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!

Therapy	ARS study	UK study
INCS and saline		
PO abx		
PO steroids		
Allergy testing		
Immunotherapy		

Dubin MG, AJR 2007
Sylvester DC, IFAR 2013

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PO abx >90% MDs used	Median 3-4 wks <3% used over 6 wk	Macrolides >6 wks
PO steroids	>50% usual/frequent 9% never/rare	66% never/rare
Allergy testing	50% usual/frequent	65% usual/frequent
Immunotherapy	N/A	98% rarely/never prescribed

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 etal, 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

Level	Studies
IA	Meta-analysis of RCTs
IB	One placebo controlled, RCT
IIA	One controlled, non-randomized study
IIB	One quasi-experimental study
III	Descriptive studies: Comparative, correlation, case-control
IV	Expert opinion, committees

Strength of recommendation

Grade	Research Quality
A	Well designed RCTs
B	RCT with minor limitations. Consistent evidence from observational studies
C	Observational studies (case control and cohort)
D	Expert opinion, case reports

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, etal 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, etal 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

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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

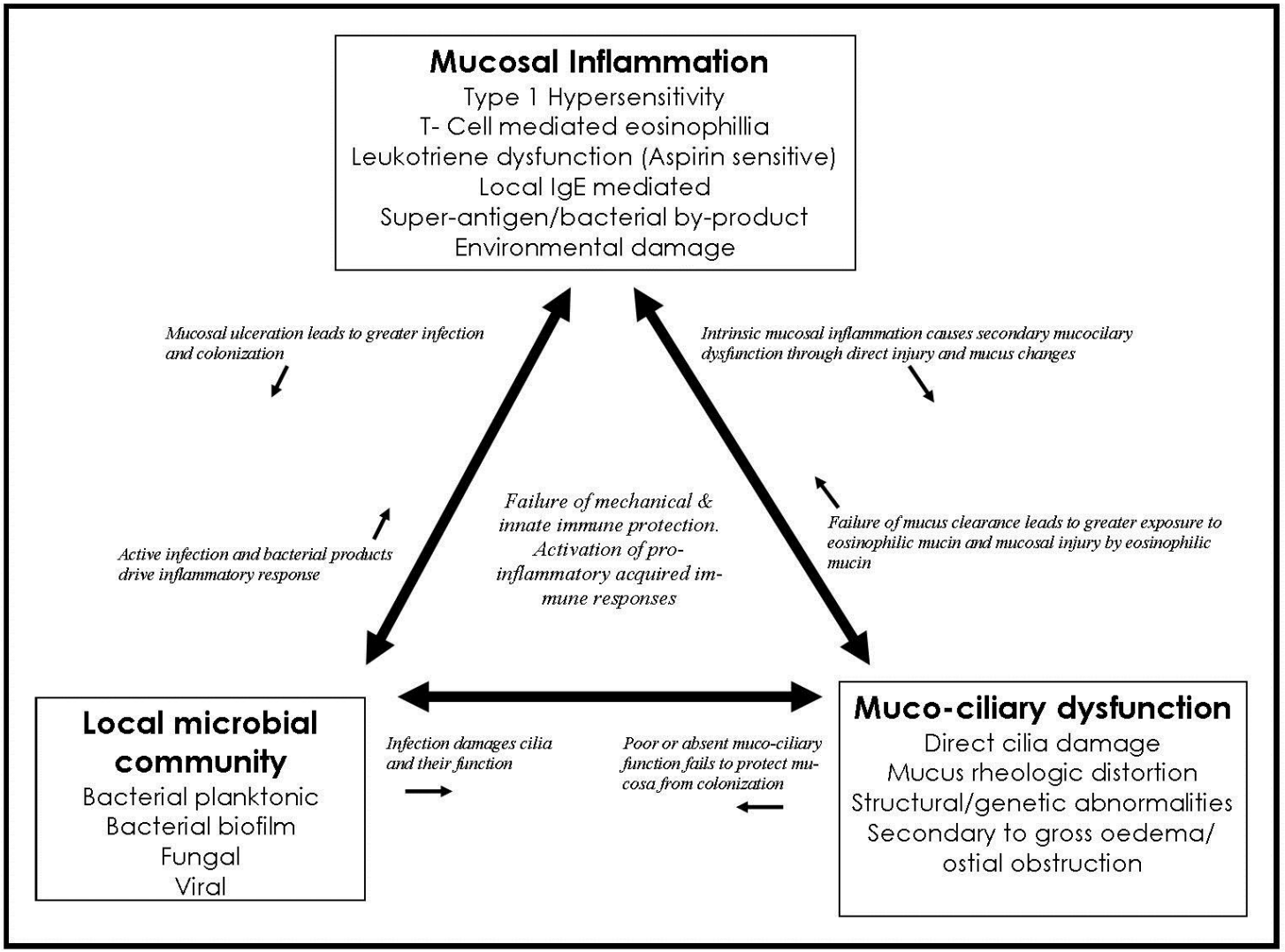
Issues with “the evidence”

- 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

Therapy	Level of evidence	Recommendation
PO steroids		
PO abx <4 wks		
PO abx >12 wks		
PO antifungals		
Immunotherapy		
Anti leukotrienes		
Anti IgE		
ASA desensitization		

CRS pathophysiology



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, etal IFAR 2012

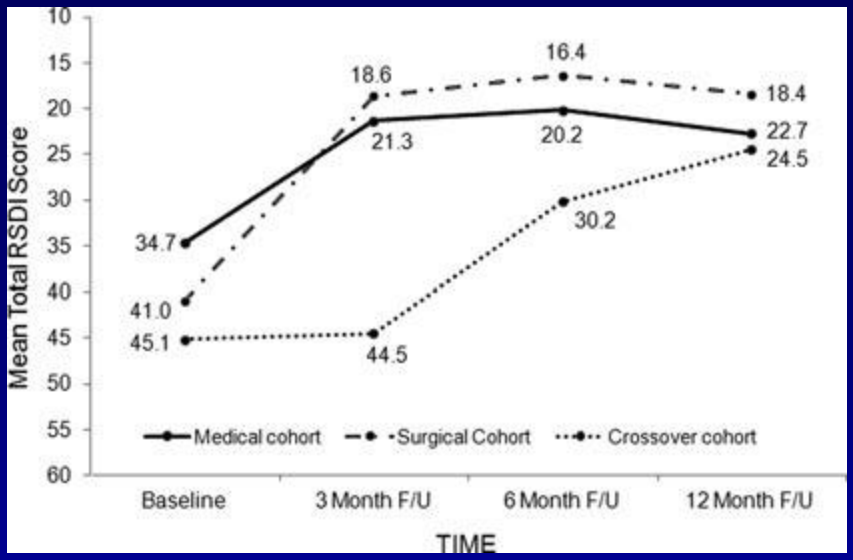
Systemic treatments for CRSwNP

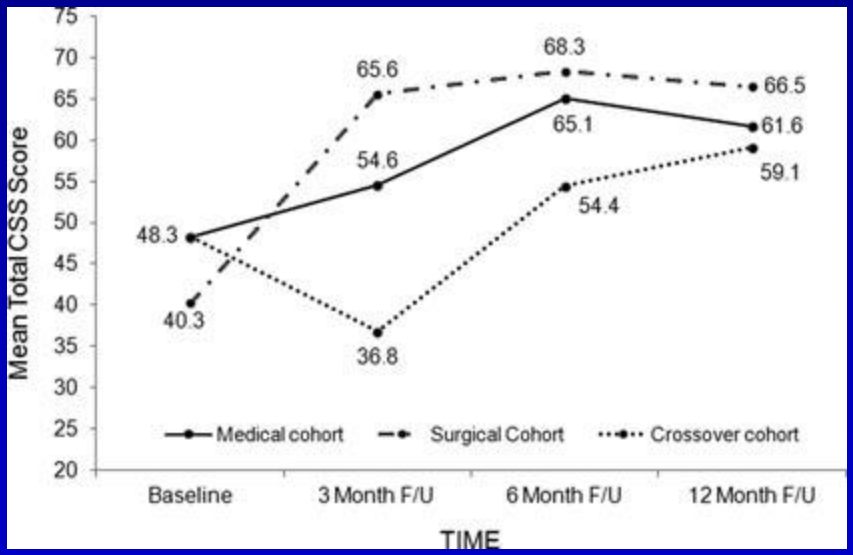
Therapy	Level of evidence	Recommendation
PO steroids	**Ia**	**A**
PO abx <3-4 wks	Ib and Ib(-)	C
PO abx >12 wks	III	C
PO antifungals		
Immunotherapy		
Anti leukotrienes		
Anti IgE		
ASA desensitization		

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 etal 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!

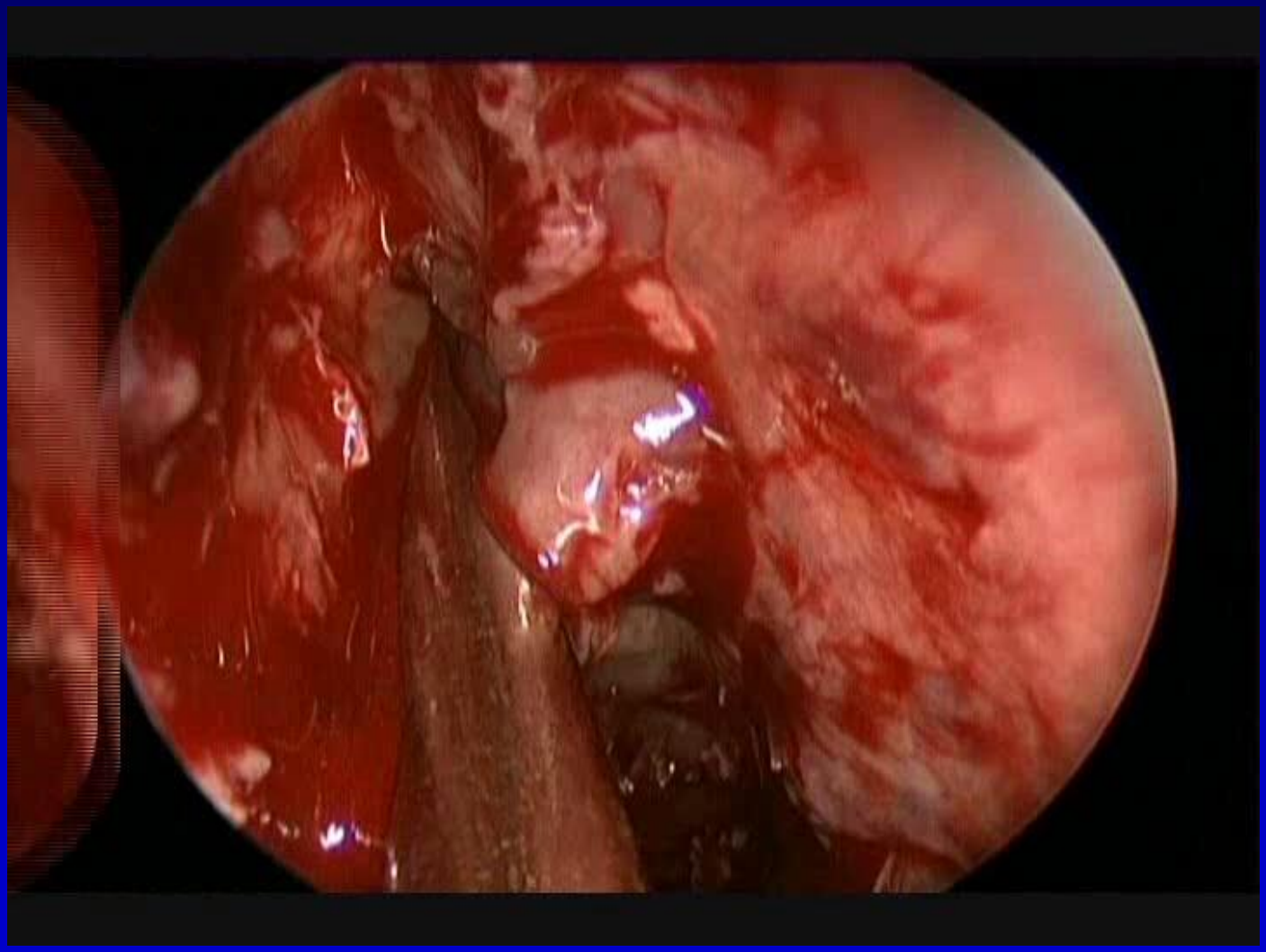
Poetker D, etal IFAR 2012

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

Panda N, etal J OHNS 2012
Sarmento JKM, etal, Braz JORL 2009
Higgins TS, etal, Laryngoscope 2011

Effects of epi 1:1,000



Adult CRSsNP

- Diffuse mucosal involvement
- NOT
  - Mucoceles
  - Fungus balls

Medical therapies for CRSsNP

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

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≤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 etal, Laryngoscope 2011

EBM of pediatric rhinosinusitis

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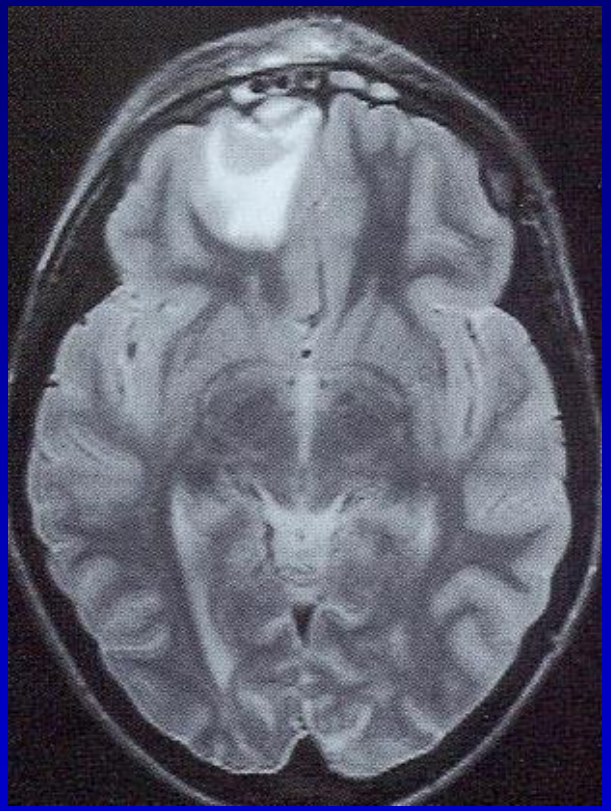
OR….
Everything I can tell you about kids with snotty noses in 30 minutes

Pediatric ABRS evidence

Therapy	Recommendation
Antibiotic	**A**
Topical nasal steroid	**A**
Antibiotic + INCS	**A**
Mucolytics	**A-**
Saline	**D**
Oral antihistamine	**D**
Decongestants	**D**

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

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

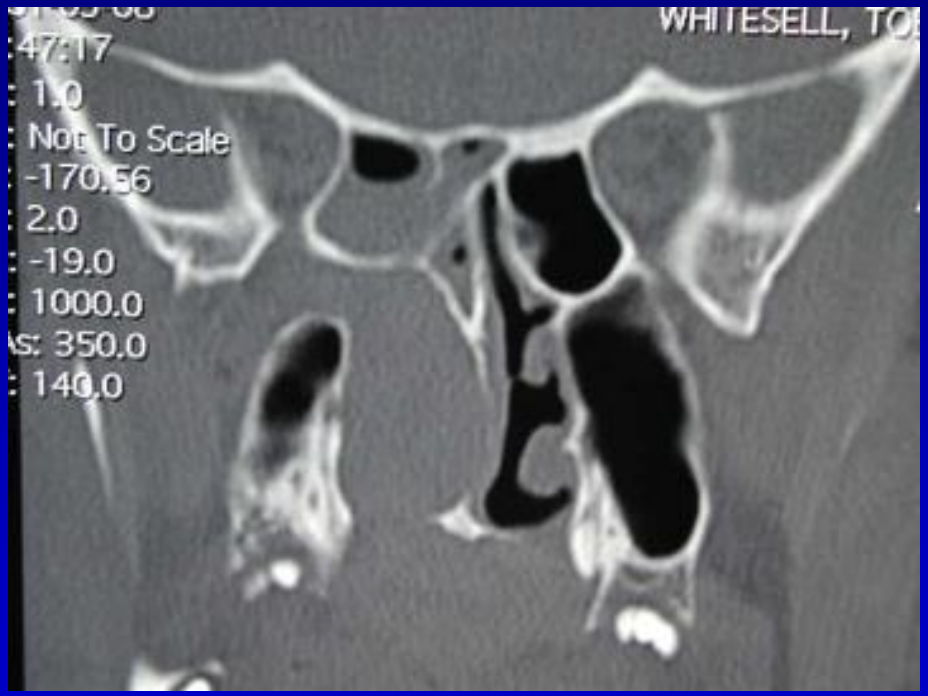
Imaging

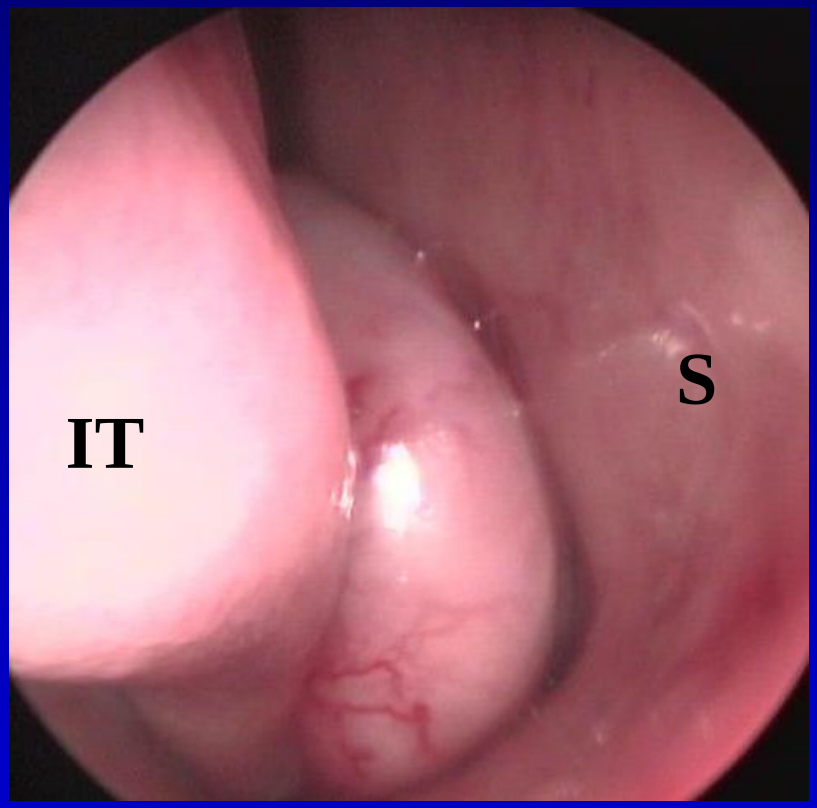
- Impossible to differentiate between CRS and adenoid hyptertrophy in young children
- Incidental CT findings 18-45%, ave LMS of 2.8
- URI sx x 3 mos
  - CT abnormalities in 73-74% of 2-10 yo
  - Only 38% of >10yo
- Plain film: Correlates with CT only 25% of time!

CT considerations

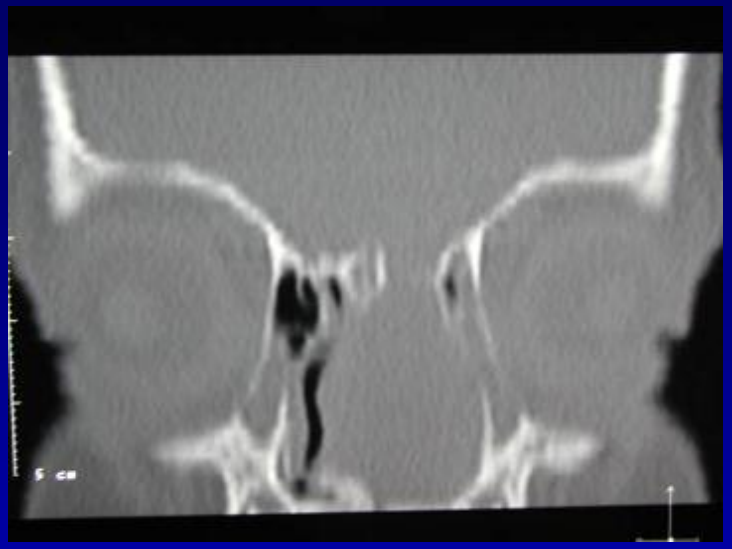
- Axial cuts for orbital, frontal, sphenoid pathology
- *Unilateral* opacification raises **red flag**
  - Allergic fungal sinusitis/antrochoanal polyp
  - Tumor (JNA)
  - Encephalocele
  - Mucocele
  - Foreign body
  - Silent sinus syndrome
  - Choanal atresia

Juvenile Nasal Angiofibroma (JNA)

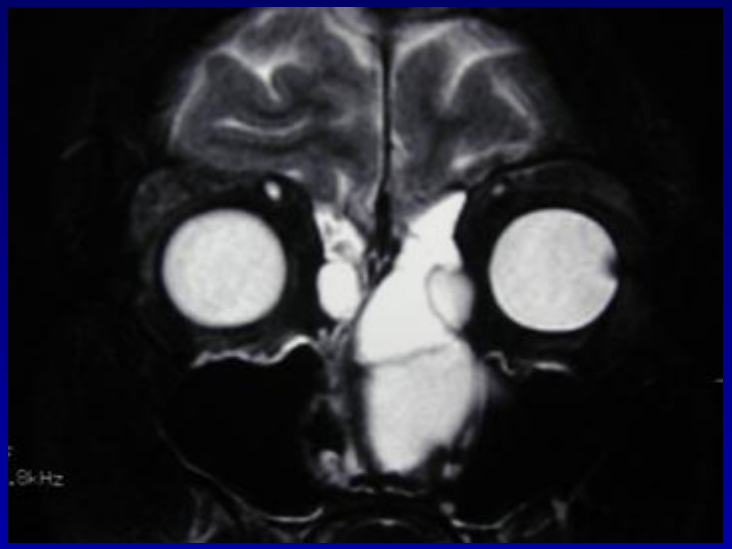


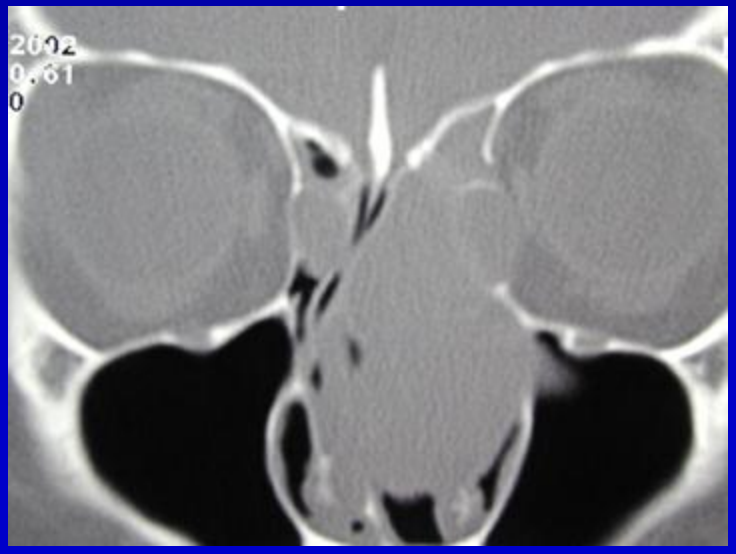


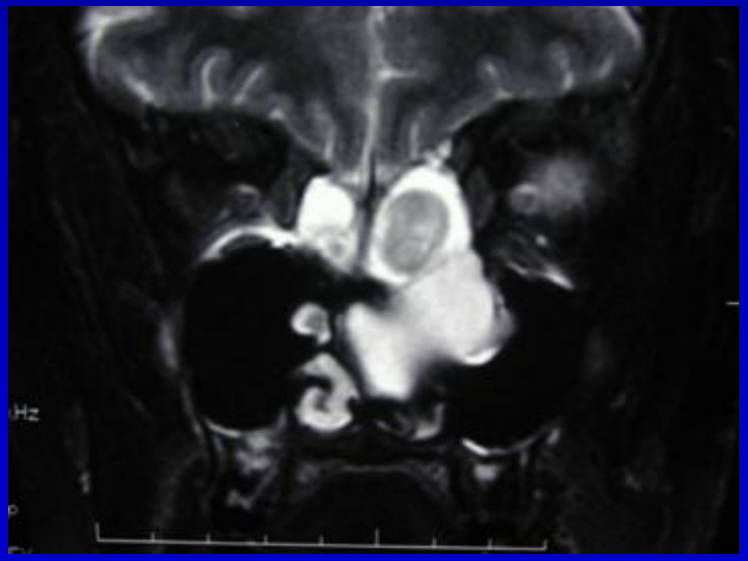
Encephalocele



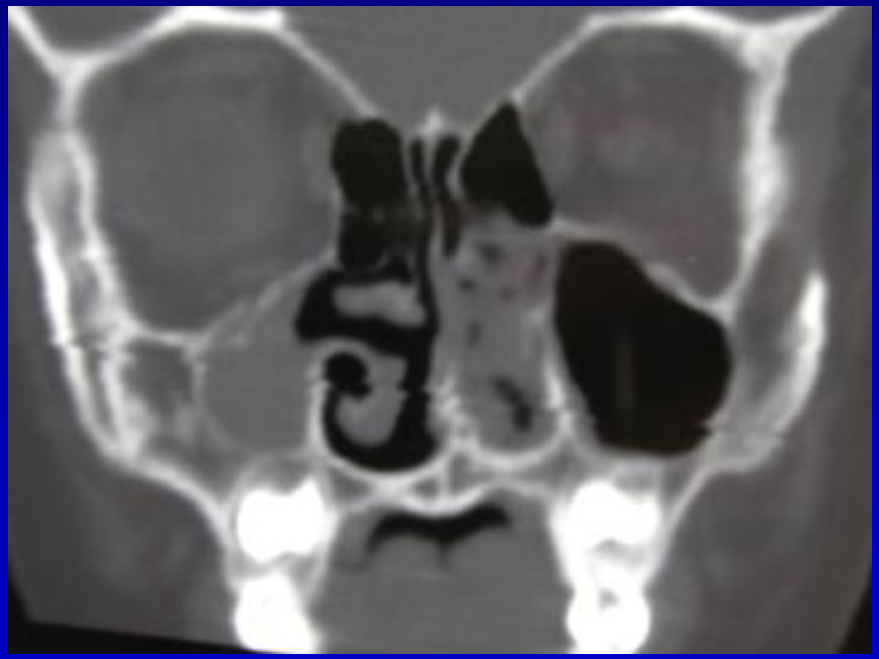
Mucoceles

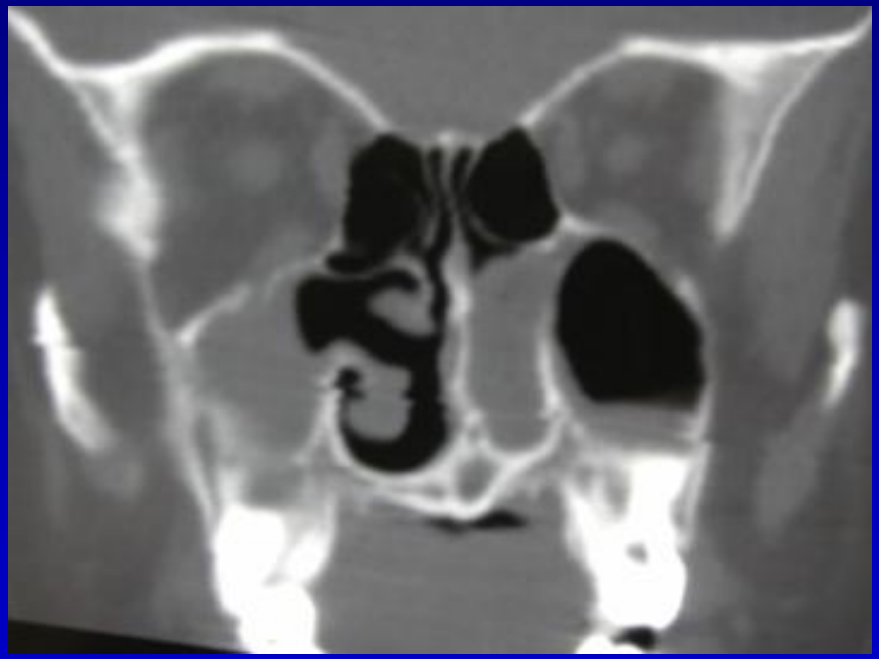




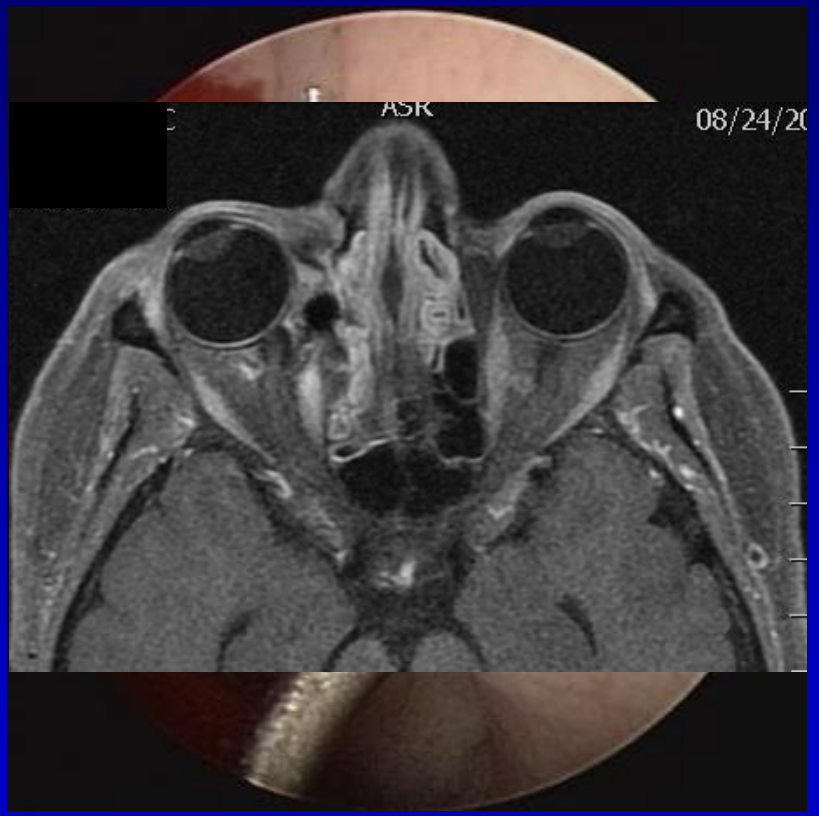


Choanal atresia and silent sinus





Silent sinus syndrome: Retrograde uncinectomy



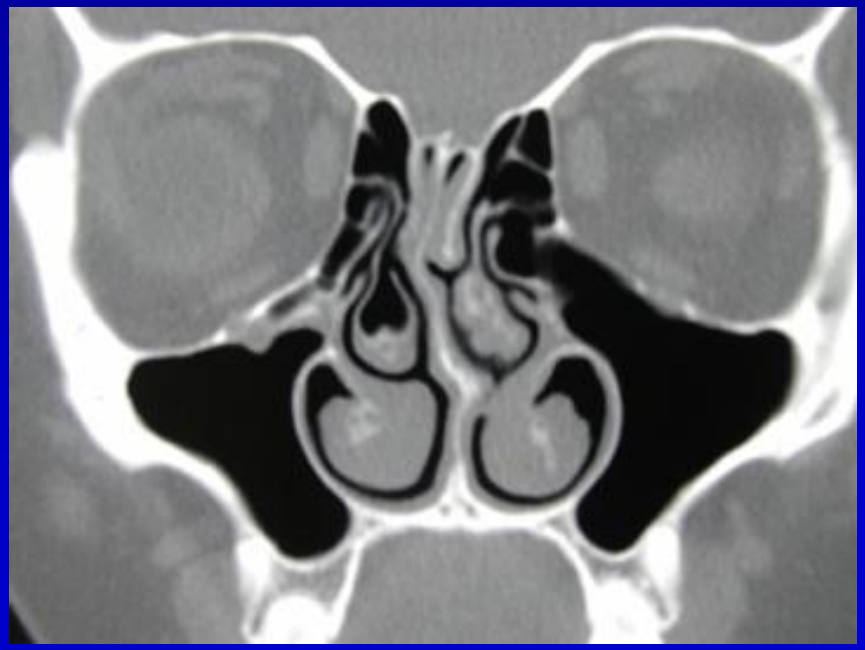
Pathophysiology of pediatric CRS

- 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

EPOS 2012

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

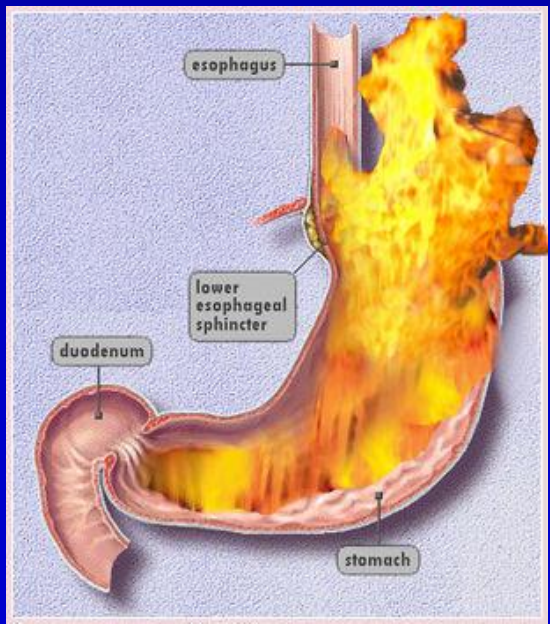
Allergic Rhinitis

- 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

EPOS 2012

GERD

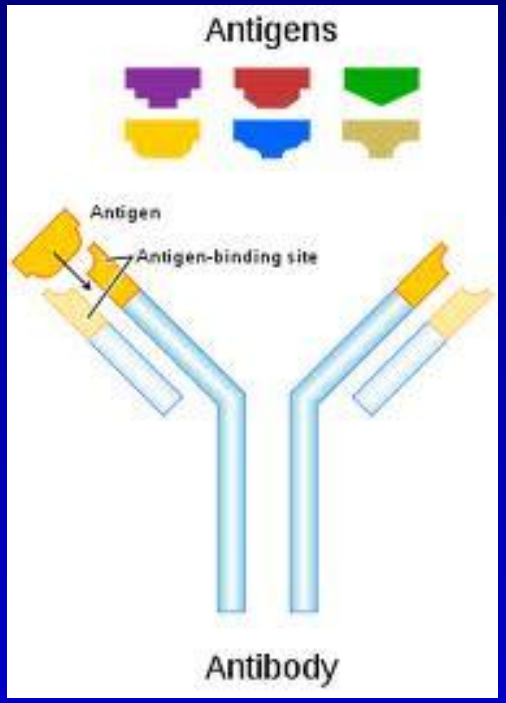
- Kids with CRS: 63% had positive pH probe
- Kids with GERD (ICD9 dx codes)
  - 4% incidence of CRS vs 1.3% in GERD negative
- Limited, level 4 retrospective non-controlled study demonstrate sx improvement and surgery avoidance with GERD Rx



EPOS 2012

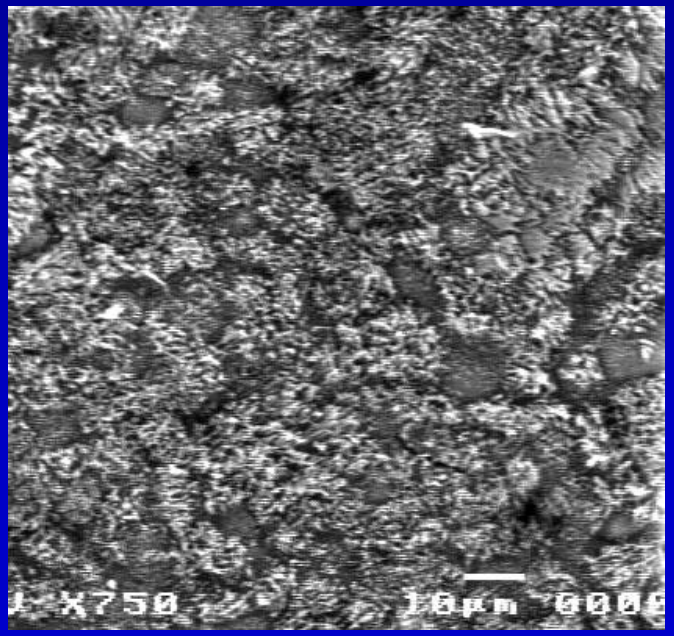
Immunodeficiency

- 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

EPOS 2012

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

EPOS 2012

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

EPOS 2012

FESS

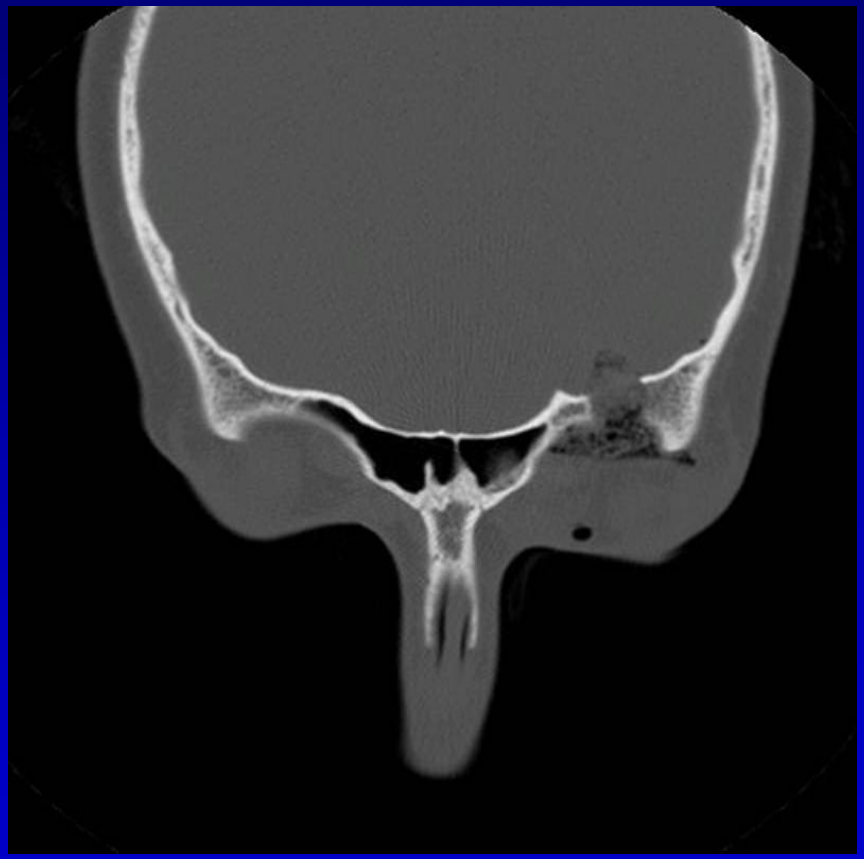
- Meta-analysis of 8 published studies + 50 unpublished
- Age: 11 mos-18 years
- 89% positive outcomes, average of 3.7 years f/u

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 (anthropometic 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

Procedure	Outcomes	Recommendation
Adenoidectomy	**69% improvement**	**A (younger children)**
Maxillary wash	**88% with adenoid**	**C**
Balloon sinuplasty	**80% with ad+max wash**	**C**
FESS	**89% success**	**A**

EPOS 2012

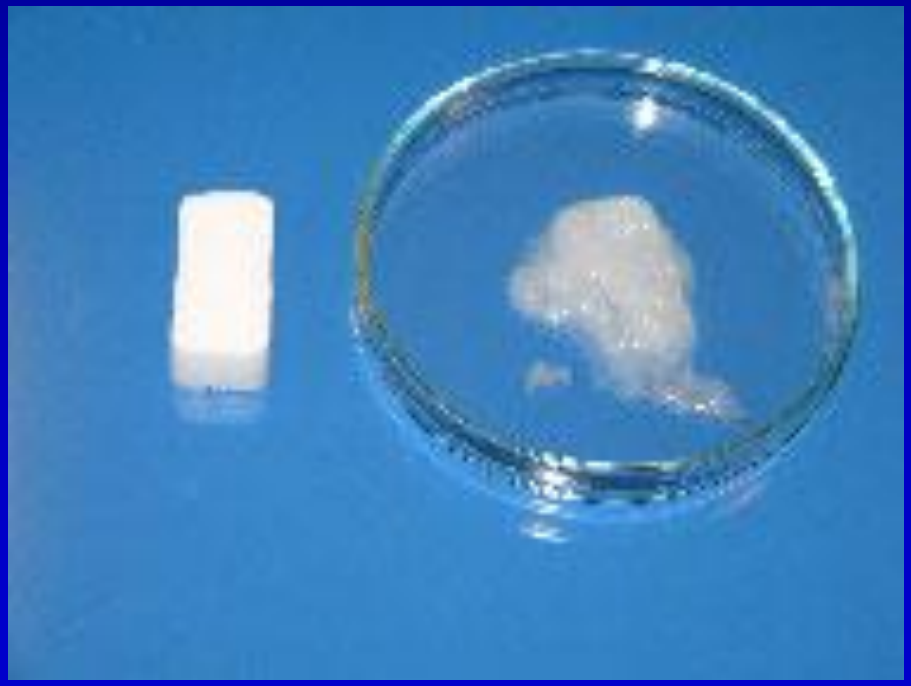
Additional considerations
Intraop steroids

- 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

Ramadan, Archives OHNS 1999

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!

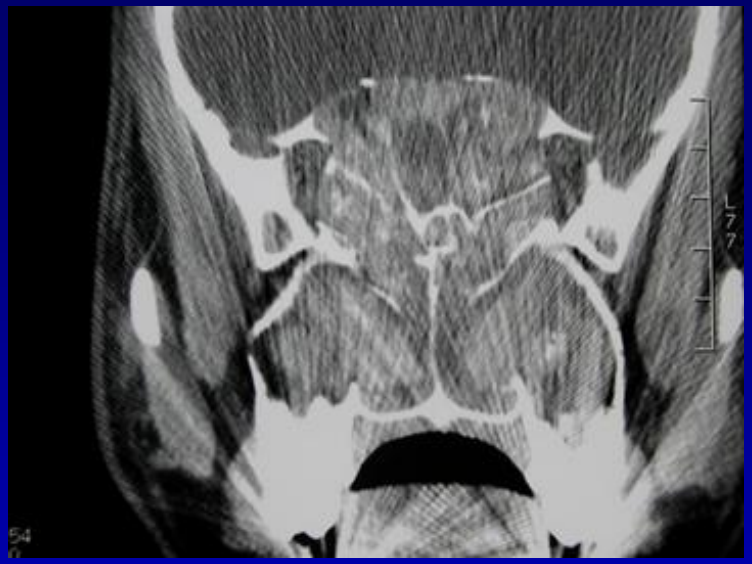
Pediatric and adult CRS cases

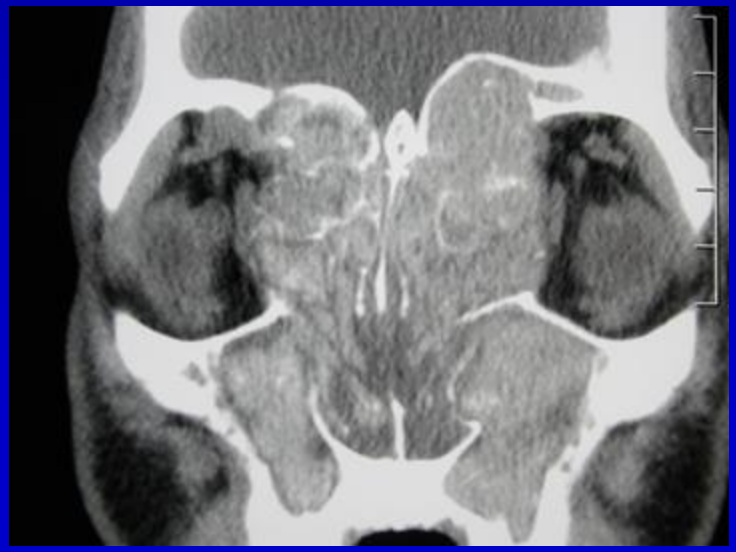
- AFRS
- AERD
- CF
- Pediatric CRSsNP

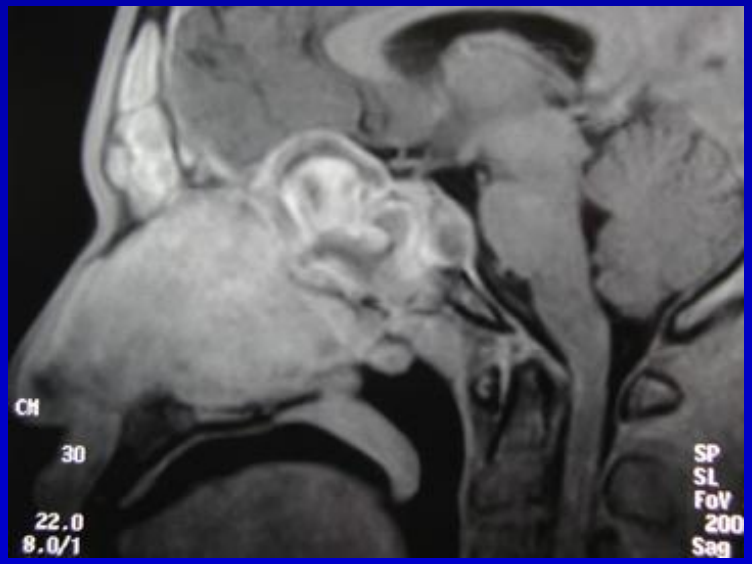
Pediatric and adult CRS cases

- Rules of the game
  - Answers brief and to the point
  - Can’t answer “I don’t treat…….”
  - Justify with evidence if possible

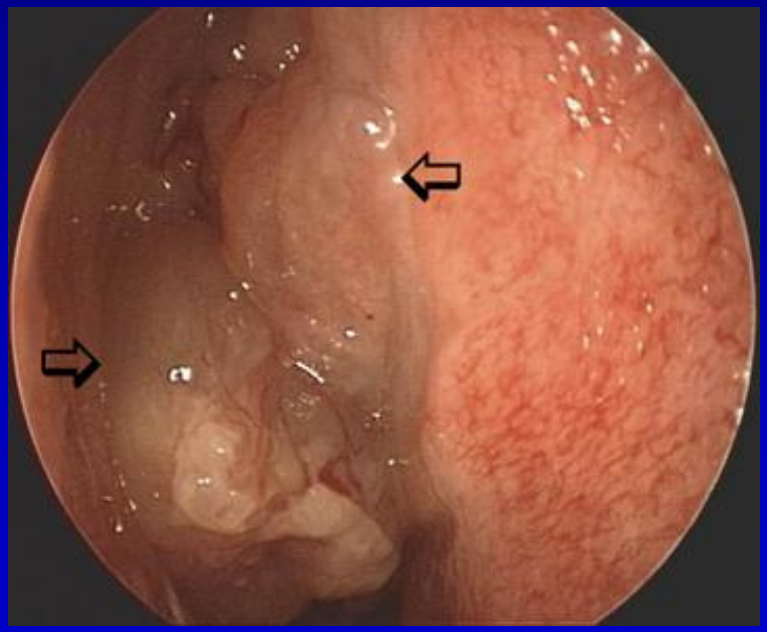
Allergic Fungal Rhinosinusitis with Polyps!







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

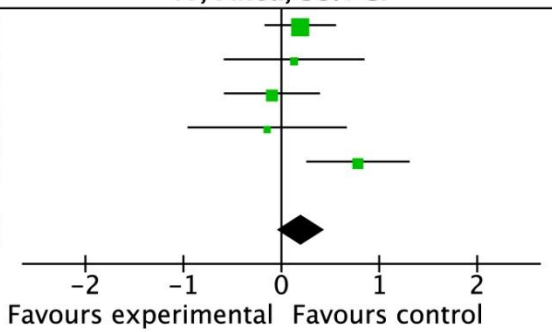
Topical (and oral) anti-fungals

No benefit in QoL, endoscopy or CT

Study or Subgroup	Antifungal (topical) Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Ebbens 2006a	-3.1	82.8	59	-21.1	101.2	57	40.1%	0.19 [-0.17, 0.56]
Gerlinger 2009	-39	13.73	14	-41	15.89	16	10.4%	0.13 [-0.59, 0.85]
Liang 2008	-120.06	112.85	32	-109.6	102	32	22.2%	-0.10 [-0.59, 0.39]
Ponikau 2005a	-0.5	0.4	10	-0.4	0.8	14	8.1%	-0.14 [-0.96, 0.67]
Weschta 2004	-2.11	8.38	28	-9.91	10.96	32	19.2%	0.78 [0.25, 1.31]
Total (95% CI)			**143**			**151**	**100.0%**	**0.21 [-0.02, 0.44]**

Heterogeneity: $Chi^2 = 6.80$, df = 4 (P = 0.15); $I^2 = 41\%$

Test for overall effect: Z = 1.77 (P = 0.08)



Sacks PL, et al. *Cochrane Database Syst Rev. 2011(8):CD008263.*

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, etal Rhinology 2010
Gevaert P, etal 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

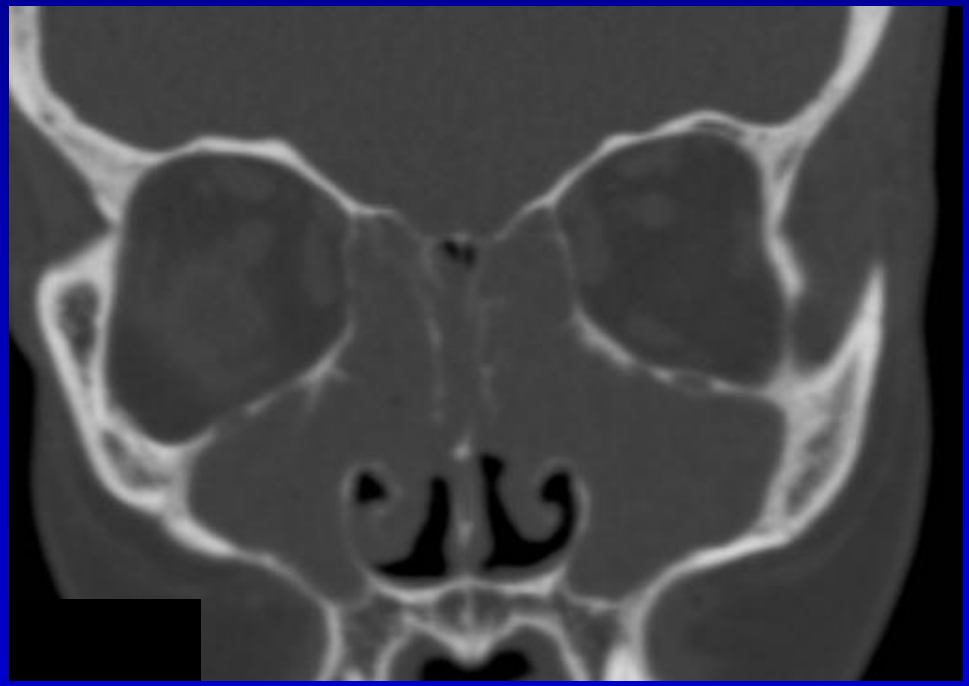
Treatment evidence for AFRS

Statement	Recommendation
Surgery with postoperative medical therapy	C
Oral steroids: Short term postop improvement, but can have significant side effects	A
Topical steroid irrigations	C (extrapolated)
SCIT improves short term outcomes, but long term benefits are unclear	C
Topical anti-fungal therapy	A- (extrapolated)

EPOS 2012

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

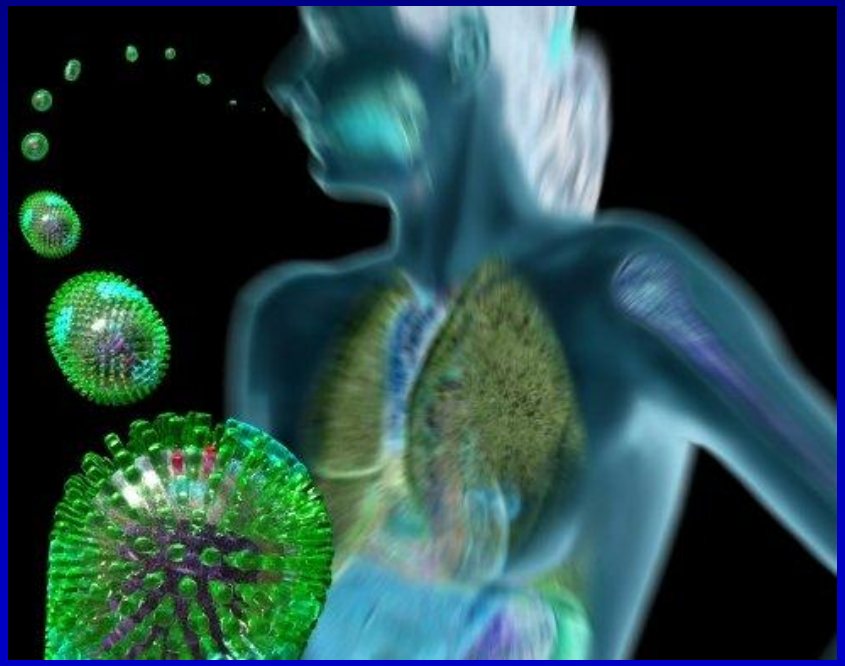
- 2 DBPCTs monteleukast
  - Some improvement in sx, but not endoscopy or immune mediators
- Non-placebo studies comparing to INCS or add on therapy
  - Some benefit, maybe sneezing, itching, HA
- Zileuton: 5% LFT elevation

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, etal IFAR 2012
Ray WA, etal 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

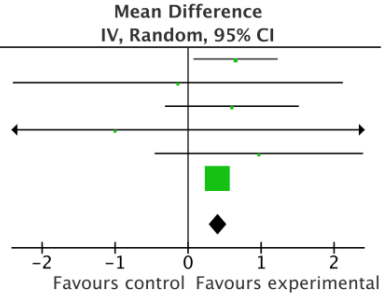
Lohia S, Schlosser RJ, etal, Allergy 2013

INCS improve asthma sx (FEV1, rescue meds)

INCS spray vs Placebo

Study or Subgroup	Favours experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Agondi 2008	3.77	0.56	16	3.12	0.97	14	4.1%	0.65 [0.07, 1.23]
Corren 1992	3.22	2.6879	10	3.36	2.2062	8	0.3%	-0.14 [-2.40, 2.12]
Henriksen 1984	8.5	0.798	17	7.9	1.7555	17	1.6%	0.60 [-0.32, 1.52]
Sandrini 2003	18	10.4293	7	19	5.9905	9	0.0%	-1.00 [-9.66, 7.66]
Stelmach 2005	2.2	1.89	19	1.23	2.55	19	0.7%	0.97 [-0.46, 2.40]
Watson 1993	2.4	0.2	21	2	0.2	21	93.3%	0.40 [0.28, 0.52]
Total (95% CI)			**90**			**88**	**100.0%**	**0.42 [0.30, 0.53]**

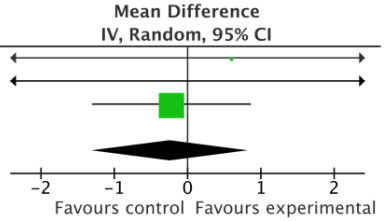
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.77$, df = 5 (P = 0.88); $I^2 = 0\%$
Test for overall effect: Z = 6.97 (P < 0.00001)



INCS spray with oral ICS vs oral ICS

Study or Subgroup	Favours experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Katial 2010	37.1	41.0122	200	36.5	38.6523	166	1.7%	0.60 [-7.58, 8.78]
Nathan 2005	20.6	52.1776	250	23.6	53.1085	259	1.4%	-3.00 [-12.15, 6.15]
Stelmach 2005	2.57	1.79	19	2.79	1.53	17	96.9%	-0.22 [-1.30, 0.86]
Total (95% CI)			**469**			**442**	**100.0%**	**-0.24 [-1.31, 0.82]**

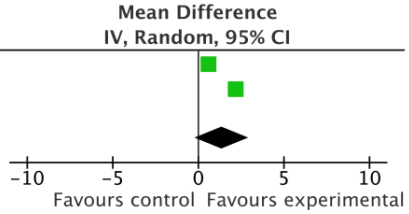
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.39$, df = 2 (P = 0.82); $I^2 = 0\%$
Test for overall effect: Z = 0.45 (P = 0.65)



Nasal inhalation vs nasal placebo

	Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
	Pedersen 1998	2.67	0.31	12	2.08	0.42	12	49.9%	0.59 [0.29, 0.89]
*	Pedersen 1998a	3.27	0.24	12	1.09	0.42	12	50.1%	2.18 [1.91, 2.45]
	Total (95% CI)			**24**			**24**	**100.0%**	**1.39 [-0.17, 2.94]**

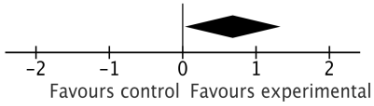
Heterogeneity: $Tau^2 = 1.24$; $Chi^2 = 59.90$, df = 1 (P < 0.00001); $I^2 = 98\%$
Test for overall effect: Z = 1.74 (P = 0.08)



Overall

Total (95% CI)	**583**		**554**	**100.0%**	**0.69 [0.04, 1.35]**

Heterogeneity: $Tau^2 = 0.70$; $Chi^2 = 140.38$, df = 10 (P < 0.00001); $I^2 = 93\%$
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

Outcome	% pts improved	95% CI
Overall asthma control	78%	72 - 82%
Frequency asthma attacks	85%	75-92%
# hospitalizations	64%	53-75%
PO steroids	73%	67-78%
Inhaled steroids	28%	23-35%
Bronchodilator use	36%	29-44%

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

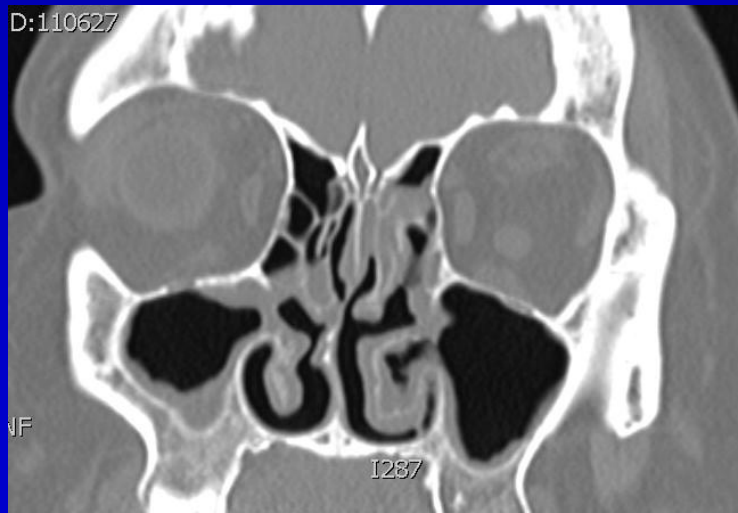
- Less systemic antibiotics, LTRAs, allergy Rx's
- My experience with macrolides and doxycycline is not great
- Role of ESS for topical access – BIG HOLES – Lothrop/medial maxillectomy?
- Use of topical steroids immediately post ESS with high concentrations, high volumes
- Be willing to consider novel approaches….

A new approach to the kickoff…

Other polyp controversies

- Topical mupirocin for staph biofilm/superAg?

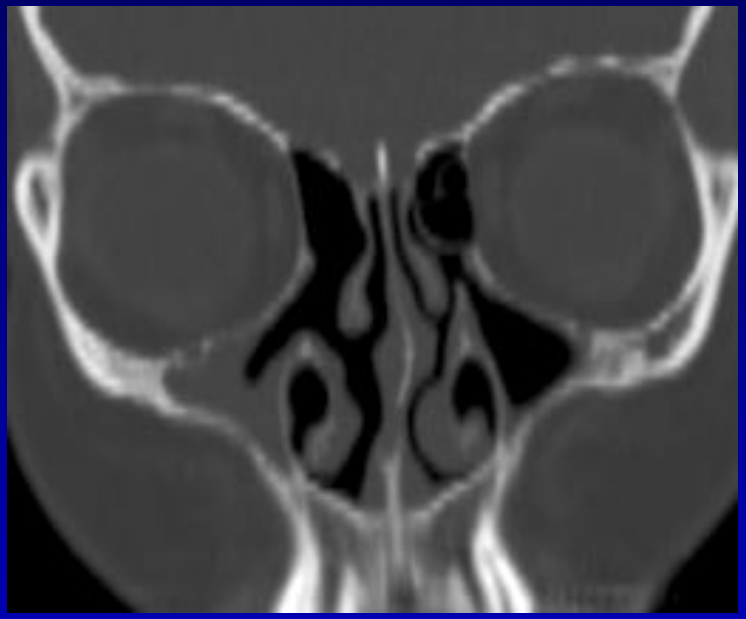
- Brittle asthmatic with minimal sinus disease?

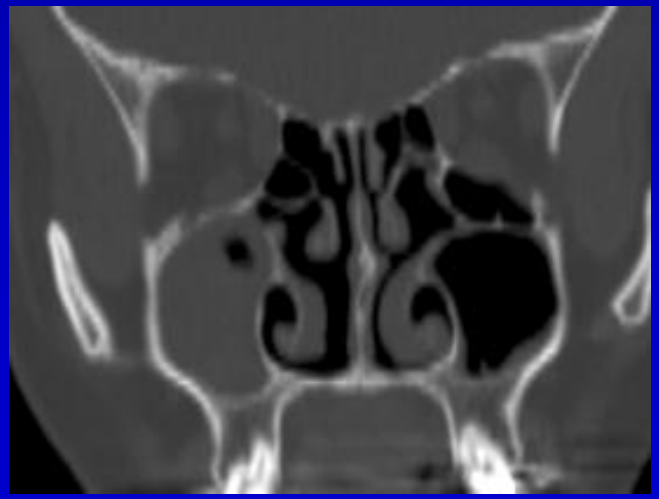


CF sinusitis… another can of worms

- 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

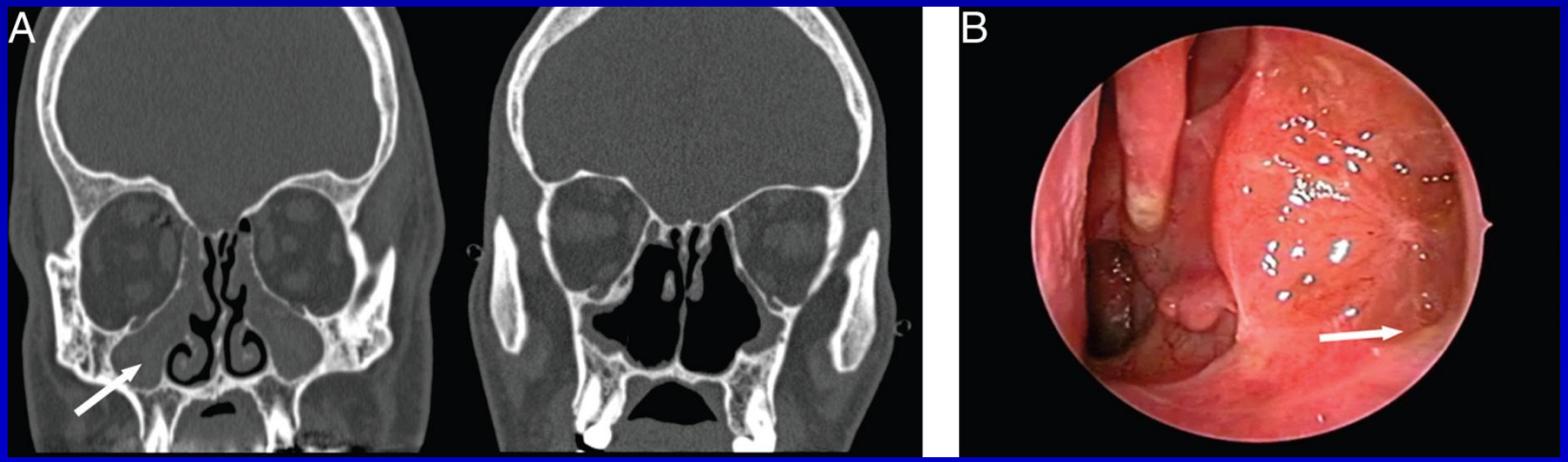
Treatment evidence for CF

Statement	Recommendation
ESS with possible MEMM (QoL & endoscopy, but NOT PFTs)	C
Post ESS topical antibiotics	B
Nasally inhaled dornase alpha	A

EPOS 2012

ESS in CF

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

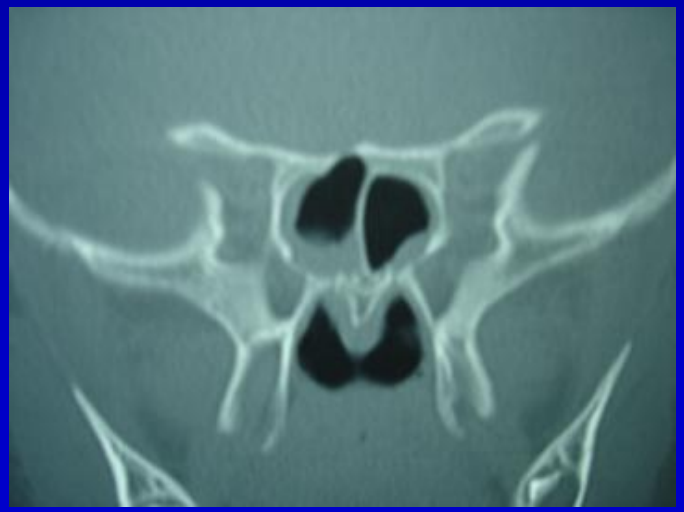


Virgin F, etal AJRA 2012
Macdonald KI etal, Rhinology 2012

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

Agent	Recommendation
Antibiotics: IV	
Antibiotics: Short term oral	
Antibiotics: Long term oral	
Antibiotics: Topical	
Steroid: Oral	
Steroid: Intranasal	
Saline: spray or rinse	
GERD Rx	
AH, LTRAs, mucolytics, decongestants	

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

EPOS 2012

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

EPOS 2012

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

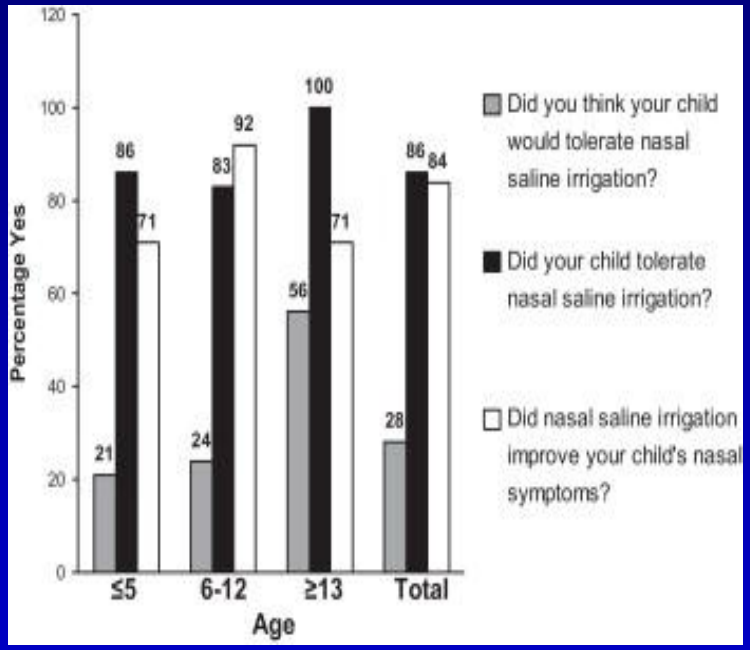
Jeffe et al Int J Pediatric ORL 2012

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



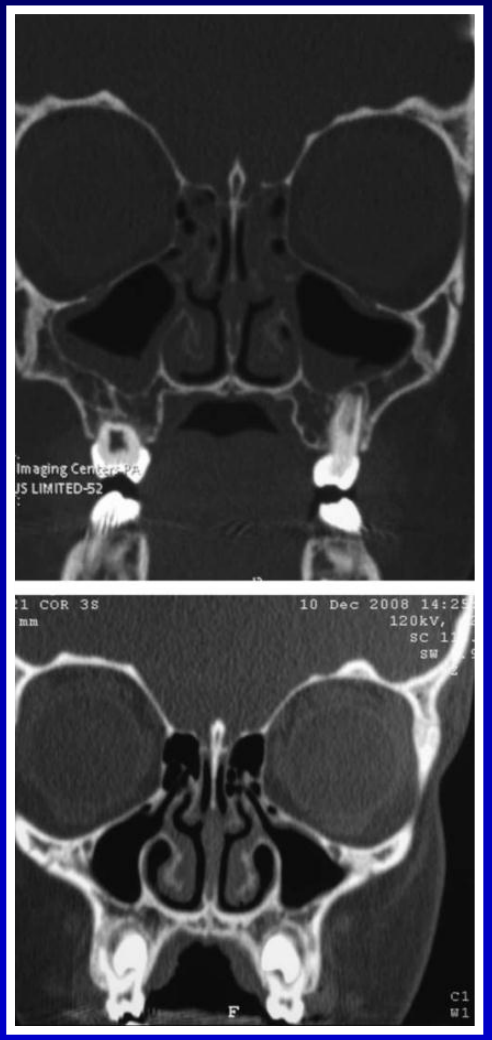
93% reported overall health improvement

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



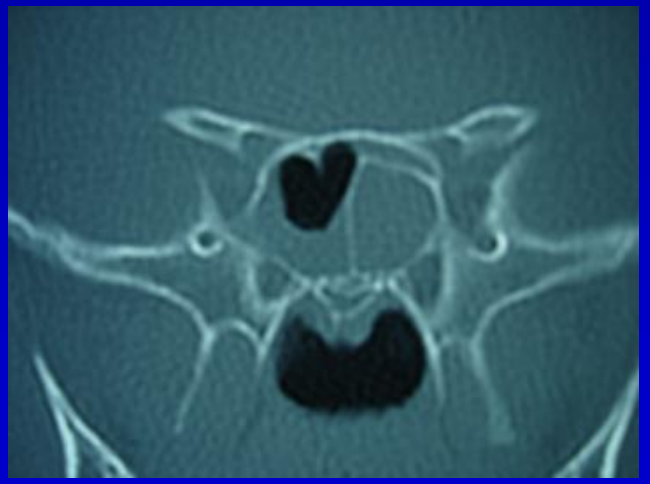
Wei et al Laryngoscope 2011

Evidence based medical Rx

Agent	Recommendation
Antibiotics: IV	
Antibiotics: Short term oral	**B-**
Antibiotics: Long term oral	
Antibiotics: Topical	
Steroid: Oral	**A (select)**
Steroid: Intranasal	**A (extrapolated)**
Saline: spray or rinse	**A**
GERD Rx	
AH, LTRAs, mucolytics, decongestants	

6 weeks of amox/clav, another CT…

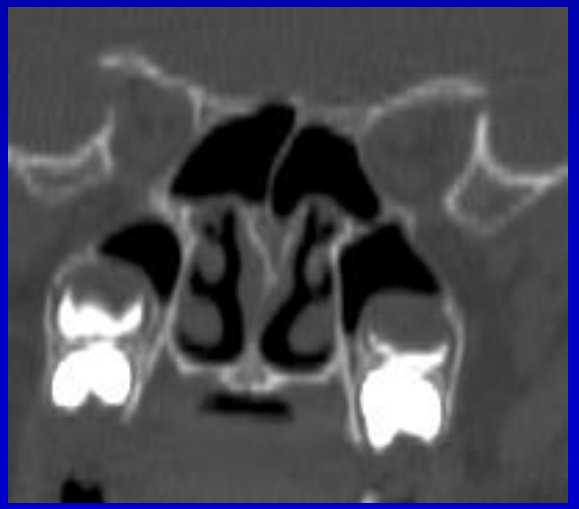
CF and immune w/u:
negative
Further medical Rx?



Evidence based medical Rx

Agent	Recommendation
Antibiotics: IV	**C-**
Antibiotics: Short term oral	**B-**
Antibiotics: Long term oral	**D (possible, extrap)**
Antibiotics: Topical	**C-**
Steroid: Oral	**A (select)**
Steroid: Intranasal	**A (extrapolated)**
Saline: spray or rinse	**A**
GERD Rx	**C**
AH, LTRAs, mucolytics, decongestants	**D**

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