Pediatric Rhinosinusitis

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Functions of the Nose

1. Function as a respiratory organ
   - Airway & Resonance
     (Nasalance, Nasality, Rhinolalia)
   - Control of inspired air
     - Temperature control

       35°C at the nasopharynx by convection between air & arterial bed
     - Humidity control

       95% at nasopharynx by the capillaries, submucosal glands, nasolacrimal ducts, and oral cavity
   - Protection & Clearance
2. Function as a sensory organ

   Olfaction, chemical sensation, sneezing reflex

Mucous Blanket

- Two layers

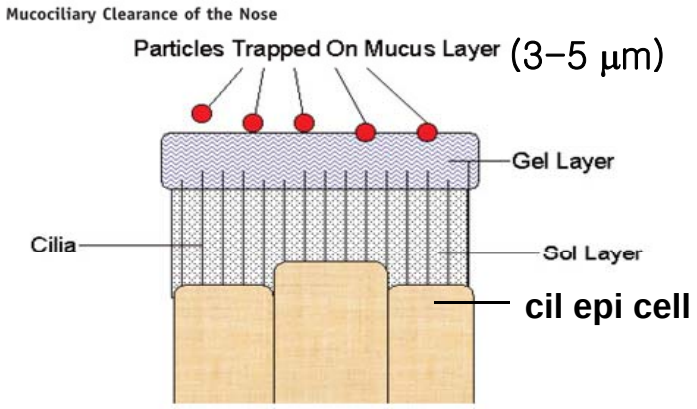
  Upper (mucous gel) layer: highly viscous, elastic

  Inner (periciliary sol) layer: less viscous

- pH=7 or slightly acidic, water 95%, mucin 3%, electrolyte 2%
- Antibacterial and antiviral substances

  neutrophils, eosinophils, lysozyme, Ig A

Mucociliary Transport (8-10 mm/min) ; Ciliary Beat Frequency (10-16/s)



Mucous Blanket

Pediatric rhinosinusitis

- Overlapping with other upper airway diseases
  - Allergic rhinitis
  - URI
  - Adenoid vegetation
  - Immune deficiencies; hypogammaglobulinemia, AIDS
  - Ciliary dyskinesia
- Diagnosis is often presumtive.
- Treatment is empirical.
- Children catch 6-8 colds/yr with an incidence of acute sinus infections (0.5% to 5%)

Classification of Rhinosinusitis

- Acute rhinosinusitis < 4 weeks
- Subacute rhinosinusitis 4-12 weeks
- Chronic rhinosinusitis > 12 weeks
- Recurrent ARS ≥ 4 episodes /year
- Acute exacerbation of CRS

Symptoms and Signs of Pediatric Acute Rhinosinusitis (Consensus Meeting)

Non-severe Acute Rhinosinusitis

- Rhinorrhea of any quality
- Nasal congestion
- Headache, facial pain, and irritability (variable)
- Low-grade or no fever

Severe Acute Rhinosinusitis

- Purulent (thick, colored, opaque) rhinorrhea
- Nasal congestion
- Facial pain or headache
- Periorbital edema (variable)
- High fever (> 39^0C)

Diagnostic Criteria in Chronic Rhinosinusitis

- Major symptoms

  Postnasal drip, Recurrent coughing,
  Mucopurulent rhinorrhea

- Minor symptoms

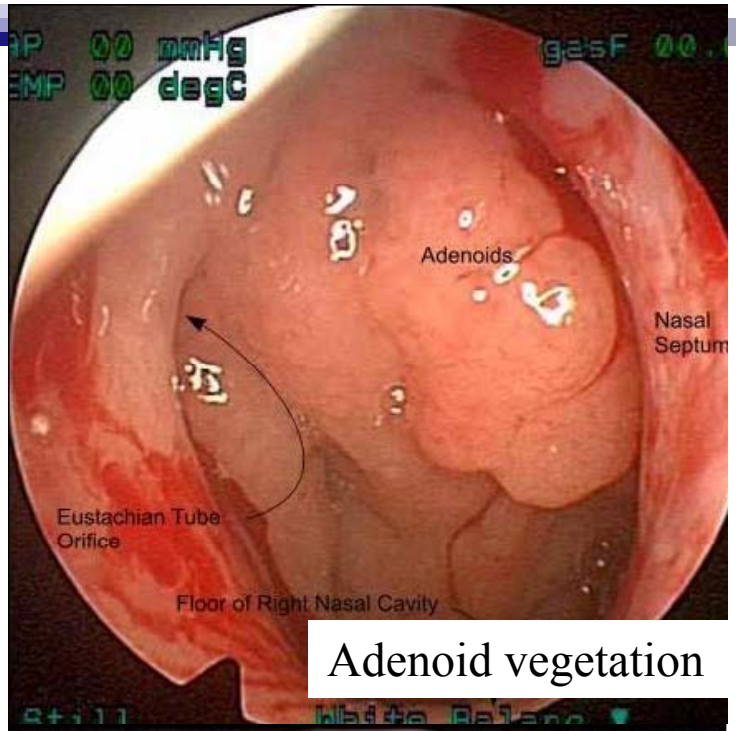
  Periorbital swelling, Headache, Facial pain,
  Toothache, Otalgia, Sore throat, **Halitosis**,
  Wheezing, Fever

Diagnosis

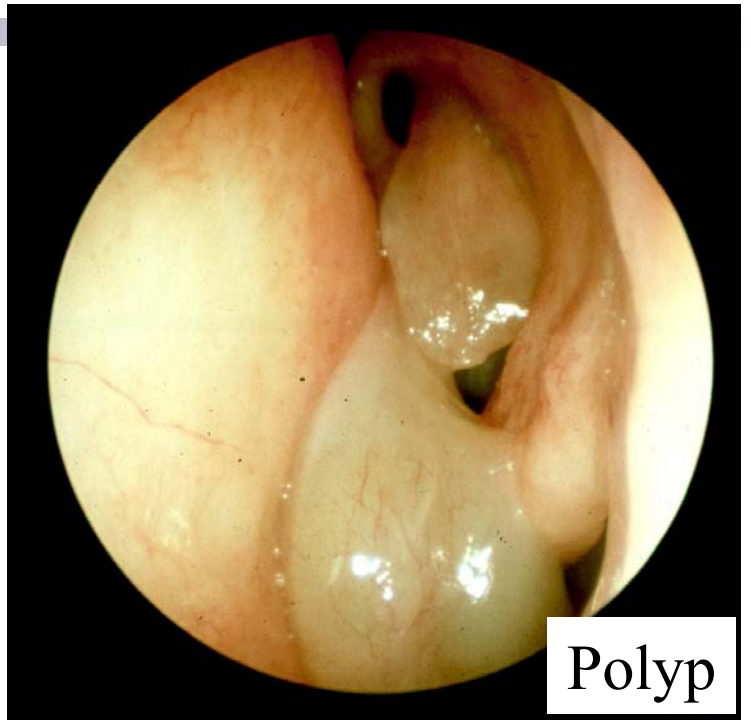
- More challenging than adults
  - Little information about the presence and severity of symptoms from children themselves
  - Frequent URI makes it difficult to distinguish it from chronic rhinosinusitis
  - Adenotonsillar hyperplasia may overlap with chronic rhinosinusitis symptoms
  - Recurrent coughing is a consistent symptom of rhinosinusitis.

Physical examination

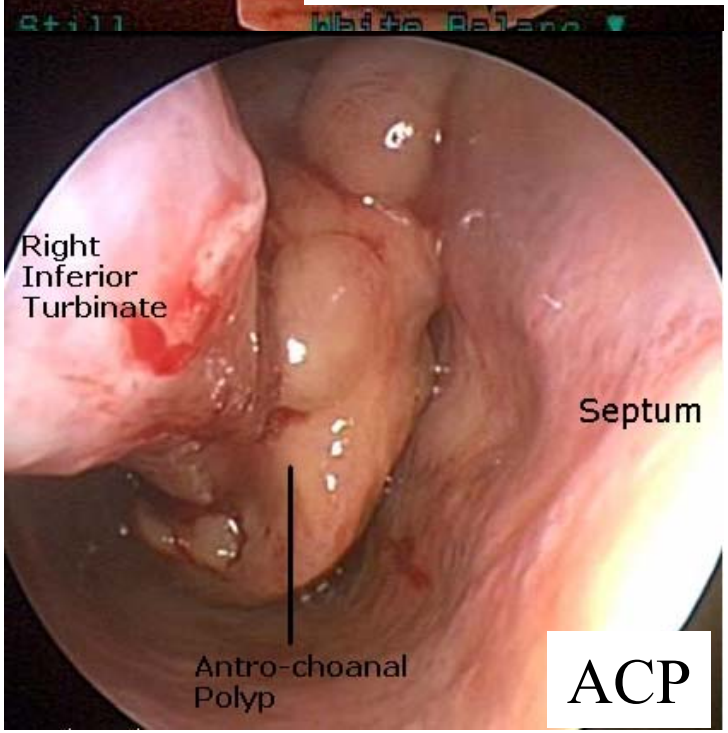
- Direct rhinoscopy with an otoscope, or with a nasal speculum & head mirror
- Fiberoptic rhinoscopy
  - Well tolerated even for younger children
- Rigid nasal endoscopy (recently better optics)
- Examine the nasal cavity before & after nasal decongestion



Adenoid vegetation



Polyp



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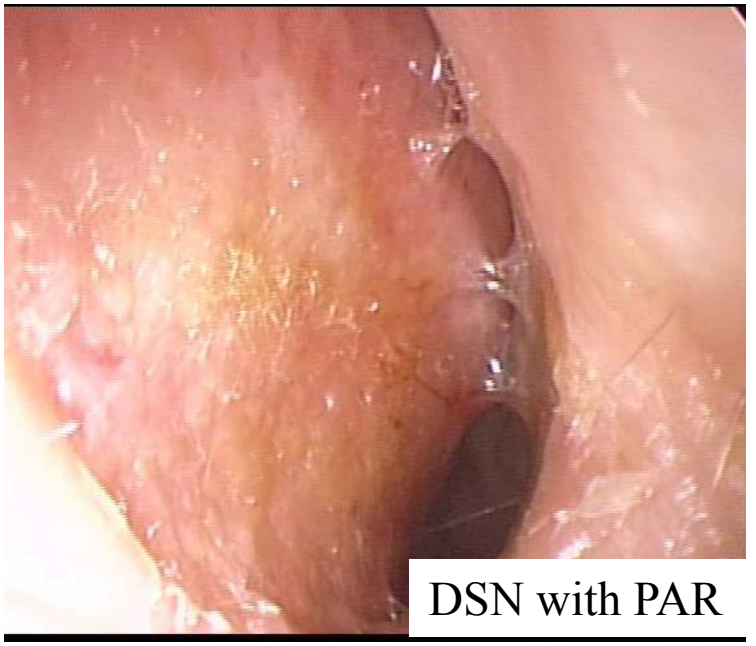


DSN with PAR

Diagnosis of Pediatric Rhinosinusitis

- Diagnosis based on clinical symptoms and signs

- Culture and isolation of causative microorganism
  - Not always feasible

- Other diagnostic tools
  - Transillumintion: no great help in children
  - Ultrasonography: sensitivity 64%, specificity 49%
  - Plain X-rays: sensitivity 85%, specificity 70%
  - PNS **CT scan or OMU CT scan**
    - Most accurate
    - **Radiation exposure risk??**

Diagnosis of the Sinusitis with Plain X-rays

- Plain X-ray
  - Sensitivity: 85%
  - Specificity: 70%
- Plain X-rays do not necessarily rule out the presence of maxillary sinus mucosal swelling.
- Additional examinations may be indicated.
- Standard: OMU CT

Indications for CT in Children

- Sinus surgery
- Severe illness or toxic conditions
- Acute illness persists with medical therapy in 48 to 72 hours
- Immunocompromised patients
- Presence of suppurative (intraorbital or intracranial) complications other than orbital cellulitis

Principle of Medical Treatment

- Relieve nasal obstruction
- Treat the inflammation
  - Antibiotics, enzymes, mucolytics
- Open the sinus ostia
- Thin the mucopurulent discharge
  - Stop antihistamines unless allergic disease
  - Improve hydration
  - Humidification of room air
  - Nasal irrigation therapy

Microbiology of Pediatric Rhinosinusitis

Acute Rhinosinusitis

S. pneumoniae

M. catarrhalis

H. influenza

Chronic Rhinosinusitis

S. pneumoniae

M. catarrhalis

H. influenza

Staphylo. aureus

α-hemolytic Streptococcus

P. aeruginosa

Anaerobes

Increasing anaerobes in CRS

Acute/Subacute RS

Therapy	Evidence level	Relevance
Antibiotics	Meta-analysis of randomized controlled study	Yes: after 5 days or in severe cases
Topical steroid	≥one randomize controlled study	Yes
Antibiotics + topical steroid	≥one randomize controlled study	Yes
Oral steroid	No evidence	No
Nasal saline douch	No evidence	No
Decongestion	No evidence	Yes as symptomatic relief
Mucolytics	No evidence	No
Oral antihistamines in AR	≥one experimental study	No

Fokkens et al, 2005

Chronic RS

Relevance (+)	Relevance (-)
Long term oral antibiotic therapy (over 12 weeks)	Short term oral antibioics (<12 weeks)
Topical steroid	Topical antibiotics
Allergen avoidance in AR	Oral steroid
Nasal saline douch for symptomatic relief	Decongestant
	Antimycotics (systemic/local)
	Oral antihistamines in AR
	Proton pump inhibitors
	Immunotherapy
	Phytotherapy

Fokkens et al, 2005

Treatment of Uncomplicated Acute Rhinosinusitis

- Usual-dose of amoxicillin (45 mg/kg/day)

- High-dose of amoxicillin (90 mg/kg/day)
- High-dose of amox-clav (90 mg/kg/day amoxicillin; 6.4 mg/kg/day clavulanate)
  - Recent antibiotic treatment (<90 days)
  - Severe symptoms

Clinical Practice Guidelines by American Academy of Pediatrics

Children Allergic to Penicillin

- Most patients with allergy to penicillin will tolerate cephalosporins.
- If allergy is manifested as anaphylaxis, macrolides should be prescribed instead of cephalosporins:
  - Cefuroxime = 30 mg/kg/day in 2 divided doses
  - Cefpodoxime = 10 mg/kg/day once daily
  - Cefdinir = 14 mg/kg/day once daily
  - Azithromycin = 10 mg/kg on day 1; 5 mg/kg x 4 days in a single daily dose
  - Clarithromycin = 15 mg/kg/day in 2 divided doses

Clinical Practice Guidelines by American Academy of Pediatrics

Duration of Antimicrobial Therapy for Acute Rhinosinusitis

- Empirical recommendation: 10-14 days of treatment for acute rhinosinusitis
- Prolonged medication for 28 days if the symptoms have improved but have not resolved completely.
- If the symptoms are unchanged at 72 hours or worsen at any time, re-evaluation is necessary; either change antibiotics or obtain a specimen of sinus secretion for culture.

Chronic Rhinosinusitis

- Antibiotic for 21-28 days
  - 2nd and 3rd-generation cephalosporins with adequate *S. pneumonias* coverage (cefprozil, cefuroxime axetil, cefpodoxime proxetil, amoxillin-clavulanate)
  - For penicillin-sensitive patients, macrolides must be considered
- Anaerobe coverage for chronic infection

(The Joint Task Force on Practice Parameters for Allergy and Immunology, Journal of Allergy Clinical Immunology 1998)

Chronic Rhinosinusitis & Macrolide Therapy

- Chronic rhinosinusitis associated with lower respiratory infections (bronchiectasis and chronic bronchitis)
- Chronic rhinosinusitis with profuse rhinorrhea and postnasal drip
- Chronic rhinosinusitis refractory to surgery
- Placebo-controlled studies are available regarding the advantages of this treatment

Rubin BK, Tamaoki J (Ed.). *Antibiotics as Anti-Inflammatory and Immunomodulatory Agents*. Basel, Switzerland. Birkhauser Verlag. 2005.193-199.

Long-term Low-dose Macrolide Therapy in CRS

- In adults
  - 400-600 mg erythromycin per day
    - More GI trouble & drug interactions
  - 150-300 mg roxithromycin (Rulid) per day
  - 250-500 mg clarithromycin (Klaricid) per day
  - For 3-6 months

  cf) Azithromycin: not proven in CRS, but in the lower airway

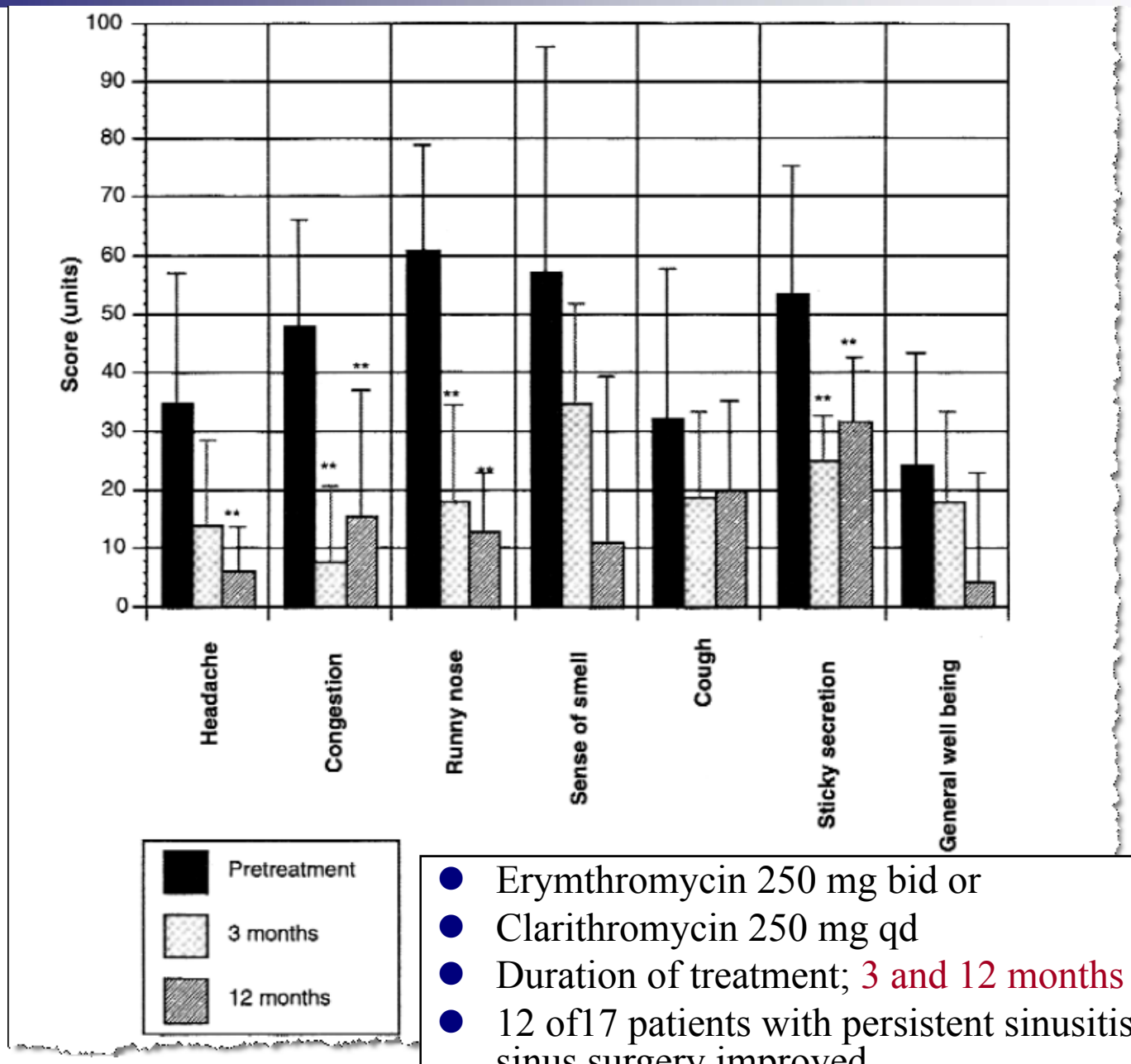
Fujita, 2000; Suzuki, 1997

- In children
  - half of the daily dose per day

Mode of Action of Macrolide-Summary

Decrease	Increase
Proinflammatory cytokines	Mucociliary clearance
Neutrophil chemotaxis	
Neutrophil apoptosis	
Bacterial adherence	
Biofilm formation	
Bacterial virulence	
Mucus hypersecretion	

Pedersen, 2001; Majima, 2004; Culic, 2001
Tamaoki 1997; Rubin, 1997; Rhee, 2000



- Erymthromycin 250 mg bid or
- Clarithromycin 250 mg qd
- Duration of treatment; 3 and 12 months
- 12 of17 patients with persistent sinusitis after sinus surgery improved

TABLE I.
Pretreatment versus Posttreatment Outcome Measures.*

Outcome	Roxithromycin Mean (SEM)	*P* value	Placebo Mean (SEM)	*P* value
PNIF (L/min)				
Pre-	102.7 (6.5)		104.3 (6.1)	
Post-	99.9 (7.8)	NS	104 (7.4)	NS
STT (min)				
Pre-	11.5 (1.2)		10.9 (0.8)	
Post-	8.2 (0.8)	<0.01	11.3 (1.0)	NS
Nasal endoscopy				
Pre-	3.2 (0.2)		3.0 (0.2)	
Post-	2.6 (0.2)	<0.01	2.9 (0.2)	NS
Olfactory function				
Pre-	22.5 (1.8)		22.7 (1.5)	
Post-	23.6 (1.7)	NS	22.3 (1.4)	NS
SNOT-20				
Pre-	2.75 (0.13)		2.83 (0.12)	
At 6 weeks	2.61 (0.14)	NS	2.87 (0.15)	NS
At 12 weeks	2.34 (0.19)	0.01	2.88 (0.12)	NS
At 24 weeks	2.49 (0.18)	NS	2.84 (0.15)	NS
Interleukin-8 (pg/ml)				

ized, Placebo-
olide in the
inosinusitis

, PhD; Lennart Greiff, PhD; Anders Cervin

required to assess their place in clinical prac-
. *Key Words:* Macrolide, chronic rhinosinusitis,
ebo-controlled,

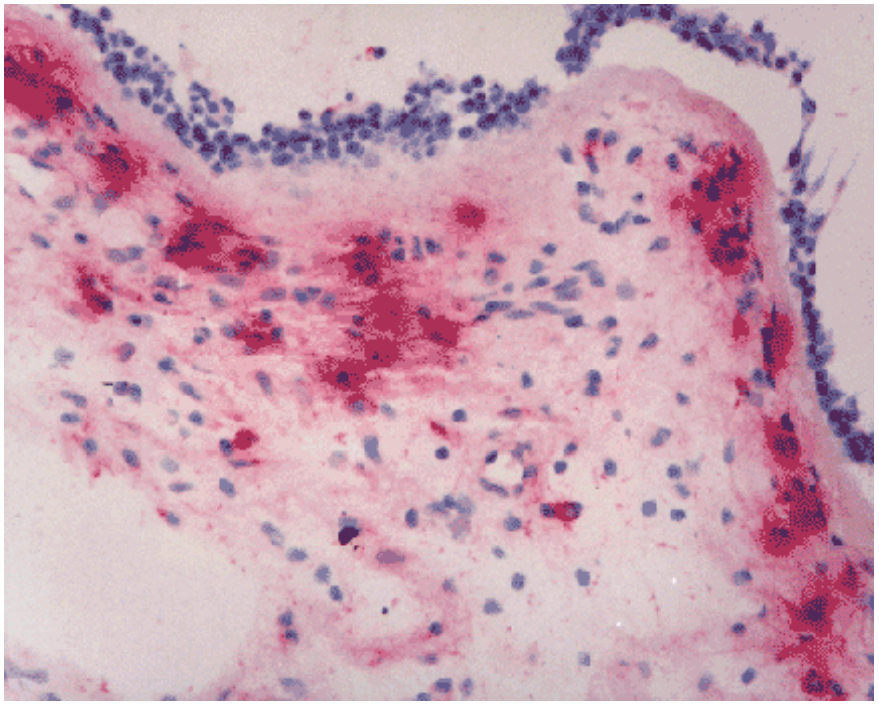
Laryngoscope, 116:189–193, 2006

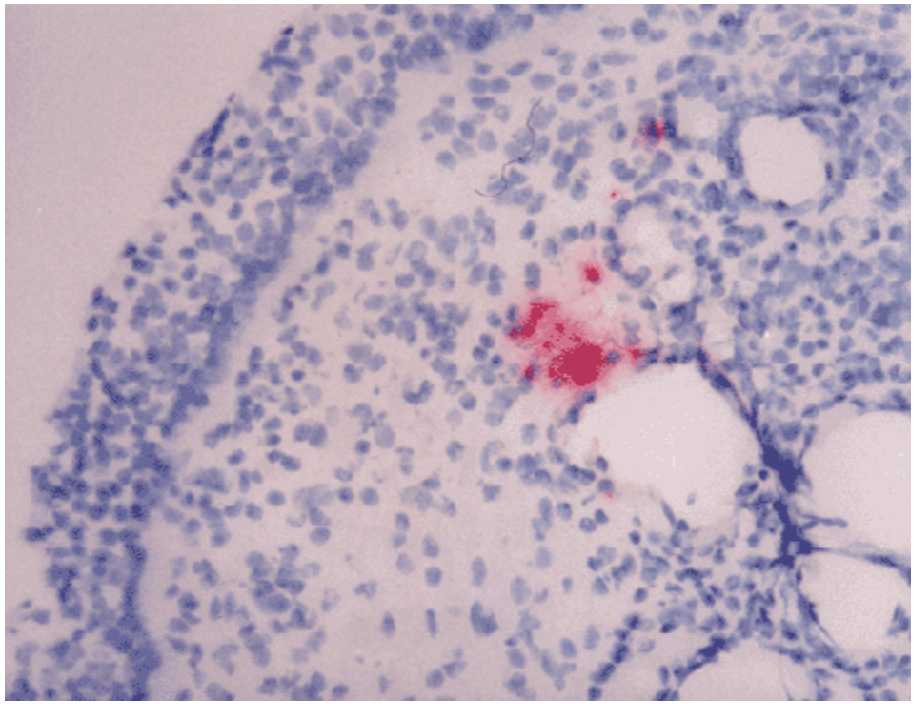
RODUCTION

In recent years, considerable evidence has emerged to
gest that macrolide antibiotics have an antiinflamma-
effect in addition to their well-established antibiotic
t. Macrolides have been shown to inhibit cytokine
luction,[1] alter bacterial biofilm formation,[2] increase

- Saccharine transit time
- Endoscopic finding
- Quality of Life questionaire

Anti-inflammatory Effect of Clarithromycin in CRS





MacLeod CM, et al. *Adv Ther.* 2001;18:75-82.

Adverse Effects

Adverse effects	Klaricid (n=2,351)
Total	**4.7%**
Nausea	3%
Diarrhea	3%
Dyspepsia	2%
Abdominal pain	2%
Headache	2%
Vomiting	1%

Mechanism of Nasal Irrigation Therapy (NIT)

- Increasing mucociliary clearance
- Decreasing inflammatory mediators (histamines, leukotrienes, prostaglandins and various cytokines)
- Removing organized pus and crust mechanically
- Decreasing mucosal edema

Increasing mucociliary clearance

- The administration of **3% hypertonic saline** results in a significantly **faster CBF** 5 min after administration, but this is a **transient** effect

(Wabnitz

Ciliary Beat Frequency (CBF) by Concentration of Saline and Time after Saline Administration (Mean ± Standard Error of the Mean).

	Baseline CBF	5 minutes	60 minutes
0.9% NaCl	10.2 ± 0.5 Hz	9.1 ± 0.6 Hz	8.8 ± 0.7 Hz
3.0% NaCl	9.0 ± 0.6 Hz	10.1 ± 0.4 Hz	9.2 ± 0.7 Hz
P value	.132	.039	.734

- **Saccarine transit time** decreases from baseline with hypertonic saline trials up to **17%,** compared with normal saline

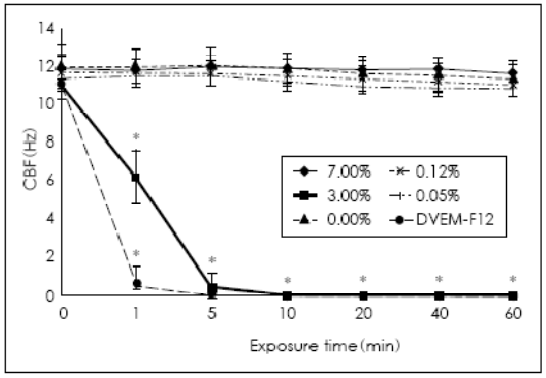
Tonicity: *in vitro* study

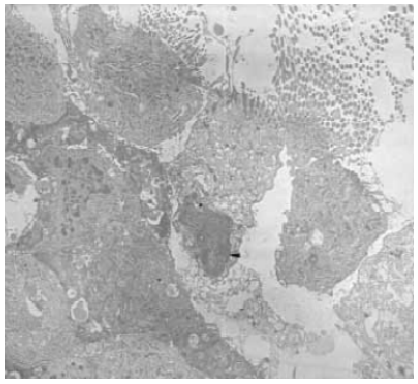
CBF measurement

- Isotonic and hypotonic (0.12%, 0.06%) saline produce no ciliary slowing, but **ciliostasis** is observed within a few minutes in hypertonic (3.0% or 7.0%) saline

Transmission Electron Microscopic Findings

- In hypertonic saline, **intercellular tight junction** and **desmosome** are disrupted and intercellular spaces are widened
- **Ciliated cells and their nuclei** are contracted and the margin of ciliated cells is irregular. No changes in the ultrastructure of the cilia.

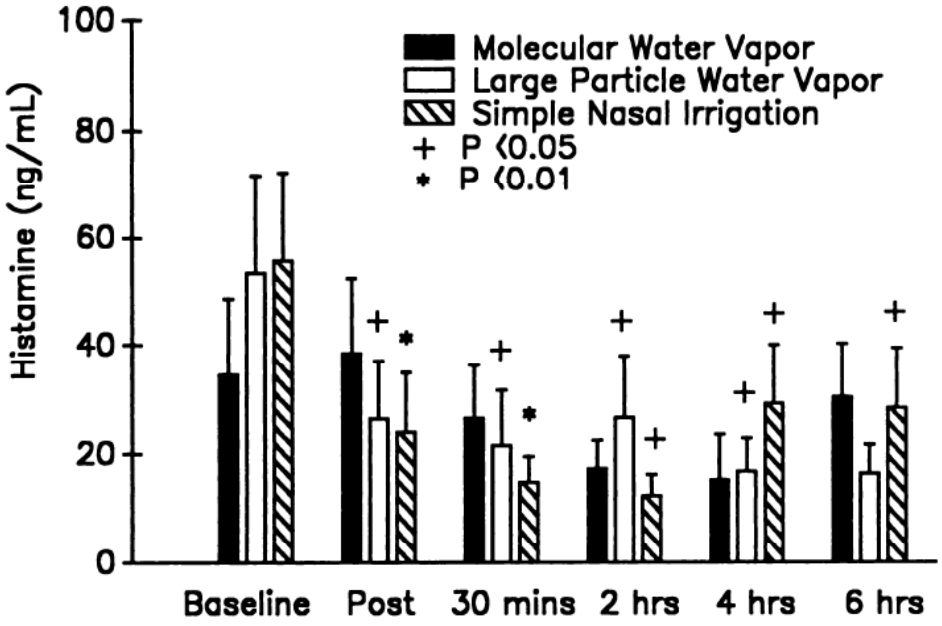


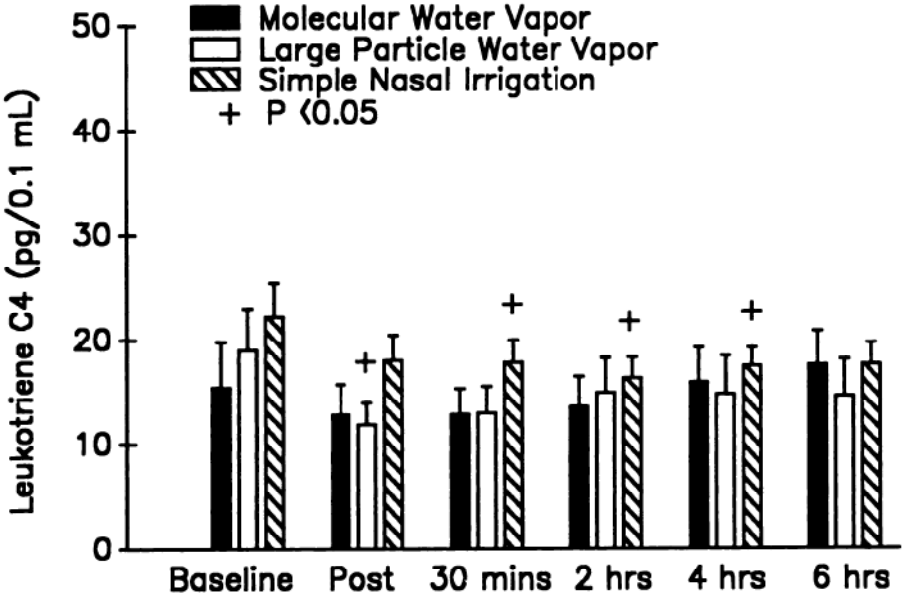


(Min *et al*, 2001)

Decreasing inflammatory mediators

- The effect of inhaled heated **vapor treatment** and saline **irrigation** on **inflammatory mediators** (histamine, leukotriene C4) production in **nasal secretion** (Georgitis, 1994)





Removing organized pus and crust

- Nasal irrigations move mucopus and crusts towards the nasopharynx via a direct physical effect
- Forceful nasal irrigations of the nasal cavity are more effective than gentle nasal irrigations
- Crusts are softened and thick tenacious secretions become less viscous
- Postoperative nasal irrigation therapy may be useful in wound healing after sinus surgery

Temperature

- A linear increase in CBF between 20 and 32˚C (the most suitable temperature to0 CBF)
- A plateau between 32 and 40˚C
- Above 40˚C, CBF declines
- Above 43˚C or below 5˚C, ciliary beating stops completely
- In summary, nasal cilia are not critically inhibited by temperature between 20 and 40˚C

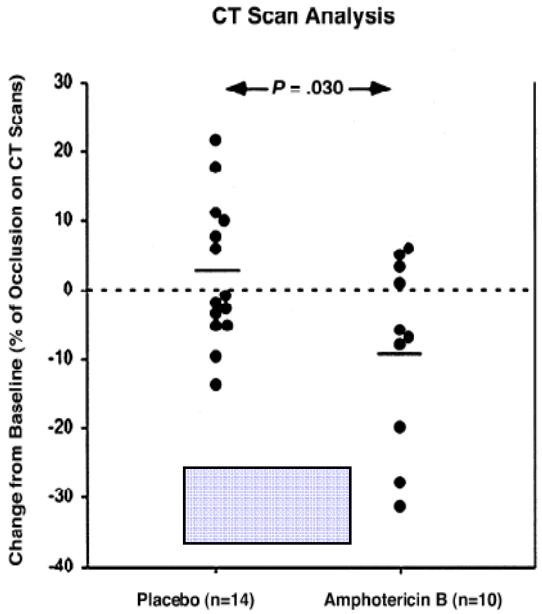
(Green A *et al*, 1995)

Additives

Antifungal agents

[1] **Amphotericin B** (N = 10)

→ significant reduction in mucosal thickening on CT, endoscopic scores, and the intranasal mucus level of eosinophil-derived neurotoxin (Ponikau, 2004)



[2] **Amphotericin B** (N=116)

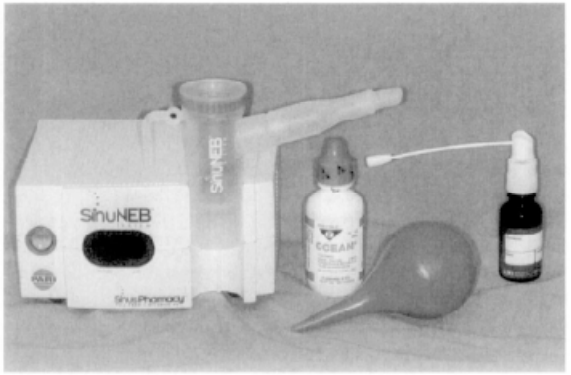
→ No significant differences in endoscopic score, polyp score, symptoms (nasal obstruction, rhinorrhea, PND, sense of smell, facial pain), and peak nasal inspiratory flow rates (Ebbens,2006)

[3] **Amphotericin B, Itraconazole** and **Clotrimazole**

: **All** decrease mucociliary clearance in a dose-dependant fashion; **Clotrimazole** induces ciliostasis, regardless of different doses (Gosepath *et al*, 2002)

Methods of Nasal Irrigation Therapy

- (1) Positive pressure irrigation
  (2) Negative pressure irrigation
  (3) Spray
  (4) Nebulization



- Devices: rubber bulb syringe, sprayer, spoid, atomizer, squeeze bottle, nebulizer,

Home Recipes

- It is ideal that temperature of solution is **at 32°C**
- When nasal irrigations are frequently used, **positive pressure method** is better than spray or nebulization
- In performing positive pressure nasal irrigation, producing a **"K" sound** as the patient administers the solution may be beneficial

	Liquid	Salt	Baking soda	Final tonicity
Univ.of Iowa	4 cup of water, boiled	1 1/2 level tsp	None	0.9%
Talbot et al	1 quart glass jar	2–3 heaping tsp	1 tsp	3.0%
Rabago et al	1 pint of tap water	1 heaping tsp	1/2 tsp	2.0%

1 cup: 240 mL, 1 pint: 480 mL, 1 quart: 950 mL

Medical Treatment of Nasal Polyposis

Relevance (+)	Relevance (-)
Long term oral antibiotic therapy (over 12 weeks)	Short term oral antibioics (less than 12 weeks)
Topical/oral steroid	Topical antibiotics
Nasal saline douch for symptomatic relief	Decongestant
	Antimycotics (systemic/local)
	Oral antihistamines in AR
	Proton pump inhibitors
	Immunotherapy
	Phytotherapy

Fokkens et al, 2005

The Laryngoscope
Lippincott Williams & Wilkins, Inc.

Evaluation of the Medical and Surgical Treatment Of Chronic Rhinosinusitis: A Prospective, Randomised, Controlled Trial

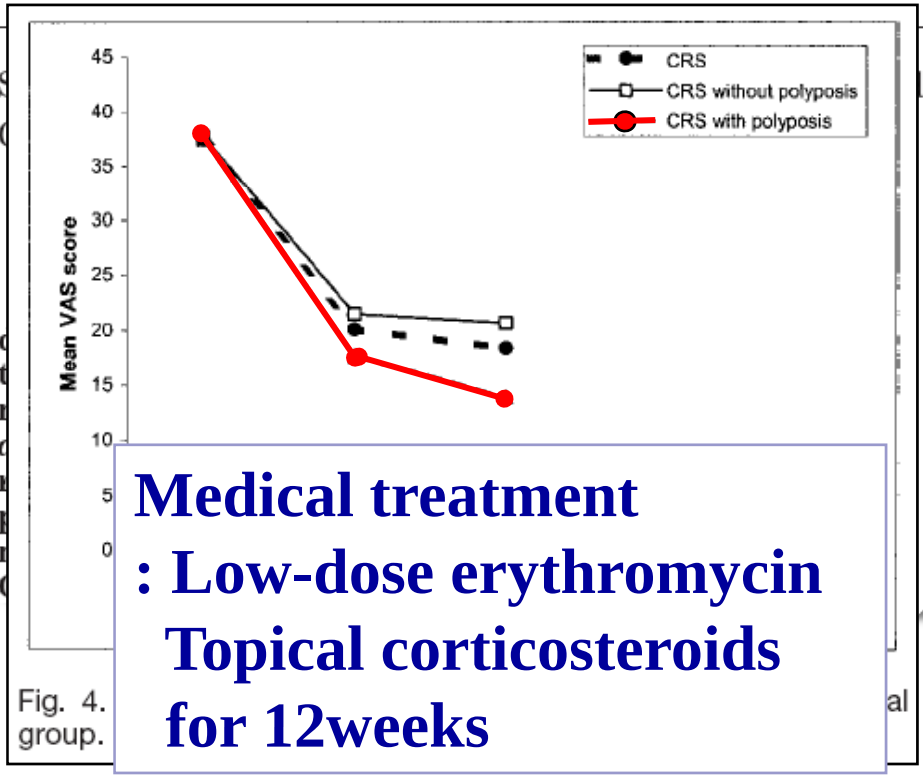


Fig. 4.
group.

Medical treatment
: Low-dose erythromycin
Topical corticosteroids
for 12weeks

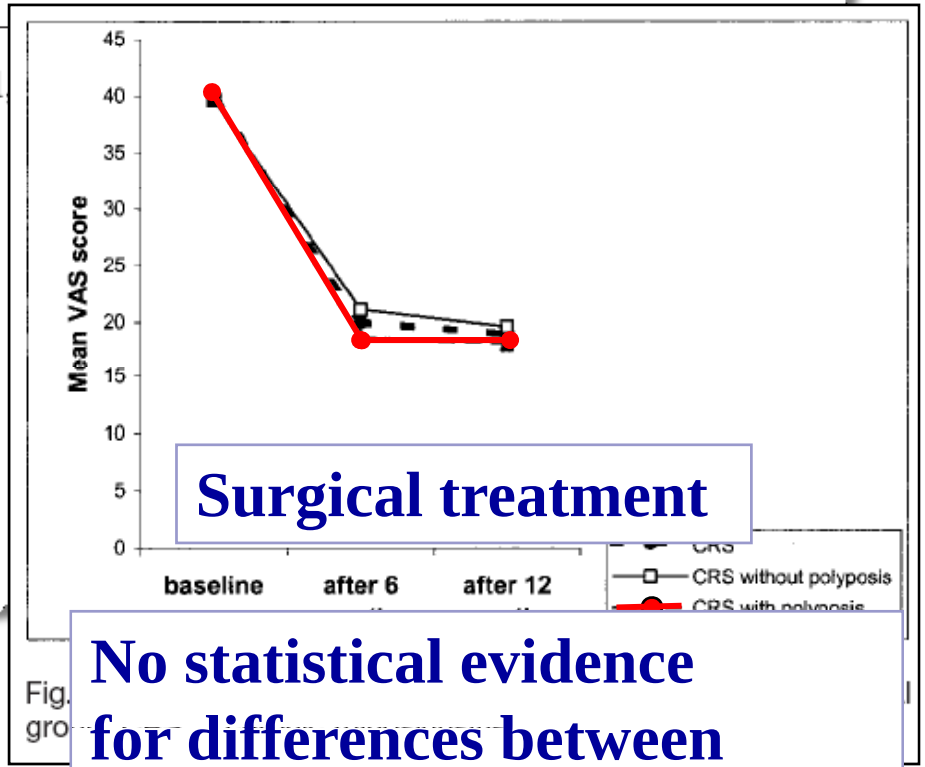


Fig.
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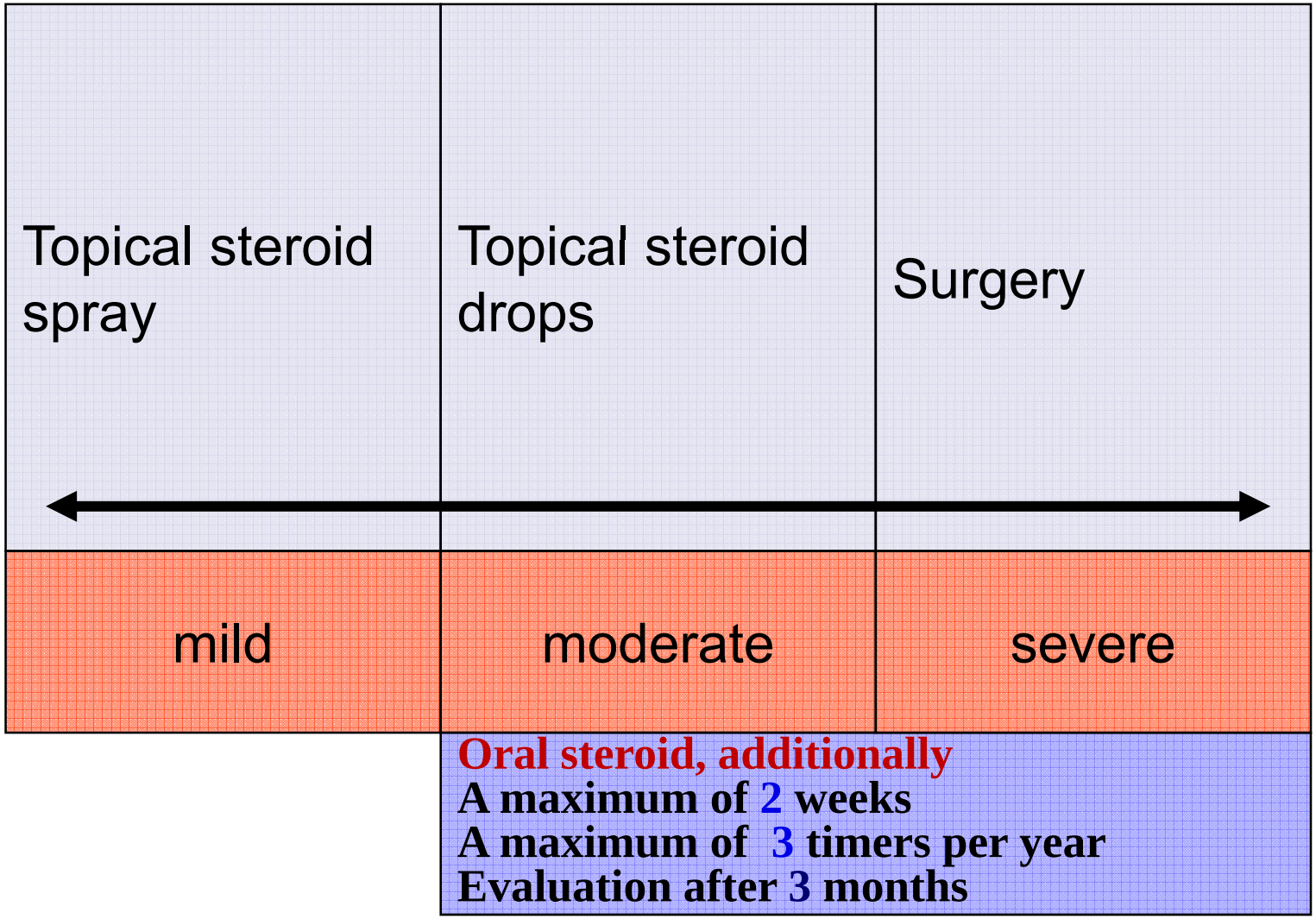
Surgical treatment

No statistical evidence for differences between medical and surgical groups

Steroids for Nasal Polyposis



- *EAACI, 2005*

NP-Intranasal Administration of Corticosteroids

- Preferred non-surgical treatment of nasal polyposis
- Effects
  - Nasal blockage, secretion and sneezing
  - Eradication or reduction in the size of polyps
  - Inhibition of the postoperative recurrence
  - Reduction in the frequency of repeated surgery
  - Evident effect on smell (steroid-dependent anosmia)

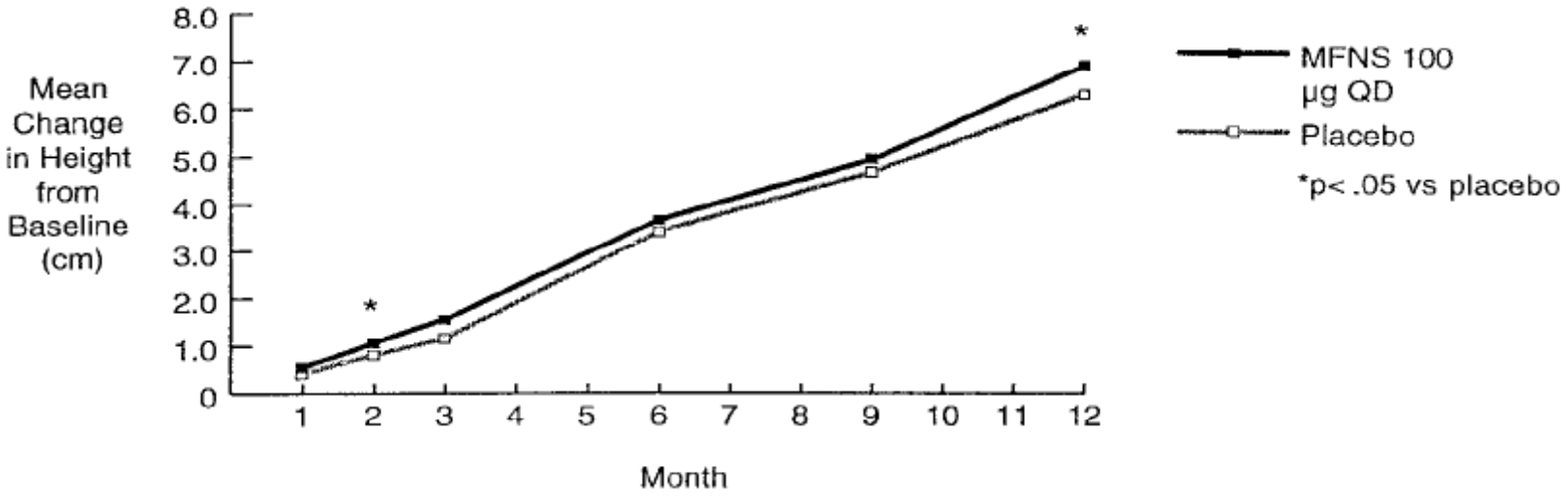
☞ [1] Intranasal spray

[2] Intranasal submucasal injection (into polyps or into the turbinate)

NP-Systemic Corticosteroids

- Dramatic effect: **“Medical Polypectomy”**
- Alternative to surgery :
  - Diffuse polyposis
  - Smell disorder
  - Delay the subsequent surgery
- A course of steroids given a few weeks prior to surgery:
  - Make the operation quicker, easier and safer
- Risk for growth retardation in children???

Growth Retardation in Allergic Rhinitis ?



- There were no significant differences in growth between treatments, between the age categories, or between male and female subjects.

Schenkel et al. ***Absence of growth retardation*** *in children with perennial allergic rhinitis after one year of treatment with* ***mometasone furoate aqueous nasal spray****. Pediatrics. 2000*

Surgical Management

- Options
  - Adenoidectomy
  - Functional Endoscopic Sinus Surgery (FESS)
  - Maxillary sinus lavage/Middle or Inferior meatal antrostomy (MMA or IMA)
    - Good initial subjective improvement *vs.* Suspicious long term results
    - Not usually recommened for pediatric sinusitis
    - No official report of treatment outcome

Biofilms on adenoid

Table 1 Patient demographics, diagnosis, and presence or absence of biofilms

Age/gender	Diagnosis	Presence of biofilms
2 years, M	CRS	+
2 years, M	CRS	+
2 years, M	CRS	+
6 years, M	CRS	+
3 years, F	CRS	+
3 years, F	CRS	+
10 years, M	CRS	+
9 months, M	OSA	–
13 months, M	OSA	–
16 months, M	OSA	–
5 years, M	OSA	–
3 years, F	OSA	–
4 years, M	OSA	–
5 years, F	OSA	–
5 years, M	OSA	–
3 months, M	OSA	–

Zuliani, 2006

Mechanical debridement of the nasopharyngeal biofilms – adenoidectomy- may explain why the clinical symptoms of sinusitis improve with surgery.

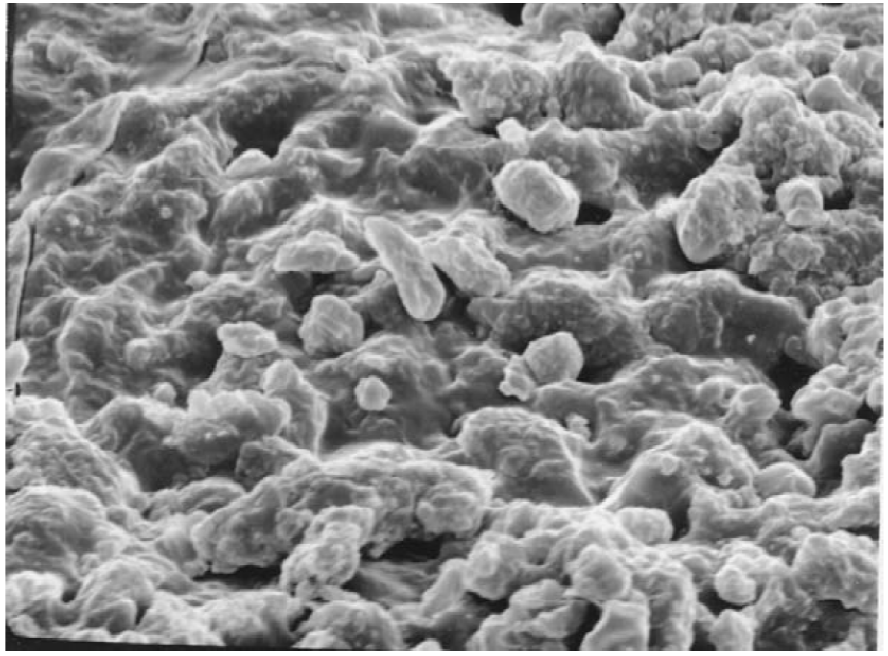


Fig. 1 High power (2000×) SEM image of biofilm architecture highlighting dense spherical colonies embedded in EPS matrix.

Adenoidectomy

- 1st line of surgical treatment
- Children whose symptoms persist after adenoidectomy should be referred for immune functions, allergy tests and CT. (*Clary, 2003*)
- Symptom improvement in 70% - 80% of pediatric sinusitis patients (*Goldsmith et al. 2003*)
- An effective option before FESS in pediatric chronic rhinosinusitis
- Indicated for 4+ nasal obstruction and selected cases of 3+ nasal obstruction (*Cassano et al.2003*)

Table 5 Mean episodes of diseases before and after surgery (number of doctor's visit for a new episode of symptoms) ($n = 37$)

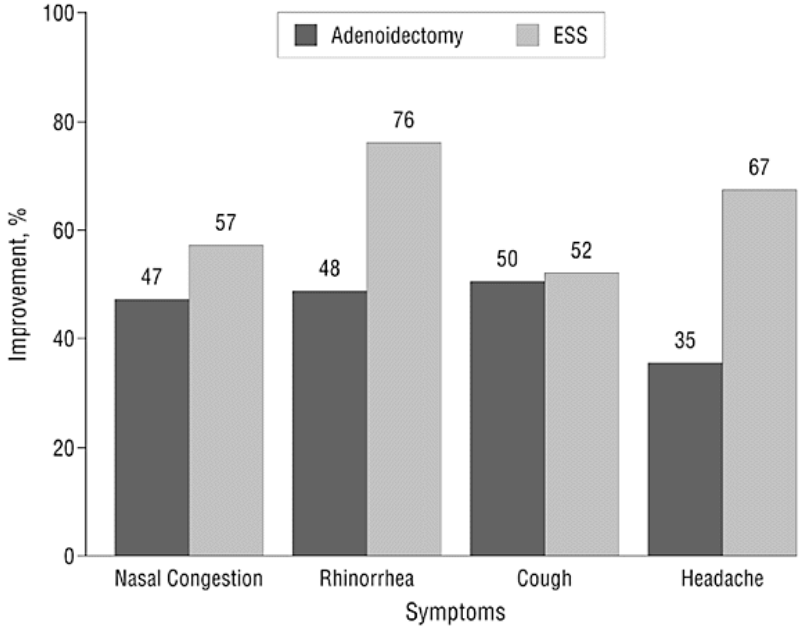
Type of infection	Episodes per year before surgery	Episodes per year after surgery	*P*-value
Rhinosinusitis	13.7	0.76	<0.001
OSD	35.1	1.2	0.008
OME	0.84	0.08	0.001

OSD: obstructive sleep disorder; OME: otitis media with effusion.

Adenoidectomy *along with* FESS

- When ESS is used as the initial treatment modality, the need for **repeated surgery** is reduced, especially in children with **asthma**, a **high CT score**, and **nasal allergy** for which medical treatment have failed and whose parents want an alternative treatment.

Ramadan, 1999



Variable	ESS*	Adenoidectomy
No. of patients who underwent surgery	33	31
No. of patients for whom no data were available	2	1
Total No. of patients	**31**	**30**
No. of patients needing further surgery	1	12
No. of patients with no improvement of symptoms	6	4
Success	24	14

**ESS indicates endoscopic sinus surgery.*

Indications of FESS in Children

- Absolute Indications:
  - Sinusitis with complications
  - Symptomatic mucocoeles
  - Systemic disease with chronic sinusitis
  - Recurrent sinusitis persisting for 6 months despite medical treatment
- Relative Indications:
  - Persistent signs and symptoms and positive CT findings
  - Symptomatic with concha bullosa
  - Chronic headache
  - Chronic nasal discharge
  - Recurrent sinusitis with normal CT findings inconsistent with clinical manifestations

Younis et al, 1996

Facial Growth after FESS

- Minimal changes in facial volume measurements have been found, specifically with subtle enlargement of the orbit on the surgical side being identified.

Senior et al, 2000

- There is no evidence that facial growth alteration will be clinically significant 10 years after FESS surgery.

Bothwell et al, 2002

Paired *t*-Test Analysis of Sinus Volume Means.

Category	Maxillary	Heminasal	Orbit	Ethmoid
Left side vs. right side (normal)	0.2392	0.1183	0.9508	0.1512
Left side vs. right side (sinusitis)	0.7522	0.5702	0.0515	0.7596
Normal mean vs. sinusitis mean	0.4329	0.6525	0.9246	0.5086
Operated side vs. nonoperated side	0.6503	0.8044	0.2214	0.896
Nonsurgical vs. surgical	0.1814	0.7831	0.0002	0.1324

Nonsurgical category is a combination of normal and sinus patients. Surgical represents operated side of surgical patients.

Refractory Rhinosinusitis

- Consider associated conditions
  - Allergy
  - Immune deficiency
  - Asthma
  - Gastroesophageal reflux disease
  - Cystic Fibrosis
  - Primary Ciliary Dyskinesia (Immotile Cilia Syndrome)
  - Allergic Fungal Sinusitis

Take Home Message

- **Rhinosinusitis** results from impaired mucociliary transport, anatomical ostial obstruction and thickened secretion.
- **Medication** in rhinosinusitis can help the antimicrobial control and symptom relief with antibiotics and saline irrigation.
- **Adenoidectomy** is the 1st line option before FESS in Pediatric chronic rhinosinusitis (CRS), particularly in younger patients with obstructive symptoms.
- **FESS** may be a safe and effective technique for special **limited cases** of Pediatric CRS, with a high success rate and a low complication rate (< 1%).


Thank You Very Much!
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