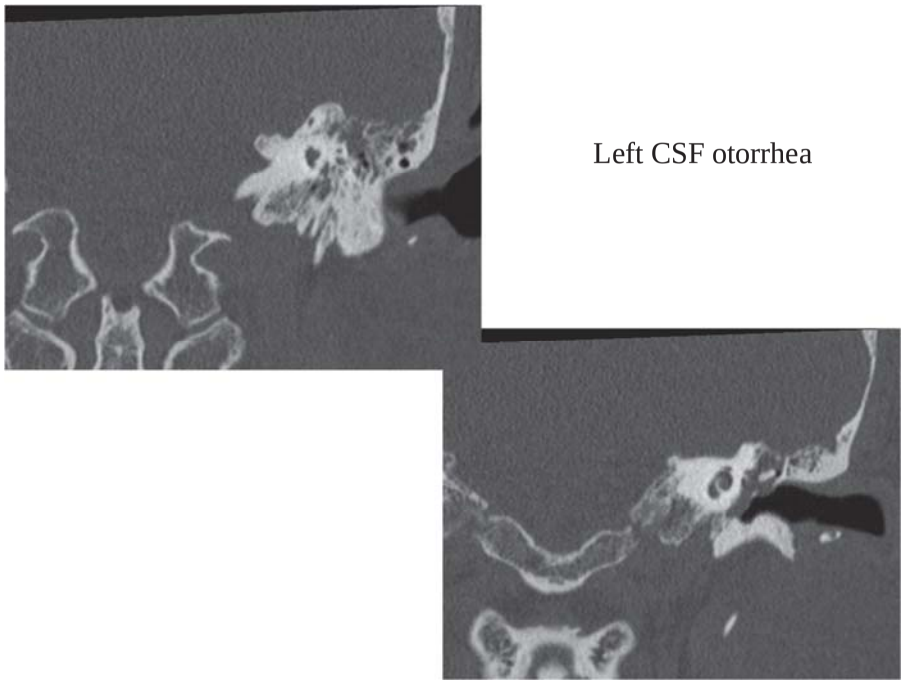


Right pulsatile tinnitus







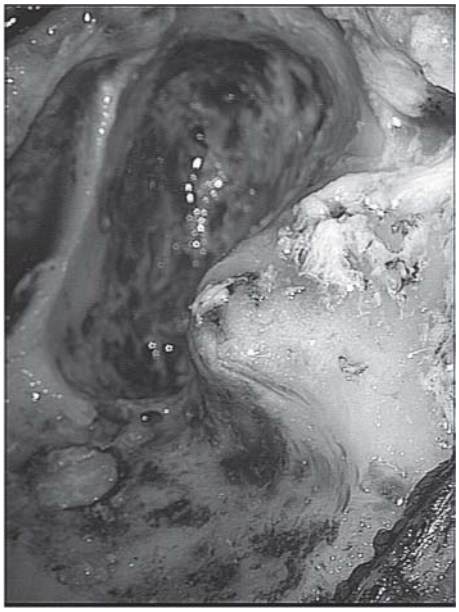
Left CSF otorrhea

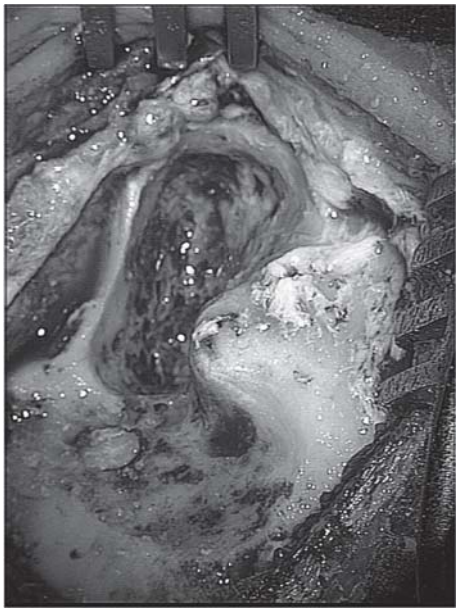
CASE REPORT #3

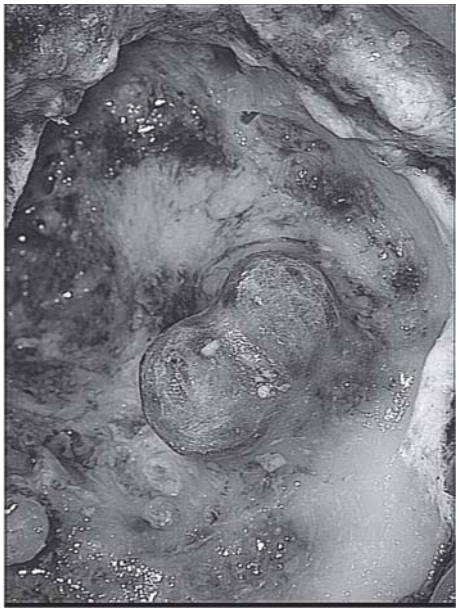
- *Surgery #1* – MCF approach: most of tegmen appeared permeative (“moth-eaten”); one encephalocele near ossicular heads

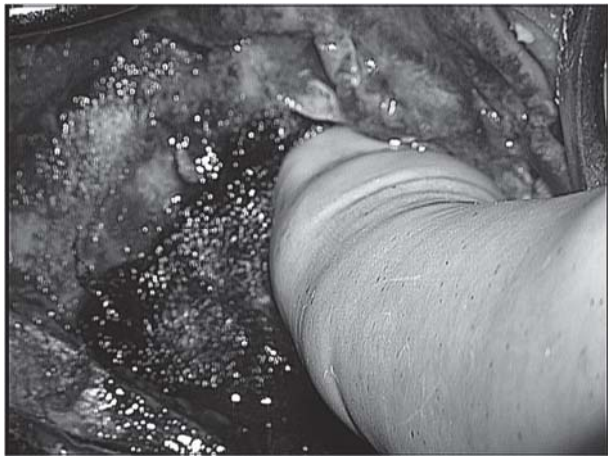
  Repaired with bone chips and fascia

- *Surgery #2* – Transmastoid obliteration of diverticulum; pulsatile tinnitus absent in recovery room; no recurrence x 3.5yrs









CASE REPORT #4

- 52 yo female with left pulsatile tinnitus x 8 years
- Compression of left neck resolved pulsatile tinnitus; often slept with rolled towel under left side of neck
- BMI 29.8
- CT: Dehiscence mid-sigmoid; small diverticulum near SD angle
- MRI: Partially empty sella

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CASE REPORT #4

- LP: OP 23 mm H_2O; developed spinal headache secondary to lumbar leak, but *pulsatile tinnitus completely resolved*.

  Blood patch placed with return of pulsatile tinnitus.

- Could not tolerate Diamox; considered VP shunt
- Negative ophthalmology exam

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CASE REPORT #4

- OR: Sigmoid sinus exposed with obliteration of small diverticulum with surgicel and bone chip
- Sigmoid sinus compressed using bone chips from cortical mastoid then covered with bone cement
- Pulsatile tinnitus resolved in recovery room; no recurrence x 3.0 yrs

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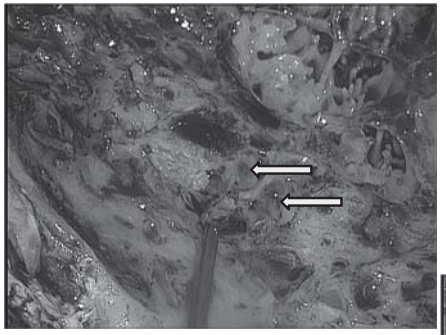
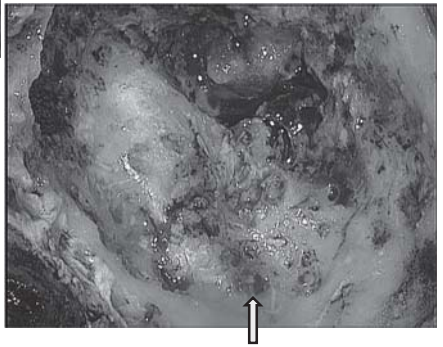
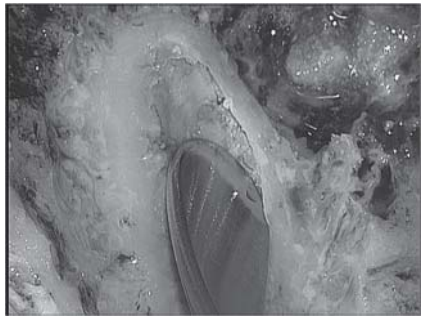
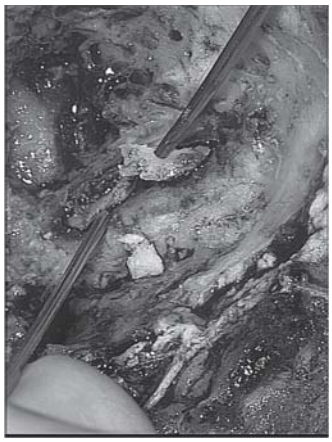


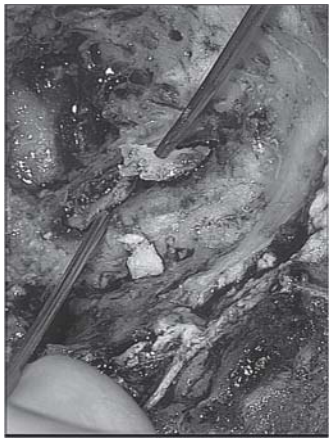
Arrows → dehiscent areas



Arrow → diverticulm







VENOUS HUM TINNITUS

Enlarged Jugular Bulb

Rx	Result	F/U (years)
1. IJV ligation	Resolved	8
2. IJV ligation	Resolved	3
3. IJV ligation	↓ 75%	6
4. IJV ligation	↓ 75%	4
5. IJV ligation	↓ 75%	3
6. IJV ligation	↓ 25%	3
7. IJV ligation SS compression	Recurred/ Resolved	9
8. IJV ligation SS compression	Recurred/ Resolved	8
9. IJV ligation SS compression	↓ 50%	3
10. SS compression x 2	Resolved	2

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VENOUS HUM TINNITUS

Abnormal Sigmoid Sinus

Rx	Result	F/U (years)
11. SS compression (*diverticulum/dehiscence*)	Resolved	2.5
12. SS compression (*diverticulum*)	Resolved	2.5
13. SS compression (*diverticulum/dehiscence*)	Resolved	3.0
13. SS compression (*diverticulum*)	Resolved	3.5
14. SS compression (*dehiscence*)	Recurred at 11mo Revision – resolved	4.0
15. SS compression (*dehiscence*) 18yo	Recurred at 2 mo Revision - resolved	0.5

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9th Annual Otolaryngology Literature Update
Rhinology & Sinus I

Rodney J. Schlosser, M.D.
Professor
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Rodney J. Schlosser, M.D. is Professor and Director of Rhinology and Sinus Surgery in the Department of Otolaryngology at the Medical University of South Carolina. He completed his Otolaryngology residency at the University of Virginia and his Rhinology fellowship at the University of Pennsylvania, and has been on staff at MUSC since 2002.

Dr. Schlosser's clinical areas of interest include complex sinus surgery, endoscopic repair of CSF leaks and skull base defects, resection of sinonasal and skull base tumors. His research interests include the mucosal immune response in various forms of chronic sinusitis, novel methods of drug delivery and clinical outcomes in patients undergoing medical and surgical treatment for chronic rhinosinusitis.

Dr. Schlosser has received research grants from the National Institute of Health, Veterans Administration, American Rhinologic Society, American Academy of Otolaryngic Allergy, American Academy of Otolaryngology – Head and Neck Surgery, Cystic Fibrosis Foundation, Johnson and Johnson, Gyrus, Xoran, Acclarent and the Flight Attendant's Medical Research Institute.

He has published a textbook on endoscopic sinus surgery, as well as over 200 peer reviewed articles and seven book chapters, and has been an invited speaker throughout the U.S. and abroad.

9th Annual Otolaryngology Literature Update
Medical University of South Carolina

Rhinology & Sinus I

Rodney J. Schlosser, M.D.

Günel C, Bleier BS, Meteoglu I. "Antibiotics in eosinophilic chronic rhinosinusitis: Rethinking maximal antimicrobial medical therapy." Laryngoscope. 2017 Apr;127(4):794-796. doi: 10.1002/lary.26415. Epub 2016 Nov 26.

Ho J, Hamizan AW, Alvarado R, Rimmer J, Sewell WA, Harvey RJ. "Systemic Predictors of Eosinophilic Chronic Rhinosinusitis." American Journal of Rhinology & Allergy. 2018 Jul;32(4):252-257. doi: 10.1177/1945892418779451. Epub 2018 Jun 4.

Oakley GM, Christensen JM, Sacks R, Earls P, Harvey RJ. "Characteristics of macrolide responders in persistent post-surgical rhinosinusitis." Rhinology. 2018 Jun 1;56(2):111-117. doi: 10.4193/Rhin17.049.

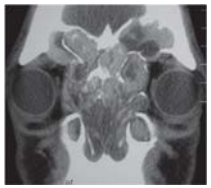
Orgain CA, Harvey RJ. "The role of frontal sinus drillouts in nasal polyposis." Current Opinion in Otolaryngology & Head and Neck Surgery. 2018 Feb;26(1):34-40. doi: 10.1097/MOO.0000000000000425.

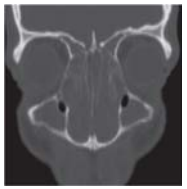
Orlandi RR, Kingdom TT, Hwang PH, Smith TL, Alt JA, Baroody FM, Batra PS, Bernal-Sprekelsen M, Bhattacharyya N, Chandra RK, Chiu A, Citardi MJ, Cohen NA, DelGaudio J, Desrosiers M, Dhong HJ, Douglas R, Ferguson B, Fokkens WJ, Georgalas C, Goldberg A, Gosepath J, Hamilos DL, Han JK, Harvey R, Hellings P, Hopkins C, Jankowski R, Javer AR, Kern R, Kountakis S, Kowalski ML, Lane A, Lanza DC, Lebowitz R, Lee HM, Lin SY, Lund V, Luong A, Mann W, Marple BF, McMains KC, Metson R, Naclerio R, Nayak JV, Otori N, Palmer JN, Parikh SR, Passali D, Peters A, Piccirillo J, Poetker DM, Psaltis AJ, Ramadan HH, Ramakrishnan VR, Riechelmann H, Roh HJ, Rudmik L, Sacks R, Schlosser RJ, Senior BA, Sindwani R, Stankiewicz JA, Stewart M, Tan BK, Toskala E, Voegels R, Wang de Y, Weitzel EK, Wise S, Woodworth BA, Wormald PJ, Wright ED, Zhou B, Kennedy DW. "International Consensus Statement on Allergy and Rhinology: Rhinosinusitis." International Forum of Allergy & Rhinology. 2016 Feb;6 Suppl 1:S22-209. doi: 10.1002/alr.21695.

Pinto Bezerra Soter AC, Bezerra TF, Pezato R, Teles Abdo TR, Pilan RM, Pinna FR, Gevaert P, van Zele T, Bachert C, Voegels RL. "Prospective open-label evaluation of long-term low-dose doxycycline for difficult-to-treat chronic rhinosinusitis with nasal polyps." Rhinology. 2017 Jun 1;55(2):175-180. doi: 10.4193/Rhin15.291.

Rudmik L, Xu Y, Alt JA, Deconde A, Smith TL, Schlosser RJ, Quan H, Soler ZM. "Evaluating Surgeon-Specific Performance for Endoscopic Sinus Surgery." JAMA Otolaryngology–Head & Neck Surgery. 2017 Sep 1;143(9):891-898. doi: 10.1001/jamaoto.2017.0752.

Smith KA, Pulsipher A, Gabrielsen DA, Alt JA. "Biologics in Chronic Rhinosinusitis: An Update and Thoughts for Future Directions." American Journal of Rhinology & Allergy. 2018 Sep;32(5):412-423. doi: 10.1177/1945892418787132. Epub 2018 Jul 19.





Precision medicine for CRSwNP

Rodney J. Schlosser, MD

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Department of Otolaryngology - HNS
Medical University of South Carolina
Charleston, SC

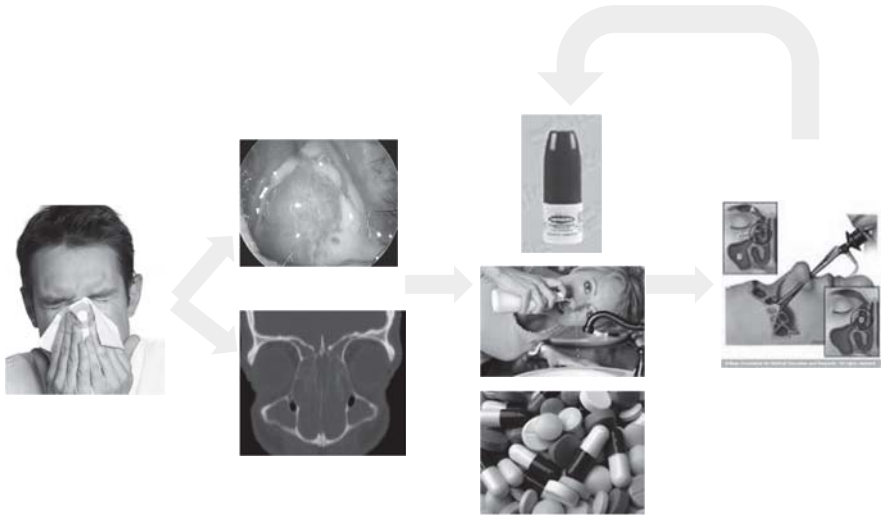
Disclosure

- Consultant: Olympus, Arrinex, Optinose, Sanofi
- Grants: Optinose, Intersect, Entellus, Sanofi, GSK, Astra Zeneca, Roche

What is precision medicine?

- An emerging approach for disease treatment and prevention that **takes into account individual variability** in genes, environment, and lifestyle for each person
- Allows doctors to **predict more accurately which treatment will work** in which groups of people
- **In contrast to a one-size-fits-all approach**, in which disease treatment and prevention strategies are developed for the average person, with less consideration for the differences between individuals

Our current CRS treatment algorithm: One size fits all



Precision med rx

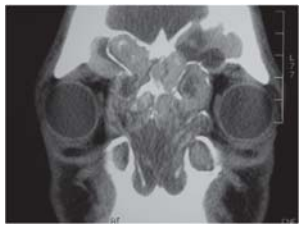
- What is success rate for medical therapy in CRSwNP?
- Are steroids successful in all CRSwNP?
- Which antibiotic, if any?

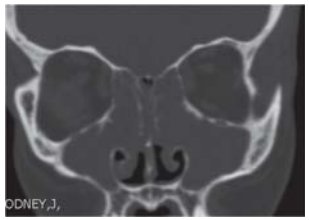
A few caveats…

- Sometimes MDs use therapies even if there is evidence AGAINST it!
  - Individual patient differences
  - Cost
  - Compliance
  - Pt demands

Why do we lack evidence regarding medical rx for CRSwNP?

- Heterogeneous
  - AFRS
  - AERD
  - Atopic v non-atopic
- Clinical parameters
  - Endoscopy
  - CT
- Eosinophilic or not?
- Postop recurrence vs primary dz





Confusion makes it difficult to understand the evidence

TABLE 2. Therapies included in maximal medical therapy criteria

Type of therapy	Prevalence within included studies % (n)	Duration of therapy (mean ± SD) (n)	95% CI
Topical steroids	91.4 (74)	8.4 ± 8.3 weeks (52)	6.2–10.8
Saline irrigation	39.5 (32)	–	–
Systemic steroids	61.7 (50)	18.0 ± 11.6 days (25)	13.2–22.8
Oral antibiotics	87.7 (71)	23.0 ± 8.4 days (47)	20.5–25.5
Oral decongestant	8.6 (7)	–	–
Systemic antihistamine	11.1 (9)	–	–
Oral mucolytic	9.9 (8)	–	–
Topical decongestant	9.9 (8)	–	–
Leukotriene inhibitor	1.2 (1)	–	–

Dautremont JF, Rudmik L, IFAR 2015

Why the confusion? Maximal Medical Therapy (MMT) guidelines

Guideline					
AAOA 2009					
AAOHNS 2015					
Canadian 2011					
EPOS 2012					
BSACI 2008					

Orlandi, etal, IFAR 2016

Why the confusion?
Maximal Medical Therapy (MMT) guidelines

Guideline	Antibiotics				
AAOA 2009	Yes, 3-4wks				
AAOHNS 2015	Cx directed, 2-4 wks				
Canadian 2011	Cx directed, "slightly longer than for ABRS"				
EPOS 2012	CRSsNP: macrolides 12 wks CRSwNP: doxy 3 wks				
BSACI 2008	Macrolides 12 wks				

Orlandi, etal, IFAR 2016

MMT guidelines

Guideline	Antibiotics	INCS			
AAOA 2009	Yes, 3-4wks	Yes, 1 mo			
AAOHNS 2015	Cx directed, 2-4 wks	Option			
Canadian 2011	Cx directed, slightly longer than for ABRS	Yes			
EPOS 2012	CRSsNP: macrolides 12 wks CRSwNP: doxy 3 wks	Yes, 3 mos except 1 mo severe NP			
BSACI 2008	Macrolides 12 wks	Yes			

Orlandi, etal, IFAR 2016

MMT guidelines

Guideline	Antibiotics	INCS	PO steroids		
AAOA 2009	Yes, 3-4wks	Yes, 1 mo	CRSwNP: yes, 8-12 days CRSsNP: if initial 2 wk Rx fails		
AAOHNS 2015	Cx directed, 2-4 wks	Option	Option		
Canadian 2011	Cx directed, slightly longer than for ABRS	Yes	CRSwNP: yes, 2 wks CRSsNP: option		
EPOS 2012	CRSsNP: macrolides 12 wks CRSwNP: doxy 3 wks	Yes, 3 mos except 1 mo severe NP	Mod/severe CRSwNP: yes, "short course" CRSsNP: no		
BSACI 2008	Macrolides 12 wks	Yes	Mod/severe CRSwNP: yes, 5-10 days CRSsNP: no		

Orlandi, etal, IFAR 2016

MMT guidelines

Guideline	Antibiotics	INCS	PO steroids	Saline	Other
AAOA 2009	Yes, 3-4wks	Yes, 1 mo	CRSwNP: yes, 8-12 days CRSsNP: if initial 2 wk Rx fails	?	PO/topical decon
AAOHNS 2015	Cx directed, 2-4 wks	Option	Option	Option	Rx AR
Canadian 2011	Cx directed, slightly longer than for ABRS	Yes	CRSwNP: yes, 2 wks CRSsNP: option	Option	LTRA option
EPOS 2012	CRSsNP: macrolides 12 wks CRSwNP: doxy 3 wks	Yes, 3 mos except 1 mo severe NP	Mod/severe CRSwNP: yes, "short course" CRSsNP: no	Yes	
BSACI 2008	Macrolides 12 wks	Yes	Mod/severe CRSwNP: yes, 5-10 days CRSsNP: no	Yes	LTRA in AERD; Antihist in AR

Orlandi, etal, IFAR 2016

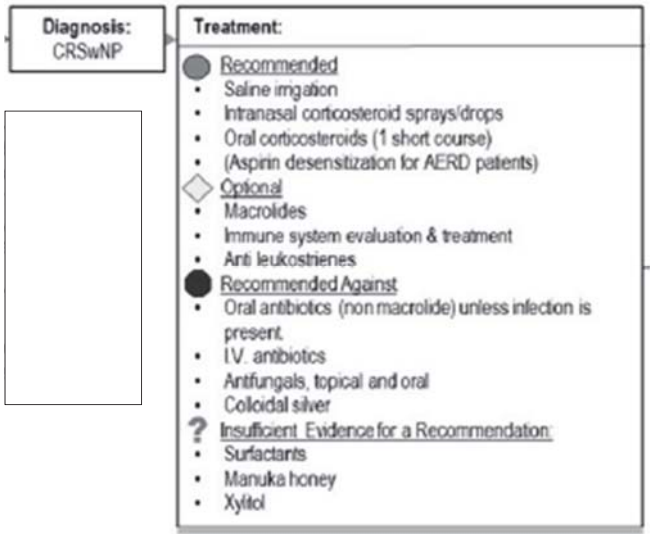
Confusing response rate to MMT

TABLE X-5. Reported response rates to medical therapy trials prior to surgery

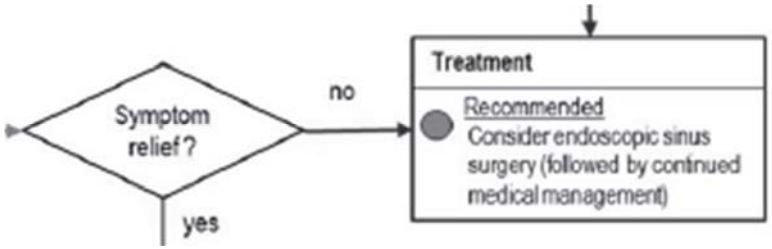
Study	Intervention	Outcome measured	Response rate
Lal[728]	4 weeks amoxicillin-clavulanate, 12 days oral corticosteroid, 4 weeks INCS, 4 weeks saline rinse	Complete resolution of symptoms Partial response	51.03% 17.8%
Dilidaer[1144]	Not specified	Complete control	30.4%
Young[1146]	3 weeks oral prednisolone, antibiotics, INCS, and saline rinses	Improvement in symptoms sufficient to avoid surgery	37.5%
Subramanian[729]	4 weeks antibiotics, INCS, saline rinses, 10 days prednisolone	Improvement in symptoms sufficient to avoid surgery	90%
Baguley[1145]	3 weeks prednisolone, 4–6 weeks INCS, saline rinse, optional 20 days antibiotics	Control = symptoms resolved or no longer bothersome	38%

Orlandi, etal, IFAR 2016

CRSwNP summary

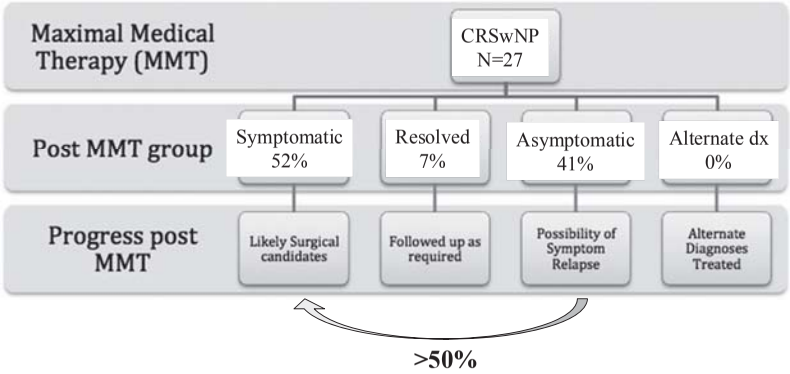


Orlandi, etal, IFAR 2016



Orlandi, etal, IFAR 2016

Likelihood of success with "maximal medical therapy"

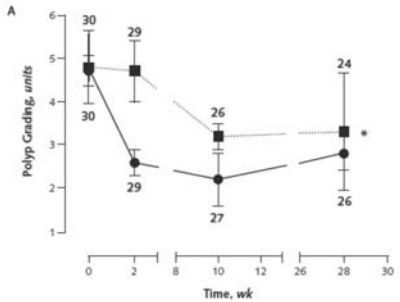


Essentially 75% "failure" rate

Baguley C, etal, IFAR 2014

Success of oral steroids in cohorts

- Prednisolone 25 mg/d x 14d vs placebo
- Fluticasone gtt x 8 wks
- Fluticasone spray x 18 wks



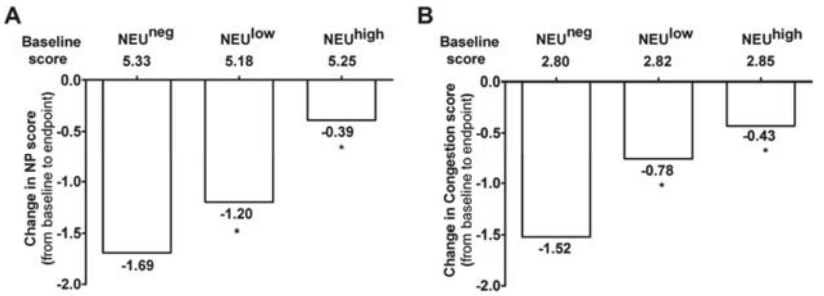
Vaidyanathan S, etal Ann Int Med 2011

Individual response rate:
MCID in NP grade or hyposmia VAS

- Prednisolone: 83%
- Placebo: 57%
- No predictors of response, including blood or tissue eos, asthma, IgE, atopic status, AERD

Vaidyanathan S, etal Ann Int Med 2011

Steroid responsiveness associated with low tissue neutrophils



Wen etal, JACI 2012

Success of amox/clav x 4 wks

TABLE I.
Characteristics of Patients With eCRS and Non-eCRS.

	eCRS (n = 25)	Non-eCRS (n = 14)	*P* Value
Age (yr)	36.8 ± 12.9	43.9 ± 16.6	.142
Gender (n)			.004
Male	10	13	
Female	15	1	
CRSsNP (n)	7	7	.305
CRSwNP (n)	18	7	
Smoking (n)	5	5	.446
Aspirin sensitivities (n)	4	13	.636
Asthma (n)	7	13	.218

CRSsNP = chronic rhinosinusitis without nasal polyps; CRSwNP = chronic rhinosinusitis with nasal polyps; eCRS = eosinophilic chronic rhinosinusitis.

Gunel C, etal, Laryngoscope 2017

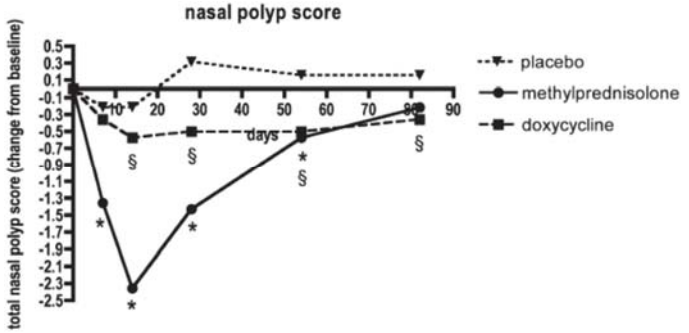
TABLE III.
The Change in Pre- and Post-treatment Endoscopy, Radiographic, and Symptom Scores Between the eCRS and Non-eCRS Groups.

	eCRS (n = 25)		Non-eCRS (n = 14)	
	Change	*P* Value	Change	*P* Value
Lund-Mackay score	0 (−2/0)	.007	−4 (−6/−2)	.002
Lund-Kennedy score	0.00 (−0.25–1.25)	.347	0.5 (0/2)	.188
SNOT-22	0.40 ± 6.22	.751	12.5 ± 9.7	<.001

The values are given are mean ± standard deviation or median (25th–75th percentiles).
eCRS = eosinophilic chronic rhinosinusitis; SNOT-22 = Sino-Nasal Outcome Test-22.

Gunel C, etal, Laryngoscope 2017

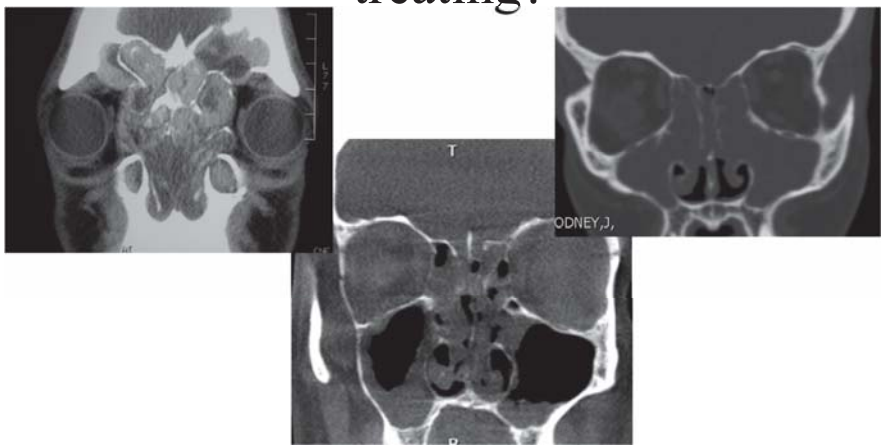
PO steroid vs doxy x 20d



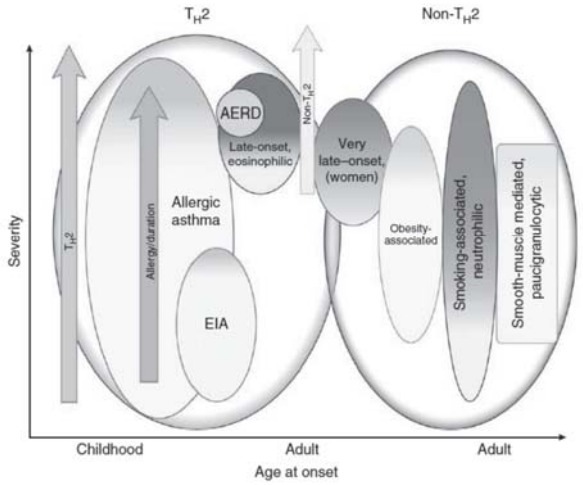
- Doxy improved PND, no other sx
- All NP recurred by 3 mos
- Predictors of success?

VanZele T, etal, JACI 2010

How do we predict what type of inflammatory disorder we are treating?



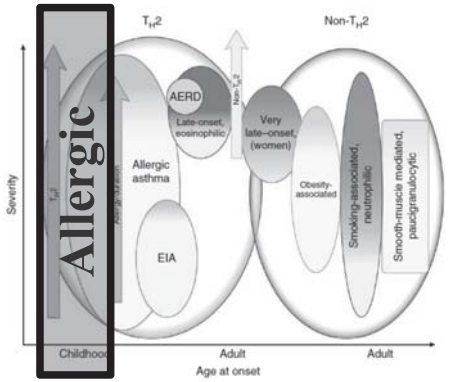
Asthma endotypes



Wenzel SE. Nat Med 2012

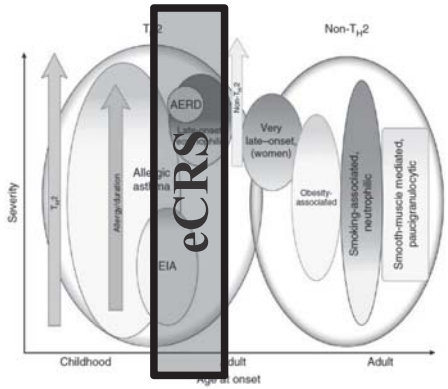
Endotype differences

- Childhood and young adult
  - Rhinitis and Asthma
  - Probably more related to common allergen exposure
  - Simple IgE mediated



Endotype differences

- Adult onset
  - Sinusitis (polyps) and asthma
  - Commonly eosinophilic (with no allergy or disparate findings)



We can't do biopsies and structured histopath on everyone, so what's the alterative?

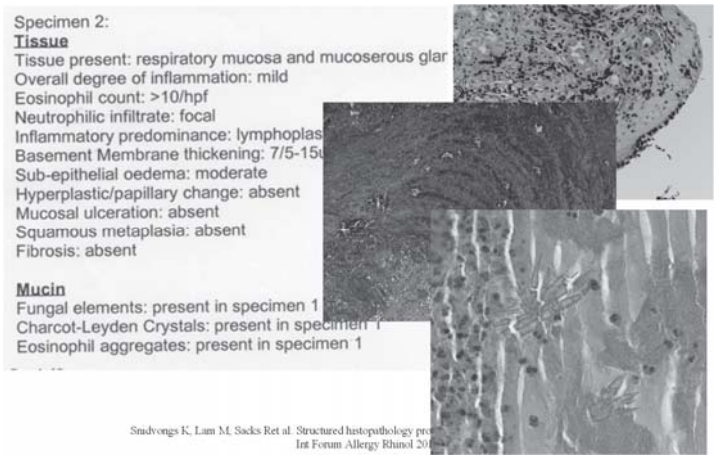
Systemic predictors of eosinophilic CRS

Table 1. Comparison of eCRS and Non-eCRS Characteristics.

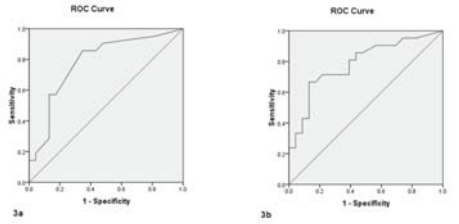
	eCRS (n=206)	Non-eCRS (n=139)	*P*
Age (years)	48.45 ± 14.34	49.12 ± 16.11	.68
Female (%)	45.1	52.5	.18
Nasal polyps (%)	70.9	10.8	<.01**
Asthma (%)	52.4	23.0	<.01**
Previous CRS surgery (%)	52.4	47.5	.37

Abbreviations: CRS, chronic rhinosinusitis; eCRS, eosinophilic chronic rhinosinusitis.
**Indicates significant results

Ho J, etal AJRA 2018



Serum eosinophilia as a biomarker



sensitivity 52%, specificity 87%, positive predictive value 79%, negative predictive value 67%

- Best test at >0.30 x10^9/L,
  - PPV 79%
  - Poor NPV 67%

Snidvongs K, Lam M, Sacks Ret al. Structured histopathology profiling of chronic rhinosinusitis in routine practice. Int Forum Allergy Rhinol 2012; 2:376-385.

Serum eosinophilia as a biomarker

Table 2. Comparison of Biomarkers Between eCRS and Non-eCRS Populations.

Patients	eCRS (n=206)	Non-eCRS (n=139)	P
Eosinophils (×10^9/L)	0.42 ± 0.34	0.17 ± 0.13	<.01**
WCC (×10^9/L)	6.94 ± 2.08	7.47 ± 2.73	.052
Eosinophil/WCC ratio (%)	6.21 ± 4.48	2.55 ± 1.84	<.01**
CRP (mg/L)	2.41 ± 3.93	3.18 ± 4.70	.11
ESR (mm/h)	8.10 ± 7.87	10.65 ± 11.91	.03**
IgE (kU/L)	182.31 ± 293.93	146.64 ± 280.72	.26
Overall ImmunoCAP +ve (%)	51.9	48.2	.50
Grass mix (%)	35.0	28.1	.19
House dust mite mix (%)	32.0	30.9	.86
Animal epithelia (%)	13.6	12.2	.73
Mold mix (%)	16.0	10.1	.13

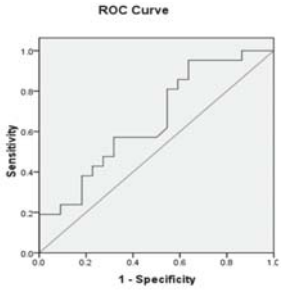
Abbreviations: CRP, C-reactive protein; eCRS, eosinophilic chronic rhinosinusitis; ESR, erythrocyte sedimentation rate; IgE, immunoglobulin E; WCC, white cell count.

- Blood eos >0.24 x 10^9/L: PPV 83%, NPV 64.5%

Ho J, etal AJRA 2018

Serum IgE is not a surrogate

- Correlate r=0.3 (p=0.05)
- Serum IgE was
  - non-predictive of high eosinophilia
  - (ROC p=0.08)



Ho J, etal AJRA 2018

"Doctor, what is your success rate with FESS?"

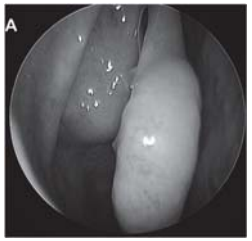
Can we personalize recommendations for ESS?

- Variability in utilization
- Outcomes
- Timing
- Extent

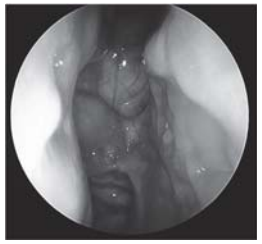
Why do we lack evidence supporting ESS success?

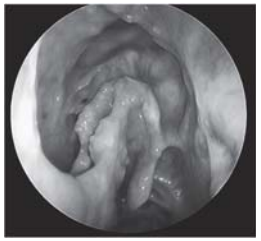
- Heterogeneous medical Rx
- Heterogeneous surgical Rx
  - Timing
  - Extent
  - Instrumentation
- Heterogeneous definition of success
  - QOL, productivity, meds, revision ESS, postop endoscopy, CT….

Unlike medications, wide variations in extent and timing of surgery



Balloon

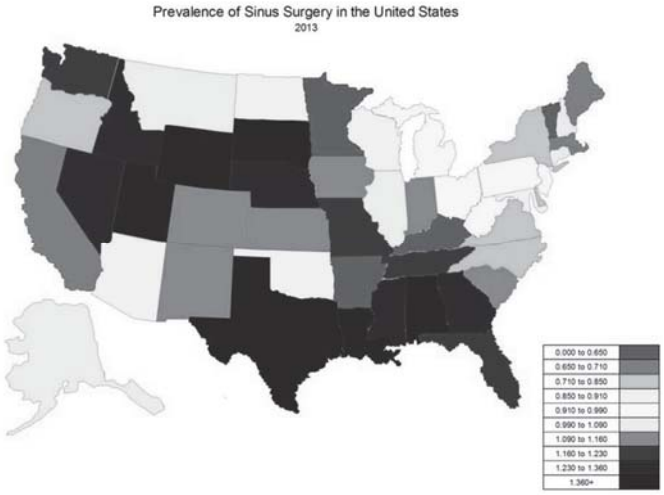

FESS


Lothrop

Variable utilization

- General consensus that ESS indicated with persistent sx, objective dz and failure of medical therapy
- Many patients "orbit" for a while before opting for surgery

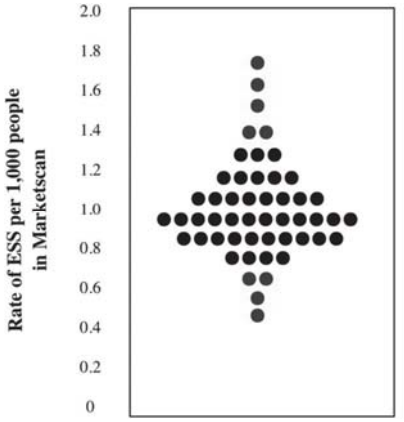
Variability in rates of ESS



Rudmik L, etal Laryngoscope 2015

Political correlation?

ESS variability



Rate of ESS per 1,000 people	
South Dakota	1.80
Alabama	1.69
Utah	1.58
Wyoming	1.45
Kentucky	1.37

Massachusetts	0.67
California	0.65
Arkansas	0.57
Vermont	0.51

- Greater variability than spine surgery, lap choly, CABG, etc.

Rudmik L, etal Laryngoscope 2015

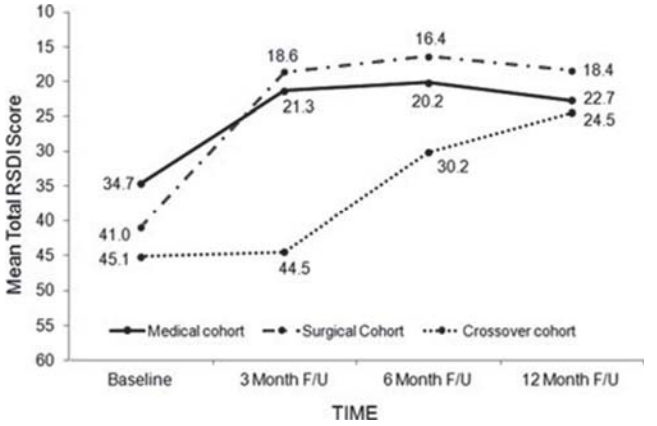
CRS outcomes and "success"

- Patient
  - **QOL**, sx scores, health utility
- Surgeon
  - Endoscopy, **revision rates**, med usage
- Society
  - Cost of care, lost productivity

Patient defined success

- Patient reported outcome measures (PROMs)
  - Overall QoL (SF12/36)
  - Disease specific QOL (SNOT22, RSDI)
  - For any PROM, magnitude of improvement?
    - Any statistical improvement
    - % achieving mean clinically important difference (MCID)
    - "Normal" QOL vs asymptomatic
- Objective metrics
  - SIT, NPIF

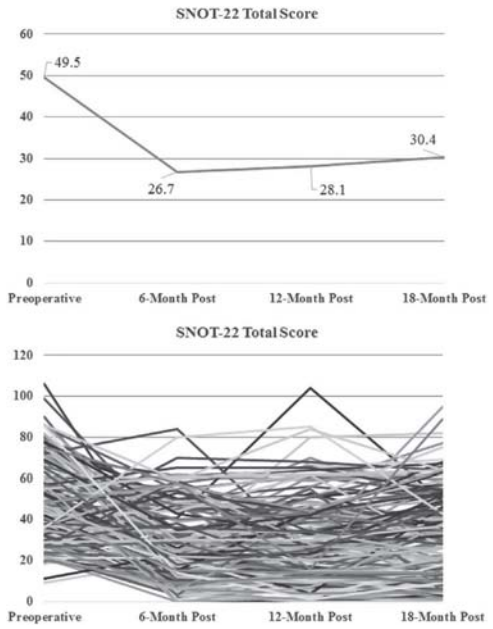
Multi-institutional prospective med vs ESS



Smith et al, IFAR 2012

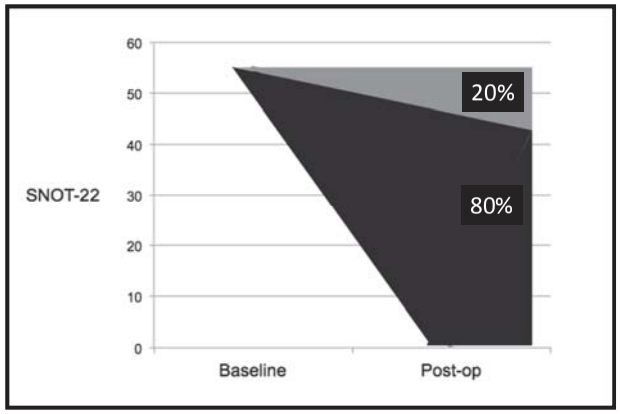
Defining success with SNOT22

Success in cohorts vs "personalized" individual outcomes?



Smith TL, IFAR 2017

Individual likelihood of achieving MCID after ESS

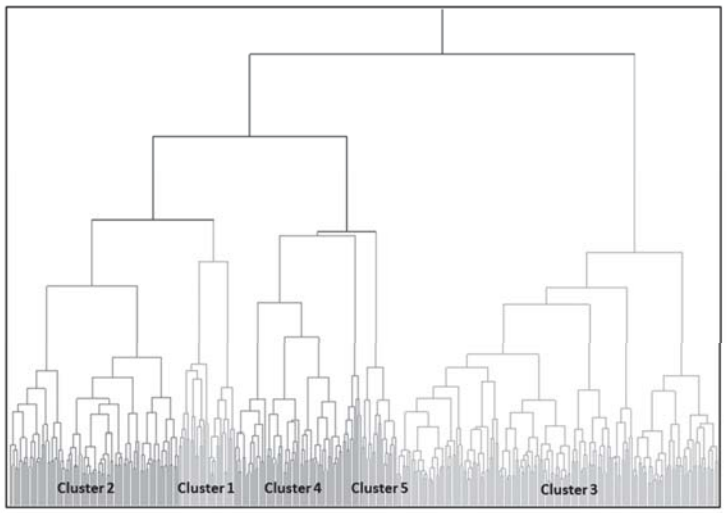


Rudmik L, et al. Laryngoscope 2015

Improving individual prognosis?

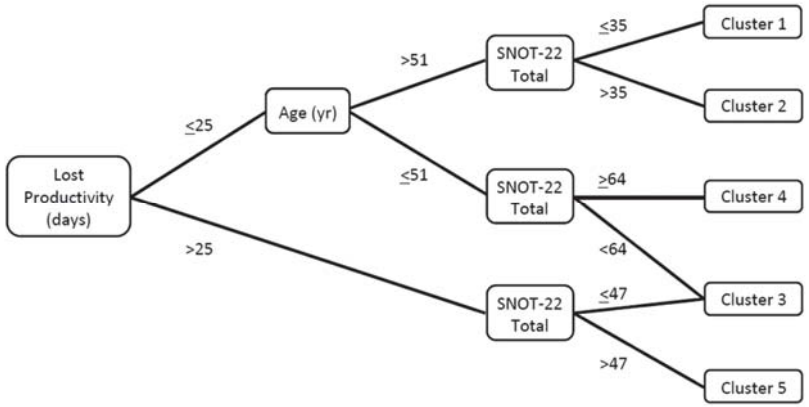
- Cluster analysis
  - Relies upon computer algorithms to group patients
  - Avoid pre-conceived biases
- Used in other heterogeneous dz (asthma)

Cluster analysis



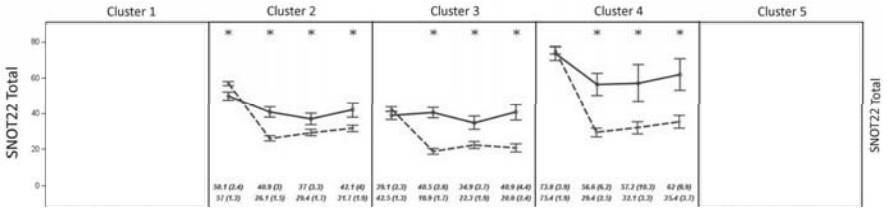
Soler, Hyer, Ramakrishnan, Smith, Schlosser, IFAR 2015

Discriminant algorithm for clinical use



Soler, Hyer, Ramakrishnan, Smith, Schlosser, IFAR 2015

Clustering can be used to predict total SNOT22 outcomes



Soler, Hyer, Ramakrishnan, Smith, Schlosser, JACI 2016

Likelihood of achieving MCID with ESS v medical Rx

Cluster	SNOT22 (99.5% CI)
1	2.1 (0.6,7.0)
2	4.7 (1.5,15.4)
3	16.9 (3.7,77.5)
4	6.2 (0.3,152.7)
5	4.9 (0.2,119.8)

Soler, Hyer, Ramakrishnan, Smith, Schlosser, IFAR 2015

More sophisticated understanding of ESS success in general

but what about extent and timing for individual patient?

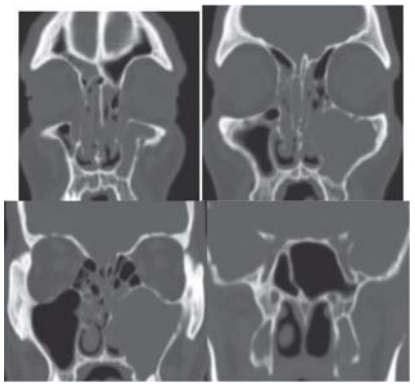
Is ESS just one single intervention?

Let's debate when and how much surgery we need to do!

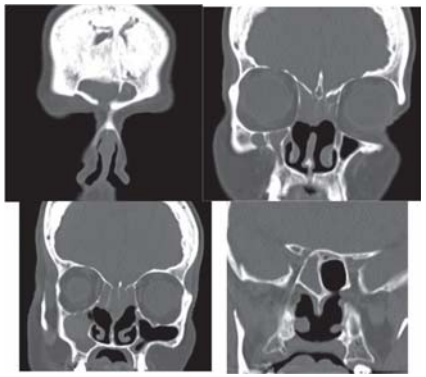
Compromise?

Two patients who have failed medical Rx

CRSsNP patient



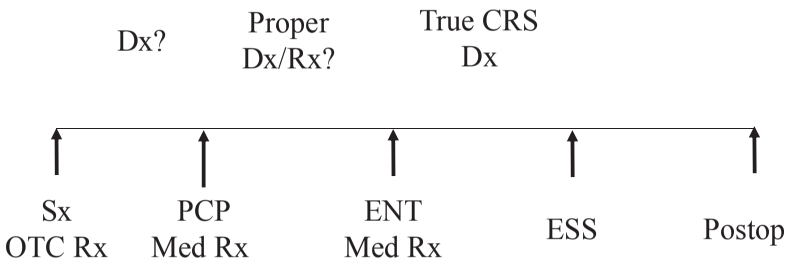
CRSwNP patient



When do you go to OR?

- Sx?
- Comorbidities?
- Severity of CT?
- Does waiting hurt?

Timing is everything



Future indications for ESS

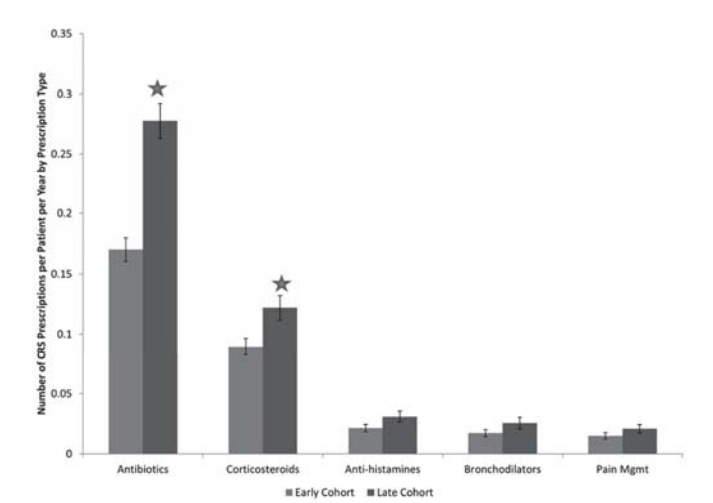
- Currently for symptom relief
- Disease prevention?

Early vs delayed ESS

- Retrospective review NHS data on 2534 pts
- 2 cohorts matched for age, gender, asthma, NP status:
  - Early ESS within 1 year of CRS dx
  - Late ESS >5 years from CRS dx

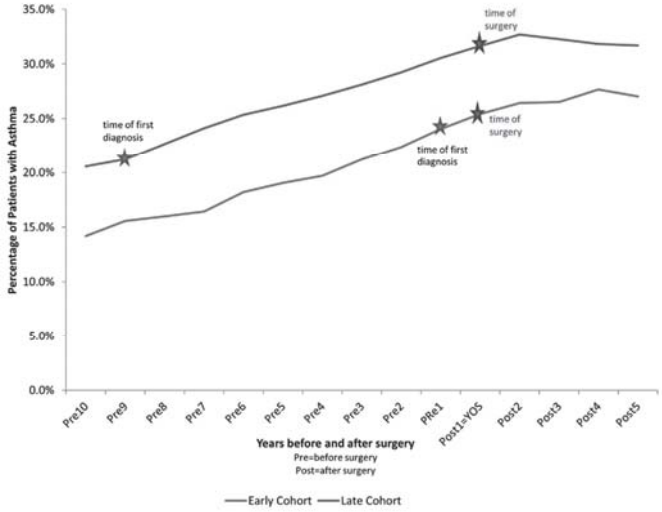
Hopkins C, etal Rhinology 2015

Decreased po abx and steroids



Hopkins C, etal Rhinology 2015

Less asthma



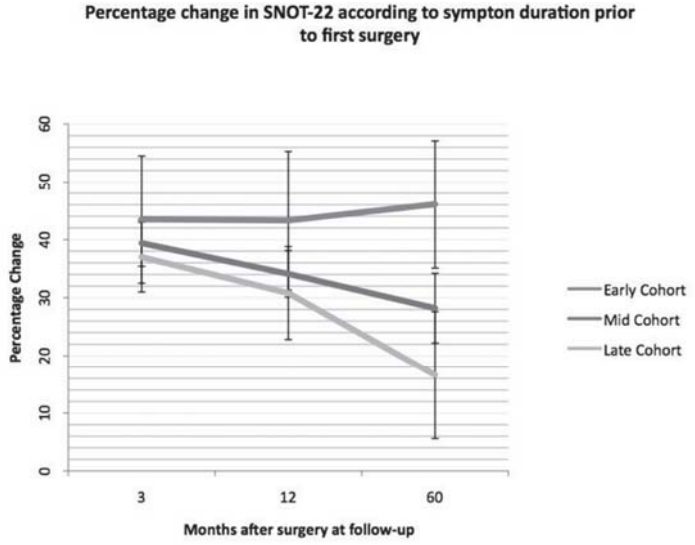
Hopkins C, etal Rhinology 2015

Early vs delayed ESS

- Prospective NHS study of 1493 pts
- 3 cohorts: Time from CRS dx to ESS
  - Early: <1 year
  - Mid: 1-5 years
  - Late: >5 years
- Late cohort with worse SNOT22, more asthma, AR

Hopkins C, etal Rhinology 2015

Sustained improvement in SNOT22



Hopkins C, etal Rhinology 2015

Early ESS with durable results
% patients achieving MCID

Followup	Early cohort (<1 yr)	Mid cohort (1-5 yrs)	Late cohort (>5 yrs)	P
3 mos	75.0	74.5	75.4	0.971
12 mos	78.0	70.8	70.5	0.05
60 mos	71.2	57.3	53.0	0.028

- Controlled for SNOT22, LM score, age, gender, asthma, extent of surgery

Hopkins C, etal Rhinology 2015

Conflicting US study

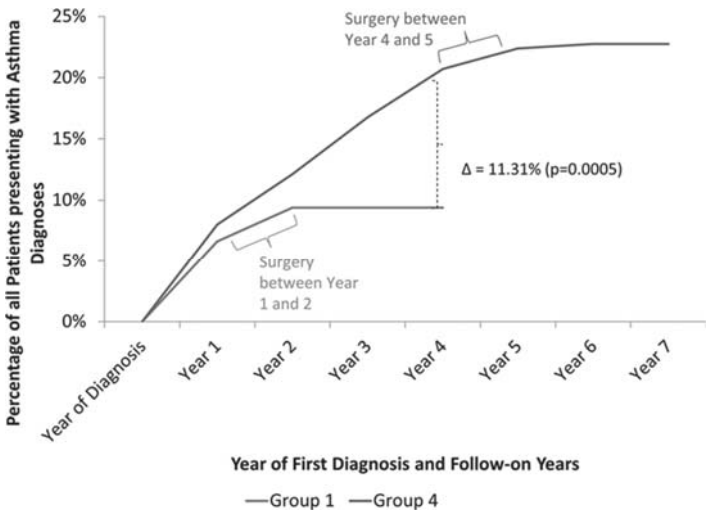
TABLE IV.
Comparison of the Prevalence of Study Participants Reporting at Least One MCID Value Following Endoscopic Sinus Surgery Between Symptom Duration Subgroups.

PROM Scores	Short Cohort (%)	Middle Cohort (%)	Late Cohort (%)	χ^2 Test Statistic	*P* Value
SNOT-22 total score	92%	83%	93%	1.65	0.438
RSDI total score	78%	59%	85%	4.32	0.115
BSIT score	50%	25%	76%	9.63	0.008

Patients asked to retrospectively estimate onset of CRS sx
Mean postop f/u 14.7 mos for all groups

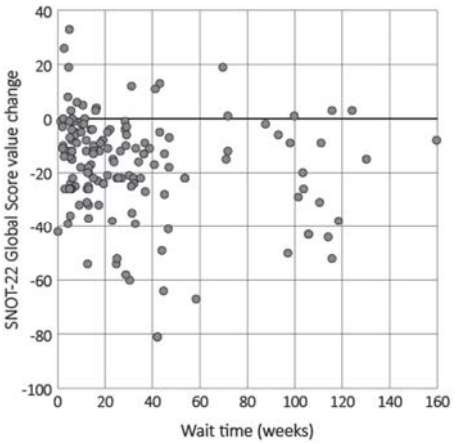
Alt et al, Laryngoscope 2019

ESS stops the "asthmatic march"



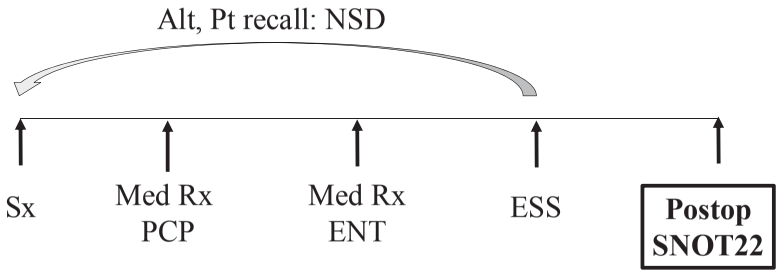
Benninger etal, IFAR 2016

Surgery wait time does not impact SNOT22 outcomes



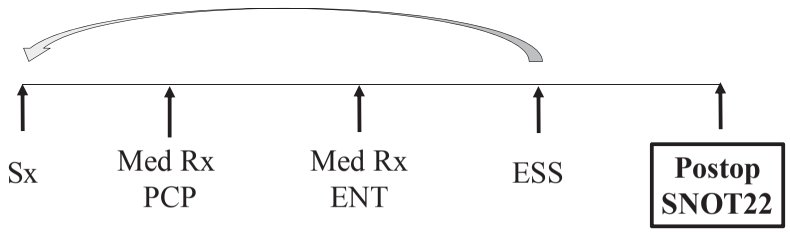
Newton E, etal, IFAR 2017

Postop SNOT22 outcomes



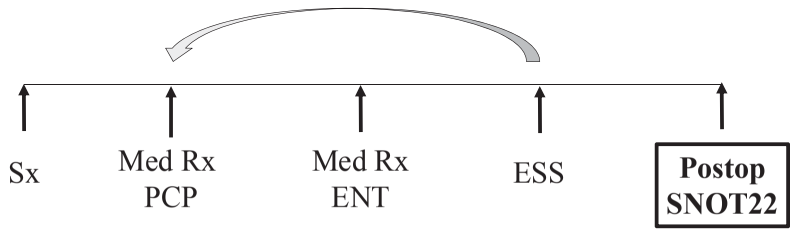
Postop SNOT22 outcomes

Hopkins, pt recall: Significant difference



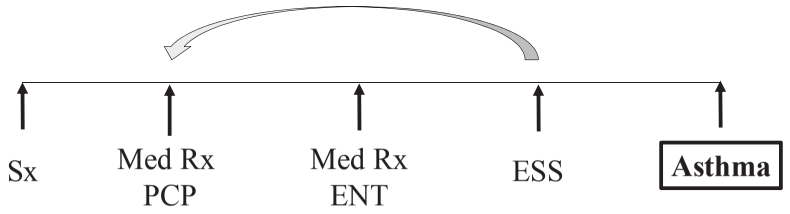
Postop SNOT22 outcomes

Hopkins retrospective database: Significant difference

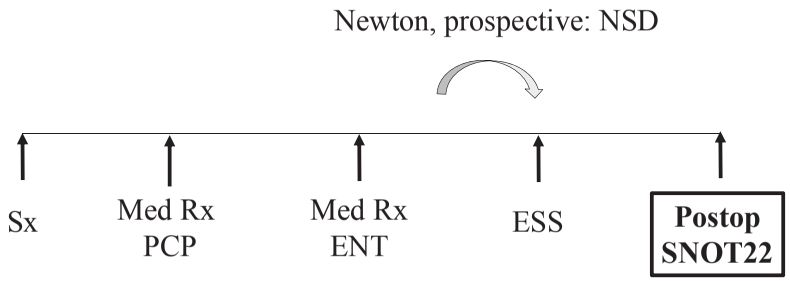


Asthma development

Benninger, retrospective database: Significant difference

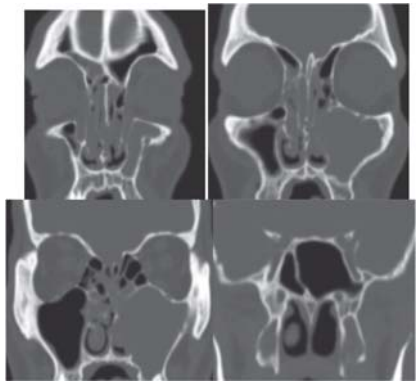


Postop SNOT22 outcomes



How much surgery?

- One size fits all?
- Location of symptoms?
- CT: Small dz=small holes, big dz=big holes?
- One sinus beyond dz
- Polyp status
- Need for postop topicals
- Insurance co tells us



What are your surgical goals in typical CRS patient?

- Establish nasal airway and relieve sinus outflow
- Decrease inflammatory load

- Improve access for topical medications

Orlandi R etal, IFAR 2016

Topical therapies

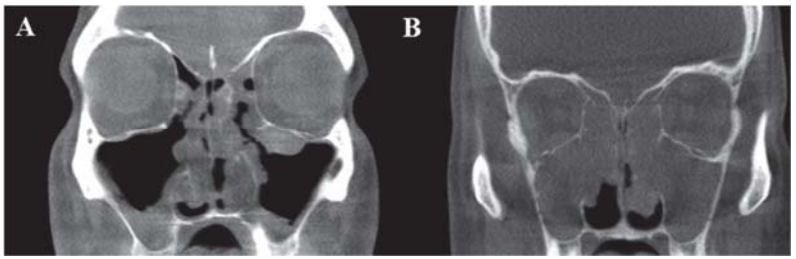
- Delivery to anatomic site (target sinus)
  - Surgical state
  - Delivery device & volume
  - Patient position
- The proper active agent

Where does the medicine need to get?

TABLE II.
Percentage of Mucosal Disease in Draining Sinuses in Each CRS Subtypes When the OMC Occlusion Was Present and Absent.

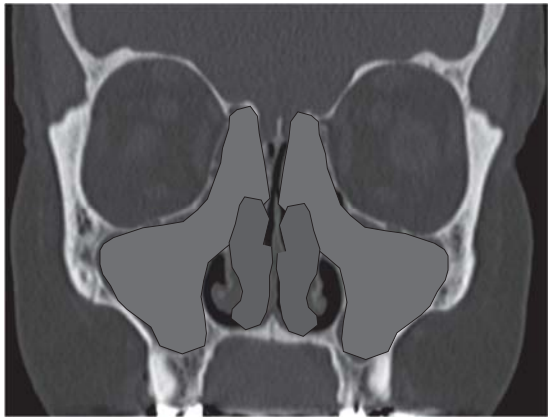
Mucosal Disease in Each Anterior Sinus	ECRS			Non-ECRS			CRSwNP			CRSsNP		
	OMC Occlusion			OMC Occlusion			OMC Occlusion			OMC Occlusion		
	Present (%)	Absent (%)	*P* Value	Present (%)	Absent (%)	*P* Value	Present (%)	Absent (%)	*P* Value	Present (%)	Absent (%)	*P* Value
Maxillary	100	100	NA	96.2	50	<.001	96.4	100	.39	100	52.6	<.001
Anterior ethmoid	94.6	90.5	.55	84.6	77.8	.56	89.3	90.0	.94	91.4	78.9	.19
Frontal	86.5	90.5	.65	84.0	52.9	.47	92.9	90.0	.72	64.7	55.6	.51

Statistical significance cannot be assessed when the event of mucosal disease is constant for OMC status.
CRSsNP = chronic rhinosinusitis without polyps; CRSwNP = chronic rhinosinusitis with polyps; ECRS = eosinophilic rhinosinusitis; NA = not applicable; OMC = ostiomeatal complex.

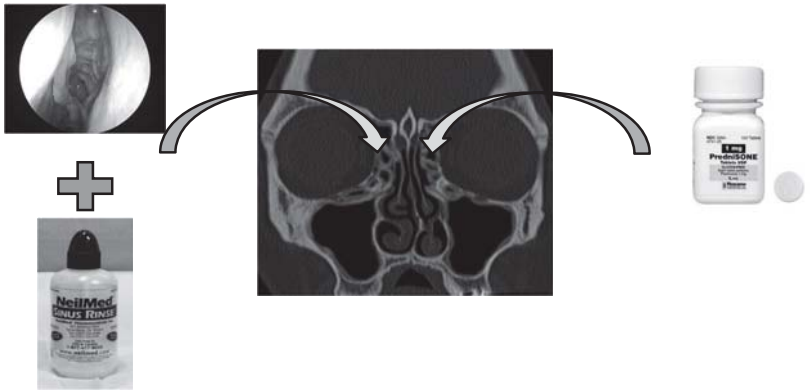


Leung R, etal AJRA 2011
Snidvongs K, etal Laryngoscope 2013

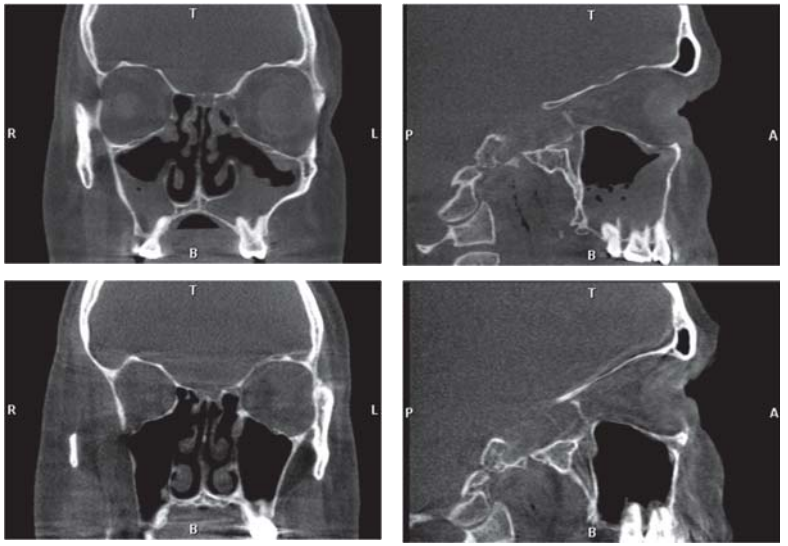
Ventilation ≠ access for topical treatments
Prior to successful ESS,
topical therapies are ONLY nasal cavity treatments



Where does our anti-inflammatory therapy need to go?



Access for topical treatments



Harvey RJ, Schlosser RJ. J OHNS, 2009

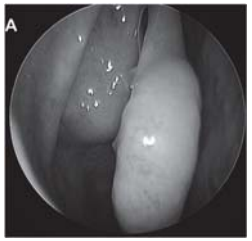
Impact of surgery

Surgical State	Findings
Unoperated	No consistent delivery regardless of device
Balloon	Sphenoid ⬆ Frontal ▬ Maxillary ⬇
ESS	Delivery increases especially with large volume
Endoscopic Lothrop or medial maxillectomy	Possible benefit

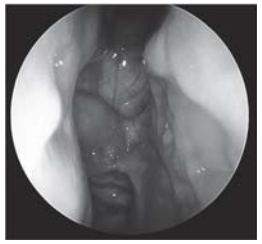
- Cadaver (n=5) and human studies (n=3)
- Conclusion: ESS optimal, critical os size 4-5 mm

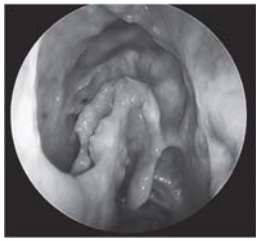
Thomas III, WT et al, IFAR 2013

What type of surgery is needed for postop topical therapies?



Balloon


FESS


Lothrop

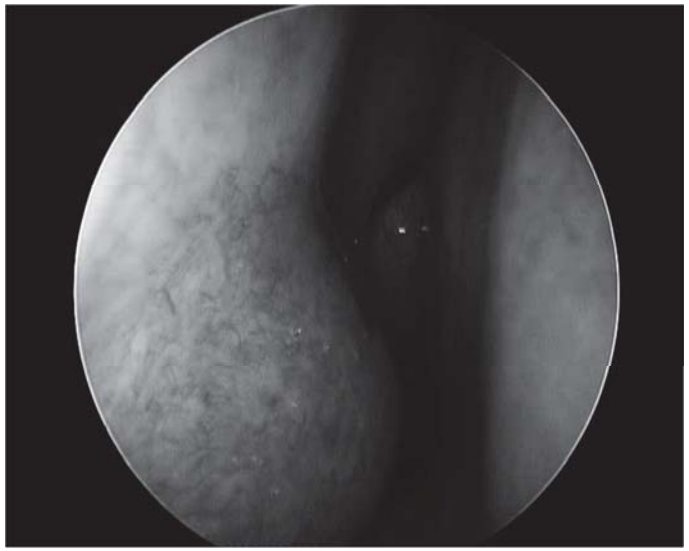
Impact of device

Device	Findings
Spray/Drops	Little sinus distribution with either technique. Some delivery to olfactory cleft/MT that may be position dependent.
Atomizer/ Nebulizer	Pulsating aerosols/nebs with some *limited* distribution to sinuses
Squeeze bottle/ Neti Pot	Larger volumes have best distribution

- Cadaver (n=5) and human studies (n=15)
- Recommend for: Large volume devices post ESS
- Recommend against: Low volume devices do not consistently reach sinuses

Thomas III, WT et al, IFAR 2013

Sprays



Large volume devices

Multi-purpose devices?

Impact of position

Position	Findings
Head upright	Inferior meatus with gtt
LHB (Mygind)	Middle meatus
LHL (Ragan)	Middle meatus
HDF (Mecca)	Increased superior distribution (Olfactory, limited ethmoid/max)

- Cadaver (n=3) & human (n=7) studies
- Recommend for: HDF with high volume devices
- Recommend for: LHB or LHL with drops and sprays

Thomas III, WT et al, IFAR 2013

Frontal distribution factors

TABLE 3. Irrigation distribution (of all irrigations performed) relative to head position in Draf IIa frontal sinusotomy or in Draf III procedure[a]

Grade	Distribution	Frankfort (%)	Vertex (%)
Draf IIa frontal sinusotomy			
0	Nasal cavity only	43.8	18.8
1	Frontal recess	37.5	0
2	Medial distribution	6.3	6.3
3	Lateral distribution	12.5	50
4	Frontal lavage	0	25

[a]Kendall's tau-b was used for ordinal values; p value (Kendall's tau-b) <0.001.

Barham H, etal, IFAR 2016

Which active agent ?

- Mechanical
  - Saline
  - Baby Shampoo
- Pharmaceutical
  - Steroids
  - Antibiotic
    - Mupirocin
    - Gentamycin / Tobramycin
    - Ampho B
  - Novel agents
    - Honey
    - Surfactants
    - Dornase Alpha

Safety and proper dose of steroids

- What % of topical steroid remains?
  - Spray, gtt, atomizer, nebs: Likely 100%
  - Rinses different story
- What is safe dose?

How much solution remains in the sinuses?

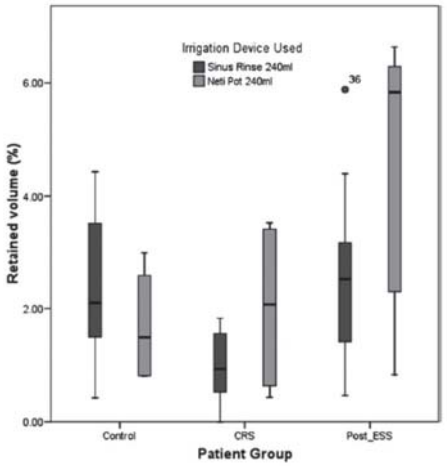


Figure 3 The effect of the irrigation device was nonsignificant among patient groups.

2.5±1.5%

Benefit to patient

Safety of budesonide irrigations

- Respules (1mg/2ml) QD = 1 mg/day
- 3% retained volume = 30 mcg drug
- Rhinocort: 32 mcg/spray=128 mcg/day

- Current irrigations are about ¼ dose of topical spray!
- Probably doesn't apply to drops or sprays which have higher retention

Safety of steroid rinse

- Calgary: 35 pts BUD 1mg bid rinse x minimum 12 mos (mean of 38 mos)
  - Serum cortisol then cosyntropin
  - No HPA suppression
- Stanford: 48 pts, BUD 0.5-1mg qd
  - 23% with abnormal cosyntropin stim
  - Risk factor: BUD rinse + spray + inhaler

Smith KA, etal IFAR 2016
Soudry E, etal IFAR 2016

Systemic side effects of intranasal steroid spray

- Dexamethasone (0.132%) 2 sprays ea nostril bid x 6 wks = 800 mcg per day
- 10/22 pts with suppressed serum cortisol
- No evidence of ocular hypertension

- Betamethasone gtt (800 mcg qd x 6 weeks) caused HPA suppression

Martino BJ etal, IFAR 2015
Gazis AG, Clin Oto 1999

What about efficacy of topical steroid?

Postop mometasone irrigations

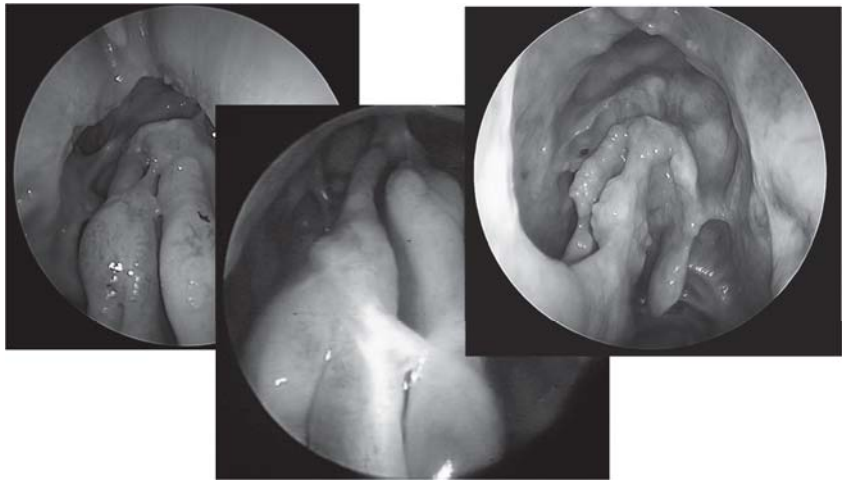
- N=44 pts sNP or wNP; blinded, randomized
- MOM 2mg qd spray (10x normal dose) vs 2mg qd rinse
- Followed 1 yr

TABLE 3. The comparison of results between baseline and 12 months*

	Intervention		
	Active spray	Active irrigation	*p*
n	23	21	
Δ VAS	−21.14 ± 14.75	−28.67 ± 17.00	0.213
Δ Blockage VAS	−36.12 ± 42.94	−69.91 ± 29.37	0.029[a]
Δ SNOT-22	−31.62 ± 21.95	−29.26 ± 13.65	0.725
Δ Global	+6.07 ± 3.94	+7.31 ± 2.68	0.347
mLKS endoscopy	21.77 ± 23.37	7.33 ± 11.55	0.018[a]
Δ Radiology (LMS)	−7.39 ± 6.94	−12.07 ± 4.43	0.031[a]

Harvey RJ etal, IFAR 2018

All CRSwNP treated similarly: Big hole ESS, steroid irrigations



Other delivery methods for topical steroids

- Unable to tolerate large volume
- Pediatric patients

Efficacy of steroid gtt

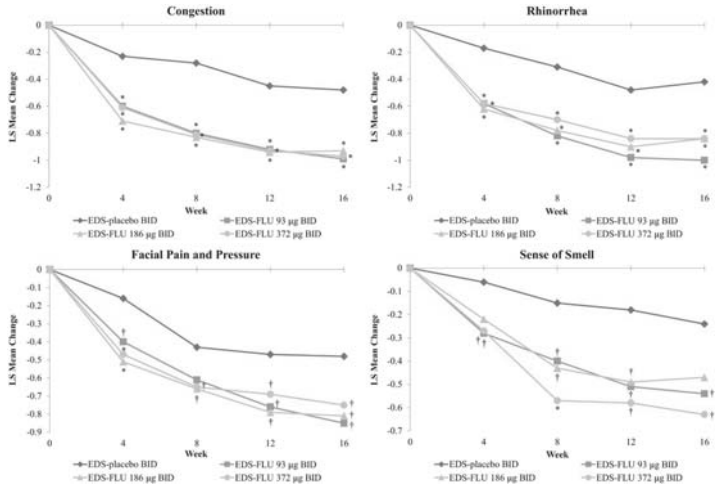
- 54 patients, failed med Rx including INCS x 3 mos were scheduled for ESS
- DBPCRCT of fluticasone gtt (400 µg) head hanging x 2 min x 12 weeks
- FP gtt improved nasal blockage, rhinorrhea, olfaction, endoscopy, PNIF
- NSD HA, PND, pain, CT

Aukema AAC, etal JACI 2005

Alternative delivery

Sagittal plane | Exhalation delivery system | Transverse plane

Leopold D, etal JACI 2019



Options for frontal sinusitis

- Ethmoidectomy ± balloon
- Frontal sinusotomy (Draf IIA)
- Extended frontal (Draf IIB or Lothrop)

Ethmoidectomy for frontal sinusitis

- Pts with at least partial opacification of one frontal on CT
  - N=196 frontal sinusotomy v 30 w/o sinusotomy
- Frontal sinusotomies: More NP, worse endo/CT, prior ESS, AERD.
- Also associated with more extensive surgery, SMRIT and MT resection

Abuzeid W, etal, IFAR 2016

Ethmoidectomy for frontal sinusitis

- Similar baseline SNOT22, med usage except for topical steroid gtt/rinse
- Similar SNOT22 and med usage outcomes at 1 yr
- Conclusion: Pts with frontal sinusitis who do not have NP, asthma, AERD and are undergoing primary ESS, ethmoidectomy is reasonable option

Abuzeid W, etal, IFAR 2016

We are doing more frontal surgery

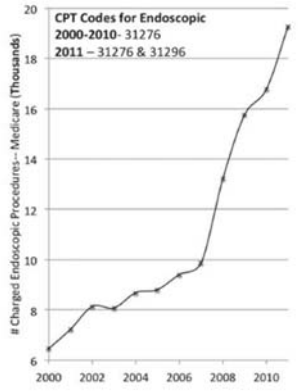
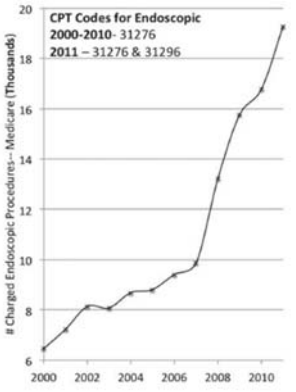


FIGURE 1. Total number of endoscopic frontal sinus procedures billed to Medicare annually. Note that balloon dilation did not have its own separate code until 2011. CPT = Current Procedural Terminology.

Svider etal, IFAR 2015

But is more better?



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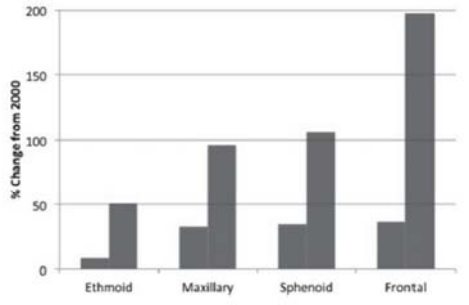


FIGURE 3. Percent increase from 2000 in the number of endoscopic procedures billed to Medicare, organized by anatomic location. Left (light blue) bars represent percent change from 2000–2005, right (Red) bars represent percent change from 2000–2011.

Svider etal, IFAR 2015

Rates of frontal sinus surgery

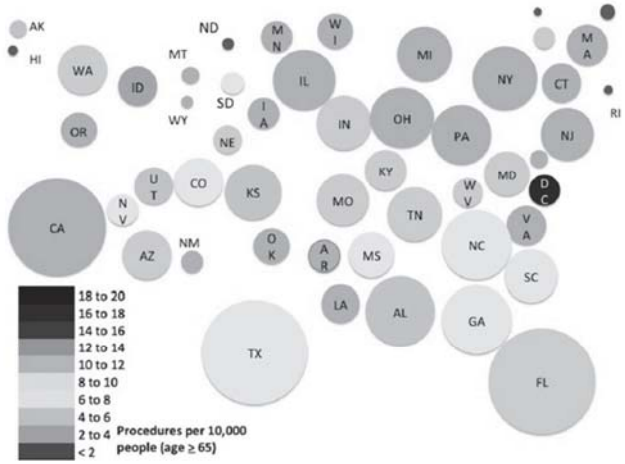


FIGURE 4. Dorling Cartogram illustrating rate of endoscopic frontal sinus surgery (shading key at inset, based on population over 65 years of age in each state as per 2010 U.S. Census). Area of each circle proportion to total number of endoscopic frontal sinus procedures (CPT 31276) performed in each state in 2010 among Medicare population. CPT = Current Procedural Terminology.

Svider etal, IFAR 2015

Extent of surgery

- Complete (all 8 sinuses) vs targeted ESS
- 311 pts at least 6 mo f/u
- Complete ESS: Higher NP, asthma, AERD, revision
- After controlling for those variables, complete ESS had nearly 6 pt greater improvement on SNOT22

- What about Lothrops?

DeConde A etal, IFAR 2015

Goals of Lothrop for CRS?

- Drug delivery
- Removal of mucin, polyps, bone, scar

Lothrop vs full house FESS

- N=338 patients, ESS=199, EMLP=139
- NP recurrence: 44% at 1 year, persisted in 23%

Primary site of recurrence	Frequency
Frontal recess	55%
Ethmoid	38%
Maxillary	3%
Olfactory cleft	2%
Middle meatus	2%

Bassiouni, Laryngoscope 2013

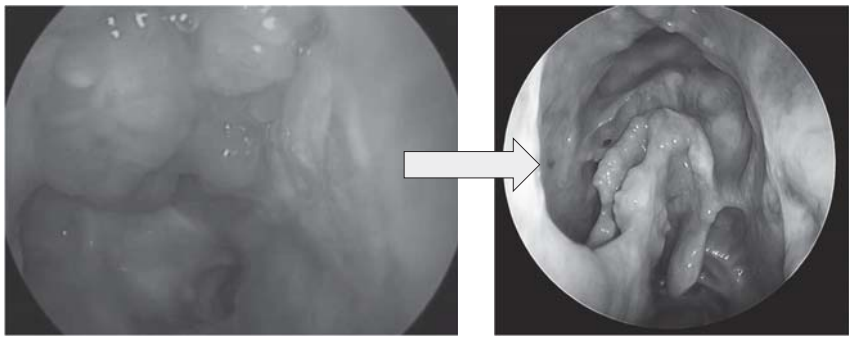
Lothrop vs full house FESS

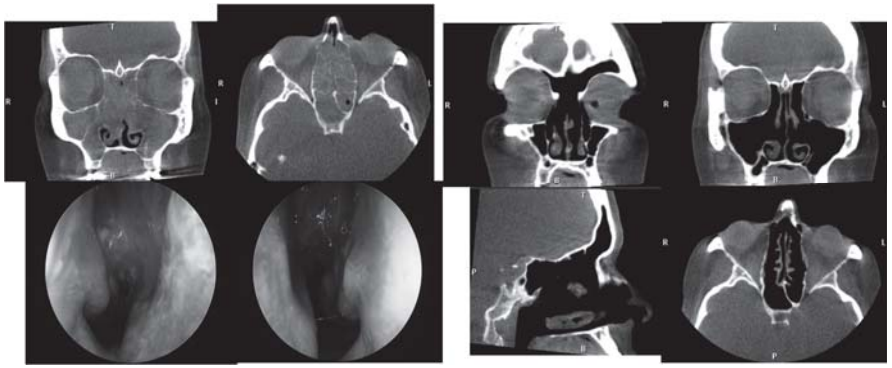
- N=338 patients: ESS=199, EMLP=139

Persistent NP (>3 mos)			
	ESS	Lothrop	P
All pts	26%	16%	0.150
Asthmatic	40%	16%	0.007
AERD	55%	11%	0.011

Bassiouni, Laryngoscope 2013

Should we just do EMLPs on all CRSwNP patients?





Harvey RJ, Kalish L, Oakley G, Christensen CL, Snidvongs K, Sacks R. Irrigation based corticosteroid therapy is more effective than simple sprays in managing post-surgical chronic rhinosinusitis: a randomized controlled trial. International Forum of Allergy & Rhinology 2016; in submission.

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The argument against routine EMLPs

Persistent NP (>3 mos)			
	ESS	Lothrop	P
All pts	26%	16%	0.150
Asthmatic	40%	16%	0.007
AERD	55%	11%	0.011

90% EMLPs would not be beneficial

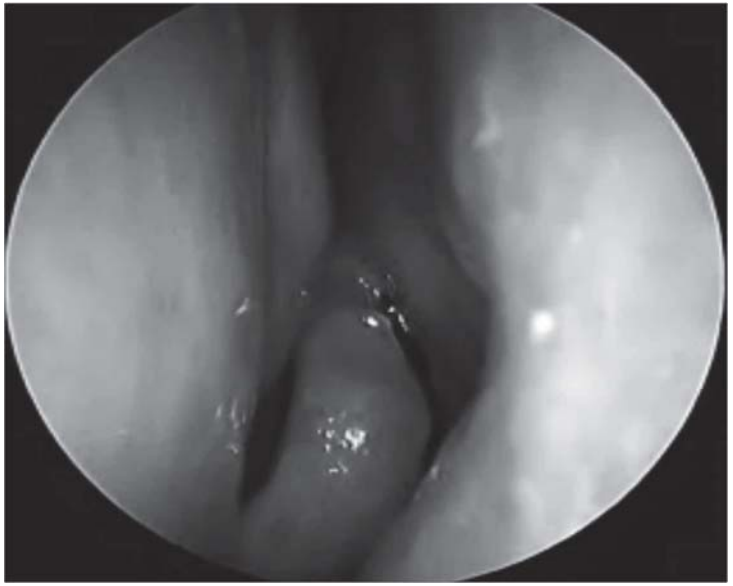
Bassiouni, Laryngoscope 2013

The argument against routine EMLPs

Persistent NP (>3 mos)		
	ESS	Lothrop
All pts	26% (30/113)	16% (12/72)
Asthmatic	40% (27/67)	16% (8/48)
Non-asthmatics	6.5% (3/46)	16% (4/24)

Bassiouni, Laryngoscope 2013

"Good" CRSwNP 3 yrs postop, no Rx

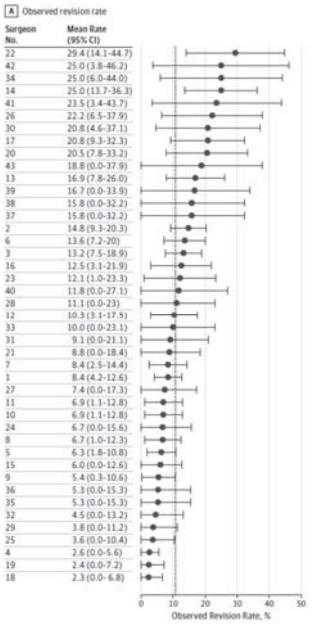


What about additional procedures?

- Septoplasty
- Turbinates

Surgeon defined: Variable Canadian ESS outcomes

- 43 surgeons in Alberta
- 5 year revision ESS rates
- Vary from 2.4% to 28.6%



Rudmik L, etal, JAMAOto 2017

Patient factors Revision ESS rates

Variables	Odd Ratio	95% CI	P value
Age	**0.568**	**0.39-0.83**	**0.003**
Sex	1.019	0.79-1.31	0.88
Geographic region (Urban/Rural)	1.203	0.90-1.61	0.21
Nasal polyps	**2.069**	**1.59-2.70**	**< 0.001**
Allergy	1.056	0.83-1.34	0.65
Asthma	1.032	0.67-1.59	0.89
Regression diagnostic	c-statistic = 0.716		

Rudmik L, etal, JAMAOto 2017

Variability in surgeon outcomes
Alberta, Canada 5 yr revision ESS rates

Surgeon ID	Adjusted mean 5-year ESS re-operation rate (95% CI)	Proportion of Nasal polyps
Top Performing Surgeons		
4	3.1% (0 – 9.0)	72.8%
18	1.8% (0 – 9.8)	73.2%
	Mean	**73%**
Lowest performing surgeons		
14	17.7% (11.3 – 24.2)	91.1%
17	23.0% (14.1 – 31.9)	22.9%
22	24.1% (15.2 – 32.9)	38.2%
26	22.7% (11.6 – 33.9)	74.1%
34	24.2% (11.2 – 37.0)	85.0%
40	28.6% (12.5 – 44.6)	47.1%
42	27.8% (11.9 – 43.6)	75.0%
	Mean	**61.9%**

Rudmik L, etal, JAMAOto 2017

Surgeon factors
Revision ESS rates

Variables	Odd Ratio	95% CI	P value
Age	**0.568**	**0.39-0.83**	**0.003**
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Nasal polyps	**2.069**	**1.59-2.70**	**< 0.001**
Allergy	1.056	0.83-1.34	0.65
Asthma	1.032	0.67-1.59	0.89
Annual quantity of topical INS (# bottles)	1.012	0.95-1.08	0.73
Annual quantity of oral antibiotic (# courses)	**1.087**	**1.01-1.17**	**0.03**
Annual quantity of oral corticosteroid (# courses)	**1.329**	**1.19-1.48**	**< 0.001**
Concurrent septoplasty	**0.695**	**0.55-0.89**	**0.001**
Number of ENT visits prior to ESS	1.191	1.03-1.39	0.02
Surgeon volume (primary ESS cases)	1.002	0.99-1.01	0.55
Frontal sinusotomy (surrogate for complete ESS)	1.277	0.99-1.64	0.05
Regression diagnostic	c-statistic = 0.716		

Rudmik L, etal, JAMAOto 2017

Variability in surgeon outcomes
Alberta, Canada 5 yr revision ESS rates

Surgeon ID	Adjusted mean 5-year ESS re-operation rate (95% CI)	Proportion of Nasal polyps	Annual number of systemic corticosteroid courses			Rate of Concurrent Septoplasty
			1	2	≥ 3	
Top Performing Surgeons						
4	3.1% (0 – 9.0)	72.8%	11.4	1.8	2.6	94.7%
18	1.8% (0 – 9.8)	73.2%	23.3	4.7	7.0	82.9%
	Mean	**73%**	**17.4**	**3.2**	**4.8**	**88.8%**
Lowest performing surgeons						
14	17.7% (11.3 – 24.2)	91.1%	16.1	3.6	1.8	44.6%
17	23.0% (14.1 – 31.9)	22.9%	2.1	0.0	0.0	75.0%
22	24.1% (15.2 – 32.9)	38.2%	5.9	5.9	5.9	70.6%
26	22.7% (11.6 – 33.9)	74.1%	3.7	3.7	7.4	66.7%
34	24.2% (11.2 – 37.0)	85.0%	10.0	0.0	0.0	20.0%
40	28.6% (12.5 – 44.6)	47.1%	23.5	5.9	0.0	70.6%
42	27.8% (11.9 – 43.6)	75.0%	0.0	0.0	0.0	37.5%
	Mean	**61.9%**	**8.8**	**2.7**	**2.2**	**55.0%**

Rudmik L, etal, JAMAOto 2017

Another study showing benefit of septoplasty!

TABLE VIII.
Unadjusted Mean SNOT-22 Total Score Improvement Across Enrollment Site and Septoplasty Groups.

Enrollment Site	Septoplasty	No Septoplasty	*P* Value
no. 1 (n = 76)	−29.5 [17.7]	−18.8 [23.2]	0.150
no. 2 (n = 76)	−31.8 [17.7]	−23.0 [16.3]	0.056
no. 3 (n = 76)	−31.5 [18.6]	−26.3 [22.3]	0.170
ALL (n = 228)	−31.3 [18.0]	−21.9 [21.2]	0.001

N = sample size; SNOT-22 = 22-Item SinoNasal Outcome Test.

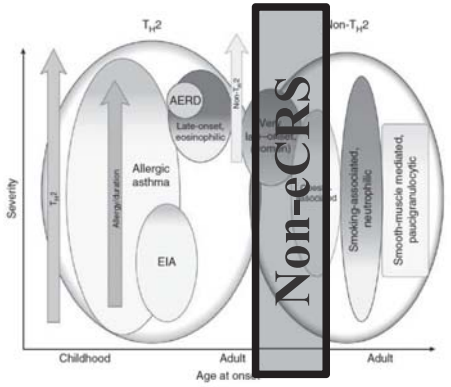
CT analysis of septal deviation unable to predict sx or performance of septoplasty (unpublished)

Rudmik L, etal, JAMAOHNS 2017
Smith TL, etal, Laryngoscope 2017

Failure of "routine care"

- Failed maximal medical therapy
- Fails complete ESS and steroid rinses

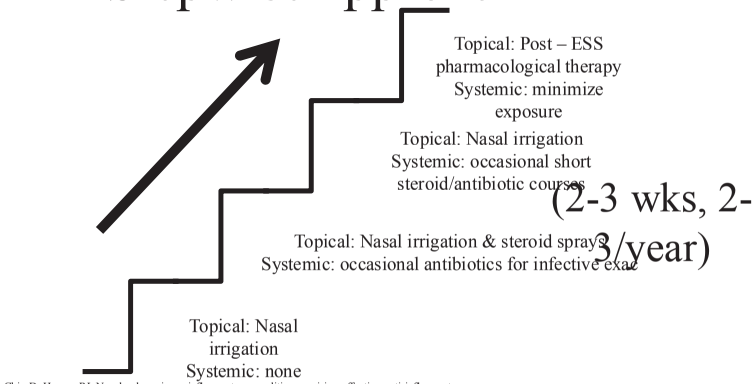
- Now what?



Wenzel SE. Asthma phenotypes: the evolution from clinical to molecular approaches. Nat Med 2012; 18:716-725.

Shifting from systemic control to regular local control

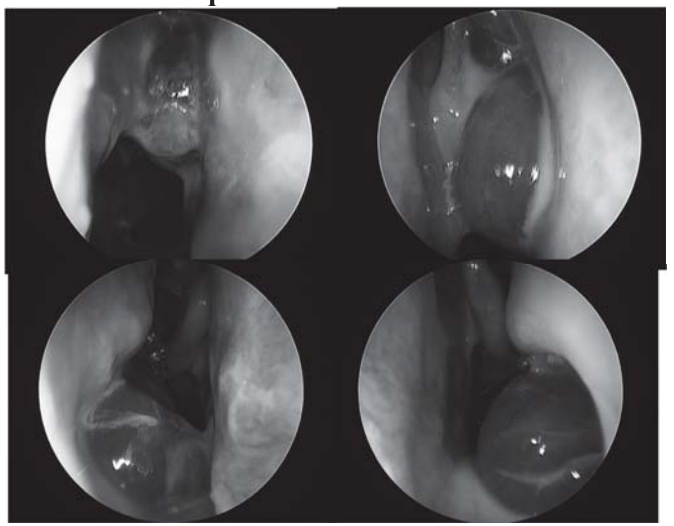
Stepwise approach



Chin D, Harvey RJ. Nasal polyposis: an inflammatory condition requiring effective anti-inflammatory treatment. Current opinion in otolaryngology & head and neck surgery 2013; 21:23-30.

Another case of CRSwNP:

50yo F 3mos post ESS and steroid rinse



Clinical *mojo: non-eCRS phenotype*

- Middle aged
- Female
- Obese
- Polyps less common
- Low IgE
- Corticosteroid insensitive (cf)

but can we be more scientific....

MICROSCOPIC:

1. and 2.
Sections show polypoidal oedematous and fibrous tissue with seromucinous glands lined by ciliated respiratory epithelium. A predominant lymphoplasmacytic infiltrate near the surface is present together with scattered eosinophils. Focal ulceration is seen in specimen (1) with associated neutrophils. The basement membrane is within normal limits. No organisms are seen on silver stain. There is no evidence of malignancy. The features are consistent with allergic/inflammatory polyps with background chronic rhinosinusitis.

SYNOPTIC REPORT FOR CHRONIC RHINOSINUSITIS

Tissue:
Tissue present:: Respiratory mucosa
Overall degree of inflammation: Moderate to focally severe
Eosinophil count: <10 per HPF
Neutrophil infiltrate: Focal
Inflammatory predominance: Lymphoplasmacytic

Basement Membrane Thickening: <7.5 micron (normal)
Subepithelial oedema: Severe (diffuse/polypoid change)
Hyperplastic/papillary change: Present
Mucosal ulceration: Present (spec 1) (with reactive changes)
Squamous metaplasia: Absent
Fibrosis: Partial

Mucin:
Fungal Elements: Absent
Charcot-Leyden Crystals: Absent
Eosinophil Aggregates: Absent

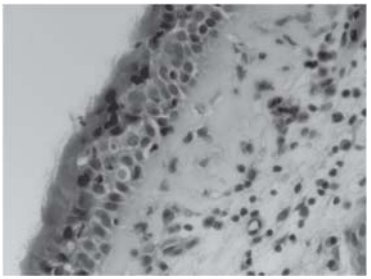
DIAGNOSIS:

1. and 2.
RIGHT AND LEFT SINUS TISSUE BIOPSY - ALLERGIC/INFLAMMATORY POLYPS

Reported by Dr Alexandra Allende (0298556251)

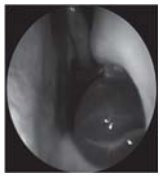
Supervising Pathologist:

NATA Accreditation No 2178

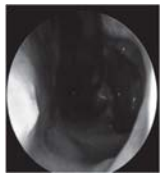


Macrolide responders

- Pts (N=28) failed complete ESS, steroid rinses x 3 mos
- Placed on clarithromycin x 3 mos
- Definition of macrolide responder
  - ≥ 3 month post-macrolide therapy endoscopy with normal or near-normal mucosa (19/28 = 68%)



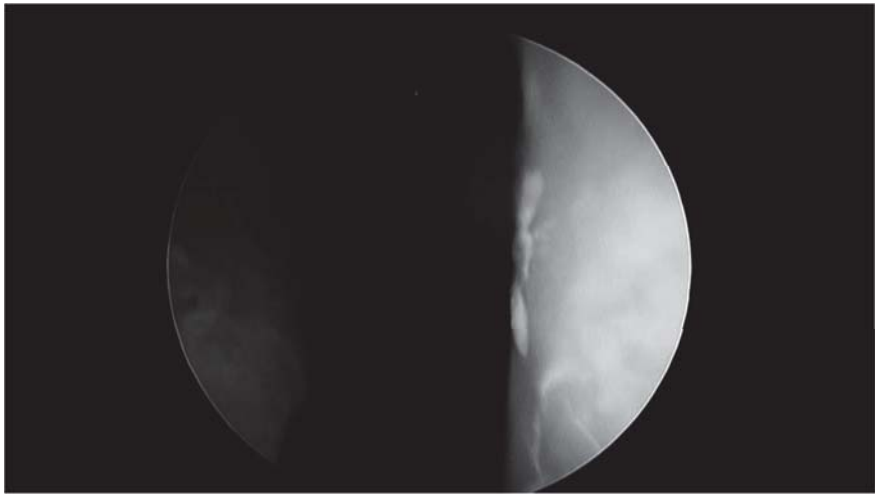
Pre-macrolide Rx



Post-macrolide Rx

Oakley GM, etal. *Rhinology* 2017.

3mth post macrolide



Results

	Macrolide responder	Macrolide non-responder	P-value
N	19	9	
Age at surgery (years), mean ± SD	53.4 ± 10.4	56.0 ± 22.2	0.68
Gender (female)	57.9%	22.2%	0.11
Smoking	0%	0%	n/a
Asthma	31.6%	22.2%	1.0
Allergy	46.7%	50.0%	1.0
Revision	57.9%	100%	0.03
SNOT-22 (mean ± SD)	2.3 ± 0.77	1.4 ± 1.2	0.04
NSS (mean ± SD)	2.5 ± 1.1	2.2 ± 1.6	0.08

Results

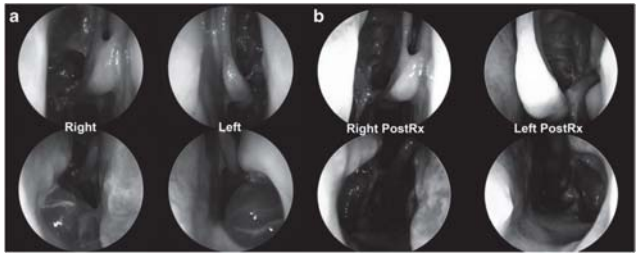
	Macrolide responder	Macrolide non-responder	P-value
Serum eosinophilia (10^9/L)	0.16 ± 0.11	0.39 ± 0.36	0.03
Serum neutrophilia (10^9/L)	4.3 ± 2.4	3.8 ± 2.2	0.67
Preoperative IgE (IU/mL)	79.4 ± 82.3	90.0 ± 96.3	0.79
Tissue eosinophil count (% >10/HPF)	17.7	62.5	0.02
Tissue neutrophil infiltrate (%focal/diffuse)	58.8	37.5	1.0
Squamous metaplasia (%present)	0	37.5	0.02
Basement membrane thickening (% with >7.5µm)	56.3	37.5	0.71
Fibrosis (% with extensive)	5.9	25.0	0.42
Subepithelial edema (% with severe)	18.8	12.5	0.43

Characteristics of macrolide appropriate CRS patient

Lack of tissue eosinophilia	More likely to have IL8-driven inflammation
Lack of serum eosinophilia	A high serum eosinophilia has a high PPV for tissue eosinophilia
Low serum IgE	Poly-IgE production associated with nasal polyposis and macrolides demonstrate effect in subgroup within RCT
Broader lower airway disease not responsive	IL8-driven disease mostly likely occurring across entire airway. Persistent upper airway 'only' disease more likely to reflect local factors
Absence of squamous metaplasia	Permeant remodeling and irreversibility of mucociliary function probably not going to improve with immunomodulation.
Lack of childhood asthma	Likely allergic or IgE-mediated association
Lack of skin or conjunctival symptoms	Atopic predispositions more likely to be associated with these organs involved.
Poor systemic corticosteroid response	Suggests non-eosinophilic disease. Lack of topical response is not the equivalent as many factors contribute to poor local effectiveness.

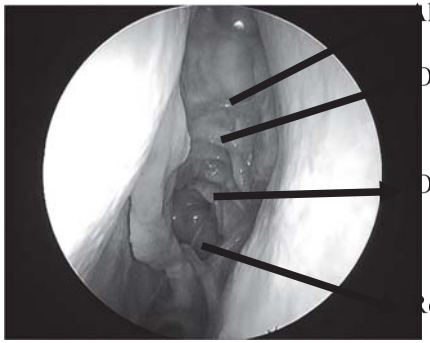
CRS chronic rhinosinusitis, *IgE* immunoglobulin E, *IL-8* interleukin-8, *CS* corticosteroids, *RCT* randomized controlled trial

Oakley GM etal CurrAllerAsthma Rep 2017



Oakley GM etal CurrAllerAsthma Rep 2017

For the inflammatory patient……

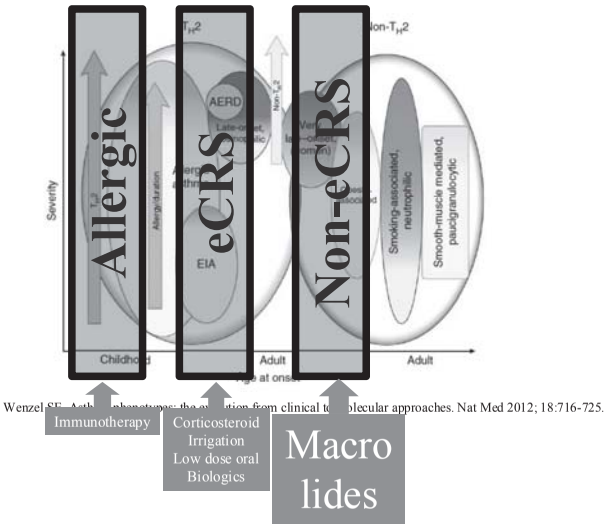


Allows topical access

Overcomes mucostasis (with irrigation)

Overcomes obstructive phenomenon

Reduces inflammatory load

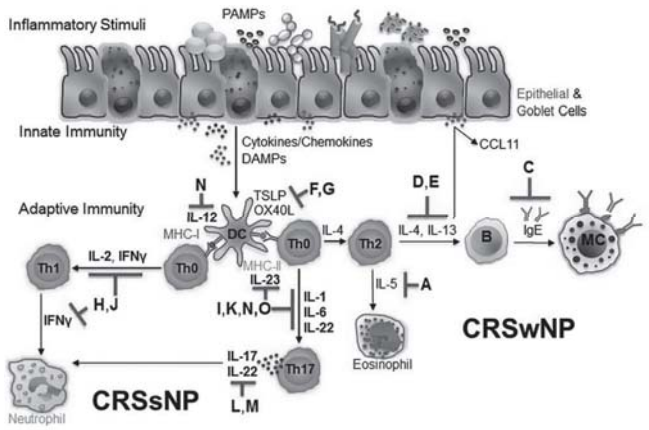


Wenzel SE. Asthma phenotypes: the evolution from clinical to molecular approaches. Nat Med 2012; 18:716-725.

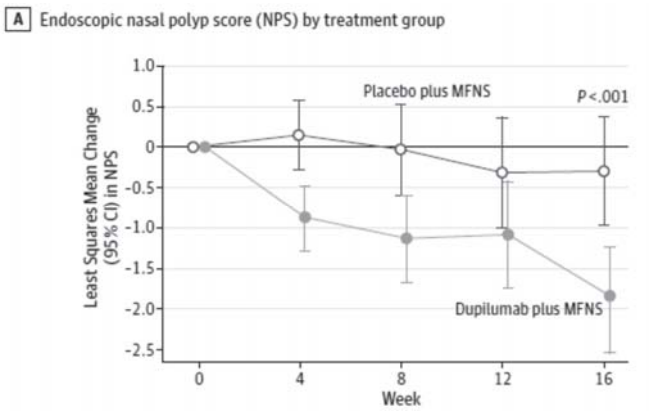
Biomarkers and monoclonals

- Serum IL5 and IgE not predictive of response to respective monoclonals
- 60% mepolizumab pts respond independent of blood eos
- Omalizumab works equally well in allergic and non-allergic
- Also unclear if changes in serum biomarkers important for clinical response
- Dupi reduced serum IgE but not eos (unpublished)

Bachert JACIPrac 2017



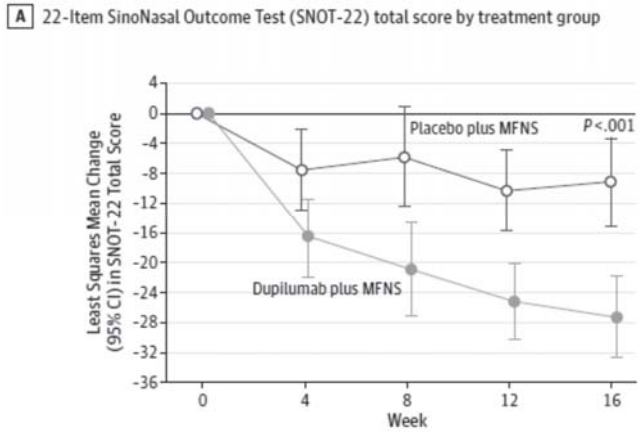
Dupilumab and CRSwNP



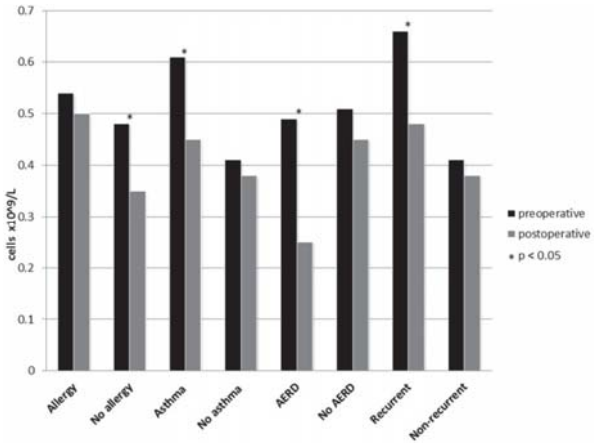
- 25% dupi pts with no change in NP score

Bachert etal, JAMA 2016

Dupilumab and CRSwNP

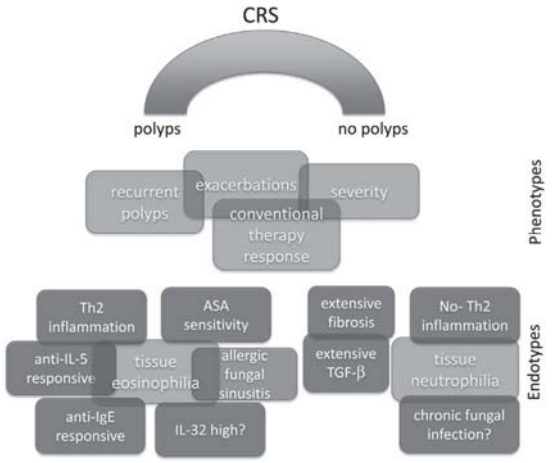


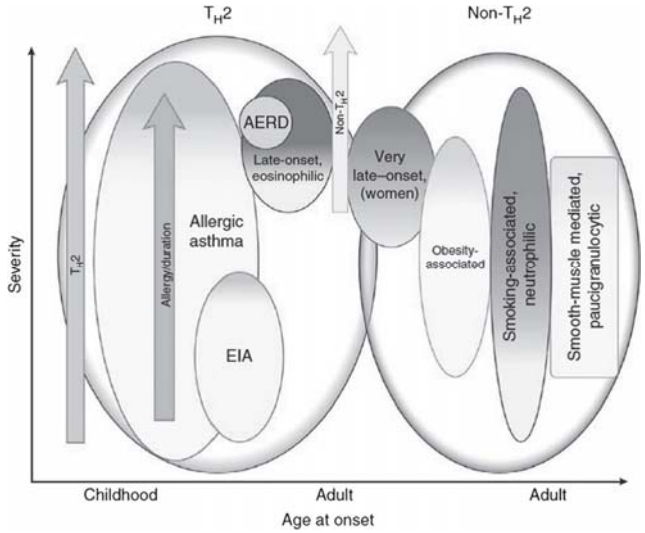
Bachert etal, JAMA 2016



Brescia G, etal AJRA 2018

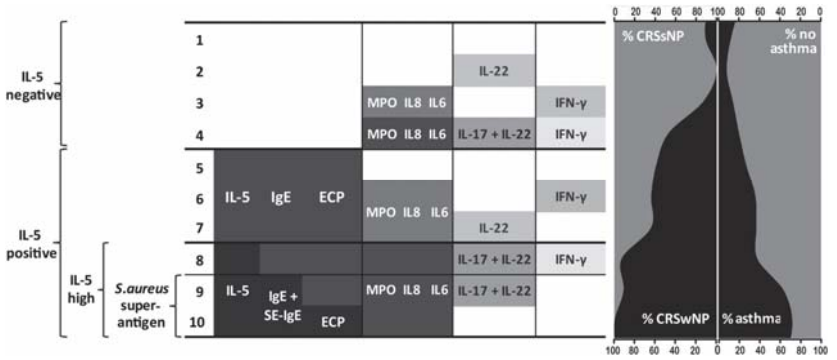
Will use of endotypes improve prognosis and success?





Oakley GM etal CurrAllerAsthma Rep 2017

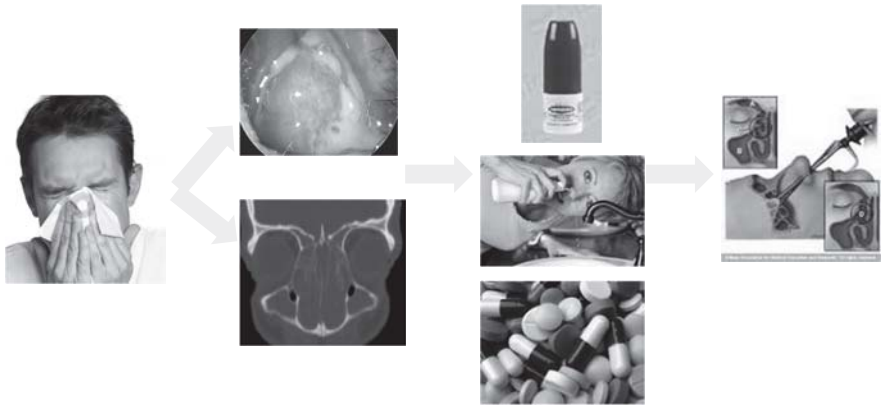
Clustering of endotypes



- Cross sectional, preop patients
- No QOL/symptom or prognostic information

Tomassen etal, JACI 2016

Our current CRS treatment algorithm

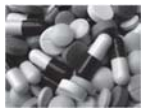


The future?

Phenotype

Endotype Biomarkers

OR



Conclusion: Personalized NP Rx

- Medical Rx: Steroids for eoNP (serum eo's)
- Standard complete ESS probably best initial surgery with postop steroid rinses
- Lothrop for AERD or ESS failures
- Non-eosinophilic NP may benefit from macrolides
- Stay tuned for biologics!

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MUSC MEDICAL UNIVERSITY of SOUTH CAROLINA

9th Annual Otolaryngology Literature Update
Pediatric Otolaryngology I

Christopher M. Discolo, M.D., MSCR
Associate Professor
Pediatric Otolaryngology
Medical Director, Craniofacial Anomalies and Cleft Lip & Palate Team
Department of Otolaryngology - Head & Neck Surgery
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Christopher M. Discolo, M.D., MSCR, joined the MUSC Department of Otolaryngology – Head and Neck Surgery and MUSC Children's Hospital in July 2008. Prior to joining MUSC, Dr. Discolo worked in the Section of Pediatric Otolaryngology within the Head and Neck Institute of the Cleveland Clinic. He completed a fellowship in Pediatric Otolaryngology at the University of Minnesota in 2006. While in Minnesota, Dr. Discolo trained under James Sidman, M.D., and participated in one of the only pediatric fellowships providing extensive training in cleft lip and palate surgery.

Dr. Discolo grew up on Long Island, N.Y., and graduated summa cum laude from Concordia College where he also played on the baseball team. In 1999, he graduated from medical school at the State University of New York Health Science Center at Brooklyn. He then traveled to Ohio to complete a residency in Otolaryngology – Head and Neck Surgery at the Cleveland Clinic. After completing a fellowship in Minnesota, he returned to the Cleveland Clinic for two years prior to joining MUSC. Dr. Discolo received board certification from the American Board of Otolaryngology in 2006 and is a fellow of the American Academy of Otolaryngology – Head and Neck Surgery.

Dr. Discolo's practice focuses entirely on the care of children. Although he cares for children with all types of ear, nose and throat problems, he has particular expertise in cleft lip and palate repair and care of children with these and other craniofacial anomalies. Other examples of his specialty areas include distraction osteogenesis, management of airway problems, head and neck masses, speech and swallowing disorders, sinus disease, and sleep apnea.

Dr. Discolo has published numerous papers and book chapters on diseases of the head and neck and has given presentations on the local, regional and national level. He is active within the American Academy of Otolaryngology – Head and Neck Surgery. He has also received a Master's Degree in Clinical Research from the MUSC Department of Biometry and Epidemiology, obtaining his degree in 2010.

9th Annual Otolaryngology Literature Update
Medical University of South Carolina

Pediatric Otolaryngology I

Christopher M . Discolo, M.D. MSCR

Baik G, Brietzke SE. "Comparison of Pediatric Intracapsular Tonsillectomy and Extracapsular Tonsillectomy: A Cost and Utility Decision Analysis." Otolaryngology-- Head & Neck Surgery. 2018 Jun;158(6):1113-1118. doi: 10.1177/0194599818760513. Epub 2018 Feb 27.

Chamseddin BH, Johnson RF, Mitchell RB. "Obstructive Sleep Apnea in Children with Down Syndrome: Demographic, Clinical, and Polysomnographic Features." Otolaryngology-- Head & Neck Surgery. Otolaryngol Head Neck Surg. 2019 Jan;160(1):150-157. doi: 10.1177/0194599818797308. Epub 2018 Aug 28.

Coppess S, Padia R, Horn D, Parikh SR, Inglis A, Bly R, Dahl J, Dudley D, Johnson K. "Standardizing Laryngeal Cleft Evaluations: Reliability of the Interarytenoid Assessment Protocol." Otolaryngology-- Head & Neck Surgery. 2019 Mar;160(3):533-539. doi: 10.1177/0194599818806283. Epub 2018 Oct 16.

Duncan DR, Mitchell PD2, Larson K, McSweeney ME, Rosen RL. "Association of Proton Pump Inhibitors With Hospitalization Risk in Children With Oropharyngeal Dysphagia." JAMA Otolaryngology-- Head & Neck Surgery. 2018 Oct 11. doi: 10.1001/jamaoto.2018.1919. [Epub ahead of print].

Kumar S, Choi S, Gupta SK. "Eosinophilic Esophagitis-A Primer for Otolaryngologists." Rhinology. 2019 Feb 21. doi: 10.1001/jamaoto.2018.4177. [Epub ahead of print].

Liming BJ, Ryan M, Mack D, Ahmad I, Camacho M. "Montelukast and Nasal Corticosteroids to Treat Pediatric Obstructive Sleep Apnea: A Systematic Review and Meta-analysis." Otolaryngology-- Head & Neck Surgery. 2019 Apr;160(4):594-602. doi: 10.1177/0194599818815683. Epub 2018 Dec 4.

Pediatric Otolaryngology

Chris Discolo, MD
Associate Professor
Director – Cleft Lip & Palate Team

JAMA Otolaryngology–Head & Neck Surgery | Review

Eosinophilic Esophagitis—A Primer for Otolaryngologists

Sanjay Kumar, MD; Sukgi Choi, MD; Sandeep K. Gupta, MD

- Why I chose this article
  - Eosinophilic esophagitis (EoE) is being increasingly recognized
    - Significant increase in published literature over 20 years
  - Likely remains under-diagnosed condition
    - Symptoms can be vague and nonspecific
  - Although technically a primary esophageal problem
    - Often has extra-esophageal symptoms
    - Enter the Otolaryngologist as the first specialist
    - Extra-esophageal symptoms are very common in younger children
    - Up to 15% of children with EoE may come to ENT first

EoE - Facts

- Prevalence of up to 1 in 1000 in western countries
  - As prevalent as inflammatory bowel disease
  - Uncertain if increased numbers represent actual increased incidence of disease or just better recognition/diagnosis
- Children with EoE are more likely to have ENT procedures such as T&A and ear tubes
- Up to 7% of adults who have EGD with biopsies have EoE on pathology
  - Number goes up to 22% if indication for EGD is dysphagia
- Up to 33% of adults who present with food impaction have EoE

EoE - Facts

- Bimodal incidence with peaks between the following ages
  - 5 – 10 years of age
  - 4th decade of life
- Males are 3 – 4 times more commonly affected
- Higher incidence in white individuals and the following…
  - Asthma
  - Eczema
  - Rhinitis
  - Food allergies

Eosinophils

- Present throughout the GI tract but NOT to any great extent within the esophageal epithelium

Box. Differential Diagnoses of Esophageal Eosinophilia

Gastroesophageal reflux disease
Eosinophilic esophagitis
Proton pump inhibitor–responsive esophageal eosinophilia
Celiac disease
Crohn disease
Hypereosinophilic syndrome
Achalasia
Vasculitis, pemphigus, connective tissue disease
Infections (viral, fungal)
Graft-vs-host disease
Drug injury

Pathogenesis (Simplified)

- Thought to be complex interplay (genetics, environment, etc)
- Likely a Th2-mediated response (similar to other allergies)
- Food or aero-allergen triggers Th2 response
  - Cytokines released ----- barrier function disrupted
  - Eosinophils recruited to microenvironment
  - Release of granule proteins leads to damage and inflammation
- Persistent inflammation ----- remodeling changes
  - Basal cell hyperplasia, fibrosis of lamina propria

Clinical Presentation

- Varies by age
- Younger patients
  - Vague symptoms that can mimic GERD
  - Feeding difficulties
  - Vomiting
  - Failure to develop normal eating habits
  - Choking with meals
  - Failure to thrive (less common)
- Adolescents – dysphagia and food impactions

Presentation – Association with Allergy

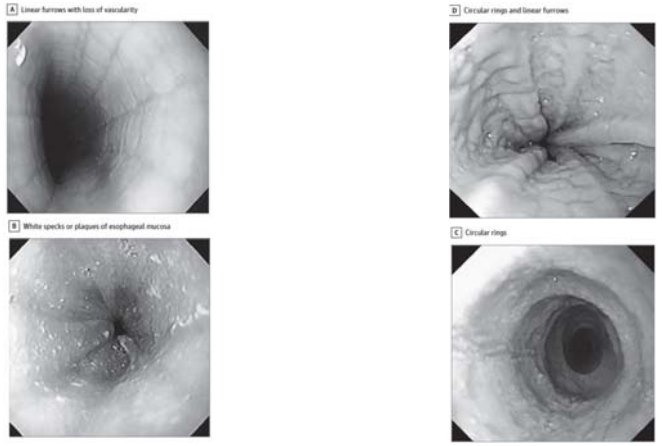
- Strong association between EoE and
  - Food allergies
  - Environmental allergies
  - Atopic dermatitis
  - Asthma
- Atopy reported in over 50% of individuals with EoE
- More than 70% of children with EoE have family history of atopy and 6% have family history of EoE

Presentation – Head and Neck Symptoms

- Rhinosinusitis
  - Reported in up to 25% of children with EoE
- Laryngeal
  - Chronic cough
  - Recurrent croup
  - Hoarseness
  - Dysphonia
- EoE has been implicated in failed airway reconstruction
  - Some centers evaluate for EoE prior to consideration of airway reconstruction

Evaluation

- EGD with biopsy is current gold standard
- Several endoscopic features have been described…



Evaluation

- Normal appearance does not rule out EoE
  - Need to obtain mucosal biopsies from multiple levels
- Studies have shown that otolaryngologists and pediatric surgeons do NOT routinely biopsy the esophagus in cases of esophageal foreign body or food impaction
- Foreign body series in our literature
  - Only 27 biopsies in 271 esophageal foreign body cases
  - 18/27 biopsies (67%) were + for EoE
- Greater than 15 eosinophils per high power field
  - Diagnostic for EoE

Treatment of EoE

- PPI is generally first line treatment
  - 8-week course of high dose PPI
    - 1mg/kg/dose, twice daily in children
  - Follow up EGD at end of treatment course (need biopsies)
  - Mechanism of benefit of PPI is not well understood

Treatment – Dietary

- Three types of diets
  - Elemental diet – sold food replaced with elemental amino acid based formula
  - Targeted elimination – eliminate foods based on allergy testing
  - Empirical elimination – no guidance from allergy testing
    - Usually a 6-food elimination
    - Milk/dairy
    - Soy
    - Wheat
    - Egg
    - Tree nuts/peanuts
    - Fish/seafood

Treatment - Pharmacologic

- Variety of corticosteroid regimens have shown improvement
- Owing to concern for long term steroid usage has led to the off-label use of topical corticosteroids
  - Swallowed fluticasone propionate (inhaler) and budesonide (slurry)
  - Side effects include candida overgrowth
  - Long term therapy needed (Up to 90% relapse rate)

EoE – Final Thoughts

- Chronic inflammatory condition of esophagus
- Risk factors and symptoms overlap into the ENT world
- Food impaction in a child is EoE until proven otherwise
- Consider EoE when standard treatments are not working
  - Needs to be on our radar
- Consider getting your GI colleagues involved in children with refractory airway symptoms that you are taking to OR for evaluation

JAMA Otolaryngology–Head & Neck Surgery | Original Investigation

Association of Proton Pump Inhibitors With Hospitalization Risk in Children With Oropharyngeal Dysphagia

Daniel R. Duncan, MD; Paul D. Mitchell, MS; Kara Larson, CCC-SLP; Maireade E. McSweeney, MD, MPH; Rachel L. Rosen, MD, MPH

- Why I chose this article
  - Growing concern over risks associated with use of PPIs
  - Acid suppression leads to changes in microbiome in gastric, oropharyngeal and lung environments
  - Patients on PPIs at increased risk for….
    - Pneumonia
    - Upper respiratory tract infections
    - GI infections
    - Sepsis
  - Despite concerns these medications are commonly prescribed by many pediatric providers

PPI and Young Children – Why?

- Often used empirically in children with dysphagia/aspiration
  - Symptom complex overlaps with GERD
    - Coughing/feeding difficulty/vomiting/etc.
  - Trying to protect the lungs from gastric acid in the aspirating child
  - There is little data to support these practices
- In adult studies of dysphagia and/or aspiration
  - PPI use associated with increased risk of pneumonia
- Authors speculate that PPI use in children carries a similar risk profile

Methods

- Retrospective review at Boston Children's Hospital
- Looked at children 2 years of age and younger
  - Abnormal swallow studies (aspiration and/or penetration)
  - One year time period
  - Determined PPI status and length of hospitalizations
- Chose children under 2 because
  - Highest incidence of dysphagia/aspiration
  - Highest incidence of PPI prescriptions
- Collected data for 1 year to include seasonal variations of hospital admissions (virus season, etc.)

Results

- Evaluated 293 patients (mean age 8.8 months at swallow study)
  - Mean follow up length was 18 months
- Overall cohort -- 45% (132/293) had at least 1 admission
  - Mean of 0.97 total admissions
  - Mean of 4.02 hospital nights
- 53% had aspiration (156/293) and 47% penetration (137/293)
  - 70% of patients did NOT have neurologic diagnosis

Table 1. Patient Characteristics (N = 293)

Characteristic	No. (%)
Demographics	
Male sex	177 (60.4)
Premature birth	100 (34.1)
Gestational age if premature [range 22-36], median (IQR), wk	33 (28-36)
Age at first VFSS [range 0.2-33.8], median (IQR), mo	7.0 (3.0-13.4)
Comorbidities	
Any comorbidities	210 (71.7)
If comorbidities, No. [range 1-7], median (IQR)	2 (2-3)
Neurologic	90 (30.7)
GI	50 (17.1)
Pulmonary	46 (15.7)
Metabolic/Genetic	37 (12.7)
Cardiac	33 (11.3)
Immunologic	2 (0.7)
Symptoms	
Coughing	173 (59.0)
Choking or gagging	112 (38.2)
Noisy breathing	81 (27.7)
Vomiting	72 (24.6)
Poor feeding	63 (21.5)
Congestion	58 (19.8)
Spells	53 (18.1)
Increased work of breathing	38 (13.0)
Pneumonia	34 (11.6)
Slow feeding	16 (5.5)
Oxygen requirement	16 (5.5)
Eyes watering	3 (1.0)

Abbreviations: IQR, interquartile range; VFSS, videofluoroscopic swallow study.

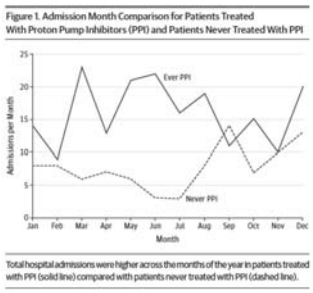
PPI Treatment Status and Confounders

- 49% of cohort never had PPI
- 51% of cohort received PPI
  - 73% taking prior to swallow study
  - 11% were taken off PPI after swallow
- Mean treatment was just over 7 months

- No differences in demographic characteristics or prevalence of comorbidities between the groups

Hospitalization Risk

- Patients treated with PPI had nearly 2-fold increase in total hospitalizations (1.77 incidence rate)
  - After adjustment for comorbid conditions
- Patients treated with PPI had 2 to 3-fold increase in hospital admission nights



Discussion Points

- This study suggests that PPI use in children with abnormal swallow function is associated with almost DOUBLE the rate of hospitalization compared to patients not on PPI
- Young children with dysphagia more often placed on PPI
  - Thought that feeding issues are GERD related
  - Try to minimize acid exposure in children who aspirate
    - No good literature to support this practice
- Exposure to PPI, and not necessarily the treatment duration, may be the key to risk
  - ? Changes in microbiome

Discussion Points

- PPI prescribing remains high despite studies like this and lack of evidence really demonstrating benefits
  - 2014 Review – 3% of hospitalized infants get started on PPI and 1.6% get started in the outpatient setting
  - PPI prescribing rates after NICU discharge have risen 7-fold from 1997-2009

Conclusion and Thoughts

- Use of PPI was associated with significantly increased hospitalization risk in children with oropharyngeal dysphagia
  - Supports growing concern about use of PPI in children
- My practice
  - Very conservative with use of acid suppression
  - Hardly ever prescribe PPI empirically (severe laryngomalacia, recalcitrant airway stenosis)
  - Tend to refer to Peds GI if I suspect clinically relevant GERD (pH testing, EGD, etc.)

Standardizing Laryngeal Cleft Evaluations: Reliability of the Interarytenoid Assessment Protocol

Steven Coppess, JD, MBA[1], Reema Padia, MD[2], David Horn, MD[2], Sanjay R. Parikh, MD[2], Andrew Inglis, MD[2], Randall Bly, MD[2], John Dahl, MD, PhD, MBA[2], Daniel Dudley[1], and Kaalan Johnson, MD[2]

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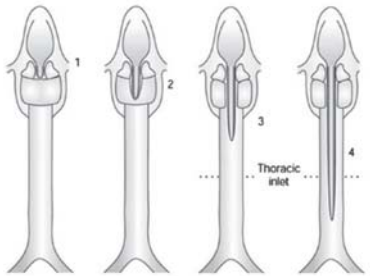
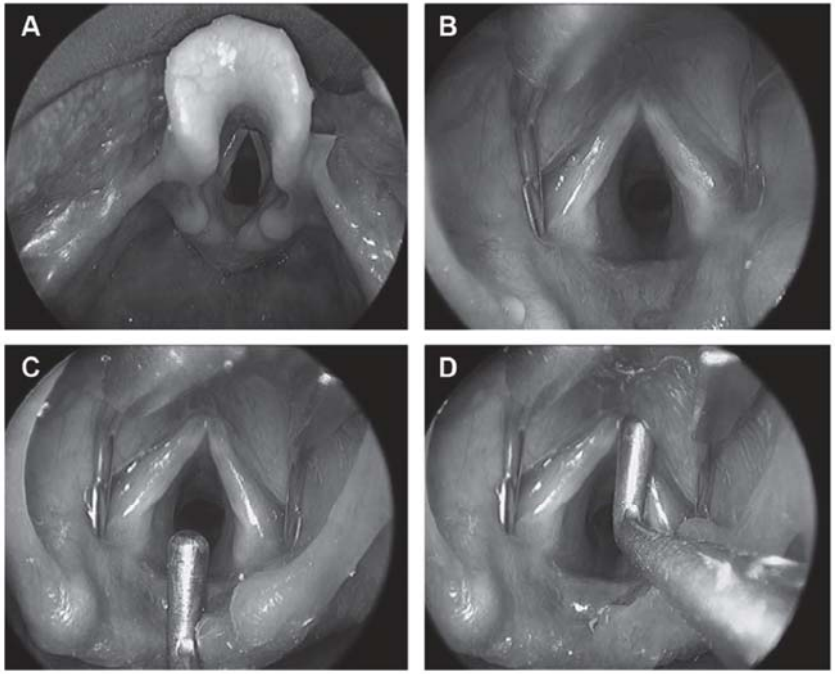
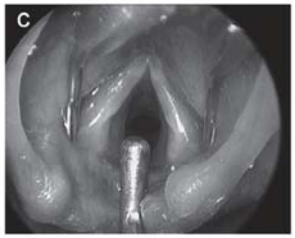
- Why I chose this article
  - The type I laryngeal cleft remains a black box
  - Many feel it is not a pathologic state
  - Injection of the interarytenoid space helps swallowing in some children with minimal findings
  - Type I vs Deep Notch???

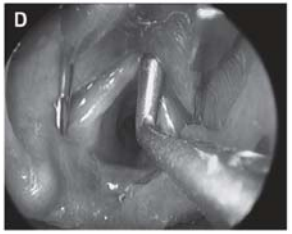


Background and Relevance

- Benjamin-Inglis classification system
  - Widely popular way to characterize clefts
  - Does NOT clearly identify the superior limit of a Type I cleft
  - There is not consistency in distinguishing Type I cleft from a deep interarytenoid notch from normal anatomy
  - Can cause issue when trying to characterize or publish research on topic
- Study designed to create standardized classification system for the interarytenoid region and to test reliability







Palpation of Interarytenoid Area
Observe bulk of muscle
Palpate surface of cricoid for cleft/defect
Check for submucosal laryngeal cleft

Assessment of Interarytenoid Mucosal Height (IAMH)
Swing probe anterolaterally in line with midpoint of membranous TVF to determine reference point
1. Above false vocal fold, 2. At false vocal fold, 3. In ventricle, 4. At TVF, 5. Below TVF

Reliability Testing

- 4 reviewers
  - 2 naïve to the protocol
  - 2 experience with protocol
  - Reviewers blinded as to type and number of clefts that they would see
  - 30 videos reviewed by each reviewer

Results

- Raters with and without instruction in the protocol showed very good interrater reliability (κ=0.61-0.80)

Discussion

- Proposed system is possible when attempted in a busy tertiary care practice
- Interrater and intrarater reliability showed substantial agreement
  - Even when compared to the findings as outlined by the surgeon who was actually there manipulating the tissue
- This study does NOT establish a normal interarytenoid mucosal height value

Obstructive Sleep Apnea in Children with Down Syndrome: Demographic, Clinical, and Polysomnographic Features

Bahir H. Chamseddin[1], Romaine F. Johnson, MD, MPH[1,2], and Ron B. Mitchell, MD[1,2]

- Why I chose this article
  - Down syndrome is most prevalent chromosome abnormality seen in live-born children
    - > 300,000 in U.S.
  - Multiple factors predispose these children to obstructive sleep apnea.
    - Up to 80% can be affected (compared to 5% of general population)
    - Disease is tougher to eradicate in this population

Down Syndrome and OSA

- Sleep apnea is #1 reason for visit to otolaryngologist
- Role of tonsillar hypertrophy and obesity are less clear in this population
- Existing studies limited by small sizes and inconsistent definitions of OSA

- Aims of study
  - Evaluate demographic, clinical and polysomnographic features of children with Down syndrome suspected of having OSA
  - Identify factors that predict severe OSA

Methods

- Looked at consecutive sample of children with Down syndrome (ages 2-18) who has polysomnogram over 7-year period
  - Excluded if previous pharyngeal/laryngeal/tracheal surgery
    - Missing data on tonsil size
  - Collected demographic and clinical information on children

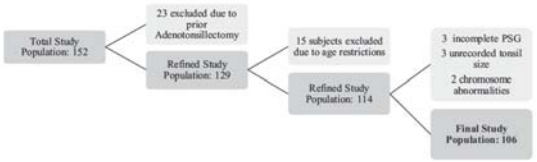


Table 1. Characteristics of Children with Down Syndrome Referred for Polysomnography.

Variable	Patients, Mean ± SD or n (%)			
	Total (N = 106)	Nonobese (n = 63)	Obese (n = 43)	*P* Value[a]
Age, y	7.3 ± 4	6.1 ± 4	9.1 ± 5	**<.001**
<12	89 (84)	58 (92)	31 (72)	**.008**
≥12	17 (16)	5 (8)	12 (28)	**.008**
Male	56 (53)	31 (49)	25 (58)	.366
Ethnicity				
Caucasian	14 (13)	10 (16)	4 (9)	.327
African American	15 (14)	5 (8)	10 (23)	**.044**
Hispanic	72 (68)	47(75)	25 (58)	.092
Other	5 (5)	1 (1)	4 (9)	.156
Weight, kg	27.4 ± 44	19.5 ± 11	39.5 ± 24	**<.001**
BMI z score[b]	1.2	0.4	2.4	**<.001**
Comorbidity				
Preterm[c]	23 (22)	15 (24)	8 (19)	.459
Allergies	32 (30)	18 (29)	14 (33)	.673
Asthma	25 (24)	16 (25)	9 (21)	.648
GERD	11 (10)	8 (13)	3 (7)	.519
Hypothyroidism	26 (25)	17 (27)	9 (21)	.477
CHD	65 (61)	45 (71)	20 (47)	**.014**
Hearing loss	29 (27)	19 (30)	10 (23)	.545
Tonsil size				
Nonhypertrophy (1+/2+)	55 (52)	31 (49)	24 (56)	.504
Hypertrophy (3+/4+)	51 (48)	32 (51)	19 (44)	.549
OSA diagnosis[d]				
None	11 (10)	7 (11)	4 (9)	>.99
Mild/moderate	49 (46)	34 (54)	15 (35)	.070
Severe	46 (44)	22 (35)	24 (56)	**.044**

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; CHD, congenital heart disease; GERD, gastrointestinal reflux; OSA, obstructive sleep apnea.
[a]*P* values are based on analysis of variance for continuous variables and Pearson chi-square or Fisher exact test for categorical variables. Significant *P* values are in bold.
[b]z score: SD score of BMI based on Centers for Disease Control and Prevention guidelines adjusted for age and sex.
[c]Preterm: born before 37 weeks of gestation.
[d]None, AHI < 1; mild/moderate, 1 ≤ AHI < 9.9; severe OSA, AHI ≥ 10.

Table 2. Polysomnographic Characteristics of Children with Down Syndrome.

Variable	Mean ± SD			
	Total	Nonobese	Obese	*P* Value[a]
AHI	16.7 ± 25	14.1 ± 24	20.6 ± 28	.170
Age <12 y	16.4 ± 26	14.8 ± 24	19.7 ± 31	.381
Age ≥12 y	18.1 ± 16	5.9 ± 5	23.1 ± 16	**.036**
Apnea index	4.4 ± 11	2.8 ± 9	5.8 ± 14	.187
Hypopnea index	11.5 ± 18	9.8 ± 15	14.0 ± 21	.263
CAI	1.4 ± 4	6.1 ± 4	9.1 ± 5	.174
REM	18.6 ± 7	18.9 ± 8	17.0 ± 7	.132
Sleep efficiency[b]	84.4 ± 12	85.7 ± 10	82.5 ± 14	.194
Arousal index	18.2 ± 13	18.3 ± 13	18.0 ± 12	.913
SaO_2 nadir[c]	83.0 ± 10	84.8 ± 7	80.3 ± 14	**.016**
Age <12 y	83.0 ± 11	84.7 ± 7	79.7 ± 16	**.050**
Age ≥12 y	82.9 ± 6	85.6 ± 7	81.8 ± 6	.264
Peak CO_2	51.7 ± 8	51.4 ± 9	52.1 ± 6	.679
TST >50 $ETCO_2$	16.0 ± 25	16.1 ± 26	15.7 ± 25	.889

Abbreviations: AHI, apnea-hypopnea index; CAI, central apnea index; REM, rapid eye movement; TST >50 $ETCO_2$, total sleep time spent at >50 mm Hg of blood end-tidal CO_2 saturation.
[a]*P* values are based on analysis of variance. Significant *P* values are in bold.
[b]Percentage of time that the patient was asleep.
[c]Lowest pulse oximetry measured hemoglobin saturation.

Table 3. Simple Logistic Regression of Demographic and Clinical Parameters for Predictors of Severe Obstructive Sleep Apnea (AHI ≥10).

	Inter	Coeff	SE	Wald χ^2	*P* Value[a]	OR	95% CI
Age	−1.2	0.1	0.05	6.42	.110	1.1	1.0-1.2
<12 y	0.9	−1.3	0.58	5.56	**.020**	0.3	0.1-0.8
≥12 y	−0.5	1.4	0.58	5.56	**.020**	1.3	0.2-2.5
Male	−0.3	0.1	0.39	1.11	.784	1.1	0.5-2.4
Female	0.2	0.1	0.39	1.11	.784	0.9	0.4-1.9
Hispanic	−0.2	−0.4	0.60	0.38	.535	0.7	0.2-2.2
African American	−0.4	1.1	0.59	3.61	.058	3.1	1.0-9.7
Caucasian	0.1	−0.6	0.42	1.84	.175	0.6	0.2-1.3
Other	−0.3	0.8	0.93	0.57	.451	2.0	0.3-13
Weight, kg	−1.2	0.03	0.01	9.90	**.002**	1.0	1.0-1.1
BMI z score	−0.4	0.1	0.14	0.89	.344	1.1	0.9-1.5
Obesity[b]	−0.6	0.9	0.40	4.47	**.035**	2.3	1.1-5.2
Tonsil size[c]							
1+/2+	−0.1	−0.3	0.39	0.54	.464	0.8	0.3-1.6
3+/4+	−0.4	0.3	0.39	0.54	.462	1.3	0.6-2.9
Allergy	−0.3	0.2	0.42	0.23	.638	1.2	0.5-2.8
Asthma	−0.4	0.5	0.45	0.98	.322	1.6	0.6-3.9
GERD	−0.2	−0.3	0.66	0.25	.620	0.7	0.2-2.6
CHD	0.5	−0.5	0.40	1.66	.200	0.6	0.2-1.3
Hypothyroid	−0.3	0.1	0.45	0.11	.744	1.2	0.5-2.8
Hearing loss	−0.8	0.8	0.46	2.44	.119	2.1	0.8-5.1

Abbreviations: AHI, apnea-hypopnea index; CHD, congenital heart disease; Coeff, coefficient of linear regression; GERD, gastroesophageal reflux; Inter, regression intercept; OR, odds ratio.
[a]*P* values are based on simple logistic regression. Significant *P* values are in bold.
[b]Body mass index z score ≥95%.
[c]Per Brodsky scale.

Table 4. Multivariable Logistic Regression Model for Predictors of Severe Obstructive Sleep Apnea (Apnea-Hypopnea Index ≥10).[a]

Variable	Coeff	SE	Wald χ^2	*P* Value	OR	95% CI
Intercept	–0.10	2.0	—	—	—	—
Age	–0.13	0.18	0.34	.560	0.87	0.6-1.3
Weight, kg	0.08	0.03	5.33	**.015**	1.10	1.0-1.1

Abbreviations: Coeff, coefficient of regression; OR, odds ratio.
[a]Chi-square goodness of fit test = 103.8. Significant *P* value is in bold.

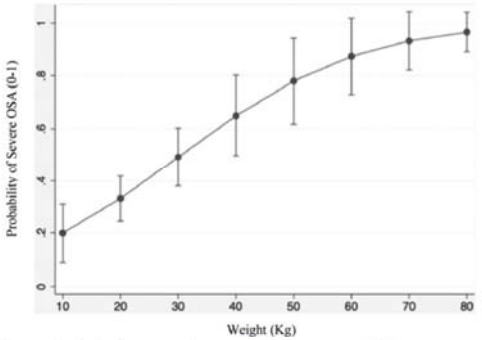


Figure 2. Risk of severe obstructive sleep apnea (OSA; apnea-hypopnea index ≥10) by weight among children with Down syndrome. Error bars indicate 95% CI

Discussion

- Only 10% of children had normal sleep study
- 44% had severe OSA
- Severe OSA more common amongst older obese children
- Hypoxemia was more severe in obese children
  - But was prevalent in both groups
- Weight but not age was a strong predictor of severe OSA
- Sex and treated comorbidities (asthma, allergies, GERD) was not associated with obesity or OSA severity

Discussion

- American Academy of Pediatrics
  - Recommends screening sleep study by age 4 regardless of symptoms
- Poor correlation between parental report of symptoms and sleep study results
- This study suggests highest yield for severe sleep apnea is in the obese pubescent Down syndrome child
- Significant difference between obese and nonobese children
  - Obese children twice as likely to have severe OSA
  - Consistent with other studies
- No association between tonsil hypertrophy and OSA

Montelukast and Nasal Corticosteroids to Treat Pediatric Obstructive Sleep Apnea: A Systematic Review and Meta-analysis

Bryan J. Liming, MD[1], Matthew Ryan[2], Douglas Mack, MD[3], Iram Ahmad, MD, MME[4], and Macario Camacho, MD[1]

- Why I chose this article
  - Obstructive sleep apnea affects up to 5% of children
  - Adenotonsillectomy is a proven treatment but has risks
  - Positive airway pressure is generally poorly tolerated in children
  - Conservative medical treatment
    - Alternative to surgery
    - To treat recurrent/refractory OSA

Pediatric Obstructive Sleep Apnea

- The case for medications
  - Adenotonsillar tissue has leukotrienes and leukotriene receptors
    - In vitro studies showed that leukotriene antagonists lead to reduction in adenotonsillar cell proliferation
    - Clinical studies have shown reduction in AHI and oxygen nadir
- Study seeks to systematically evaluate the effect of montelukast on OSA
  - With or without nasal steroid use
  - Had to have pre and post sleep study data

Results

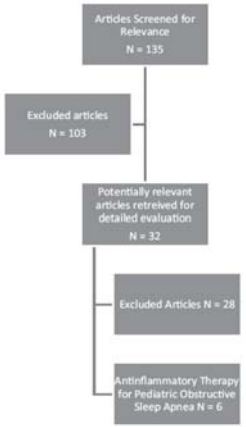


Table 1. Summary and Characteristics of Included Studies.

Characteristic	Design	No.	Age, Mean (SD), y	BMI, kg/m^2	AHI Events/h, Mean (SD)			Low O_2 %, Mean (SD)		
					Pretreatment	Posttreatment	% Change	Pretreatment	Posttreatment	% Change
OM + ICS										
Yang et al[21] OM + ICS group	Prospective cohort	57	3.9 (1.6)	0.7 (1.3[a])	6.9 (1.5)	1.6 (1.3)	76.8	90.2 (2.0)	94.8 (1.2)	5.1
Kheirandish-Gozal et al[3]	Retrospective cohort	445	6.2 (1.9)	1.2 (0.8[a])	4.5 (2.0)	1.4 (0.9)	68.9	87.5 (3.1)	92.3 (2.1)	5.5
Subtotal		502	5.94 (2.0)		4.7 (2.1)	1.4 (1.0)	70.2	87.8 (3.1)	92.6 (2.2)	5.5
OM										
Yang et al[21] OM leg	Prospective RCT, open label	65	4.2 (1.3)	0.8 (1.0[a])	7.3 (1.5)	1.3 (0.7)	82.2	90.7 (8.5)	93.6 (3.3)	3.2
Sunkonkit et al[24]	Cross-sectional	28	7.3 (2.9)	18.6 (3.6[b])	3.5 (1.2)	4.7 (4.3)	−34.3	89.8 (3.3)	90.6 (4.8)	0.9
Kheirandish-Gozal et al[23]	RCT montelukast vs placebo, prospective randomized double blind	28	5.5 (2.5)	1.4 (0.5[a])	9.2 (4.1)	4.2 (2.8)	54.3	85.2 (7.4)	91.0 (2.5)	6.8
Goldbart et al[24]	RCT montelukast vs placebo, prospective double blind	23	4.8 (2.0)	0.8 (1.1[a])	6.0 (3.2)	3.6 (2.3)	40.0	90.3 (3.1)	92.5 (3.0)	2.4
Goldbart et al[22]	Prospective cohort	24	5.4 (2.0)	19.6 (0.9[b])	3.0 (0.2)	2.0 (0.3)	33.4	90.3 (3.1)	90.5 (3.0)	0.2
Subtocal		166	5.2 (2.3)		6.2 (3.1)	2.8 (2.7)	54.8	89.5 (6.9)	92.1 (3.6)	2.9
Total		668	5.8 (2.1)		5.1 (2.5)	1.8 (1.7)	64.7	88.2 (4.4)	92.5 (2.6)	4.9

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; ICS, intranasal corticosteroids; Low O_2, lowest oxygen saturation; OM, oral montelukast; RCT, randomized controlled trial.
[a]Mean (z score).
[b]Mean (SD).

Quality of Studies

- Of the 6 studies
  - 1 prospective cross-sectional trial
  - 2 prospective cohorts
  - 1 retrospective cohort
  - 2 placebo-controlled prospective RCTs

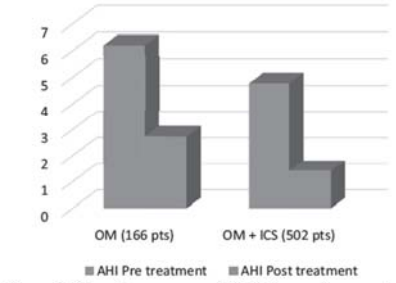


Figure 2. Effect of treatment on AHI. AHI, apnea-hypopnea index; ICS, intranasal corticosteroids; OM, oral montelukast.

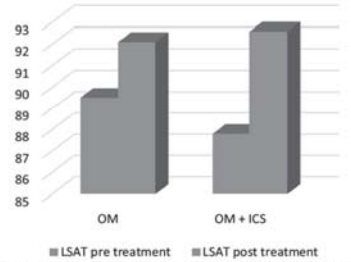


Figure 3. Effect of treatment on LSAT. ICS, intranasal corticosteroids; LSAT, lowest oxygen saturation; OM, oral montelukast; SaO_2, saturation of oxygen.

Adverse Events

- 4 studies (n=511) reported adverse reactions
  - 3 events reports (0.59%)
  - All were mild (nausea, headache, epistaxis)

- Other studies have reported more significant side effects of montelukast therapy in children
  - Depression
  - Aggression
  - Anxiety
  - Suicidal behavior
  - Label change by FDA in 2009 to reflect this

Discussion

- Study suggests oral montelukast improves both AHI and oxygen saturation parameters
  - The addition of nasal steroids further improves results
  - Data was heterogenous
- Medical management may be a reasonable alternative in children with MILD OSA
  - Not enough data to comment on these medications to treat moderate or severe OSA

Discussion

- Treatment length
  - Studies treated for variable amounts of time (6-16 weeks)
  - Unknown what optimal treatment length is
    - Or if treatment beyond 16 weeks results in ongoing improvement

My Practice

- I will offer montelukast and nasal steroid spray to young children with mild sleep apnea
  - 12 week course with follow up in clinic
  - If symptoms improved then continue to treat
  - If no improvement then usually refer to surgery
  - Many parents do not like the idea of chronic medication and will refuse medication in order to have surgery

Comparison of Pediatric Intracapsular Tonsillectomy and Extracapsular Tonsillectomy: A Cost and Utility Decision Analysis

Grace Baik, MD[1] and Scott E. Brietzke, MD, MPH[1]

- Why I chose this article
  - Tonsillectomy common part of my practice
  - Remains morbid with fixed rate of complications
  - Perform intracapsular tonsillectomy routinely but not very often
  - Intracapsular associated with less pain and likely lower complications rates (bleeding, dehydration)
    - Risk of tonsil regrowth which could negate early benefits
    - Regrowth from 1 – 16% depending on who you read

Decision Analysis

- Helps to examine alternatives with competing trade-offs to estimate potential best option
- Decision tree is plotted
  - Starts with a choice with alternative treatment option (traditional versus intracapsular tonsillectomy) and relevant outcomes
  - The value of each alternate in the decision tree is determined by multiplying the likelihood of that outcome with the value of that outcome

Table 1. Key Model Parameters.

Parameter[a]	Starting Value, %	Range Used for Sensitivity Analysis %
Post-ICT		
Bleed rate[7,22]	1	0.5-6
Dehydration rate[5]	2	0.5-3.5
Tonsillar regrowth rate[10,11,21]	10	0.6-17
Post-ECT		
Bleed rate[6,10,23]	3	1.5-7
Dehydration rate[5]	3	1.5-5

Abbreviations: ECT, extracapsular tonsillectomy; ICT, intracapsular tonsillectomy.
[a]References used to establish parameter starting value and estimated range that was used for sensitivity analysis.

Decision Analysis Model

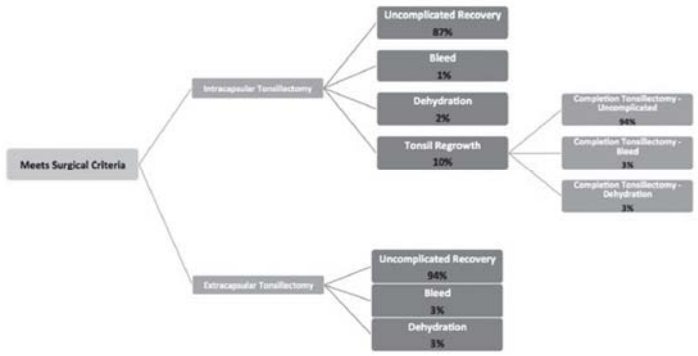


Table 3. Model Cost Values.

Condition/Endpoint	Estimated Total Cost, $[15,16]	Range Used for Sensitivity Analysis, $
Initial surgery (ICT or ECT)	2892	2000-3500
Postoperative		
Tonsil bleed	2706	2200-3200
Dehydration (requiring IV hydration)	326	200-400
Completion tonsillectomy	3072	2500-3500
Recovery (per day)	155	100-300

Abbreviations: ECT, extracapsular tonsillectomy; ICT, intracapsular tonsillectomy; IV, intravenous.

Results

- Intracapsular tonsillectomy was superior to total tonsillectomy for the overall utility-based analysis
- Authors then reran data changing the parameters for one variable (bleed rate, dehydration, tonsil regrowth, etc.)
- Key variables that affected model
  - Having a single surgical procedure
  - Tonsil regrowth
    - Cumulative utility becomes EQUAL at a regrowth rate of 1. 64%
    - Regrowth rates about this level favor total tonsillectomy

Results - Cost

- Intracapsular tonsillectomy is cheaper
  - $4177 versus $4546
  - Factors in differences in bleeding rates, days of recovery, etc.
  - Intracapsular with regrowth carried the overall highest cost
  - Total cumulative cost was EQUAL at a regrowth rate of 17.8%

My Practice

- Offer intracapsular tonsillectomy to the following patients
  - Children under the age of 3
  - Any child that I worry about the recovery from traditional tonsillectomy
    - Down syndrome
    - Autism
    - GI disorders/dysphagia
  - Parental request

9th Annual Otolaryngology Literature Update
Pediatric Otolaryngology II

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Clarice S. Clemmens, M.D., joined the Department of Otolaryngology-Head and Neck Surgery and MUSC Children's Hospital in October of 2015. Prior to joining MUSC, Dr. Clemmens completed a fellowship in pediatric otolaryngology at the Children's Hospital of Philadelphia.

Dr. Clemmens grew up in Idaho, and graduated summa cum laude from Clemson University where she played varsity soccer. In 2009, she graduated from Medical School at the Medical University of South Carolina, and then completed a residency in otolaryngology at the University of Pennsylvania. Dr. Clemmens received her board certification from the American Board of Otolaryngology in 2015.

Since completing her fellowship, Dr. Clemmens limited her clinical practice to the care of children. Dr. Clemmens has dedicated her practice to the care of children with all types of ear, nose, and throat problems, with a particular emphasis on neonatal airway disorders and thyroid disorders. She has authored multiple papers and book chapters and has given presentations at both the regional and national levels.

9th Annual Otolaryngology Literature Update
Medical University of South Carolina

Pediatric Otolaryngology II

Clarice S. Clemmens, M.D.

Diercks GR, Comins J, Bennett K, Gallagher TQ, Brigger M, Boseley M, Gaudreau P, Rogers D, Setlur J, Keamy D, Cohen MS, Hartnick C. "A Comparison of Ibuprofen vs Acetaminophen and Severe Bleeding Risk After Pediatric Tonsillectomy: A Noninferiority Randomized Clinical Trial." JAMA Otolaryngology-- Head & Neck Surgery. 2019 Apr 4. doi: 10.1001/jamaoto.2019.0269. [Epub ahead of print].

Friedman NR, Ruiz AG, Gao D, Jensen A, Mitchell RB. "Pediatric Obstructive Sleep-Disordered Breathing: Updated Polysomnography Practice Patterns." Otolaryngology-- Head & Neck Surgery. 2019 Apr 30:194599819844786. doi: 10.1177/0194599819844786. [Epub ahead of print].

Lavin J, Lehmann D, Silva AL, Bai G, Hebal F, Manworren R, Stake C, Rychlik K, Billings KR. "Variables associated with pediatric emergency department visits for uncontrolled pain in postoperative adenotonsillectomy patients." International Journal of Pediatric Otorhinolaryngology. 2019 Aug;123:10-14. doi: 10.1016/j.ijporl.2019.04.038. Epub 2019 Apr 26.

Riga M, Korres G, Chouridis P, Naxakis S, Danielides V. "Congenital cytomegalovirus infection inducing non-congenital sensorineural hearing loss during childhood; a systematic review." International Journal of Pediatric Otorhinolaryngology. 2018 Dec;115:156-164. doi: 10.1016/j.ijporl.2018.10.005. Epub 2018 Oct 4.

Socarras MA, Landau BP, Durr ML. "Diagnostic techniques and surgical outcomes for persistent pediatric obstructive sleep apnea after adenotonsillectomy: A systematic review and meta-analysis." International Journal of Pediatric Otorhinolaryngology. 2019 Jun;121:179-187. doi: 10.1016/j.ijporl.2019.02.030. Epub 2019 Mar 3.

Vandjelovic ND, Brown JR, Traboulsi HT, Thottam PJ. "Impact of Infant Supraglottoplasty on Quality of Life." Otolaryngology-- Head & Neck Surgery. 2018 Sep;159(3):564-571. doi: 10.1177/0194599818775091. Epub 2018 May 15.

2019 Pediatric Otolaryngology Literature Review

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Department of Otolaryngology – Head and Neck Surgery

Overview

Original Research

Original Research—Pediatric Otolaryngology

International Journal of Pediatric Otorhinolaryngology 115 (2018) 156–164

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

Review Article

Congenital cytomegalovirus infection inducing non-congenital sensorineural hearing loss during childhood; a systematic review

Maria Riga[a,*], George Korres[b], Pantelis Chouridis[a], Stephanos Naxakis[c], Vasilios Danielides[c]

International Journal of Pediatric Otorhinolaryngology 123 (2019) 10–14

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

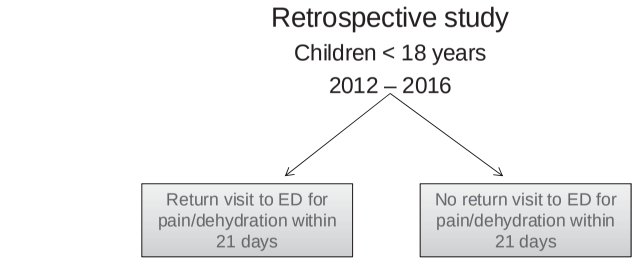
Variables associated with pediatric emergency department visits for uncontrolled pain in postoperative adenotonsillectomy patients

Jennifer Lavin[a,b], David Lehmann[c], Astrid Leon Silva[d], Guangyu Bai[c], Ferdynand Hebal[d], Renee Manworren[d,e], Christine Stake[d], Karen Rychlik[b,g], Kathleen R. Billings[a,b,*]

Introduction

- Tonsillectomy +/- adenoidectomy
  - Common surgical procedure
  - Disproportionately higher rates for return emergency department (ED) visits
- Return to ED
  - Related to pain and dehydration
- Variability in pain management prescribing patterns
- FDA black box warning against Codeine
  - Increase in ED return visits
- Study investigating demographics and comorbidities associated with return ED visits

Methods



Exclusions:
1. Other procedures impacting postoperative course
2. Hemorrhage, respiratory issues, other complaints unrelated to perioperative period

Ann & Robert H. Lurie Children's Hospital of Chicago®

Methods

- 7,493 T&A during study period
  - 554 (7.4%) return to ED
  - 144 (1.9) return to ED for pain/dehydration and met criteria
- Matched by age, gender, and payer status
  - 285 patients compared to ED cohort
- From EMR: demographics, indication for surgery, surgeon, surgical technique postoperative pain regimen, and comorbidities

Variable	No ED Return	ED Return
Average Age	5.54 (range 1–17)	5.53 (range 1–17)
Gender		
Female	126 (45.3%)	62 (45.3%)
Male	152 (54.7%)	75 (54.7%)
Payer status		
PPO	97 (34.9%)	45 (32.8%)
Medicaid	181 (65.1%)	90 (65.7%)
HMO	0 (0.0%)	2 (1.5%)

Demographics

- ED returns
  - 144 patients
- Average time to return
  - 4.7 days

Variable	No ED Return (%)	ED Return (%)	OR (95% CI)	p
Race				
Caucasian	143 (51.4)	43 (31.4)		
African American	33 (11.9)	21 (15.3)	N/A	**0.0005**
Other/Unknown	102 (36.7)	73 (53.3)		
Ethnicity				
Hispanic	86 (31.3)	73 (53.3)	2.49 (1.64–3.8)	**< 0.0001**
Non-Hispanic	188 (68.7)	64 (46.7)		
Primary language				
Spanish	27 (9.9)	33 (24.1)	2.92 (1.67–5.1)	**0.0002**
English	246 (90.1)	103 (75.9)		
Surgical indication				
Hypertrophy	262 (94.2)	133 (97.1)		
Chronic/Recurrent Tonsillitis	16 (5.8)	4 (2.9)	2.03 (0.67–6.19)	0.31
Surgical Technique			N/A	**0.01**
Cautery	200 (70.1%)	112 (77.8%)		
Coblator	64 (22.5%)	32 (22.2%)		
Microdebrider (partial)	17 (6.0%)	0 (0%)		
Cold	4 (1.4%)	0 (0%)		

Comorbidities

Variable	No ED Return (%)	ED Return (%)	OR (95% CI)	p
Global Developmental Delay				
Yes	28 (10.1)	16 (11.7)	1.18 (0.62–2.26)	
No	250 (89.9)	121 (88.3)		0.74
Down syndrome				
Yes	2 (0.7)	7 (5.1)	2.49 (1.64–3.8)	**0.01**
No	276 (99.3)	130(94.9)		
Preterm delivery				
Yes	29 (10.4)	4 (2.9)	2.92 (1.67–5.1)	**0.01**
No	249 (89.6)	133 (97.1)		
Asthma/RAD				
Yes	37 (13.4)	7 (5.1)	0.35 (0.15–0.81)	**0.02**
No	240 (86.6)	130 (94.9)		
Cardiac comorbidity				
Yes	16 (5.8)	4 (2.9)	0.49 (0.16–1.5)	0.31
No	262 (94.2)	133 (97.1)		
Neurological comorbidity				
Yes	17 (6.1)	6 (4.4)	0.70 (0.27–1.83)	0.62
No	261 (93.9)	131 (95.6)		
Anxiety/depression				
Yes	6 (2)	2 (1)	0.66 (0.13–3.32)	0.91
No	272 (98)	135 (99)		
Autistic spectrum disorder				
Yes	5 (2.2)	3 (2.2)	1.22 (0.29–5.19)	1.0
No	273 (97.8)	134 (97.8)		
ADHD				
Yes	2 (0.7)	7 (5.1)	7.43 (1.52–36.27)	**0.011**
No	276 (99.3)	130 (94.9)		

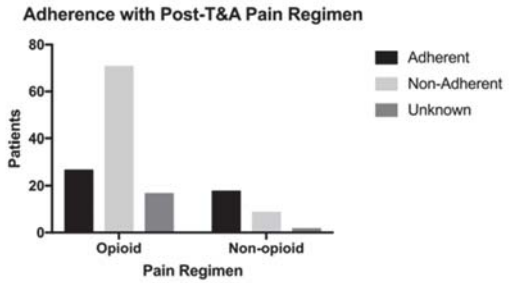
Telephone Calls

- No difference in return to ER with or without opioids
  - > 80% discharged with opioids
- More likely to report poor PO and be counseled on signs of dehydration
- No difference if pain regimen changed by phone

Variable	No ED Return (%)	ED Return (%)	p
Pain regimen discussed?			
Yes	62 (76.5)	64 (87.6)	
No	19 (23.5)	9 (12.3)	0.09
Pain regimen changed?			
Yes	22 (27.2)	24 (32.9)	0.48
No	59 (72.8)	49(67.1)	
Poor PO reported by parent?			
Yes	54 (66.7)	13 (17.8)	**< 0.0001**
No	27 (33.3)	60 (82.2)	
Counseled on fluid intake?			
Yes	55 (67.9)	53 (72.6)	0.60
No	26 (32.1)	20 (27.4)	
Counseled on signs of dehydration?			
Yes	58 (71.6)	25 (34.2)	**< 0.0001**
No	23 (28.4)	48 (65.8)	

Readmission and Adherence

- 30.6% return to ER patients admitted
- 64% with sub-optimal adherence to pain regimen



Conclusion

- T&A is an ideal procedure for readmission reduction efforts
  - Common procedure
  - High return to ED rate
- Down Syndrome and ADHD higher risk for return to ED
  - Difficult patient cooperation
  - Difficulties with oral intake
  - Inability to judge pain levels
- High rate of non-adherence
  - Need to identify drivers (e.g. language barrier, patient cooperation)
  - Improve communication

Research

JAMA Otolaryngology–Head & Neck Surgery | Original Investigation

Comparison of Ibuprofen vs Acetaminophen and Severe Bleeding Risk After Pediatric Tonsillectomy
A Noninferiority Randomized Clinical Trial

Gillian R. Diercks, MD, MPH; Jill Comins, NP; Kara Bennett, MS; Thomas Q. Gallagher, DO, CDR, MC, USN; Matthew Brigger, MD, MPH; Mark Boseley, MD; Philip Gaudreau, MD, LCDR, MC, USN; Derek Rogers, MD, LTC, MC, USA; Jennifer Setlur, MD; Donald Kearny, MD, MPH; Michael S. Cohen, MD; Christopher Hartnick, MD, MS Epi

Introduction

- T&A associated with risk of postoperative pain and hemorrhage
- Post-tonsillectomy bleeding (PTB)
  - Categorized by severity or timing
  - Rates 3.3 – 20% (mean 4.5%)

Nonsteroidal anti-inflammatory drugs (NSAIDs)

- Block prostaglandin-induced inflammation
- Do not cause respiratory or central nervous system depression
- May interfere with platelet aggregation → increased risk of bleeding
- Several meta-analyses have NOT shown an increase in PTB

Methods

- Design
  - Multi-center randomized double-blind noninferiority trial
- Participants
  - Ages 2 – 18
  - Sleep disordered breathing (SDB), Obstructive sleep apnea (OSA), Adenotonsillar hypertrophy, Tonsillitis
  - Extracapsular tonsillectomy

Intervention

- All patients received:
  - Preoperative Tylenol (15 mg/kg up to 650 mg)
  - Intraoperative steroids
  - Extracapsular tonsillectomy using electrocautery
    - 12W tonsillectomy
    - 12W – 18W hemostasis
    - 30W adenoidectomy
- Postoperative pain control
  - Ibuprofen OR Tylenol
  - Given every 6 hours for 9 days
  - Oxycodone per surgeon's discretion

Outcomes

- Questionnaire regarding dosage and bleeding
- Bleeding types
  - Type 1: no intervention
  - Type 2: readmission
  - Type 3: return to operating room

Statistics

- Noninferiority study
  - Null hypothesis: rate of type 3 bleeding differed between groups
  - Alternative hypothesis: rate of type 3 bleeding not different than more than the noninferiority margin (3%)

Results

- N = 688 subjects

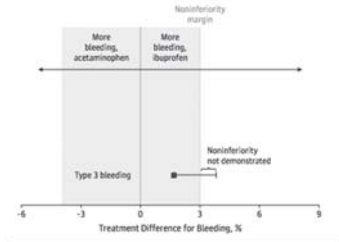
Table 1. Characteristics of Study Patients

Characteristic	Ibuprofen (n = 345)	Acetaminophen (n = 343)
Age, median (IQR), y	5 (4-8)	5 (3-7)
Boys	177 (51.3)	189 (55.1)
Reason for surgery		
OSA and/or ATH	274 (79.4)	264 (77.0)
Tonsillitis only	39 (11.3)	45 (13.1)
Tonsillitis and OSA and/or ATH	29 (8.4)	34 (9.9)
Other only	3 (0.9)	0
Surgery type		
Tonsillectomy alone	23 (6.7)	22 (6.4)
Tonsillectomy with adenoidectomy	321 (93.0)	321 (93.6)
Unknown	1 (0.3)	0
Study location		
MAMC	62 (18.0)	63 (18.4)
MEEI	155 (44.9)	152 (44.3)
NMCP	55 (15.9)	57 (16.6)
NMCSD	73 (21.2)	71 (20.7)

Bleeding

- 65 children (9.4%) developed at least one PTB event
  - 27 (7.9%) children in acetaminophen group
  - 38 (11%) children in ibuprofen group
- Noninferiority of ibuprofen could not be concluded for type 3 bleeding
  - The possibility that ibuprofen causes more severe hemorrhage than acetaminophen could not be excluded.

Figure 2. Type 3 Bleeding Event Rate by Noninferiority Modified Intention-to-Treat Analysis



Treatment difference determined as ibuprofen treatment minus acetaminophen treatment.

Original Research

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery 1–7

DOI: 10.1177/0194599819844786
http://otojournal.org

SAGE

Pediatric Obstructive Sleep-Disordered Breathing: Updated Polysomnography Practice Patterns

Norman R. Friedman, MD[1,2], Amanda G. Ruiz[1,2], Dexiang Gao, PhD[3], Alexandria Jensen, MS[4], and Ron B. Mitchell, MD[5]

Polysomnography Guidelines

- 2011 American Academy of Otolaryngology (AAO)
  - "Polysomnography (PSG) for Sleep Disordered Breathing (SDB) Prior to Tonsillectomy in Children"
  - 5 key action statements
  - Specifically stated that children with Down Syndrome or obesity should undergo PSG prior to T&A
- American Academy of Pediatrics (AAP)
  - Recommend PSG prior to T&A or referral to otolaryngologist or sleep medicine specialist
- American Academy of Sleep Medicine (AASM)
  - Recommend PSG prior to T&A

Practice Patterns before 2011

- PSG patterns
  - 20% of respondents always ordered PSG for Down Syndrome
  - 8% always ordered PSG for obesity
  - 58% ordered for inconsistent history (most common)
- Overnight observation patterns
  - 83% "most of the time" for Down Syndrome
  - 83% "most of the time" for age < 3 years
  - 70% "most of the time" for obesity

Objective

- Examine practice patterns 6 years after the publication of the AAO CPG

*** Side Note***

Updated tonsillectomy guidelines were published in 2019

Methods

- Survey of ASPO Members
  - 17 questions
  - 5 minutes
  - Electronic survey
- Sent to 427 ASPO Members
  - 170 (40%) completed

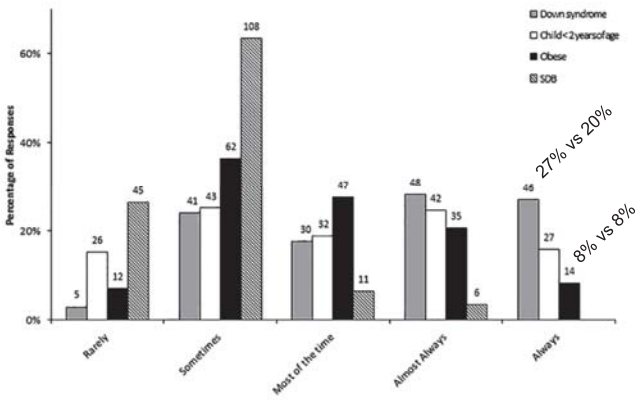
Demographics

- Practice setting
  - 124 (73%) academic practice
  - 46 (27%) private practice
- Length of time in practice
  - 66 (39%) > 21 years
  - 53 (31%) 11 - 20 years
  - 45 (26%) 5 – 10 years
  - 6 (4%) < 5 years
- Snoring 48% of practice (range 8 – 99%)
- 89% referred to dedicated pediatric sleep lab
  - Mean estimated wait time 6.8 weeks

Survey Results

- PSG prior to Tonsillectomy in Healthy 5 Year Old?
  - 58% inconsistent history
  - 25% caregiver uncertainty
  - 7% facilitate perioperative management

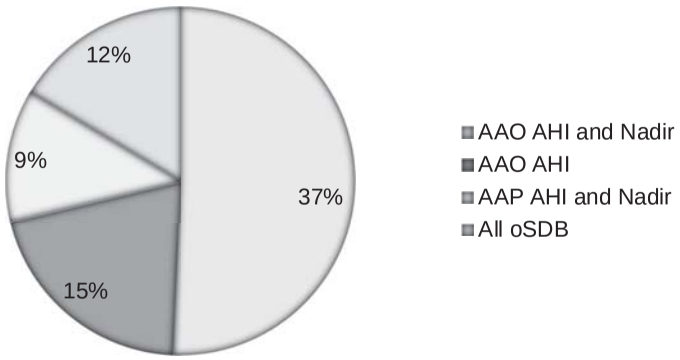
PSG Prior to T&A



Admission patterns without PSG

	n (%)
Respondents[a]	149 (100)
Child with Down syndrome	
Rarely (<10%)	5 (3)
Sometimes (10%-49%)	16 (11)
Most of the time (50%-89%)	19 (13)
Almost always (≥90%)	109 (73)
Child <3 y of age for sleep-disordered breathing	
Rarely (<10%)	7 (5)
Sometimes (10%-49%)	15 (10)
Most of the time (50%-89%)	15 (10)
Almost always (≥90%)	112 (75)
Obese child[b]	
Rarely (<10%)	15 (10)
Sometimes (10%-49%)	46 (31)
Most of the time (50%-89%)	36 (24)
Almost always (≥90%)	51 (34)

Overnight Observation Criteria



Additional Findings

- Increase in use of appropriate BMI metric (58%)
- Down Syndrome
  - Practitioners less likely to order also less likely to admit
- Children < 2 years old
  - Practitioners in academic settings more likely to admit
  - Practitioners with > 21 years experience less likely to admit regardless of practice setting
- Obesity
  - Practitioners in academic settings more likely to admit

Conclusions

- PSG is underutilized by ASPO Members
- Practice patterns not aligned with AAO, AAP, or AASM Guidelines

International Journal of Pediatric Otorhinolaryngology 121 (2019) 179–187

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International Journal of Pediatric Otorhinolaryngology

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Diagnostic techniques and surgical outcomes for persistent pediatric obstructive sleep apnea after adenotonsillectomy: A systematic review and meta-analysis

Melissa A. Socarras[a,b], Barcleigh P. Landau[a], Megan L. Durr[a,*]

Obstructive Sleep Apnea (OSA)

- 1 – 4% of children
- Associated with daytime sleepiness, behavioral and cognitive deficits, developmental delay, pulmonary hypertension, cor pulmonale
- Adenotonsillar hypertrophy = primary cause
  - T&A recommended first line treatment
- 25 – 75% of patients with persistent OSA following T&A
  - Risk factors = obesity, craniofacial anomalies, preoperative severe OSA
- What are the options?

Persistent OSA

- Treatment options
  - Weight loss
  - CPAP
  - Surgery
- Assessment
  - Awake flexible fiberoptic laryngoscopy
    - Poorly tolerated
    - Not dynamic
  - Drug Induced Sleep Endoscopy (DISE)
  - Cine MRI

Study Purpose

- Evaluate efficacy of surgery for children with persistent OSA s/p T&A
- Evaluate surgical outcomes with respect to diagnostic measure employed

Methods

- Systematic review and meta-analysis
- January 2000 - April 2018
- 11 studies included

Results

- 11 studies
  - 5 DISE
  - 4 Cine MRI
  - 2 alternative imaging
- 214 patients
  - Age range 3.1 – 23 years (mean 10.3 years)
- 102/189 (54%) of patients with comorbidities
  - 77 Trisomy 21
  - 23 neuromuscular dysfunction
  - 2 mucopolysaccharidosis
  - 1 Noonan Syndrome
  - 8 unspecified syndrome
- 47/124 (38%) obese

DISE Studies (5)

Study	AHI: Mean (SD), e/hr		MinSaO2: Mean (SD), %	
	Pre	Post	Pre	Post
DISE				
Chan (2012) [22]	12.8 (10.08)	5.7 (6.42)	88.5 (5.5)	90.3 (3.67)
DeMarcantonio (2016) [30]	13.2 (4.6)	24.2 (24.1)	67 (13)	58.2 (31.8)
Slaats (2017) [31]	15.14 (12.26)	7.95 (6.12)	83.9 (7.3)	90.2 (4.1)
Thottam (2015) [32]	27.1 (20.3)	10.9 (11)	74.2 (12.2)	83.2 (8.4)
Wootten (2014) [33]	7.0 (5.8)	3.6 (1.8)	NR	NR

- 120 patients
- Age 10 (+/- 1.2)
- 35% comorbidities
- Most common procedure
  - Lingual tonsillectomy (75%)
- 4/5 with decreased AHI and increased MinSaO2

Cine MRI

Study	AHI: Mean (SD), e/hr		MinSaO2: Mean (SD), %	
	Pre	Post	Pre	Post
CINE MRI				
Propst (2017) [34]	44.3 (30.6)	34.1 (36.4)	74.8 (36.4)	73.7 (18.2)
Prosser (2017) [35]	13.0 (11.8)	4.9 (5.7)	84.0 (8.0)	89.0 (5.0)
Shott (2004) [36]	8.67 (4.08)	3.8 (5.09)	NR	NR
Wootten (2010) [37]	14.1 (10.1)	6.4 (6.5)	86.1 (5.4)	89.1 (7.2)

- 68 patients
- Age 11.4 (+/- 4.2)
- 82% comorbidities
- Most common procedure
  - Lingual tonsillectomy (57%)
- All with decreased AHI
- 2/3 increased MinSaO2

Meta-analysis

- DISE
  - Change in AHI - 6.01
  - Change in MinSaO2 4.07%
- Cine MRI
  - Change in AHI – 7.37
  - Change in MinSaO2 3.53%
- Overall
  - Change in AHI – 6.51
  - Change in MinSaO2 3.24%

Conclusion

- Many surgical options for persistent OSA
- Surgery provides statistically significant improvement in AHI and MinSaO2
- Both DISE and Cine MRI, when used to direct surgery results in improvement in AHI and MinSaO2

Original Research—Pediatric Otolaryngology

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

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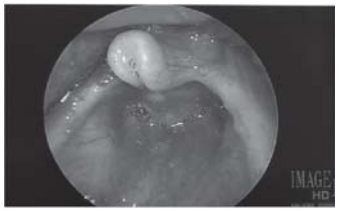
SAGE

Impact of Infant Supraglottoplasty on Quality of Life

Nathan D. Vandjelovic, DO[1], Jason R. Brown, DO[1], Henri T. Traboulsi, MD[2], and Prasad John Thottam, DO[3,4]

Introduction

- Laryngomalacia (LM)
  - Most common cause of pediatric stridor
  - High-pitched inspiratory noise associated with agitation, excitement, feeding, or supine positioning
  - Stridor begins in first weeks of life and peaks around 6 months
  - Mild-moderate disease management conservatively
  - 20% with severe LM
    - Require surgical intervention



Supraglottoplasty

- Standard surgical management
- High success rate

- This study examines quality of life (QOL) in patients with moderate-severe LM
  - Pre and post-supraglottoplasty

Methods

- Cohort study
- 47-item QOL survey
- 121 patients presented with LM
  - N = 39 included in study

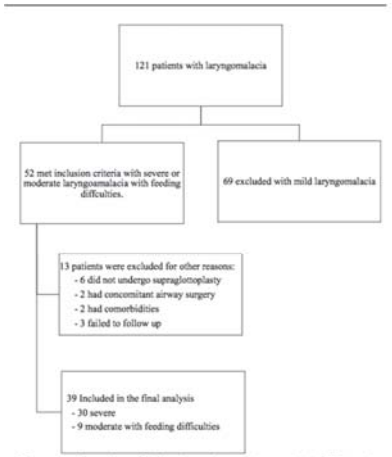


Figure 1. Flowchart of inclusion and exclusion criteria. Thirty-nine patients were included in the final analysis.

Results

- Mean age at surgery = 4 months
- Supraglottoplasty technique:
  - 94.9% AE fold release
  - 56.4% excision of redundant arytenoid mucosa
  - 7.7% laser epiglottopexy

QOL Results

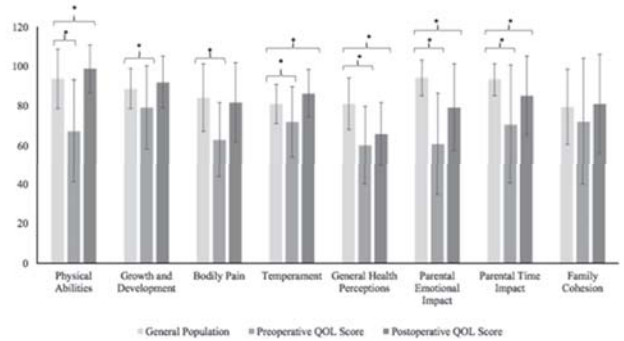
Significant improvement in overall health, physical abilities, satisfaction with growth and development, bodily pain, temperament and mood.

Table 2. Comparison of QOL Scores Following Supraglottoplasty.[a]

	Paired-Samples *t* Test, Mean ± SD				One-way ANOVA	
ITQOL-SF47	Preoperative Score	Postoperative Score	*t*	*p*	*F* (*df*)	*p*
→ Overall health	63.3 ± 19.8	84.4 ± 12.4	−5.3	**<.001**	7.16 (1, 35)	**.011**
→ Physical abilities	67.2 ± 26.5	98.8 ± 11.9	−6.4	**<.001**	9.17 (1, 33)	**.005**
→ Satisfaction with growth and development	79.3 ± 21.5	92.1 ± 13.2	−4.3	**<.001**	7.02 (1, 35)	**.012**
→ Bodily pain	62.8 ± 19.8	81.9 ± 19.9	−4.6	**<.001**	20.0 (1, 35)	**<.001**
→ Temperament and mood	72.0 ± 18.0	86.4 ± 12.2	−5.3	**<.001**	12.72 (1, 35)	**<.001**
General health perception	60.0 ± 20.3	65.8 ± 15.6	−1.7	.095	0.02 (1, 35)	.901
Impact on caregiver						
Emotional impact	60.7 ± 26.2	79.3 ± 21.9	−3.6	**.001**	9.09 (1, 35)	**.005**
Caregiver's time	70.6 ± 29.6	85.3 ± 19.7	−3.1	**.004**	10.38 (1, 35)	**.003**
Family cohesion	72.1 ± 32.0	81.1 ± 24.5	−2.0	.05	0.92 (1, 35)	.344

Abbreviations: ANOVA, analysis of variance; ITQOL-SF47, 47-item short form of the Infant and Toddler Quality of Life Questionnaire–47; QOL, quality of life.
[a]The left columns denote improved QOL scores in most categories after supraglottoplasty. The right columns denote similar improvement when age and sex are controlled. Significant values are set in bold ($P < .05$).

QOL vs. general population



- Significantly worse pre-operative QOL scores compared to general population
- QOL similar to general population post-op in most categories

Conclusion

- Pre-supraglottoplasty QOL significantly worse than general population for patients with severe LM
- Physical ability, temperament and mood, growth and development, bodily pain, and family cohesion score after supraglottoplasty were similar or better than those of the general population
- General health perception, emotional impact on the caregiver, and impact on the caregiver's time remained lower than the general population

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Review Article

Congenital cytomegalovirus infection inducing non-congenital sensorineural hearing loss during childhood; a systematic review

Maria Riga[a,*], George Korres[b], Pantelis Chouridis[a], Stephanos Naxakis[c], Vasilios Danielides[c]

Introduction

- Hearing loss in children
  - Time-critical importance of etiological diagnosis and treatment
    - Important step: Universal Newborn Hearing Screen
    - 40 – 50% of patients with bilateral moderate-severe SNHL during education years
      - No programs to identify late-onset, acquired, or progressive hearing loss
- Congenital CMV Infection (cCMVI)
  - Birth prevalence ~ 0.7%
  - Accounts for 10 – 40% SNHL
    - 30 – 65% in symptomatic
    - 7 – 15% in asymptomatic
  - No guidelines for monitoring hearing

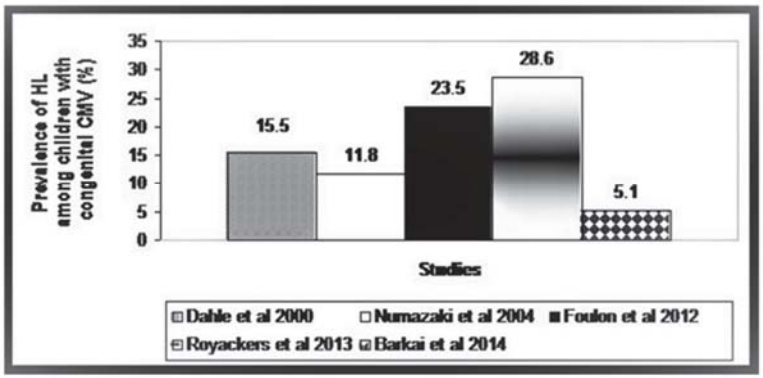
Methods

- Systematic Review
  - Clinic studies referring to neonates with cCMVI with progressive, fluctuating, and late-onset hearing loss
  - Minimum 2 years audiologic follow-up
  - Retrospective or prospective
- 11 studies included

Significant heterogeneity

- Ratios of symptomatic vs asymptomatic
  - +/- gancyclovir
- Diagnostic method
  - Urine, saliva, dried blood spot
- Prospective vs retrospective
- Primary vs non-primary maternal infection
- Etiology of SNHL
  - May have had multiple etiologies – not excluded
- Reported laterality and degree of hearing loss
- Hearing evaluation process

Prevalence of Hearing Loss



Synthesis of Results

- 1089 cCMVI
  - 181 children with cCMVI-induced SNHL (16.6%)
    - 70/784 asymptomatic (8.9%)
    - 107/242 symptomatic (44.2%)
    - Symptomatic children twice as likely to present with SNHL as asymptomatic
- Laterality
  - Unilateral 44.1%

Follow-up

- No conclusions drawn based on lack of data
- Late-onset hearing loss
  - 15.2 years asymptomatic
  - 16.4 years symptomatic
- Progressive hearing loss
  - 15.5 years asymptomatic
  - 17.4 years symptomatic

Suggested Follow-up Principles

- cCMVI testing within first 2-3 weeks
- Audiologic evaluation every 3 months for 2 years
  - Subsequent testing every 6 - 12 months until 5 – 6 years old
- Present data lacking to develop more consensus guidelines

Bibliography

1. Lavin J, Lehmann D, Silva AL, Bai G, Hebal F, Manworren R, Stake C, Rychlik K, Billings KR. Variables associated with pediatric emergency department visits for uncontrolled pain in postoperative adenotonsillectomy patients. Int J Pediatr Otorhinolaryngol. 2019 Apr 26;123:10-14.

2. Friedman NR, Ruiz AG, Gao D, Jensen A, Mitchell RB. Pediatric Obstructive Sleep-Disordered Breathing: Updated Polysomnography Practice Patterns. Otolaryngol Head Neck Surg. 2019 Apr 30:

3. Vandjelovic ND, Brown JR, Traboulsi HT, Thottam PJ. Impact of Supraglottoplasty on Quality of Life. Otolaryngol Hed Neck Surg. 2018 Sep; 159 (3) 564-571

4. Diercks GR, Comins J, Bennett K, Gallagher TQ, Brigger M, Boseley M, Gaudreau P, Rogers D, Setlur J, Keamy D, Cohen MS, Hartnick C. Comparison of Ibuprofen vs Acetaminophen and Severe Bleeding Risk After Pediatric Tonsillectomy: A Noninferiority Randomized Clinical Trial. JAMA Otolaryngol Head Neck Surg. 2019 Apr 4. doi: 10.1001/jamaoto.2019.0269.

5. Socarras MA, Landau BP, Durr ML. Diagnostic techniques and surgical outcomes for persistent pediatric obstructive sleep apnea after adenotonsillectomy: A systematic review and meta-analysis. Int J Pediatr Otorhinolaryngol. 2019 Jun;121:179-187

6. Riga M, Korres G, Chouridis P, Naxakis S, Danielides V. Congenital cytomegalovirus infection inducing non-congenital sensorineural hearing loss during childhood; a systematic review. Int J Pediatr Otorhinolaryngol. 2018 Dec;115:156-164

9th Annual Otolaryngology Literature Update
Head & Neck Oncology I

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David M. Neskey, M.D., MSCR, FACS joined the MUSC Department of Otolaryngology (Ear, Nose and Throat, ENT) in the Head and Neck Surgical Oncology division in 2014. Originally from Massachusetts he received his medical degree from Albany Medical College with a distinction in research in 2006 followed by a residency in ENT at the University of Miami. He then completed a fellowship in head and neck surgical oncology at MD Anderson Cancer Center in Houston.This training experience was comprised of two years dedicated to basic science research followed by a year committed to the management of patients with head and neck cancer.

Dr. Neskey's clinical focus is on the care of patients with benign and malignant growths of the head and neck including oral cavity, oropharyngeal, laryngeal lesions, and skullbase, advanced melanoma and nonmelanoma skin cancers, and lesions of the salivary glands, thyroid and parathyroids. His specific interests are squamous cell carcinoma of the oral cavity and oropharynx along with advanced skin cancer and skull base tumors.

Dr. Neskey has published over 30 peer reviewed articles and book chapters focused on the molecular pathways and genomic alterations associated with head and neck squamous cell carcinoma. Based on this work he is currently funded through the National Institute of Health to study the mechanisms of invasion and metastases in head and neck cancer.

In addition to his lab based studies, Dr. Neskey is the principle investigator in several ongoing trials, including an investigator initiated trial investigating immunotherapy a presurgical treatment for patients with oral cavity cancer.He is board certified by the American Board of Otolaryngology and is a member of the American Head and Neck Society, American Academy of Clinical Research, and a Fellow of the American College of Surgeons.

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Medical University of South Carolina

Head & Neck Oncology I

David M. Neskey, M.D., MSCR

Ebrahimi A, Gil Z, Amit M, Yen TC, Liao CT, Chaturvedi P, Agarwal JP, Kowalski LP, Köhler HF, Kreppel M, Cernea CR, Brandao J, Bachar G, Villaret AB, Fliss DM, Fridman E, Robbins KT, Shah JP, Patel SG, Clark JR; International Consortium for Outcome Research (ICOR) in Head and Neck Cancer. "Depth of invasion alone as an indication for postoperative radiotherapy in small oral squamous cell carcinomas: An International Collaborative Study." Head & Neck. 22019 Jun;41(6):1935-1942. doi: 10.1002/hed.25633. Epub 2019 Feb 24.

Moeckelmann N, Ebrahimi A, Tou YK, Gupta R, Low TH, Ashford B, Ch'ng S, Palme CE, Clark JR. "Prognostic implications of the 8th edition American Joint Committee on Cancer (AJCC) staging system in oral cavity squamous cell carcinoma." Oral Oncology. 2018 Oct;85:82-86. doi: 10.1016/j.oraloncology.2018.08.013. Epub 2018 Sep 4.

Rettig EM, Zaidi M, Faraji F, Eisele DW, El Asmar M, Fung N, D'Souza G, Fakhry C. "Oropharyngeal cancer is no longer a disease of younger patients and the prognostic advantage of Human Papillomavirus is attenuated among older patients: Analysis of the National Cancer Database." Oral Oncology. 2018 Aug;83:147-153. doi: 10.1016/j.oraloncology.2018.06.013. Epub 2018 Jun 27.

Sathasivam HP, Bhatia R, Bradley P, Robson A, Paleri V, Cocks H, Oozeer N, Milne D, Sloan P, Robinson M. "Concurrent HPV-related oropharyngeal carcinoma in four couples." Oral Oncology. 2018 Nov;86:33-37. doi: 10.1016/j.oraloncology.2018.09.003. Epub 2018 Sep 11.

Suhas Kodasoge Rajappa, Udip Maheshwari, Jiten Jaipuria, Anupam Kumar Singh, Sumit Goyal, Ullas Batra, Rajeev Kumar, Ajay Kumar Dewan. "Number of positive nodes – Current relevance in determining prognosis of oral cavity cancer after the recent AJCC staging update." Oral Oncology. 2019 March; 90:1-5. doi.org/10.1016/j.oraloncology.2019.01.001.

Torrecillas V, Shepherd HM, Francis S, Buchmann LO, Monroe MM, Lloyd S, Cannon D, Hitchcock YJ, Weis JR, Hunt JP, Houlton JJ, Cannon RB. "Adjuvant radiation for T1-2N1 oral cavity cancer survival outcomes and utilization treatment trends: Analysis of the SEER database." Oral Oncology. 2018 Oct;85:1-7. doi: 10.1016/j.oraloncology.2018.07.019. Epub 2018 Aug 6.

Presentation not available at press time; handouts are available at the registration desk.

9th Annual Otolaryngology Literature Update
Audiology

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Dr. Camposeo grew up in the suburbs of New York City. She is a cum laude graduate of Emerson College in Boston and received her graduate degree from Northwestern University in Chicago. She completed her clinical externship year at NYU Cochlear Implant Center. Dr. Camposeo joined the faculty at MUSC in 2011.

Dr. Camposeo has focused clinically on cochlear implants and adult diagnostics. She evaluates potential adult cochlear implant candidates and manages a caseload of implant recipients. Dr. Camposeo is involved in independent and industry-sponsored research looking at cochlear implant performance.

Current Trends in Audiology

Elizabeth Camposeo, AuD
Clinical Assistant Professor
Interim Clinical Director- CI Program

Topics

- Hearing aids, Over-the-counter (OTC) hearing aids, & Personal sound amplification products (PSAPs)
- Osseointegrated devices (OIDs)
- Cochlear implants (CIs)

Current (Traditional) Hearing Aid technology

Mild to profound hearing loss

May be sensorineural, conductive, or mixed

Tinnitus management (Tunkel et al 2014)

Bilateral is better than unilateral

CROS system can route sound to poor ear in cases of asymmetrical hearing loss

Unaddressed hearing loss associated with higher risk of dementia (Rutherford et al 2018), social isolation, and depression in older adults

Current (Traditional) Hearing Aid technology

- Wireless Bluetooth streaming
- Rechargeable batteries
- Applications for remote control
- Faster, smarter noise algorithms
- Smaller size
- Built in fitness tracker

Personal sound amplification products- PSAPs

- ***Not*** intended for people with hearing loss
- Not allowed to be marketed for hearing loss
- May use “hearing enhancement”
- Readily available in drug stores and online
- Can be very inexpensive but there is a range ($20-$500)

How helpful are they?

One study found that low-end devices had excessive circuit noise but that more expensive devices performed adequately (Callaway & Punch 2018)

Another study found similar to near similar improvement from unaided to aided between traditional hearing aids and some PSAPs. There was one PSAP that resulted in a significant decrease in performance (Reed et al 2017).

OTC Hearing aids

2017 FDA Reauthorization Ace

- FDA will create a new category of device- in place by 2020
- Can be marketed for hearing loss but does not require a professional
- Mild-to-moderate hearing loss

Lower cost than traditional HA!

Benefit is yet to be determined- no devices available until 2020

Assume better benefit than PSAPS but still limited fitting range

What's the best option?

May be better for bargain hunter patients to wear something instead of nothing

OTC hearing aids are for MILD TO MODERATE hearing losses only

- Unlikely that patients can accurately self-identify degree of hearing loss = poor fit
- Poor fit at best just not helpful, at worst potentially harmful
- Study found that there was benefit to wearers, but significantly more benefit with Audiology follow up

Unclear at this time if OTC hearing aids will have all the same functions as traditional hearing aids

For most patients the best outcomes will be from traditional hearing aids

- Audiologists can:
  - Pick the most appropriate device
  - Optimize the fit and programming for functional outcomes
    - Hearing aids fit using Real ear verification measures produce better speech recognition outcomes than manufacturer software fit alone (Valente et al 2018)
  - Counsel realistic expectations
  - Suggest assistive technology

Osseointegrated Devices

1. Cochlear Baha and 2. Oticon Ponto

May use:

Magnetic coupling- transcutaneous

Abutment- percutaneous (most power)

Softband- transcutaneous

3. ADHEAR uses adhesive on the skin (least power)

Osseointegrated Devices

Can be used for

- Conductive hearing loss
- Mixed hearing loss
- Unilateral sensorineural hearing loss/Single sided deafness (SSD)

Osseointegrated Devices- Cochlear & Oticon

Conductive HL

- Air-bone gap of at least 30 dB
- May consider magnetic retention

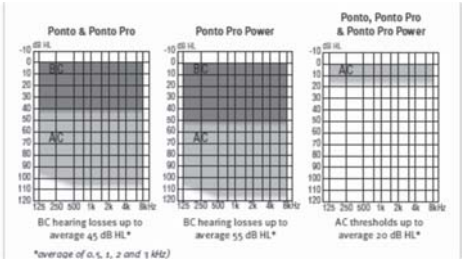
Mixed HL

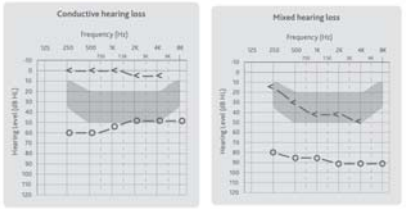
- Bone scores no worse than 65 dB (*may require power product)*
- Mild loss- may consider magnetic retention
- *Greater degree of loss will require abutment*

Unilateral sensorineural HL/SSD

- Depends on normal hearing good ear
- May consider magnetic retention (depends on transcranial attenuation)

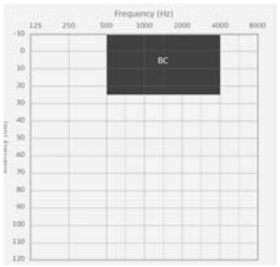
Osseointegrated Devices- Cochlear & Oticon





Osseointegrated Devices- ADHEAR

ONLY mild conductive



SSD

Cochlear implants

Adult: Moderate-to-profound sensorineural hearing loss and poor aided word recognition (*sentences*)

Pediatric: Severe-to-profound sensorineural hearing loss and poor language development

Recent approval of hybrid/electroacoutic devices- good low frequency hearing but poor high frequency hearing & poor aided word recognition (WORDS)

Cochlear implants

Bimodal patients- use 1 hearing aid and 1 CI

- More common than ever before
- Patients with asymmetrical hearing are being implanted

All bilateral listeners perform better than unilateral CI users (Firszt et al 2008; Dunn et al 2010; van Schoonhoven et al 2013)

If patient has PTA better than 55 dB HL (Yoon et al 2012) or CNC word score of 40% or better in the hearing aid ear (Blamey et al 2105), than bimodal is typically the best option

Off-label CI

Cochlear implants have been used for SSD

Typically have some other justification besides SSD

- Bothersome, intractable tinnitus
- Reason to believe the good ear is susceptible to hearing loss
  - IE- Meniere's disease, EVA, etc

SSD- So many options

CROS or BiCROS hearing aid

Osseointegrated device

Cochlear implant

CI is the only option that restores hearing in the poorer ear as other options route sound to the better ear

Significantly better speech discrimination and localization ability with CI than OI or CROS (Arndt et al 2017)

Articles

Arndt, S., Kaszig, R., Aschendorff, A., Hassenpass, F., Beck, R., & Wesarg, T. Cochlear implant treatment of patients with single-sided deafness or asymmetric hearing loss. *HNO, 65 Supplement 2:* 98-108.

Blamey, P.J., Maat, B., Baskent, D., Mawman, D., Burke, E., Dillier, N., … Lazard, D.S. (2015) A retrospective multicenter study comparing speech perception outcome for bilateral implantation and bimodal rehabilitation. *Ear & Hearing,* Epub.

Callaway, S.L., & Punch, J.L. (2008). An electroacoustic analysis of over-the-counter hearing aids. *American Journal of Audiology, 17(1): 12-24.*

Dunn, C.C., Noble, W., Tyler, R.S., Kordus, M., Gantz, B.J., Ji, H. (2010). Bilateral and unilateral cochlear implant users compared on speech perception in noise. *Ear & Hearing, 31,* 296–298.

Firszt, J. B., Reeder, R. M., Skinner, M. W. (2008). Restoring hearing symmetry with two cochlear implants or one cochlear implant and a contralateral hearing aid. *Journal of Rehabilitation Research & Development, 45*, 749–767.

Humes, L.E., Kinney, D.L, Main, A.K., & Rogers, S. E. (2019). A follow-up clinical trial evaluating the consumer-decides service delivery model. *American Journal of Audiology, 15* (1): 69-84.

Reed, N.S., Betz, J., Kendig, N., Korczak, M., & Lin, F.R. (2017). Personal sound amplification products vs a conventional hearing aid for speech understanding in noise. *JAMA, 318(1):* 89-90.

Rutherford, B.R., Brewster, K., Golub. J.S., Kim, A.H., & Roose, S.P.(2018). Sensation and Psychiatry: Linking age-related hearing loss to late-life depression and cognitive decline. *American Journal of Psychiatry, 175 (3):*215-224.

Tunkel, D., Bauer, C., Sun, G., Rosenfeld, r., Chandrasekhar, S., Cunningham, E., … Whamond, E. (2014). Clinical practice guideline. *Otolaryngology- Head and Neck Surgery,* 151(4): 533-541.

Valente, M., Oeding, K., Brockmeyer, A., Smith, S., Kallogjeri, D. (2018). Differences in word and phoneme recognition in quiet, sentence recognition in noise, and subjective outcomes between manufacturer first-fit and hearing aids programmed to NAL-NL2 using real-ear measures. *Journal of the American Academy of Audiology, 29(8)*: 706-721.

van Schoonhoven, J., Sparreboom, M., van Zanten, B. G., Scholten, R.J., Mylanus, E.A., Dreschler, W.A., Grolman, W., Maat, B. (2013). The effectiveness of bilateral cochlear implants for severe-to-profound deafness in adults: A systematic review. *Otology & Neurotology, 34,* 190–198.

Yoon, Y., Shin, Y., & Fu, Q. (2012). CIlinical selection criteria for a second cochlear implant for bimodal listeners. *Otology & Neurotology, 33:1161-1168*

9th Annual Otolaryngology Literature Update
Thyroid & Parathyroid Surgery

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A native of New York City, Eric J. Lentsch, M.D. moved to Louisville, KY, early in childhood and spent most of his formative years there. He received a bachelor's degree in Zoology from the University of Kentucky and a medical degree from the University of Louisville in 1992.

After completing a residency in Otolaryngology - Head and Neck Surgery at the University of Louisville, he served as a fellow in Head and Neck Surgery at the M.D. Anderson Cancer Center in Houston, Texas, from 1999 until 2001. In 2001, he returned to the University of Louisville as the Louisa Bumgardner Professor of Otolaryngologic Research within the Division of Otolaryngology - Head and Neck Surgery. There, he served as the director of research and received the Vincent J. Hyams Award for Excellence in Resident Education three times. In addition, he established and led the Multidisciplinary Head and Neck Cancer Clinic at the James Graham Brown Cancer Center.

In December 2006, Dr. Lentsch moved from Louisville to Charleston to join the Department of Otolaryngology - Head and Neck Surgery at the Medical University of South Carolina. Dr. Lentsch's clinical interests include head and neck oncology, general otolaryngology, endoscopic sinus surgery, and endocrine surgery using minimally invasive techniques for thyroid and parathyroid surgery.

For the past eight years, Dr. Lentsch has used a video-assisted technique for thyroidectomy and currently has one of the largest series of patients who have undergone this technique in the United States. Dr. Lentsch's research interests focus on prognostic factors related to head and neck and endocrine cancer. Using national databases, he has studied oral, laryngeal, oropharyngeal, and sino-nasal cancers, as well as thyroid and skin cancers. His efforts are made to improve prognosis and survival in these cancers.

9th Annual Otolaryngology Literature Update
Medical University of South Carolina

Thyroid & Parathyroid Surgery

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Amendoeira I, Maia T, Sobrinho-Simões M. "Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): impact on the reclassification of thyroid nodules." Endocrine Related Cancer. 2018 Apr;25(4):R247-R258. doi: 10.1530/ERC-17-0513. Epub 2018 Feb 9.

Ladurner R, Al Arabi N, Guendogar U, Hallfeldt K, Stepp H, Gallwas J. "Near-infrared autofluorescence imaging to detect parathyroid glands in thyroid surgery." Annals of the Royal College of Surgeons of England. 2018 Jan;100(1):33-36. doi: 10.1308/rcsann.2017.0102. Epub 2017 Sep 15.

Moskalenko M, Asai M, Beem K, Pezzi TA, Brophy CL, Noonan K, Pezzi CM. "Incidence of Surgical Site Infections after Thyroid and Parathyroid Surgery: No Role for Antimicrobial Prophylaxis." The American Surgeon. 2018 Jun 1;84(6):897-901.

Perrier ND, Brierley JD, Tuttle RM. "Differentiated and anaplastic thyroid carcinoma: Major changes in the American Joint Committee on Cancer eighth edition cancer staging manual." CA: A Cancer Journal for Clinicians. 2018 Jan;68(1):55-63. doi: 10.3322/caac.21439. Epub 2017 Nov 1.

Schneider R, Randolph GW, Dionigi G, Wu CW, Barczynski M, Chiang FY, Al-Quaryshi Z, Angelos P, Brauckhoff K, Cernea CR, Chaplin J, Cheetham J, Davies L, Goretzki PE, Hartl D, Kamani D, Kandil E, Kyriazidis N, Liddy W, Orloff L, Scharpf J, Serpell J, Shin JJ, Sinclair CF, Singer MC, Snyder SK, Tolley N, Van Slycke S, Volpi E, Witterick I, Wong RJ, Woodson G, Zafereo M, Dralle H. "International neural monitoring study group guideline 2018 part I: Staging bilateral thyroid surgery with monitoring loss of signal." The Laryngoscope. 2018 Oct;128 Suppl 3:S1-S17. doi: 10.1002/lary.27359. Epub 2018 Oct 5.

Vidal Fortuny J, Sadowski SM, Belfontali V, Guigard S, Poncet A, Ris F, Karenovics W, Triponez F. "Randomized clinical trial of intraoperative parathyroid gland angiography with indocyanine green fluorescence predicting parathyroid function after thyroid surgery." The British Journal of Surgery. 2018 Mar;105(4):350-357. doi: 10.1002/bjs.10783. Epub 2018 Feb 6.

Wu CW, Dionigi G, Barczynski M, Chiang FY, Dralle H, Schneider R, Al-Quaryshi Z, Angelos P, Brauckhoff K, Brooks JA, Cernea CR, Chaplin J, Chen AY, Davies L, Diercks GR, Duh QY, Fundakowski C, Goretzki PE, Hales NW, Hartl D, Kamani D, Kandil E, Kyriazidis N, Liddy W, Miyauchi A, Orloff L, Rastatter JC, Scharpf J, Serpell J, Shin JJ, Sinclair CF, Stack BC Jr, Tolley NS, Slycke SV, Snyder SK, Urken ML, Volpi E, Witterick I, Wong RJ, Woodson G, Zafereo M, Randolph GW. "International neuromonitoring study group guidelines 2018: Part II: Optimal recurrent laryngeal nerve management for invasive thyroid cancer-incorporation of surgical, laryngeal, and neural electrophysiologic data." The Laryngoscope. 2018 Oct;128 Suppl 3:S18-S27. doi: 10.1002/lary.27360. Epub 2018 Oct 6.

Thyroid and Parathyroid

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7

Pre-Test

Pre-Test

T or F? Although surgical infections are rare in thyroid and parathyroid surgery, perioperative antibiotic prophylaxis substantially decreases them.

Pre-Test

When RLN monitoring is performed during thyroidectomy and loss of signal (LOS) is seen on the first side, what is the rate of LOS on the second side?

A. 1%

B. 3%

C. 7%

D. 20%

Pre-Test

T or F? In patients with thyroid cancer undergoing surgery, recurrent laryngeal nerve invasion does not impact survival.

Pre-Test

T or F? Patients who have differentiated thyroid cancers staged T3 N2 M1 have what stage of disease.

A. I
B. II
C. III
D. IV

Post-Test

The newly created tumor category non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) has had what effect on cancer rates within the different Bethesda categories?

A. Increased rates
B. Decreased rates

Extra Credit: What category is affected the most?

Pre-Test

T or F? Near-infrared autofluorescence imaging can not only detect parathyroid glands during thyroid surgery, but can also predict their function after surgery

1

Incidence of Surgical Site Infections after Thyroid and Parathyroid Surgery: No Role for Antimicrobial Prophylaxis

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- To better define the value of antimicrobial prophylaxis (AMP) and antiseptic skin preparation (ASP) in thyroid and parathyroid surgery, we examined the rate of surgical site infections (SSIs) with and without AMP.
- Patients undergoing thyroid or parathyroid surgery with data entered into the National Surgical Quality Improvement Program database at our institution between November 2007 and June 2015 were studied, including patient demographics, wound classification, other risk factors for SSI, and wound outcome.
- Charts were retrospectively reviewed for AMP, ASP, and use of drains.

- 534 patients
  - Type of surgery
    - 358 thyroidectomy
    - 176 parathyroidectomy
  - Comorbidites
    - Diabetes (10.9%)
    - Smokers (10.1%)
    - Steroids (2.6%)steroids
  - Atimicrobial prophylaxis
    - Yes (26%) using cefazolin, vancomycin, or clindamycin. T
    - No (74%)
  - Surgical site infections
    - Zero infections occurred in the group who did not receive AMP. One (0.7%) superficial, nonpurulent SSI occurred in the group that received AMP which was not statistically significantly different (*P* = 0.319).

TABLE 1. *Demographics, Risk Factors, Details of Operative Procedures, and Rate of SSI in 534 Patients Undergoing Thyroid and Parathyroid Surgery, 2007 to 2015*

Characteristics	Prophylactic Antibiotics (n = 141)	No Antibiotics (n = 393)	*P* Value	Total (n = 534)
Age, mean (years)	59.6	60.6	0.429	60.5
Female, n (%)	108 (76.8)	308 (78.3)	0.702	416 (77.9)
Male, n (%)	33 (23.2)	85 (21.7)		118 (22.1)
BMI (mean)	28.7	28.3	0.517	28.4
Diabetes, n (%)	23 (16.2)	35 (8.9)	0.017	58 (10.9)
Steroids, n (%)	2 (1.4)	12 (3.1)	0.291	14 (2.6)
Tobacco smoking, n (%)	18 (12.8)	36 (9.2)	0.237	54 (10.1)
Procedure				
Parathyroidectomy	35 (24.6)	141 (36.0)	0.038	176 (33.0)
Thyroid lobectomy	59 (41.5)	148 (37.8)	0.298	207 (38.8)
Total thyroidectomy	48 (33.8)	103 (26.3)		151 (28.3)
OR time, minutes (median)	79	105	0.341	97
Drain placed	7 (5.0)	4 (1.0)	0.001	11 (2.1)
Skin preparation				
Betadine	134 (95.0)	379 (96.4)	0.776	513 (96.1)
Cloraprep	5 (3.6)	12 (3.1)		17 (3.2)
Wound classification				
Clean	141 (100)	391 (99.5)	0.394	532 (99.6)
Clean, contaminated	0	2 (0.51)		2 (0.4)
SSI, n (%)	1 (0.7)	0 (0)	0.319	1 (0.2)

Take Home Pearl

Patients undergoing routine thyroidectomy and parathyroidectomy do not require antimicrobial prophylaxis

Questions

Notes

Contemporary Review

International Neural Monitoring Study Group Guideline 2018 Part I: Staging Bilateral Thyroid Surgery With Monitoring Loss of Signal

Rick Schneider, MD; Gregory W. Randolph, MD, FACS, FACE; Gianlorenzo Dionigi, MD, FACS; Che-Wei Wu, MD, PhD; Marcin Barczynski, MD, PhD, FEBS-ES; Feng-Yu Chiang, MD; Zaid Al-Quaryshi, MD, MPH; Peter Angelos, MD, PhD; Katrin Brauckhoff, MD; Claudio R. Cernea, MD; John Chaplin, MB, ChB FRACS; Jonathan Cheetham, VetMB, PhD, DACVS; Louise Davies, MD, MS; Peter E. Goretzki, MD; Dana Hartl, MD; Dipti Kamani, MD; Emad Kandil, MD, MBA, FACS; Natalia Kyriazidis, MD; Whitney Liddy, MD; Lisa Orloff, MD, FACS; Joseph Scharpf, MD; Jonathan Serpell, MD, FACS, Med; Jennifer J. Shin, MD; Catherine F. Sinclair, MD; Michael C. Singer, MD, FACS; Samuel K. Snyder, MD, FACS; Neil S. Tolley, MD; Sam Van Slycke, MD; Erivelto Volpi, MD; Ian Witterick, MD, FRCSC; Richard J. Wong, MD, FACS; Gayle Woodson, MD; Mark Zafereo, MD, FACS; Henning Dralle, MD, FRCS, FACS, FEBS

- The International Neural Monitoring Study Group (INMSG) is a multidisciplinary international group established in 2006 comprising otolaryngologists, general surgeons, laryngologists, voice and laryngeal electromyography specialists, and anesthesiologists
- The INMSG recognizes that neural monitoring adds a new functional dynamic to thyroid surgery and most importantly, nerves that appear morphologically intact to a surgeon's eye are not always functionally intact.

- Accurate RLN paralysis rates can be difficult to obtain
- Isolated expert reports of low rates (1-3%) by high-volume surgeons are of little significance to the patient undergoing routine thyroidectomy around the world.
- Evidence from two large national databases (the Scandinavian Quality Register and the British Association of Endocrine and Thyroid Surgeons audit) suggests that the rates of paralysis based on symptomatic assessment double when patients routinely undergo postoperative laryngeal exam.
  - Jeannon et al., in a recent meta-analysis of more than 25 thousand patients, found a postsurgery VCP rate of 9.8%.
  - Francis reviewed over 5 thousand patients undergoing thyroidectomy and found a unilateral VCP rate of 9%.
  - Steurer et al. reported a 6% rate of temporary and a 3% rate of permanent VCP

- Bilateral VCP rates may also be difficult to obtain, given the associated symptom variability, inconsistency in performing postoperative laryngeal exam, and variability in the need to secure the airway surgically.
- In existing English literature reporting on bilateral VCP, when bilateral VCP occurs after thyroidectomy, it is found to be permanent in 45% of patients.
- The risk of tracheotomy with bilateral VCP averages 30%, with an additional 21% requiring other varieties of acute airway surgery.
- Thus, overall 50% of the patients with bilateral VCP require acute airway intervention

- One of the benefits of neural monitoring is not only to inform when injury has occurred but also to potentially identify the mechanism and the site of injury.
- LOS is a significantly worrisome intraoperative adverse electromyography (EMG) event. The definition of LOS as 100 μV or less was proposed by the INMSG in 2011.
- Two articles by German and American authors have defined our initial understanding of adverse EMG events during surgery; both found that nearly 80% of neural injury was due to traction at the ligament of Berry.
- In a study by Dionigi et al. consisting of 281 injured nerves associated with temporary or permanent postoperative VCP identified intraoperatively by LOS, only 14% of such injuries were visually evident intraoperatively, emphasizing the importance of neural signal loss information and the lack of sensitivity of visual neural inspection.

- Injury mechanisms in order of frequency were: traction > thermal > compression > clamping > ligature entrapment > suction-related injury > transection.

- The initial rates of RLN paralysis with permanent postoperative VCP rates listed in parenthesis were, respectively:
  - Traction 98% (1.4%),
  - Thermal 72% (28%),
  - Compression 100% (0%)
  - Clamping injury 50% (50%)
  - Ligature-associated injury 100% (0%)
  - Suction-related injury 100% (0%)
  - Transection 100% (100%).
  - Thus, thermal, clamping, and transection are the most serious injuries in terms of risk for long-term VCP.

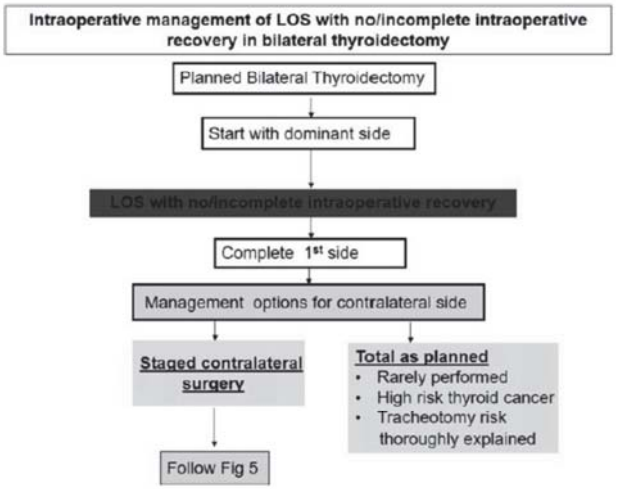
Clinical Evidence for Neural Monitoring-Based Surgical Staging

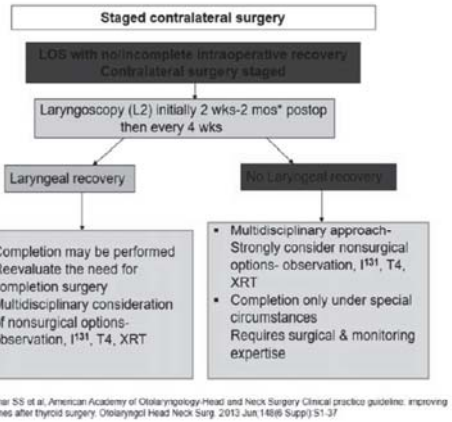
- Goretzki et al. found in a series of over 2,600 nerves at risk that the rate of bilateral cord paralysis was 17% if LOS was undetected or disregarded despite detection, and it was zero if the second side was aborted or performed as a staged procedure.
- Similarly, Melin et al. found that continuation of the surgery on the second side after initial LOS resulted in a 16% rate of bilateral VCP versus zero ($P = 0.017$) in patients undergoing staged procedure after ipsilateral LOS.
- Melin et al. subsequently reported that in 3,426 nerves at risk after ipsilateral LOS, the contralateral nerve injury rate was 28.6%.
- Sarkis et al., reporting on over 7,400 patients from a high-volume tertiary center, described seven patients with bilateral cord paralysis and noted that five of these patients (including one resultant death) would have been prevented by routine use of monitoring with staged surgery after ipsilateral LOS.
- Sadowski et al., in a single arm study of 220 patients utilizing a staged approach for LOS occurring on the first side, found no cases of bilateral cord paralysis.

- Why the rate of contralateral cord paralysis after ipsilateral LOS leading to bilateral VCP is as high as the literature suggests is unclear, but it may be in part due to both patient and surgeon related factors.
- LOS is a relatively rare event and suggests a rare and complex surgical patient. This surgical complexity may not be localized solely to one side, and thus contralateral injury may be increased due to that surgical thyroid host complexity.
- Surgeon issues such as increased concern and decreased ease during contralateral surgery—realizing the first side has not gone well and that the second side now risks potential tracheotomy—may also impact the situation. Surgical complications and procedures not going as planned are among the top stressors that impair a surgeon's performance.

INMSG recommendation I.
The INMSG recommends that neural monitoring information should be obtained and utilized in the strategy of a planned bilateral procedure by staging the surgery in the setting of ipsilateral LOS. This algorithm should be shared and discussed with the patient during the preoperative informed consent process.

INMSG recommendation II.
The INMSG feels a surgeon should prioritize concern for the obvious significant medical and psychological morbidity of bilateral VCP and possible tracheotomy (even temporary) over perceived surgical convenience, the routine of doing the "planned procedure" or the potential perceived impact on surgical reputation by openly acknowledging the surgical complication of ipsilateral loss of signal. The full benefit of neural monitoring information in this surgical setting is appreciated through both optimization of the patient's quality of life as well as surgical cost. [102]





*Chandrasekhar SS et al, American Academy of Otolaryngology-Head and Neck Surgery Clinical practice guideline: improving voice outcomes after thyroid surgery. Otolaryngol Head Neck Surg. 2013 Jun;148(6 Suppl):S1-37

Fig. 5. Staged contralateral surgery management when there is intraoperative loss of signal with no/incomplete intraoperative recovery. LOS = loss of signal.

Take Home Pearl

When there is LOS on the first side, with inadequate recovery in a procedure planned as a total thyroidectomy, the surgeon should expect at least temporary ipsilateral nerve paralysis, which means that proceeding with contralateral surgery may increase the risk of bilateral VCP postoperatively. In such a setting, a surgeon should consider a staged completion surgery

Questions

Notes

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3

Contemporary Review

International Neuromonitoring Study Group Guidelines 2018: Part II: Optimal Recurrent Laryngeal Nerve Management for Invasive Thyroid Cancer—Incorporation of Surgical, Laryngeal, and Neural Electrophysiologic Data

Che-Wei Wu, MD, PhD; Gianlorenzo Dionigi, MD, FACS; Marcin Barczynski, MD, PhD, FEBS-ES; Feng-Yu Chiang, MD; Henning Dralle, MD, FRCS, FACS, FEBS; Rick Schneider, MD; Zaid Al-Quaryshi, MD, MPH; Peter Angelos, MD, PhD; Katrin Brauckhoff, MD; Jennifer A. Brooks, MD, MPH; Claudio R. Cernea; John Chaplin, MB, ChB, FRACS; Amy Y. Chen, MD, MPH, FACS; Louise Davies, MD, MS; Gill R. Diercks, MD, MPH; Quan Yang Duh, MD; Christopher Fundakowski, MD; Peter E. Goretzki, MD; Nathan W. Hales, MD, FACS; Dana Hartl, MD; Dipti Kamani, MD; Emad Kandil, MD, MBA, FACS; Natalia Kyriazidis, MD; Whitney Liddy, MD; Akira Miyauchi, MD; Lisa Orloff, MD, FACS; Jeff C. Rastatter, MD; Joseph Scharpf, MD; Jonathan Serpell, MD, FACS Med; Jennifer J. Shin, MD; Catherine F. Sinclair, MD; Brendan C. Stack Jr. MD, FACS, FACE; Neil S. Tolley, MD; Sam Van Slycke, MD; Samuel K. Snyder, MD, FACS; Mark L. Urken, MD; Erivelto Volpi, MD; Ian Witterick, MD, FRCSC; Richard J. Wong, MD, FACS; Gayle Woodson, MD; Mark Zafereo, MD, FACS and Gregory W. Randolph, MD, FACS, FACE

- The RLN is one of the most frequent sites of invasion for locally aggressive thyroid cancer, but the preoperative detection of RLN invasion is problematic.
- RLN dysfunction may present with voice related and/or aspiration issues. However, many patients with RLN invasion are completely asymptomatic.
- Nerve invasion is a gradual process that takes weeks, months, or years. Glottic function may be supported during this process through compensation by the contralateral functioning cord, thereby offsetting the symptoms of neural dysfunction. .

- It is the clinicians' responsibility to diagnose potential invasive disease by looking for related risk factors in addition to careful assessment of clinical presentation including comprehensive clinical, laryngeal, and radiologic workup.
- Preoperative diagnosis of potential RLN invasion demands this meticulous preoperative approach, and in turn optimizes thoughtful preoperative discussion with the patient during the informed consent process, further helping to manage the patient's consequent postoperative expectations.

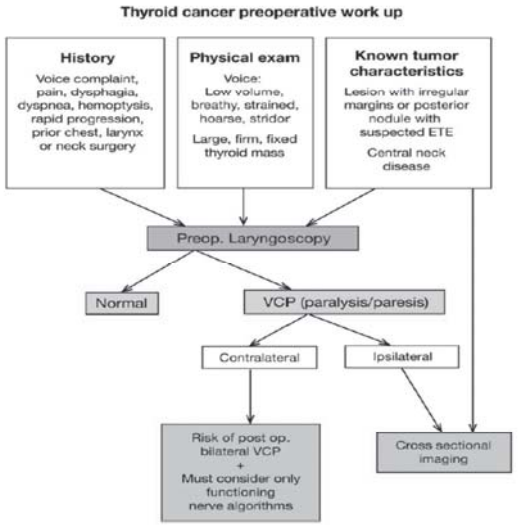


TABLE I.
Recurrent Laryngeal Nerve Risk–Benefit Factors

Laryngeal Factors

1. Preoperative ipsilateral laryngeal function
2. Preoperative contralateral nerve status (nerve function as well as disease involvement)
3. IONM: Intraoperative proximal nerve EMG signal status
4. Impact of nerve resection on the patient (e.g. professional voice-users, aspiration in geriatric patients)

Oncologic Factors

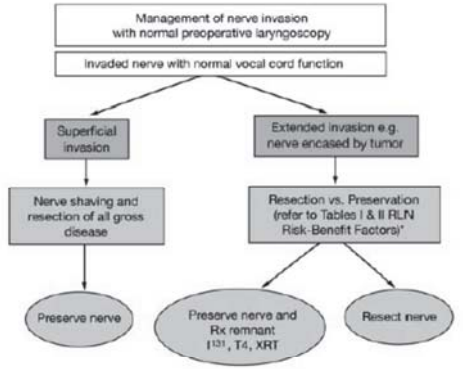
5. Possibility of complete resection of all gross disease with nerve resection
6. Prognostic impact of leaving residual tumor on the nerve:
   - -amount and histology of tumor left
   - -invasion site/likelihood of subsequent visceral axis invasion
7. Distant metastasis - presence, critical location and activity
8. Perceived responsiveness to postoperative adjuvant nonsurgical treatment - most notably RAI avidity, Thyroxine (T4) suppression and in some circumstances external beam.

EMG = electromyogram; IONM = intraoperative nerve monitoring; RAI = radioactive iodine.

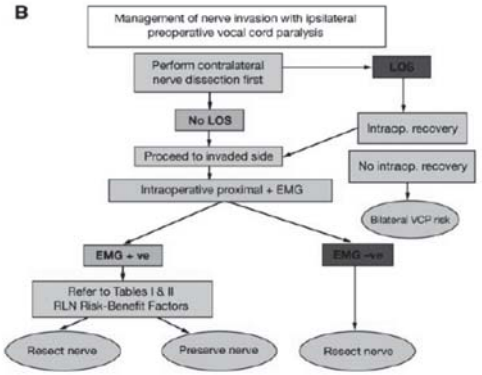
TABLE II.
Factors in Favor of Nerve Sparing Versus Nerve Sacrifice

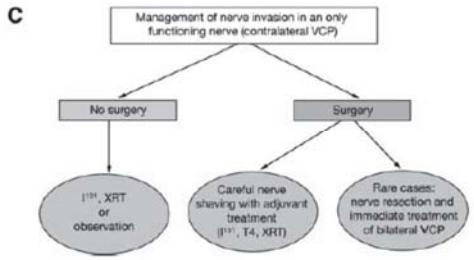
Factors in favor of nerve sparing (even if incomplete tumor resection)	**Factors in favor of nerve sacrifice** (with complete tumor resection) to improve disease-free or overall survival
Young patients, generally iodine-avid patients, papillary thyroid carcinoma	Aggressive histopathological and genetic variants
Efficiency of adjuvant therapy (iodine or external beam radiation therapy) judged to be good	Iodine-refractory disease (recurrences) Previous external beam radiation therapy
Elderly patients (increased risk of aspiration pneumonia)	
Reduced pulmonary capacity, chronic bronchitis (lower tolerance of microaspiration)	
Voice professionals/ Patient preferences	Nerve invasion at the neural entry point to the larynx (this may increase risk of subsequent visceral axis invasion with persistent gross disease)
Contralateral vocal cord paralysis	Normal contralateral vocal fold function
Known active distant metastases	No/ indolent distant metastases

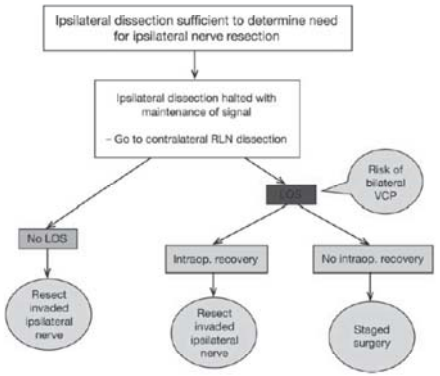
A



B




C
Management of nerve invasion in an only functioning nerve (contralateral VCP)
No surgery
Surgery
I131, XRT or observation
Careful nerve shaving with adjuvant treatment (I131, T4, XRT)
Rare cases: nerve resection and immediate treatment of bilateral VCP


Ipsilateral dissection sufficient to determine need for ipsilateral nerve resection
Ipsilateral dissection halted with maintenance of signal
– Go to contralateral RLN dissection
Risk of bilateral VCP
No LOS
Intraop. recovery
No intraop. recovery
Resect invaded ipsilateral nerve
Resect invaded ipsilateral nerve
Staged surgery

Questions

Notes

4

Differentiated and Anaplastic Thyroid Carcinoma: Major Changes in the American Joint Committee on Cancer Eighth Edition Cancer Staging Manual

Nancy D. Perrier, MD, FACS [1]; James D. Brierley, MS, MB[2]; R. Michael Tuttle, MD[3]

- Authors used a

DEFINITION OF PRIMARY TUMOR (T)	
T CATEGORY	**T CRITERIA**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 2 cm in greatest dimension limited to the thyroid
T1a	Tumor ≤ 1 cm in greatest dimension limited to the thyroid
T1b	Tumor > 1 cm but ≤ 2 cm in greatest dimension limited to the thyroid
T2	Tumor > 2 cm but ≤ 4 cm in greatest dimension limited to the thyroid
T3[a]	Tumor > 4 cm limited to the thyroid or gross extrathyroidal extension invading only strap muscles
T3a[a]	Tumor > 4 cm limited to the thyroid
T3b[a]	Gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles) from a tumor of any size
T4	Includes gross extrathyroidal extension into major neck structures
T4a	Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size
T4b	Gross extrathyroidal extension invading prevertebral fascia or encasing carotid artery or mediastinal vessels from a tumor of any size

DEFINITION OF REGIONAL LYMPH NODE (N)	
N CATEGORY	**N CRITERIA**
NX	Regional lymph nodes cannot be assessed
N0	No evidence of regional lymph nodes metastasis
N0a[a]	One or more cytologic or histologically confirmed benign lymph node
N0b[a]	No radiologic or clinical evidence of locoregional lymph node metastasis
N1[a]	Metastasis to regional nodes
N1a[a]	Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian, or upper mediastinal) lymph nodes; this can be unilateral or bilateral disease
N1b[a]	Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (levels I, II, III, IV, or V) or retropharyngeal lymph nodes
DEFINITION OF DISTANT METASTASIS (M)	
M CATEGORY	**M CRITERIA**
M0	No distant metastasis
M1	Distant metastasis

DIFFERENTIATED THYROID CANCER				
WHEN AGE AT DIAGNOSIS IS...	AND T IS...	AND N IS...	AND M IS...	THEN THE STAGE GROUP IS...
<55 y	Any T	Any N	M0	I
	Any T	Any N	M1	II
≥55 y	T1	N0/NX	M0	I
	T1	N1	M0	II
	T2	N0/NX	M0	I
	T2	N1	M0	II
	T3a/T3b	Any N	M0	II
	T4a	Any N	M0	III
	T4b	Any N	M0	IVA
	Any T	Any N	M1	IVB

ANAPLASTIC THYROID CANCER			
T IS...	AND N IS...	AND M IS...	THEN THE STAGE GROUP IS...
T1-T3a	N0/NX	M0	IVA
T1-T3a	N1	M0	IVB
T3b	Any N	M0	IVB
T4	Any N	M0	IVB
Any T	Any N	M1	IVC

TABLE 1. Major Changes to the American Joint Committee on Cancer TNM Staging of Differentiated and Anaplastic Thyroid Cancers in the Eighth Edition

Differentiated

1. The age cutoff used for staging was increased from 45 to 55 y at diagnosis.
2. Minor extrathyroidal extension detected only on histologic examination was removed from the definition of T3 disease and therefore has no impact on either T category or overall stage.
3. N1 disease no longer upstages a patient to stage II; if the patient is age <55 y at diagnosis, N1 disease is stage I; if age ≥ 55 y of age, N1 disease is stage II.
4. T3a is a new category for tumors >4 cm confined to the thyroid gland.
5. T3b is a new category for tumors of any size demonstrating gross extrathyroidal extension into strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles)
6. Level VII lymph nodes, previously classified as lateral neck lymph nodes (N1b), were reclassified as central neck lymph nodes (N1a) to be more anatomically consistent and because level VII presented significant coding difficulties for tumor registrars, clinicians, and researchers.
7. In differentiated thyroid cancer, the presence of distant metastases in older patients is classified as stage IVB disease rather than stage IVC disease; distant metastasis in anaplastic thyroid cancer continues to be classified as stage IVC disease.

Anaplastic

1. Unlike previous editions, where all anaplastic thyroid cancers were classified as T4 disease, anaplastic cancers will now use the same T definitions as differentiated thyroid cancer.
2. Intrathyroidal disease is stage IVA, gross extrathyroidal extension or cervical lymph node metastases is stage IVB, and distant metastases is stage IVC.

Take Home Pearl

- **All patients aged 55 years or older who have tumors less than or equal to 4 cm (T1-T2) confined to the thyroid (N0, NX) have stage I disease.**
- **All patients aged 55 years or older who have tumors greater than 4 cm confined to the thyroid (T3a) have stage II disease regardless of lymph node status.**
- **In patients aged 55 years or older who demonstrate gross extrathyroidalextension, the disease is considered stage II if only the strap muscles are grossly invaded (T3b); stage III if there is gross invasion of the subcutaneous tissue, larynx, trachea, esophagus, or recurrent laryngeal nerve (T4a); or stage IVA if there is gross invasion of the prevertebral fascia or tumor encasing the carotid artery or internal jugular vein (T4b).**

Questions

Notes

Endocrine-Related Cancer | I Amendoeira, T Maia *et al.* | NIFTP, impact on the reclassification | 25:4 | R247–R258

REVIEW

Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): impact on the reclassification of thyroid nodules

Isabel Amendoeira[1,2,3,*], **Tiago Maia**[1,2,*] and **Manuel Sobrinho-Simões**[1,2,3,4]

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*(I Amendoeira and T Maia contributed equally to this work)

- The fourth edition of the WHO book on Classification of Tumours of Endocrine Organs includes a new section entitled ‘Other encapsulated follicular-patterned thyroid tumours’
- This includes ‘Follicular tumour of Uncertain Malignant Potential’, ‘Well differentiated tumour of Uncertain Malignant Potential’ and the newly created NIFTP (Non-invasive follicular thyroid neoplasm with papillary-like nuclear features)

- Within the group of follicular variant of papillary thyroid carcinoma (FVPTC), three clinicopathological entities were recognized:
  - Encapsulated/well-circumscribed, non-invasive FVPTC (E/NI-FVPTC), with a more indolent behavior,
  - I-FVPTC, whose behavior is closer to cPTC
  - Multinodular/diffuse form of FVPTC. This multinodular FVPTC is characterized by an aggressive clinical behavior, giving rise to nodal and distant (lung and bone) metastases

- The crucial distinction between non-invasive and invasive forms of PTC has been reinforced by the finding of a molecular profile in E-FVPTC which is more similar to that of follicular adenoma and FTC than to that of cPTC

- The concept and the designation NIFTP was intended to constitute a way of solving the aforementioned problems through the utilization of terms (‘non-invasive’ and ‘tumor’ instead of ‘carcinoma’) that will induce a more conservative treatment.
- This option will reduce the iatrogeny, psycho-social burden and high economical costs for patients and medical care.
- Despite deleting the word ‘carcinoma’ from its name, NIFTP is not a benign tumor either and is best regarded as a neoplasm with ‘very low malignant potential’

- Strict inclusion and exclusion criteria are absolutely necessary to support the diagnosis of NIFTP.
- Inclusion criteria are the following: follicular pattern, encapsulation/good circumscription and nuclear grade equal or above 2.
- Assuming the aforementioned entry criteria are present, the final diagnosis of NIFTP may be rendered unless any of the following exclusion features are present: vascular or capsular invasion, more than 1% papillae, presence of psamomma bodies, more than 30% solid-trabecular architecture, more than 3 mitoses/10 HPF and presence of tumor necrosis
- .

- Genotypic abnormalities in NIFTP have been reported
- They are somewhat heterogeneous but the most frequent genetic abnormalities found in NIFTP are
  - *RAS* (*N-RAS*, *H-RAS* or *K-RAS*)
  - *BRAF*
  - *PAX8-PPARg* rearrangements.
- Overall, the pattern of genetic abnormalities of NIFTP is closer to that of FA/FTC and to cases formerly classified as E-FVPTC, but there is also some overlap with cPTC.

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- Overall, the pattern of genetic abnormalities of NIFTP is closer to that of FA/FTC and to cases formerly classified as E-FVPTC, but there is also some overlap with cPTC.

Table 2 Summary of the most important data reported in studies addressing cytomorphologic features of NIFTP in pre-surgical FNA cytology (Brandler *et al.* 2017).

	Study aim	Cytomorphologic features	Most frequent TBRSTC for NIFTP cases	Results	Conclusions
Strickland *et al.* (2016)	NIFTP DD cPTC	Microfollicular architecture, papillae, psammomatous calcifications, sheet-like architecture, nuclear pseudoinclusions	SM	62% NIFTP 12.5% FVPTC 25% FA	cPTC can be separated from NIFTP/FVPTC on FNA
Howitt *et al.* (2015)	FNA diagnosis of NIFTP; impact on ROM	Microfollicular vs sheet, papillae, pseudoinclusions	SM	cPTC: 96% sheets 79% pseudoinclusions 50% papillae 4% microfollicles NIFTP: 0% papillae 0%pseudo inclusions 36% sheets 55%microfollicles	Cytology and molecular features can help to identify NIFTP at the time of diagnosis
Ibrahim & Wu (2016)	Cytopathology and NIFTP DD IFVPTC	Cellularity, nuclear irregularity, grooves, pseudoinclusions, nuclear enlargement	AUS/FLUS	NIFTP diagnosed as AUS/FLUS (61%) IFVPTC diagnosed as SM (44%)	Cytology can distinguish between NIFTP and IFVPTC
Maletta *et al.* (2016)	To characterize cytological features of NIFTP cases with histological outcome correlates	Nuclear enlargement, nuclear abnormalities, microfollicular pattern, colloid, prominent nucleoli, tridimensional clusters	FN	Nuclear features with good correlation with histology The NIFTP nuclear features different from those of benign nodules but not from E/IFVPTC	E/IFVPTC and NIFTP cannot be reliably separated
Bizarro *et al.* (2016)	Compare the morphologic features of NIFTP and IFVPTC on liquid-based cytology	Colloid, papillae, isolated cells, N/C ratio, follicular architecture, pseudoinclusions, grooves	AUS/FLUS	Larger nuclear size and grooves more frequent in IFVPTC	NIFTP usually lack pseudoinclusions and papillary structures NIFTP and IFVPTC may be discriminated on cytology, based on nuclear size and microfollicular clusters

AUS/FLUS, atypia of undetermined significance/follicular lesion of undetermined significance; DD, differential diagnosis; E/I-FVPTC, encapsulated invasive FVPTC; FA, follicular adenoma; FN, follicular neoplasm; FNA, fine-needle aspiration; I-FVPTC, invasive FVPTC; NIFTP, noninvase follicular tumor with papillary-like nuclear features; ROM, risk of malignancy; SM, suspicious for malignancy; TBRSTC, the Bethesda reporting system for thyroid cytology.

- The majority of NIFTP cases are classified in the Bethesda 'Indeterminate' categories – atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), suspicious for follicular neoplasm/follicular neoplasm (SFN/FN) or even suspicious for malignancy (SM)
- Taking into consideration the morphological and molecular heterogeneity of NIFTP, it is not surprising the spreading of cytological diagnosis of NIFTP through different Bethesda categories, depending on the assessment of nuclear atypia and on institutional recommendations.

Table 3 Distribution of NIFTP (non-invasive follicular tumor with papillary-like nuclear features) according to Bethesda system in the indeterminate categories.

	AUS/FLUS (%)	SFN/FN (%)	SM (%)
Brandler *et al.* (2017)		82.10	
Maletta *et al.* (2016)	15	56	27
Bizzarro *et al.* (2016)	13.50	40.60	35.10
Faquin *et al.* (2016)	31.20	26.60	24.30
Strickland *et al.* (2015)	14.80	13.40	14.40
Lee *et al.* (2017)	57		19
Maia & Amendoeira*	23.80	25.60	13.70

*Unpublished observations.
AUS/FLUS, atypia of unknown significance/follicular lesion of unknown significance; SFN/FN, suspicious for follicular neoplasm/follicular neoplasm; SM, suspicious of malignancy.

- As a consequence of the spread of cytological diagnoses and absence of strict cytological criteria, the risk of malignancy (ROM) for each category is changing

- The decrease of the risk of malignancy (ROM) varies from series to series and is reported to be
  - SM from 13.5% to 48%
  - SFN/FN from10–36
  - AUS/FLUS from 4.9–45%
  - For the Bethesda VI (malignant) category, the decrease of ROM secondary to the introduction of NIFTP is not relevant

Table 4 Risk of malignancy for Bethesda indeterminate and malignant categories.

		AUS/FLUS	SFN/FN	SM	Mal
Strickland *et al.* (2015)	Before NIFTP	66.6%	45.5%	87.2%	98.6%
	After NIFTP	21.6% (45% decrease)	37.5% (18% decrease)	45.7% (48% decrease)	93.6% (5% decrease)
Brandler *et al.* (2017)	Before NIFTP	36%	42%	95%	100%
	After NIFTP	20% (16% decrease)	6% (36% decrease)	63% (32% decrease)	99% (1% decrease)
Faquin *et al.* (2016)	Before NIFTP	31.2%	33.2%	82.6%	99.1
	After NIFTP	17.6% (13.6% decrease)	18% (15.2% decrease)	59.2% (23.4% decrease)	95.7% (3.4% decrease)
Maia & Amendoeira*	Before NIFTP	17.8%	37.5%	80.2%	97.8%
	After NIFTP	12.9% (4.9% decrease)	27.5% (10% decrease)	66.7% (13.5% decrease)	92.8% (5% decrease)

*Unpublished observations.
AUS/FLUS, atypia of unknown significance/follicular lesion of unknown significance; Mal, malignant; NIFTP, non-invasive follicular tumor with papillary-like nuclear features; SFN/FN, suspicious for follicular neoplasm/follicular neoplasm; SM, suspicious of malignancy.

- The introduction of NIFTP concept has changed the utility of predictive values of molecular tests
- Rule out test: Reassessment of NIFTP with previous categories AUS/FLUS and SFN/FN and found
  - A drop on ROM from 24% to 15%
  - An increase of NPV from 88% to 94%
  - A decrease of PPV from 50% to 34%
- Rule-in tests: Variable sensitivities and positive predictive value could potentially harm the usefulness of this test

Table 5 'Ruling-out' malignancy according to Bethesda indeterminate categories.

	AUS/FLUS	SFN/FN	SM
Rule-out Afirma GEC	NPV 95%	NPV 94%	NPV 85%
Alexander *et al.* (2012), Eszlinger *et al.* (2017)		PPV 16–26%	

AUS/FLUS, atypia of unknown significance/follicular lesion of unknown significance; NPV, negative predictive value; PPV, positive predictive value; SFN/FN, suspicious for follicular neoplasm/follicular neoplasm; SM, suspicious of malignancy.

Table 6 'Ruling-in' malignancy (NGS) according to Bethesda indeterminate categories.

	AUS/FLUS	SFN/FN	SM
Nikiforov *et al.* (2016)	PPV 88% Sensitivity 63% Specificity 99%	PPV 87% Sensitivity 57%	
Beaudenon-Huibregtse *et al.* (2014)	PPV 67% Sensitivity 36%		
Labourier *et al.* (2016)		PPV 71% Sensitivity 69%	
Eszlinger *et al.* (2017)	Sensitivity 58% Specificity 82%		

AUS/FLUS, atypia of unknown significance/follicular lesion of unknown significance; PPV, positive predictive value; SFN/FN, suspicious for follicular neoplasm/follicular neoplasm; SM, suspicious of malignancy.

Take Home Pearls

Table 7 Main impacts of NIFTP on cytopathology.

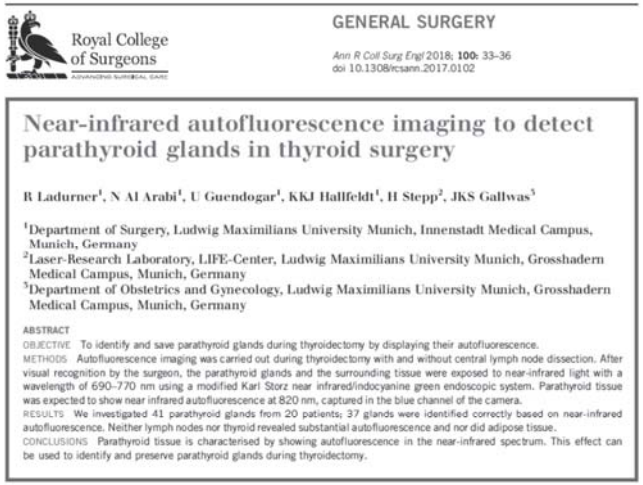
1. Drop of rates of malignancy for each Bethesda category
2. Striking relative decrease of risk of malignancy for atypia of unknown significance/follicular lesion of unknown significance (4.9–45%), suspicious of follicular neoplasm/follicular neoplasm (10–36%) and SM (13–48%)
3. Very low impact of risk of malignancy in the malignant category (1–5%) – most nodules still keep the diagnosis of malignancy
4. The biggest impact will be seen in institutions where the rate of FVPTC is highest
5. Molecular testing will probably switch to rule-out approach
6. Selection for surgery will be mostly determined by clinical, cytological and ultrasound suspicious features

Questions

Notes

Questions

6



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Near-infrared autofluorescence imaging to detect parathyroid glands in thyroid surgery

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ABSTRACT

OBJECTIVE To identify and save parathyroid glands during thyroidectomy by displaying their autofluorescence.

METHODS Autofluorescence imaging was carried out during thyroidectomy with and without central lymph node dissection. After visual recognition by the surgeon, the parathyroid glands and the surrounding tissue were exposed to near-infrared light with a wavelength of 690–770 nm using a modified Karl Storz near infrared/indocyanine green endoscopic system. Parathyroid tissue was expected to show near infrared autofluorescence at 820 nm, captured in the blue channel of the camera.

RESULTS We investigated 41 parathyroid glands from 20 patients; 37 glands were identified correctly based on near-infrared autofluorescence. Neither lymph nodes nor thyroid revealed substantial autofluorescence and nor did adipose tissue.

CONCLUSIONS Parathyroid tissue is characterised by showing autofluorescence in the near-infrared spectrum. This effect can be used to identify and preserve parathyroid glands during thyroidectomy.

- Autofluorescence imaging was carried out during thyroidectomy with and without central lymph node dissection.
- After visual recognition by the surgeon, the parathyroid glands and the surrounding tissue were exposed to near-infrared light with a wavelength of 690–770 nm using a modified Karl Storz near infrared/indocyanine green endoscopic system.
- Parathyroid tissue was expected to show near infrared autofluorescence at 820 nm, captured in the blue channel of the camera.

- Authors investigated 41 parathyroid glands from 20 patients
- 37 glands were identified correctly based on near-infrared autofluorescence.
- Neither lymph nodes nor thyroid revealed substantial autofluorescence and nor did adipose tissue.

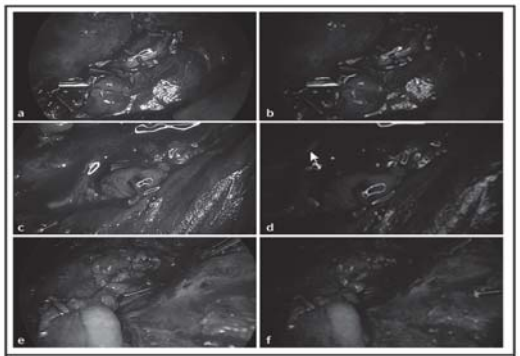
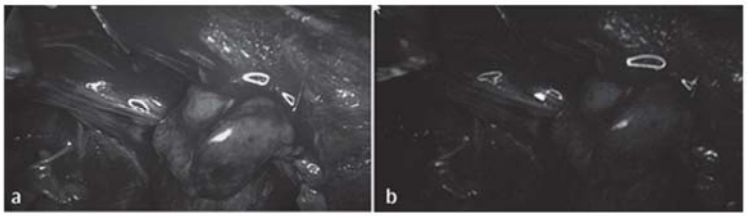


Figure 1 Autofluorescence of parathyroid glands. Parathyroid glands exposed to normal white light (a, c, e) and near infrared light (b, d, f). Parathyroid tissue displays a well-recognisable bluish violet colour representing autofluorescence; the surrounding structures remain nonfluorescent. Images (e) and (f) display two parathyroid glands.



Take Home Pearl

Parathyroid tissue is characterized by showing autofluorescence in the near-infrared spectrum. This effect can be used to identify and preserve parathyroid glands during thyroidectomy.

Questions

7

Randomized clinical trial

Randomized clinical trial of intraoperative parathyroid gland angiography with indocyanine green fluorescence predicting parathyroid function after thyroid surgery

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[1]Department of Thoracic and Endocrine Surgery and Faculty of Medicine, [2]Department of Clinical Epidemiology, and [3]Department Visceral Surgery, University Hospitals of Geneva, Geneva, Switzerland

This study was undertaken to determine whether intraoperative parathyroid gland angiography with indocyanine green (ICG) could predict postoperative hypoparathyroidism, and obviate the need for systematic blood tests and oral calcium supplementation.

- Between September 2014 and February 2016, patients who had at least one well perfused parathyroid gland on ICG angiography were randomized to receive
  - Standard follow-up - measurement of calcium and parathyroid hormone on postoperative day 1 and systematic supplementation with calcium and vitamin D (control group) or
  - No supplementation and no blood test on POD 1 (intervention group).
- In all patients, calcium and PTH levels were measured 10–15 days after thyroidectomy.
- The primary endpoint was hypocalcemia on POD 10–15.

- A total of 196 patients underwent ICG angiography during thyroid surgery
  - 146 had at least one well perfused parathyroid gland on ICG angiography.
  - 50 patients had no well perfused parathyroid gland on ICG angiography

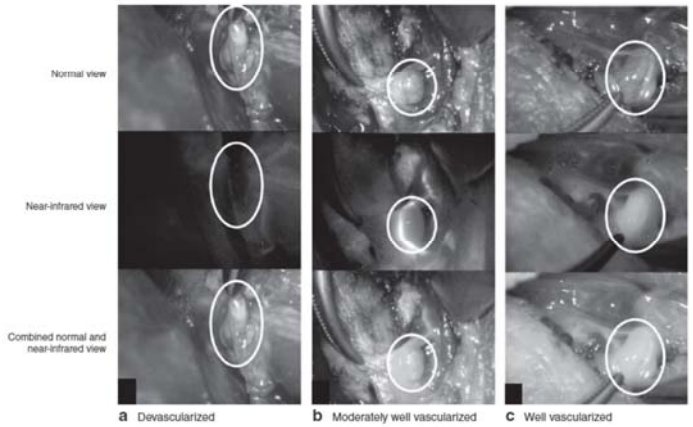

Fig. 1 Representative images of **a** devascularized (indocyanine green (ICG) score 0), **b** moderately well vascularized (ICG score 1) and **c** well vascularized (ICG score 2) parathyroid gland assessed using ICG angiography (*Video S1*, supporting information). Circles indicate the parathyroid gland

Table 1 Number of parathyroid glands evaluated in each patient

No. of glands evaluated	Control group ($n = 73$)	Intervention group ($n = 73$)	Excluded group* ($n = 50$)	Total ($n = 196$)
1	13	8	14	35 (17·9)
2	21	24	19	64 (32·7)
3	19	25	8	52 (26·5)
4	20	16	9	45 (23·0)

Values in parentheses are percentages. *Patients were excluded from the study before randomization if indocyanine green (ICG) angiography showed none of the parathyroid glands to have an ICG score of 2.

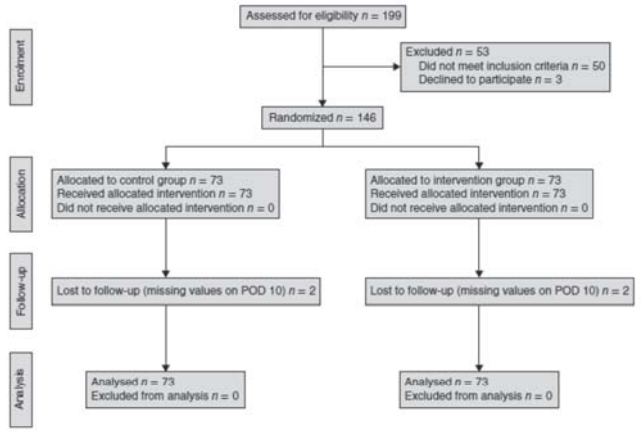

Fig. 2 CONSORT diagram showing randomization and allocation of the study cohort. POD, postoperative day

Table 2 Demographic and clinical characteristics

	Control group ($n = 73$)	Intervention group ($n = 73$)	Excluded group† ($n = 50$)
Age (years)*	50·9(15·4)	53·9(15·9)	50·6(12·1)
Sex ratio (M : F)	11 : 62	11 : 62	17 : 33
ASA score*	1·91(0·43)	1·95(0·45)	1·90(0·46)
Indication for surgery			
Multinodular goitre	41 (56)	33 (45)	30 (60)
Thyroid cancer	17 (23)	30 (41)	15 (30)
Graves' disease	15 (21)	10 (14)	5 (10)
Extent of surgery			
Completion thyroidectomy	5 (7)	11 (15)	5 (10)
Total thyroidectomy	59 (81)	45 (62)	37 (74)
Total thyroidectomy + central neck dissection	6 (8)	15 (21)	2 (4)
Total thyroidectomy + central + lateral neck dissection	3 (4)	2 (3)	6 (12)
Duration of hospital stay (days)*	1·53(1·15)	1·48(0·98)	1·38(0·69)

Values in parentheses are percentages unless indicated otherwise; *values are mean(s.d.). †Patients were excluded from the study before randomization if indocyanine green (ICG) angiography showed none of the parathyroid glands to have an ICG score of 2.

- A total of 196 patients underwent ICG angiography during thyroid surgery
  - 146 had at least one well perfused parathyroid gland on ICG angiography.
    - None of these patients developed hypoparathyroidism, including those who did not receive calcium supplementation.
  - 50 patients had no well perfused parathyroid gland on ICG angiography
    - 17 of these patients developed hypoparathyroidism
      - 11 on POD 1
      - 6 on POD 10–15

Table 3 Comparison of calcium and parathyroid levels between the randomized groups

	Control group ($n = 73$)	Intervention group ($n = 73$)	Difference†	P§
Calcium (mmol/l)*				
POD 1	2·27(0·10)	n.a.		
POD 10	2·31(0·10)‡	2·30(0·11)	0·012 (−0·022, 0·046)	0·480
PTH (pmol/l)*				
POD 1	3·28(1·39)	n.a.		
POD 10	4·44(2·19)‡	4·88(2·05)	−0·441 (−1·144, 0·262)	0·217

*Values are mean(s.d.); †values in parentheses are 95 per cent confidence intervals. ‡Calcium and parathyroid hormone (PTH) levels were significantly higher on POD 10 than POD 1 in the control group (mean difference in calcium 0·039 (95 per cent c.i. 0·012 to 0·067) mmol/l, $P = 0·006$; mean difference in PTH 1·13 (0·66 to 1·61) pmol/l, $P < 0·001$). POD, postoperative day; n.a., not available. §Paired t test.

Take Home Pearl

ICG angiography reliably predicts the vascularization of the parathyroid glands and obviates the need for postoperative measurement of calcium and PTH, and supplementation with calcium in patients with at least one well perfused parathyroid gland.

Questions

Notes

Post-Test

Post-Test

T or F? Although surgical infections are rare in thyroid and parathyroid surgery, perioperative antibiotic prophylaxis substantially decreases them.

Post-Test

T or F? Although surgical infections are rare in thyroid and parathyroid surgery, perioperative antibiotic prophylaxis substantially decreases them.

False

Post-Test

When RLN monitoring is performed during thyroidectomy and loss of signal (LOS) is seen on the first side, what is the rate of LOS on the second side?

A. 1%

B. 3%

C. 7%

D. 20%

Post-Test

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Post-Test

T or F? In patients with thyroid cancer undergoing surgery, recurrent laryngeal nerve invasion does not impact survival.

Post-Test

T or F? In patients with thyroid cancer undergoing surgery, recurrent laryngeal nerve invasion does not impact survival.

TRUE

Post-Test

T or F? Patients who have differentiated thyroid cancers staged T3 N2 M1 have what stage of disease.

A. I
B. II
C. III
D. IV

Post-Test

T or F? Patients who have differentiated thyroid cancers staged T3 N2 M1 have what stage of disease.

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B. II
C. III
D. IV

UNABLE TO ANSWER – NO AGE GIVEN

Post-Test

T or F? Patients who have differentiated thyroid cancers staged T3 N2 M1 have what stage of disease.

A. I – if less than 55 years old
B. II
C. III
D. IV

UNABLE TO ANSWER – NO AGE GIVEN

Post-Test

T or F? Patients who have differentiated thyroid cancers staged T3 N2 M1 have what stage of disease.

- **A. I**
- **B. II**
- **C. III – if more than 55 years old**
- **D. IV**

UNABLE TO ANSWER – NO AGE GIVEN

Post-Test

The newly created tumor category non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) has had what effect on cancer rates within the different Bethesda categories?

- **A. Increased rates**
- **B. Decreased rates**

Extra Credit: What category is affected the most?

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Post-Test

The newly created tumor category non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) has had what effect on cancer rates within the different Bethesda categories?

A. Increased rates

B. Decreased rates – biggest decreases in Bethesda V – SM

Extra Credit: What category is affected the most?

Post-Test

T or F? Near-infrared autofluorescence imaging can not only detect parathyroid glands during thyroid surgery, but can also predict their function after surgery

Post-Test

T or F? Near-infrared autofluorescence imaging can not only detect parathyroid glands during thyroid surgery, but can also predict their function after surgery

TRUE

Thank You

Thank You

Thank You

Thank You