Evidence based treatment of pediatric and adult CRS

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Disclosure

- Consultant: BrainLAB, Olympus, United Allergy, Sunovion
- Grants: VA Merit, FAMRI, NeilMed, Medtronic, Arthrocare, Sunovion
- Text book

- Essentially all therapies for CRS are off label
We all know how to treat CRS!

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Sylvester DC, IFAR 2013
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<td>66% never/rare</td>
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<td>50% usual/frequent</td>
<td>65% usual/frequent</td>
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<tr>
<td>Immunotherapy</td>
<td>N/A</td>
<td>98% rarely/never prescribed</td>
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Dubin MG, AJR 2007
Sylvester DC, IFAR 2013
Why should we care about EBM?

• An older sinus surgeon
  – Rod, where do you think all this EBM “stuff” is going?

• McGlynn et al., NEJM 2003
  – Only 55% of primary care in US based upon accepted evidence in applicable cases

• Carriers and the govt do/will require it!

• We should too!
Category of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Meta-analysis of RCTs</td>
</tr>
<tr>
<td>IB</td>
<td>One placebo controlled, RCT</td>
</tr>
<tr>
<td>IIA</td>
<td>One controlled, non-randomized study</td>
</tr>
<tr>
<td>IIB</td>
<td>One quasi-experimental study</td>
</tr>
<tr>
<td>III</td>
<td>Descriptive studies: Comparative, correlation, case-control</td>
</tr>
<tr>
<td>IV</td>
<td>Expert opinion, committees</td>
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# Strength of recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Research Quality</th>
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<tbody>
<tr>
<td>A</td>
<td>Well designed RCTs</td>
</tr>
<tr>
<td>B</td>
<td>RCT with minor limitations. Consistent evidence from observational studies</td>
</tr>
<tr>
<td>C</td>
<td>Observational studies (case control and cohort)</td>
</tr>
<tr>
<td>D</td>
<td>Expert opinion, case reports</td>
</tr>
</tbody>
</table>
Types of EBM documents

• Meta-analysis/Cochrane review/systematic review
  – Focused topic, single author group, transparent, objective data analysis

Nasal saline irrigations for the symptoms of chronic rhinosinusitis (Review)

  – No recommendations or harm/benefit judgment
  – Do not define action or incorporate values

Rosenfeld RM, et al. OHNS 2006
Clinical practice guidelines

– “Systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances”

Clinical practice guideline on adult sinusitis

– Make value judgments and recommendations based upon strength of evidence
– 17 statements regarding dx, imaging, endoscopy and treatment for adult ABRS and CRS

Rosenfeld RM, etal OHNS 2006
Clinical practice guidelines

- Multidisciplinary:
  - Allergy, ER, FM, insurance carriers, immunology, ID, IM, informatics, nursing, OHNS, radiology
- Face-to-face meetings, conference calls, 1 yr
- CPGs are NOT INTENDED to be:
  - Reimbursement policies
  - Performance measures or measures of certification
  - Legal precedents
  - For provider selection/public posting/cookbook medicine

Rosenfeld RM, et al OHNS 2006
Evidence based reviews & recommendations

• CPG drawbacks
  – Time (1 yr), cost (travel etc), inconvenient

• EBRR as an alternative

Early postoperative care following endoscopic sinus surgery: an evidence-based review with recommendations

• Single discipline, done via email, rapid

Rudmik L, etal IFAR 2011
A few caveats...

• Lack of evidence doesn’t mean something doesn’t work, it just means we haven’t studied it
A few caveats...

• Lack of evidence doesn’t mean something doesn’t work, it just means we haven’t studied it

Criminal Trial

Guilty

Innocent

Not Guilty
Studying new approaches to old problems....
Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

Contributors: GCSS had the original idea. JPP tried to talk him out of it. JPP did the first literature search but GCSS lost it. GCSS drafted the manuscript but JPP deleted all the best jokes. GCSS is the guarantor, and JPP says it serves him right.

Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials.
A few caveats...

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

- Mixed CRSsNP and CRSwNP
- Even CRSwNP studies are heterogeneous
  - AFRS, AERD, non-atopic, +/- eosinophils
- Postop studies exam recurrence
- Primary studies begin with larger disease burden
# Systemic treatments for CRSwNP

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<td>ASA desensitization</td>
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CRS pathophysiology

**Mucosal Inflammation**
- Type 1 Hypersensitivity
- T-Cell mediated eosinophilia
- Leukotriene dysfunction (Aspirin sensitive)
- Local IgE mediated
- Super-antigen/bacterial by-product
- Environmental damage

**Local microbial community**
- Bacterial planktonic
- Bacterial biofilm
- Fungal
- Viral

**Infection damages cilia and their function**
- Poor or absent muco-ciliary function fails to protect mucosa from colonization

**Muco-ciliary dysfunction**
- Direct cilia damage
- Mucus rheologic distortion
- Structural/genetic abnormalities
- Secondary to gross oedema/ostial obstruction

- Mucosal ulceration leads to greater infection and colonization
- Intrinsic mucosal inflammation causes secondary muco-ciliary dysfunction through direct injury and mucus changes
- Failure of mechanical & innate immune protection. Activation of pro-inflammatory acquired immune responses
- Failure of mucus clearance leads to greater exposure to eosinophilic mucin and mucosal injury by eosinophilic mucin

Harvey RJ et al, J OHNS 2009
Oral Steroids

- Aggregate evidence: A
- At least 5 PCRCTs, doses 25-50 mg qd, f/u up to 12 weeks, universal benefit
- Potential harm with side effects (290 mg cumulative dose)
- Strong recommendation for: short term use

Poetker D, etal IFAR 2012
Short Term PO Antibiotics

- Aggregate evidence: B
- 4 RCT’s, but only 2 had placebo control!
- Doxycycline (20d) vs placebo in NP
  - Improved endoscopy (12 wks) & PND (2 wks)
  - NSD: Congestion, rhinorrhea, olfaction, NPIF
- Anti-staph abx x 3wk (TMP, amox/clav, quinolones, no benefit 3-6 mos
- Recommend: Option

Soler ZM, etal IFAR 2012
Long Term PO Antibiotics

- Aggregate evidence: N/A
- 1 CRSsNP study of questionable benefit
- Recommend: Against due to potential harm (C dif), resistance, cost

Soler ZM, et al IFAR 2012
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<td>A</td>
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<td>Ib and Ib(-)</td>
<td>C</td>
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Systemic medical therapies fail, what’s the evidence for surgery in CRSwNP?
Evidence for ESS?

- ESS = Med Rx
- QoL Improvement: CRSwNP > CRSsNP
- ARS Study
  - N=115 pts (40% CRSwNP)
  - 55% in ESS arm
  - 34% crossover within year
  - Surgery better than med Rx

Smith TL, et al, IFAR 2011
Fokkens W et al, EPOS 2012
Periop Oral Steroids

- Aggregate evidence: B
- Improves intraop conditions and postop outcomes
- Recommendation for: periop use
  - Apparent dosing: 30 mg qd x 5 d preop and continue 9 d postop

- Most studies done in pre-epinephrine and steroid irrigation era!

Poetker D, etal IFAR 2012
Epinephrine evidence

• Aggregate evidence: B
• DBRCT, epi 1:5,000 and 1:20,000
  – 1:5,000 group with less EBL, but required more rescue meds for HTN, no clinical consequence
• DBRCT, epi 1:2,000; 10,000; 50,000
  – Shorter OR time, lower EBL favoring 1:2,000
  – Trend toward elevated BP in 1:2,000
• Systematic review
  – Epi 1:1,000 and 1:2,000 generally safe

Effects of epi 1:1,000
Adult CRSsNP

- Diffuse mucosal involvement
- NOT
  - Mucoceles
  - Fungus balls
### Medical therapies for CRSsNP

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<th>Therapy</th>
<th>Grade</th>
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<td>INCS</td>
<td>A</td>
<td>Yes</td>
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<tr>
<td>Saline irrigation</td>
<td>A</td>
<td>Yes</td>
</tr>
<tr>
<td>Xylitol irrigation postop</td>
<td>A</td>
<td>Yes</td>
</tr>
<tr>
<td>Bacterial lysates (OM85 BV)</td>
<td>A</td>
<td>Unclear</td>
</tr>
<tr>
<td>Short term PO abx</td>
<td>B</td>
<td>During exacerbation</td>
</tr>
<tr>
<td>Macrolides x 12 weeks</td>
<td>C</td>
<td>If low IgE</td>
</tr>
<tr>
<td>PO steroid</td>
<td>C</td>
<td>Unclear</td>
</tr>
<tr>
<td>Mucolytics</td>
<td>C</td>
<td>No</td>
</tr>
<tr>
<td>Antihistamine, PPI, decongestants</td>
<td>D</td>
<td>No data</td>
</tr>
<tr>
<td>SCIT</td>
<td>D</td>
<td>No data</td>
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Bacterial lysates (OM-85 BV)

- Enhance Th1 response
- Multicenter, DBPCT 284 pts purulent CRSsNP
- OM-85 BV plus abx, mucolytics, inhalants
- Rx 10 days per month x 3 months
- Outcomes: Sx and Xray improved at 6 mos
Xylitol irrigations

• Effects airway surface liquid ionic composition
• Improved sx compared to saline alone
Surgery for minimal CRSsNP

- Low stage: CT score $LM \leq 3$, $n=17$
- High stage $n=207$
- No prior surgery, mucoceles and HA patients excluded
- Baseline QoL the same, endoscopy worse in high stage
- Both groups improve to the same degree

Rudmik L et al, Laryngoscope 2011
EBM of pediatric rhinosinusitis

Rodney J. Schlosser, MD

Professor and Director of Rhinology
Department of Otolaryngology - HNS
Medical University of South Carolina
Charleston, SC
OR....
Everything I can tell you about kids with snotty noses in 30 minutes
### Pediatric ABRS evidence

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<td>A</td>
</tr>
<tr>
<td>Topical nasal steroid</td>
<td>A</td>
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<tr>
<td>Antibiotic + INCS</td>
<td>A</td>
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<tr>
<td>Mucolytics</td>
<td>A-</td>
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<td>Saline</td>
<td>D</td>
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<tr>
<td>Oral antihistamine</td>
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<td>Decongestants</td>
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Surgical indications

- Severely ill child
- No improvement on medical rx after 48-72 hours
- Immunocompromised
- Suppurative complications (intraorbital or intracranial)
Surgical steps

- Atraumatic decongestion
- Slow, deliberate movements
- Complete uncinectomy usually provides adequate exposure
- No need for turbinectomy or septoplasty
- Use of pediatric instruments
  - Backbiter
  - Stapes curette
  - Upbiting forceps
  - Shaver blades & scopes
  - Suctions 7Fr
  - Ball tipped probes
Pediatric FESS

3yro Male - Right subperiostieal orbital abscess
What about CHRONIC rhinosinusitis in kids?

- Two or more of the sx, must include one of the following:
  - Nasal blockage/obstruction/congestion
  - Nasal discharge (anterior or posterior)
- Can also include
  - Facial pain/pressure
  - Cough
- AND endoscopic or CT evidence of dz
Imaging

- Impossible to differentiate between CRS and adenoid hypertrophy in young children
- Incidental CT findings 18-45%, ave LMS of 2.8
- URI sx x 3 mos
  - CT abnormalities in 73-74% of 2-10 yo
  - Only 38% of >10yo
- Plain film: Correlates with CT only 25% of time!
CT considerations

• Axial cuts for orbital, frontal, sphenoid pathology

• *Unilateral* opacification raises red flag
  – Allergic fungal sinusitis/antrochoanal polyp
  – Tumor (JNA)
  – Encephalocele
  – Mucocele
  – Foreign body
  – Silent sinus syndrome
  – Choanal atresia
Juvenile Nasal Angiofibroma (JNA)
Encephalocele
Mucoceles
Choanal atresia and silent sinus
Silent sinus syndrome: Retrograde uncinectomy
Pathophysiology of pediatric CRS

- Inflammatory reaction with more lymphocytes and fewer eosinophils and epithelial disruption than adults
- Bacteria:
  - No consistent findings
  - Staph, strep, H flu, M catarrhalis, anaerobes
  - 99% bacteria exist in biofilm state
Anatomic factors

• Few studies, limited control groups without CRS
• No significant correlation to septal deviation, concha bullosa, paradoxical MT
Adenoid

- CRS: 88-99% surface with biofilm
- OSA: 0-6.5% surface with biofilm
- High correlation between adenoid and middle meatal bacterial cultures
- Adenoid size correlates with nasal discharge, but not CT staging
- Role as bacterial reservoir probably more important than size

EPOS 2012
Allergic Rhinitis

- In mixed adult and pediatric population, positive RAST had higher CT score
- 3 other studies fail to demonstrate relationship between atopic status and CT
- Bottom line: probably no causal relationship, but rather comorbid disease modifier
GERD

- Kids with CRS: 63% had positive pH probe
- Kids with GERD (ICD9 dx codes)
  - 4% incidence of CRS vs 1.3% in GERD negative
- Limited, level 4 retrospective non-controlled study demonstrate sx improvement and surgery avoidance with GERD Rx
Immunodeficiency

- Kids presenting with CRS
  - Just over half may have immunodeficiency
  - IgG1/2/3, IgA deficiency
  - Impaired response to pneumococcal Ag
- Rx with IVIG decreases antibiotic use and improves CT
Primary Ciliary Dyskinesia

- Autosomal recessive, affects 1/15,000
- Only half have situs inversus
- Suspect: Atypical asthma, bronchiectasis, COM
- Requires EM evaluation
Smoke exposure

- Conflicting data in adults
- No demonstrable adverse effect upon ESS outcomes
- Likely a disease modifier, rather than sole cause
Cystic Fibrosis

- Autosomal recessive: 1/3,500 newborns
- Nasal polyps in 7-50% pediatric CF patients
- Common cause of pediatric NP
Medical therapy

- Antibiotics: IV, oral, topical
- Steroids: Oral, topical
- Saline
- GERD Rx
- Antihistamine, LT antagonist, mucolytic, decongestant
Topical steroids

• No RCTs for INCS, but given evidence in adults, probably reasonable
IV Antibiotics

• Max irrigation + 1-4 wks culture directed IV antibiotics via PICC line

• Adenoidectomy in 53%
  – Only had f/u on 52/70 pts (mean 25 mos)
  – 89% resolution of sx, unclear impact of adenoidectomy
  – 11% FESS, 14% PICC complication

• May be appropriate for select patients, nonsurgical candidates

Don et al, Arch OHNS 2001
Topical antibiotics

- Evidence based review and recommendation:
  - Recommend against for routine CRS
  - Option for difficult cases (CF, etc)

Rudmik L, etal IFAR 2012
Antihistamines, LTRAs, GERD

- AH/LTRA/mucolytics: No evidence for CRS
- GERD: Level 4 evidence, no control group
Surgery

• Adenoidectomy
• Balloon sinuplasty
• Maxillary lavage
• FESS
Adenoidectomy

- Meta-analysis of 9 studies
- Mean 5.8 years old (4.4-6.9)
- 69% improvement
- Adenoidectomy alone if 50% or greater obstruction of choanae
- Also perform endoscopically-directed cultures and possibly cilia biopsy
Maxillary lavage

• Improved success of adenoidectomy from 61% to 88% at 12 months
Balloon sinuplasty

- Adenoidectomy vs adenoid + balloon + irrigation:
  - 53% success vs 80% at 1 year f/u
  - Difficult to separate effects of irrigation from balloon
FESS

- Meta-analysis of 8 published studies + 50 unpublished
- Age: 11 mos-18 years
- 89% positive outcomes, average of 3.7 years f/u
Impact of FESS on facial growth?

- Mair: Piglets with unilateral surgery – reduction in bony growth of operated side
- Bothwell, Lusk:
  - 10 year f/u using quantitative analysis (anthropometric measurements) and qualitative analysis (facial plastic surgeon)
  - No difference in prognathia, occlusion, facial symmetry when compared to non-FESS patients
Pediatric ESS

- CT guidance may be helpful for complicated cases
- Be aware of anatomic differences between adults and children
Adenoidectomy vs. ESS

• Multivariate analysis of 202 pts
• Adjusted for age, sex, allergy, asthma, day care, CT stage
• Best outcomes if >6yo, no asthma, no smoke exposure
• Conclusion: ESS better than adenoidectomy
• Recommend: Adenoid alone for <6yo, no asthma, mild disease

Ramadan, Laryngoscope, 2004
## Evidence based surgical Rx

**PCRS**

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<tr>
<th>Procedure</th>
<th>Outcomes</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenoidectomy</td>
<td>69% improvement</td>
<td>A (younger children)</td>
</tr>
<tr>
<td>Maxillary wash</td>
<td>88% with adenoid</td>
<td>C</td>
</tr>
<tr>
<td>Balloon sinuplasty</td>
<td>80% with ad+max wash</td>
<td>C</td>
</tr>
<tr>
<td>FESS</td>
<td>89% success</td>
<td>A</td>
</tr>
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Additional considerations
Intraop steroids

- IV dexamethasone decreased maxillary sinus edema, closure of antrostomy, and ethmoid scarring
- Steroid group: 29% abnormal 2nd look
- Non-steroid group: 62% abnormal 2nd look
- Most effective in mild disease and those without passive smoke exposure
Stenting summary

- Comparisons using various hyaluronic acid materials, Merocel sponges, Gelfilm
- Currently no definitively proven benefit

Tom, AJR, 1997
Maccabee, AJR, 2003
Catalano, OHNS, 2003
Miller, OHNS, 2003
Second look endoscopy (SLE)

- N=147 pts, outcome=revision surgery
- 94 pts underwent SLE at 2-3 wks
- 53 pts did not
- SLE had 21% revision rate
- Non-SLE group had 19% revision rate
- Questions necessity of SLE

Walner, Arch OHNS, 1998
Our Goal: A Happy Patient!
Pediatric and adult CRS cases

- AFRS
- AERD
- CF
- Pediatric CRSsNP
Pediatric and adult CRS cases

• Rules of the game
  – Answers brief and to the point
  – Can’t answer “I don’t treat…….”
  – Justify with evidence if possible
Allergic Fungal Rhinosinusitis with Polyps!
Or in a 10 yo boy
AFRS

- PO/topical steroids
- Antibiotics
- Antifungals (PO/topical)
- Immunotherapy
- Antihistamines
- Monoclonal antibodies
- Surgical philosophy: Big or small?
Oral Antifungals

• Aggregate evidence: B
  – Level 1 (terbinafine), level 4 (15), level 5 (12) evidence
  – 19 AFRS studies: 2 with validated outcome measures
  – N=55 pts, 3-6 mo f/u, 56-70% clinical improvement

• Considerable risks/harm

• Recommend: Against for routine CRS

• ABPA and itraconazole (controlled studies)
  – Reduction in PO steroids, IgE and eosinophilia, improved PFTs

Soler ZM, etal IFAR 2012
Thanasumpun, IFAR 2011
Topical (and oral) antifungals

No benefit in QoL, endoscopy or CT

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antifungal (topical)</th>
<th>Placebo</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
</tr>
<tr>
<td>Ebbens 2006a</td>
<td>-3.1</td>
<td>8.28</td>
<td>59</td>
</tr>
<tr>
<td>Gerlinger 2009</td>
<td>-39</td>
<td>13.73</td>
<td>14</td>
</tr>
<tr>
<td>Liang 2008</td>
<td>-120.06</td>
<td>112.85</td>
<td>32</td>
</tr>
<tr>
<td>Ponikau 2005a</td>
<td>-0.5</td>
<td>0.4</td>
<td>10</td>
</tr>
<tr>
<td>Weschta 2004</td>
<td>-2.11</td>
<td>8.38</td>
<td>28</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>143</strong></td>
<td></td>
<td><strong>151</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 6.80, df = 4 (P = 0.15); I² = 41%
Test for overall effect: Z = 1.77 (P = 0.08)
Immunotherapy

• Aggregate evidence: C

• 22 AFRS pts all with surgery, steroids, abx
  – 11 SCIT, 11 no SCIT: Rx all reactors
  – Mean f/u: 33mo
  – SCIT improved: endoscopy, QoL, PO and topical steroid use

• Subsequent study
  – 10 SCIT, 7 no SCIT
  – Mean f/u 82 mos (46-138 mos)
  – 76% pts with normal/mild edema
  – No benefit from SCIT

Folker et al. (1998)
Mabry & Mabry (2000)
Antihistamines

• One RCT of cetirizine for 3 months postop
• No benefit in endoscopy, possibly some benefit in sneezing, rhinorrhea
Anti IgE

- Aggregate evidence: B
- 2 RDBPCTs omalizumab SQ x 4-8 mos
- Outcomes: CT, QoL, endoscopy, NPIF, UPSIT, rescue meds, inflammatory mediators
- One study positive, one negative

Pinto JM, et al. Rhinology 2010
Gevaert P, et al. JACI 2012
Anti IL5

• Evidence: B
• 2 DBPCTs both found improvement in some outcome measures in 50% CRSwNP pts
• High nasal IL5 predicts response
• Concerns over cost, duration, rebound eosinophilia
### Treatment evidence for AFRS

<table>
<thead>
<tr>
<th>Statement</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery with postoperative medical therapy</td>
<td>C</td>
</tr>
<tr>
<td>Oral steroids: Short term postop improvement, but can have significant side effects</td>
<td>A</td>
</tr>
<tr>
<td>Topical steroid irrigations</td>
<td>C (extrapolated)</td>
</tr>
<tr>
<td>SCIT improves short term outcomes, but long term benefits are unclear</td>
<td>C</td>
</tr>
<tr>
<td>Topical anti-fungal therapy</td>
<td>A- (extrapolated)</td>
</tr>
</tbody>
</table>
ASA triad

- 35 yo s/p 4 prior ESS
- AERD, requiring oral steroids for asthma
AERD or ASA triad

- Steroids
- Antibiotics
- ASA desensitization
- Leukotriene antagonists
- Macrolides
- Surgical plan
- Impact upon asthma
ASA desensitization

- Usually 1 month postop for recurrence
- Only one prospective placebo controlled cross over study with 2 doses ASA
  - Improved nasal sx and less INCS w ASA
  - NSD: Lower airway sx, FEV1, asthma meds
- Other non-placebo controlled studies report sx benefit, but effects upon NP unclear
- Dose from 300 qd to 650 bid
- Side effects: up to 56%
- Newer routes, agents in development
Leukotriene antagonists

- 2 DBPCTs monteleukast
  - Some improvement in sx, but not endoscopy or immune mediators
- Non-placebo studies comparing to INCS or add on therapy
  - Some benefit, maybe sneezing, itching, HA
- Zileuton: 5% LFT elevation
Long Term Macrolides

- Aggregate evidence: A
  - Meta-analysis benefit when low IgE
  - Japanese neutrophilic NP benefit?
- Cost: high with ave 3 month duration
- Risk: Proarrhythmic, cardiac effects?
- Recommend: Option especially with low IgE

Soler ZM, et al. IFAR 2012
Ray WA, et al. NEJM 2012
Does any of this sinus stuff apply to the lower airway?
Medical and surgical Rx for CRS improve asthma

- CRSsNP and CRSwNP failed INCS, lavage
- Medical: erythromycin x 12 wks, lavage, fluticasone gtt (some got prednisone)
- Surgery: erythromycin x 2 wks postop, INCS, lavage
- Both improved asthma QoL at 1 yr, medical better PFTs (but unclear prednisone effects)

Ragab A, etal Eur Resp J 2006
Topical steroids for upper airway and asthma

• CRS study: Uncontrolled budesonide irrigation study with improved asthma sx

• MA: INCS in AR with asthma
  – 18 studies, 2162 patients
  – 3 subgroups
  – INCS vs placebo spray
  – INCS plus oral ICS vs oral ICS alone
  – Nasal inhalation vs nasal placebo

Lohia S, Schlosser RJ, et al, Allergy 2013
INCS improve asthma sx (FEV1, rescue meds)

INCS spray vs Placebo

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Favours experimental</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agondi 2008</td>
<td>3.77</td>
<td>0.56</td>
<td>16</td>
<td>3.12</td>
<td>0.97</td>
<td>14</td>
<td>4.1%</td>
<td></td>
<td>0.65</td>
<td>0.65 [0.07, 1.23]</td>
<td></td>
</tr>
<tr>
<td>Corren 1992</td>
<td>3.22</td>
<td>2.6879</td>
<td>10</td>
<td>3.36</td>
<td>2.2062</td>
<td>8</td>
<td>0.3%</td>
<td></td>
<td>-0.14</td>
<td>-0.14 [-2.40, 2.12]</td>
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</tr>
<tr>
<td>Henrikson 1984</td>
<td>8.5</td>
<td>0.798</td>
<td>17</td>
<td>7.9</td>
<td>1.7555</td>
<td>17</td>
<td>1.6%</td>
<td></td>
<td>0.60</td>
<td>0.60 [-0.32, 1.52]</td>
<td></td>
</tr>
<tr>
<td>Sandrini 2003</td>
<td>18 10.4293</td>
<td>7</td>
<td>19</td>
<td>5.9905</td>
<td>9</td>
<td>0.0%</td>
<td></td>
<td>-1.00</td>
<td>-1.00 [-9.66, 7.66]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stelmach 2005</td>
<td>2.2</td>
<td>1.89</td>
<td>19</td>
<td>1.23</td>
<td>2.55</td>
<td>19</td>
<td>0.7%</td>
<td></td>
<td>0.97</td>
<td>0.97 [-0.46, 2.40]</td>
<td></td>
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<tr>
<td>Watson 1993</td>
<td>2.4</td>
<td>0.2</td>
<td>21</td>
<td>2</td>
<td>0.2</td>
<td>21</td>
<td>93.3%</td>
<td></td>
<td>0.40</td>
<td>0.40 [0.28, 0.52]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>90</td>
<td>88</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.42</td>
<td>0.30, 0.53</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 1.77, df = 5 (P = 0.88); I² = 0%</td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 6.97 (P &lt; 0.00001)</td>
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</tbody>
</table>

INCS spray with oral ICS vs oral ICS

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Favours experimental</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Katal 2010</td>
<td>37.1</td>
<td>41.0122</td>
<td>200</td>
<td>36.5</td>
<td>38.6523</td>
<td>166</td>
<td>1.7%</td>
<td></td>
<td>0.60</td>
<td>0.60 [-7.58, 8.78]</td>
<td></td>
</tr>
<tr>
<td>Nathan 2005</td>
<td>20.6</td>
<td>52.1776</td>
<td>250</td>
<td>23.6</td>
<td>53.1085</td>
<td>259</td>
<td>1.4%</td>
<td></td>
<td>-3.00</td>
<td>-3.00 [-12.15, 6.15]</td>
<td></td>
</tr>
<tr>
<td>Stelmach 2005</td>
<td>2.57</td>
<td>1.79</td>
<td>19</td>
<td>2.79</td>
<td>1.53</td>
<td>17</td>
<td>96.9%</td>
<td></td>
<td>-0.22</td>
<td>-0.22 [-1.30, 0.86]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>469</td>
<td>442</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>-0.24</td>
<td>-1.31, 0.82</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 0.39, df = 2 (P = 0.82); I² = 0%</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.45 (P = 0.65)</td>
<td></td>
<td></td>
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</tbody>
</table>

Nasal inhalation vs nasal placebo

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pedersen 1998</td>
<td>2.67</td>
<td>0.31</td>
<td>12</td>
<td>2.08</td>
<td>0.42</td>
<td>12</td>
<td>49.9%</td>
<td></td>
<td>0.59</td>
<td>0.59 [0.29, 0.89]</td>
<td></td>
</tr>
<tr>
<td>Pedersen 1998a</td>
<td>3.27</td>
<td>0.24</td>
<td>12</td>
<td>1.09</td>
<td>0.42</td>
<td>12</td>
<td>50.1%</td>
<td></td>
<td>2.18</td>
<td>2.18 [1.91, 2.45]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>24</td>
<td>24</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>1.39</td>
<td>-0.17, 2.94</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 1.24; Chi² = 59.90, df = 1 (P &lt; 0.00001); I² = 98%</td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 1.74 (P = 0.08)</td>
<td></td>
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</tr>
</tbody>
</table>

Overall

| Total (95% CI)    | 583           | 554  | 100.0%| |       | 0.69  | [0.04, 1.35]| |
| Heterogeneity: Tau² = 0.70; Chi² = 140.38, df = 10 (P < 0.00001); I² = 93% |
| Test for overall effect: Z = 2.08 (P = 0.04) |
Meta-analysis: Impact of ESS upon asthma

- N=21 studies, 812 patients, mean f/u 26 mos
- NSD in FEV1

<table>
<thead>
<tr>
<th>Outcome</th>
<th>% pts improved</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall asthma control</td>
<td>78%</td>
<td>72 - 82%</td>
</tr>
<tr>
<td>Frequency asthma attacks</td>
<td>85%</td>
<td>75-92%</td>
</tr>
<tr>
<td># hospitalizations</td>
<td>64%</td>
<td>53-75%</td>
</tr>
<tr>
<td>PO steroids</td>
<td>73%</td>
<td>67-78%</td>
</tr>
<tr>
<td>Inhaled steroids</td>
<td>28%</td>
<td>23-35%</td>
</tr>
<tr>
<td>Bronchodilator use</td>
<td>36%</td>
<td>29-44%</td>
</tr>
</tbody>
</table>

Vashishta R, Schlosser RJ, etal, IFAR 2013 (in press)
All CRSwNP treated similarly: Big hole ESS, steroid irrigations

AFRS 13 months  
s/p 3rd ESS

ASA triad 8 months  
s/p 5th ESS
All CRSwNP treated similarly:
Big hole ESS, steroid irrigations

AFRS 13 months
s/p 3rd ESS

ASA triad 8 months
s/p 5th ESS
How EBM has changed my management of nasal polyposis

• Less systemic antibiotics, LTRAs, allergy Rx’s
• My experience with macrolides and doxycycline is not great
• Role of ESS for topical access – BIG HOLES – Lothrop/medial maxillectomy?
• Use of topical steroids immediately post ESS with high concentrations, high volumes
• Be willing to consider novel approaches…. 
A new approach to the kickoff...
Other polyp controversies

• Topical mupirocin for staph biofilm/superAg?

• Brittle asthmatic with minimal sinus disease?
CF sinusitis… another can of worms

- Small sinuses
- Thick mucus
- Definite bacterial issues
  - Staph, Pseudomonas
- Use of topical antibiotics
- Nutrition/vitamin D?
- Compliance
An unusual (well pneumatized) CF CT scan
dF508 CT scan
Options

- IV/PO/topical antibiotics
- PO/topical steroids
- Mucolytics
- Irrigations
- Surgical philosophy
## Treatment evidence for CF

<table>
<thead>
<tr>
<th>Statement</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESS with possible MEMM (QoL &amp; endoscopy, but NOT PFTs)</td>
<td>C</td>
</tr>
<tr>
<td>Post ESS topical antibiotics</td>
<td>B</td>
</tr>
<tr>
<td>Nasally inhaled dornase alpha</td>
<td>A</td>
</tr>
</tbody>
</table>

*EPOS 2012*
ESS in CF

- 19 studies, 586 pts
- ESS improves sinonasal QoL, not PFTs
- Conflicting data on hospitalizations, abx used, endoscopy scores

Virgin F, et al. AJRA 2012
Macdonald KI et al., Rhinology 2012
Case: Routine Pediatric CRS

• 4 ½ year old WM otherwise healthy, no PMH, FHx, SHx
• CC: Cough, nasal congestion, PND x 3-4 months
• PCP: Z Pack, negative allergy w/u
• PE: purulent rhinorrhea, IT hypertrophy
A 4 ½ year old with a cough...
## Evidence based medical Rx

<table>
<thead>
<tr>
<th>Agent</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics: IV</td>
<td></td>
</tr>
<tr>
<td>Antibiotics: Short term oral</td>
<td>←</td>
</tr>
<tr>
<td>Antibiotics: Long term oral</td>
<td></td>
</tr>
<tr>
<td>Antibiotics: Topical</td>
<td></td>
</tr>
<tr>
<td>Steroid: Oral</td>
<td>←</td>
</tr>
<tr>
<td>Steroid: Intranasal</td>
<td>←</td>
</tr>
<tr>
<td>Saline: spray or rinse</td>
<td>←</td>
</tr>
<tr>
<td>GERD Rx</td>
<td></td>
</tr>
<tr>
<td>AH, LTRAs, mucolytics, decongestants</td>
<td>←</td>
</tr>
</tbody>
</table>
PO Antibiotics

• N=141 kids, 3-10 yo EPOS + dx
• Underwent 10d Rx, 26 wks f/u:
  – Saline drops
  – Xylometazoline gtt + PO amox
  – Max tap and indwelling catheter irrigation x 5d
  – Max tap, cathether + xylometazoline + amox
  – 69% cure regardless of Rx
• No evidence to justify short term oral abx in PCRS
PO Steroids

- N=48 kids, EPOS dx, ave 8yo, CT mod dz
  - All Rx with amox/clav x 30d
  - Methylprednisolone vs placebo x 15d
  - Both groups improved sx and CT
  - PO steroids over placebo for cough, nasal obstruction, PND, total sx score and CT
Saline and Pediatric CRS - Tolerability

• Only 65% of ASPO members prescribe

• Less than 25% of parents think it will be tolerated

Sobol et al Laryngoscope 2005
Jeffe et al Int J Pediatric ORL 2012
Saline and Pediatric CRS - Tolerability

61 children, median age 8 years

23% parents thought it would be tolerated

93% attempted
86% tolerated it
77% continued use

93% reported overall health improvement

Jeffe et al Int J Pediatric ORL 2012
Saline and Pediatric CRS

40 CRS RCT saline vs gent/saline 25ml od

- 90% compliance
- QOL improvement after 3 weeks
- Improved CT scores after 6 weeks
- No difference between groups

Wei et al Laryngoscope 2011
## Evidence based medical Rx

<table>
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<tr>
<td>Antibiotics: IV</td>
<td></td>
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<tr>
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<td>B-</td>
</tr>
<tr>
<td>Antibiotics: Long term oral</td>
<td></td>
</tr>
<tr>
<td>Antibiotics: Topical</td>
<td></td>
</tr>
<tr>
<td>Steroid: Oral</td>
<td>A (select)</td>
</tr>
<tr>
<td>Steroid: Intranasal</td>
<td>A (extrapolated)</td>
</tr>
<tr>
<td>Saline: spray or rinse</td>
<td>A</td>
</tr>
<tr>
<td>GERD Rx</td>
<td></td>
</tr>
<tr>
<td>AH, LTRAs, mucolytics, decongestants</td>
<td></td>
</tr>
</tbody>
</table>
6 weeks of amox/clav, another CT...

CF and immune w/u: negative
Further medical Rx?
## Evidence based medical Rx

<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics: IV</td>
<td>C-</td>
</tr>
<tr>
<td>Antibiotics: Short term oral</td>
<td>B-</td>
</tr>
<tr>
<td>Antibiotics: Long term oral</td>
<td>D (possible, extrap)</td>
</tr>
<tr>
<td>Antibiotics: Topical</td>
<td>C-</td>
</tr>
<tr>
<td>Steroid: Oral</td>
<td>A (select)</td>
</tr>
<tr>
<td>Steroid: Intranasal</td>
<td>A (extrapolated)</td>
</tr>
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<td>Saline: spray or rinse</td>
<td>A</td>
</tr>
<tr>
<td>GERD Rx</td>
<td>C</td>
</tr>
<tr>
<td>AH, LTRAs, mucolytics, decongestants</td>
<td>D</td>
</tr>
</tbody>
</table>
10 weeks after reflux therapy, the cough is gone!
The saga continues…

• Returns after 1 month with cough again
• CT looks like first 2 scans
• Pulmonary eval negative for RAD/asthma

• Time to operate?
• What surgery?
What surgery to perform?
Pediatric Chronic Sinusitis

• Adenoidectomy?
• Endoscopically-directed cultures (possibly antral puncture)?
• Balloon sinuplasty?
• FESS (how extensive)?
• Some combination of the above?
PCRS Summary

- Aggressive EBM diagnostic work-up and medical treatment
- Adenoidectomy for “routine CRS”
  - Congestion, PND, < 6 years old
- Maxillary lavage +/- BSP may be beneficial
- ESS for “difficult CRS”
  - CF, AFS, polyps, mucoceles, silent sinus, older patients
- Intra-op steroids and mucosal sparing technique to avoid second look