# A practical Approach to Sinusitis

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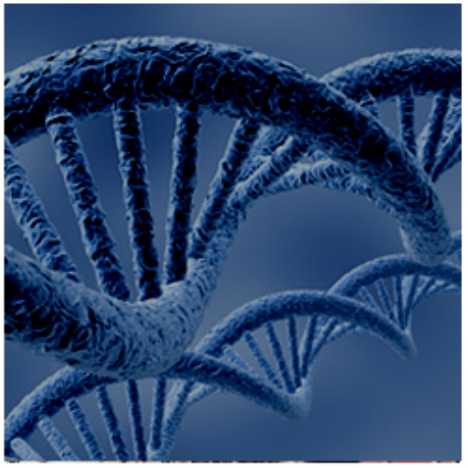


# Disclosures





- Principal Investigator
  - Sanofi, AstraZeneca
- Speaker/Consultant
  - Stryker, Novartis, Mylan, Pentax, GSK
- Royalties for book sales: Thieme

# Learning Objectives





As a result of attending this session, participants will be able to:

1. Differentiate the various types and presentation of sinusitis;
2. Investigate patients' sinonasal symptoms using an appropriate diagnositic workup;
3. Apply the latest treatment recommendations for sinusitis.

# A typical case…

- 42 year old receptionist
- URTI 1 week ago
- Now worsening R congestion, colored discharge, and malar pressure
- Purulence seen below R middle turbinate

# Case continued…







- **Previous treatments**
  - Saline
  - INCS
  - Decongestant
- Would imaging be helpful?
- Are antibiotics indicated?



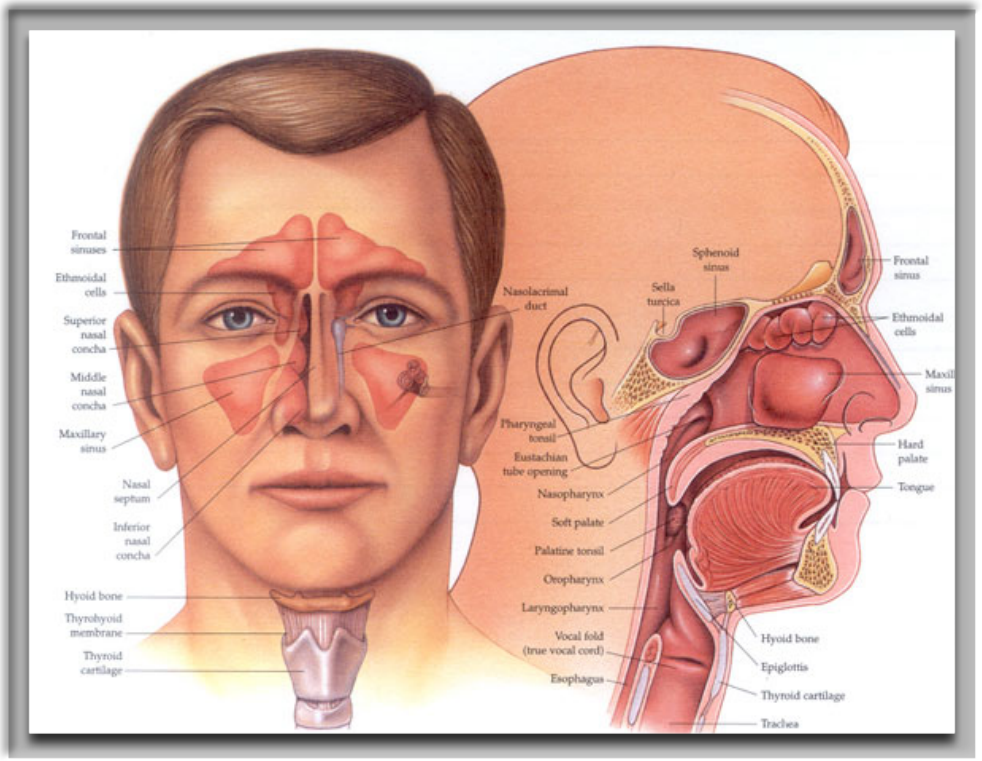




# BACK TO BASICS

# Paranasal Sinuses

- Mucosa lined air spaces within the bones of the face and skull
- 4 paired sinuses:
  - Maxillary
  - Ethmoid: A & P
  - Sphenoid
  - Frontal

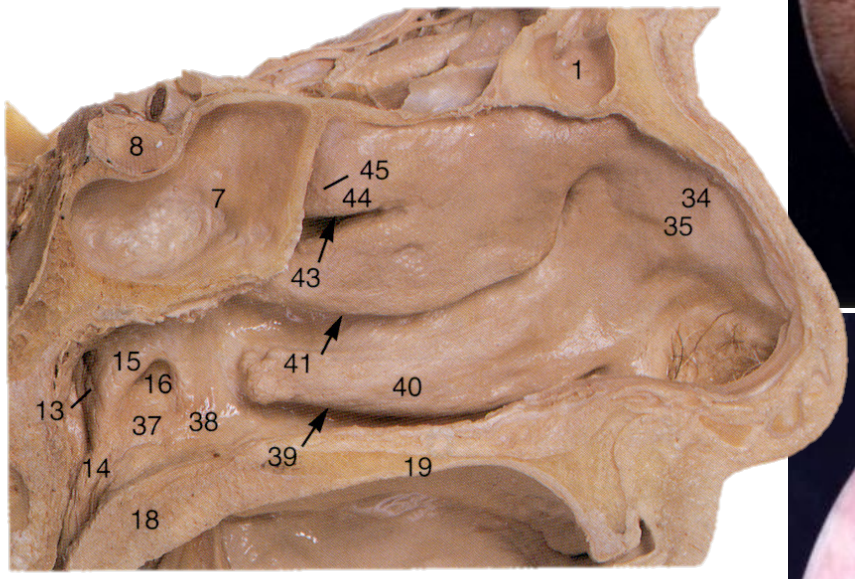


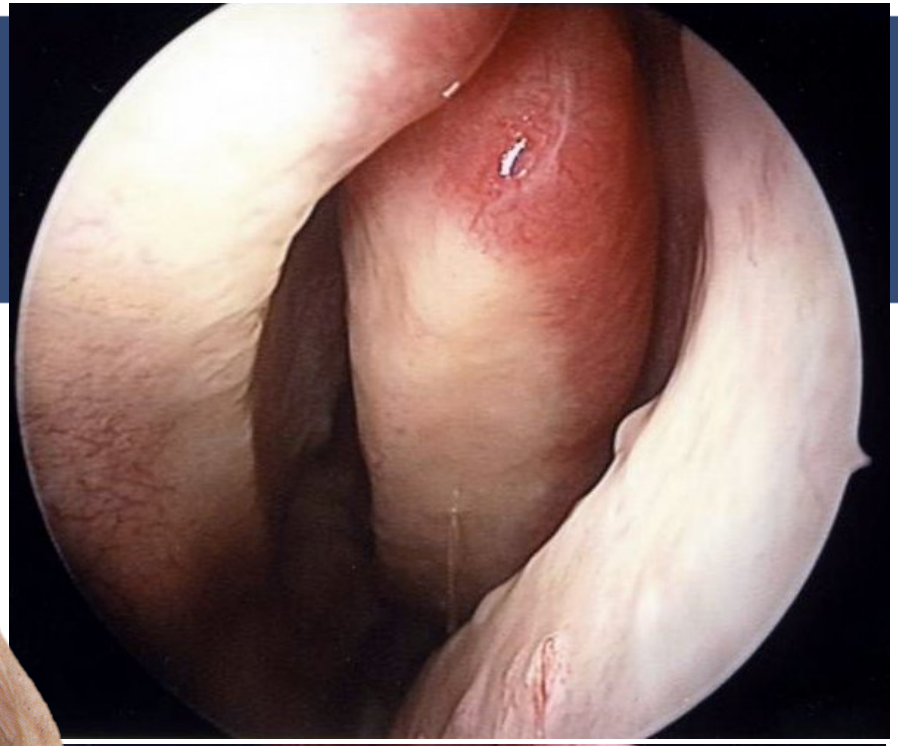
# Nasal Anatomy

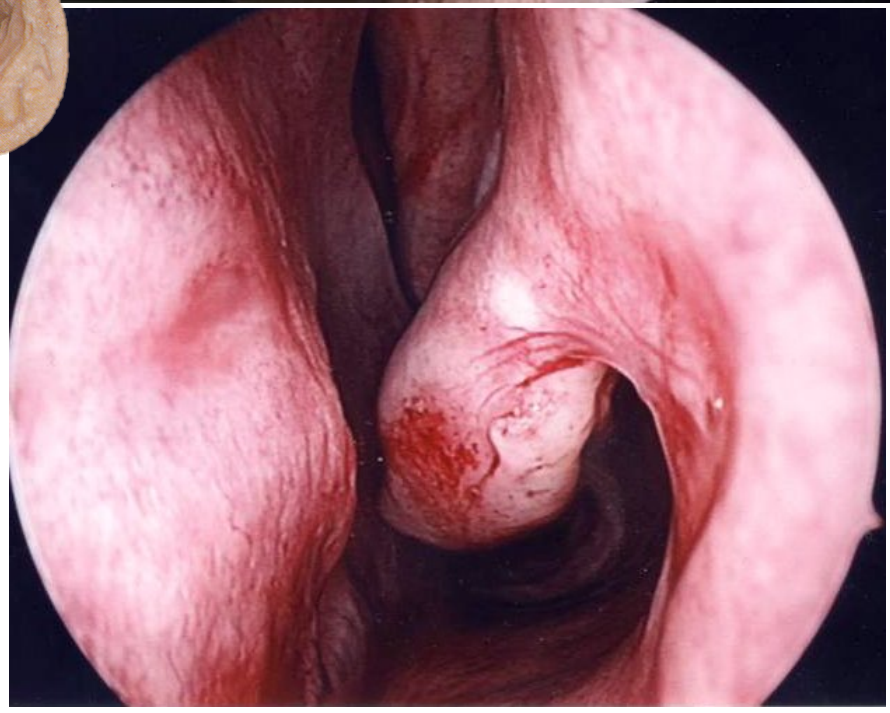




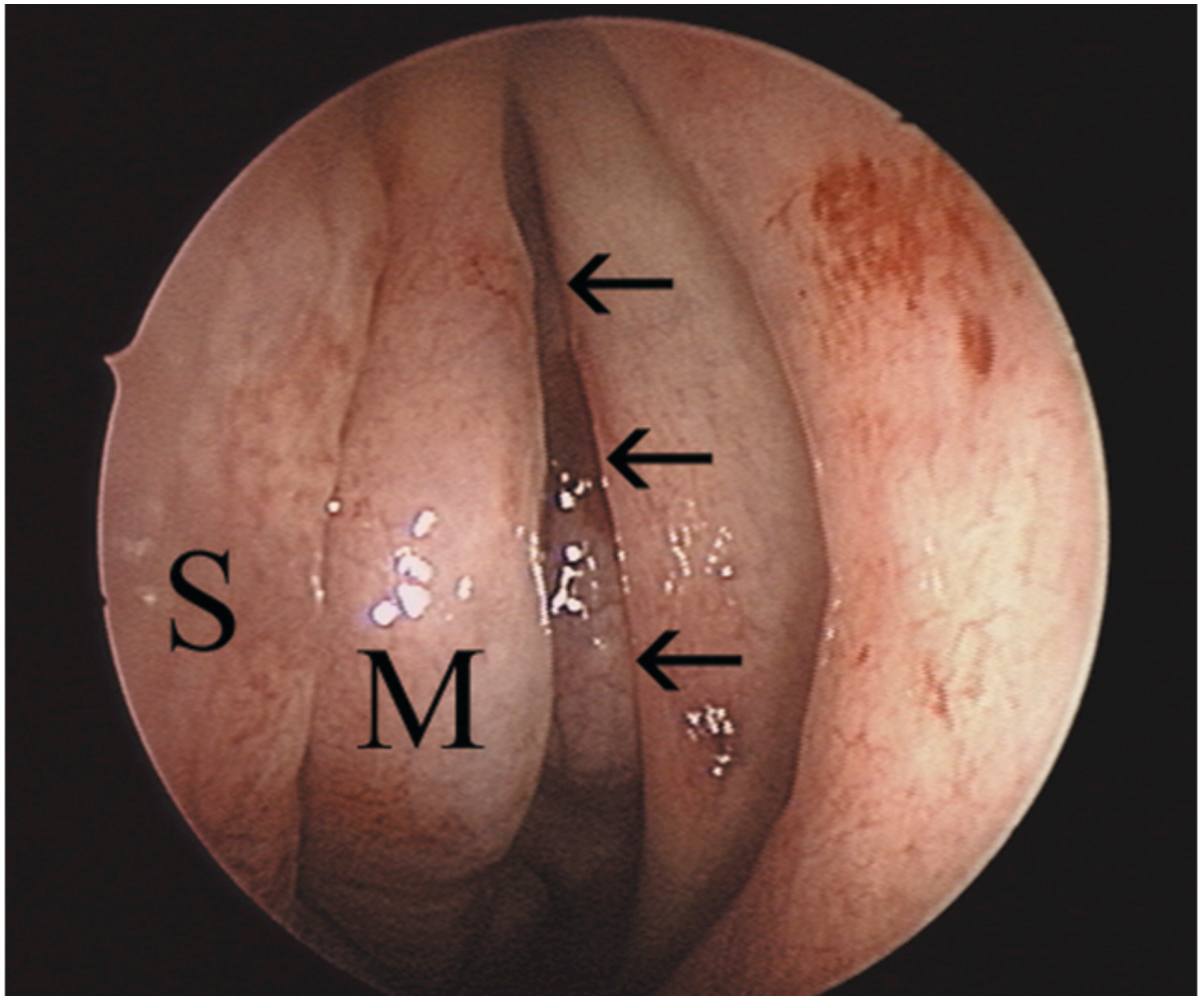






# Endoscopic View of the OMC




Scott-Brown's, 7th Ed

# Endoscopic View of the OMC

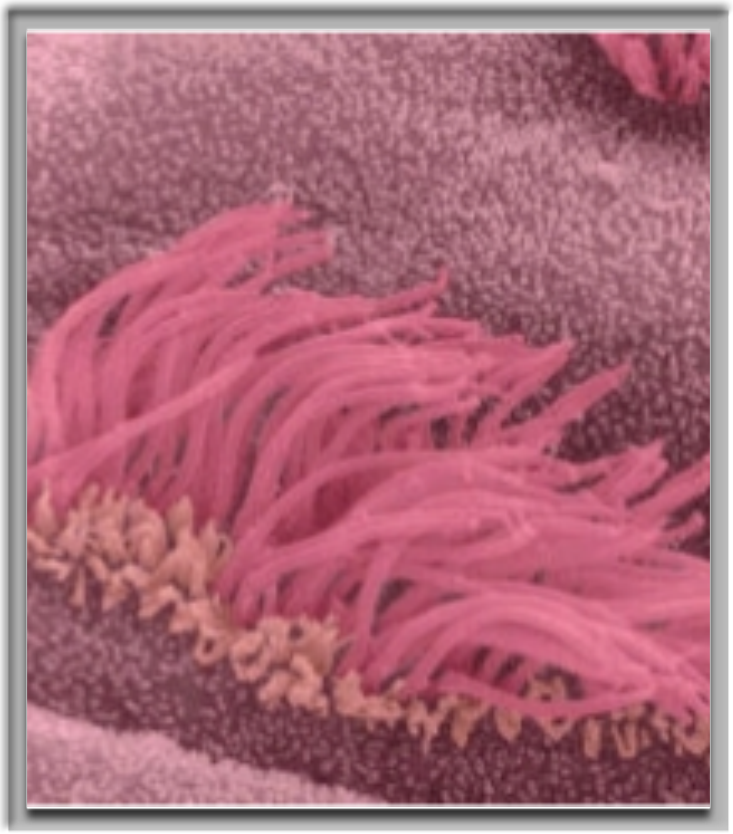
# Mucociliary Flow



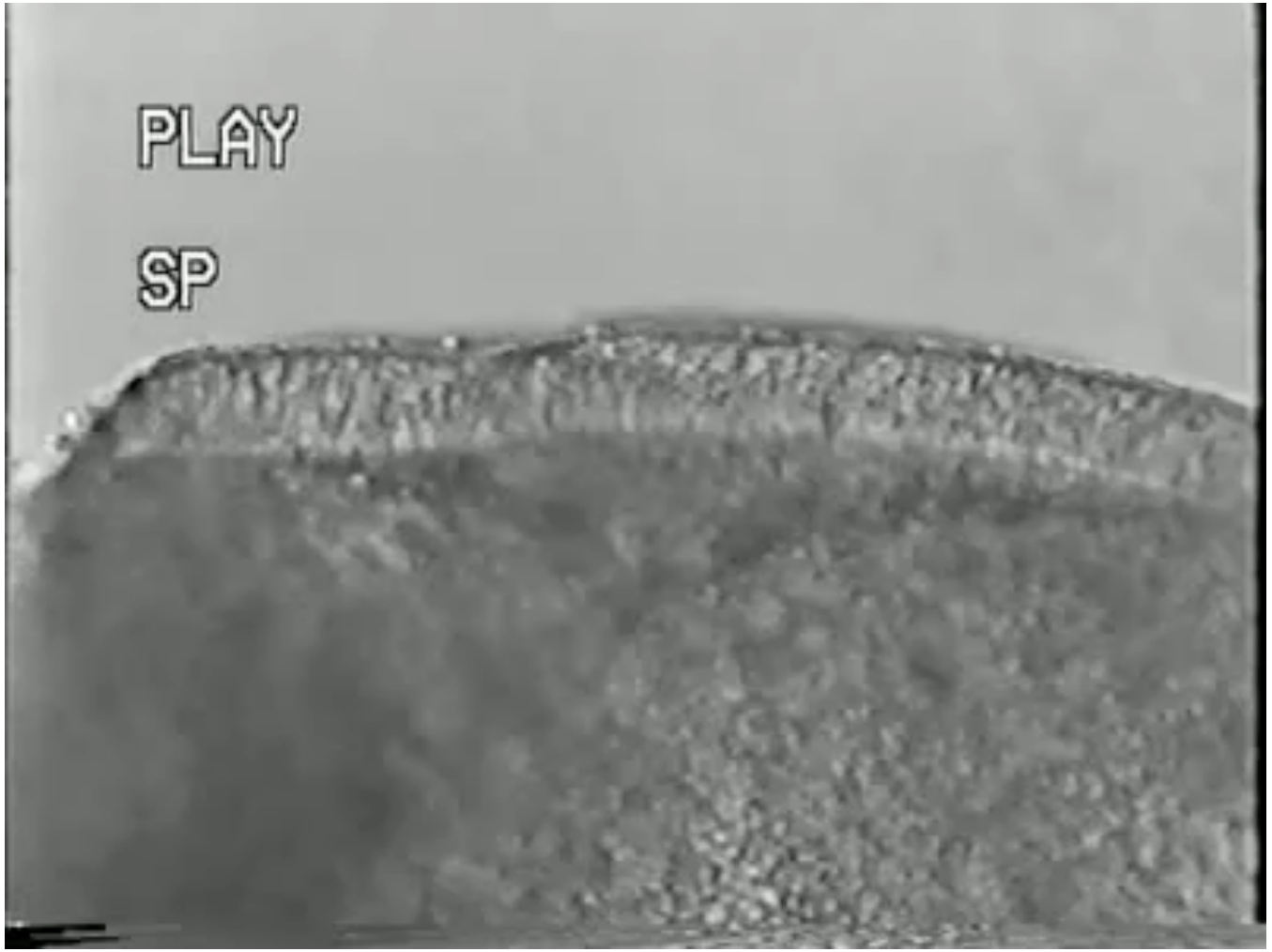




- Thick mucus layer
- Traps bacteria and particulate
- Cilia push mucus layer
- Natural ostia
- Osteomeatal unit
- Postnasal space
- Swallow



# Ciliary Beat Frequency

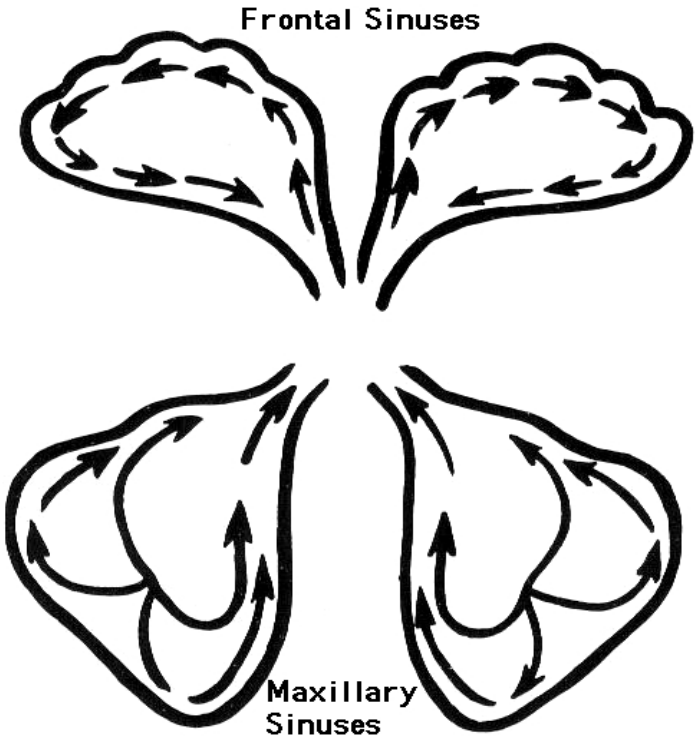


# Mucociliary Clearance













# RHINOSINUSITIS

# Rhinosinusitis Definitions - Duration





- Acute rhinosinusitis (ARS)
- Recurrent acute rhinosinusitis (RARS)
- Chronic rhinosinusitis (CRS)
  - Chronic rhinosinusitis with nasal polyps (CRSwNP)
  - Chronic rhinosinusitis without nasal polyps (CRSsNP)

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# ACUTE RHINOSINUSITIS

# Acute Rhinosinusitis

- Children: 3-8 URTI / year on average
- Adults: 2-3 URTI / year

- Sinusitis = Inflammation / thickening of sinus mucosa

- Occurs in ~90% of viral URTI's as evaluated by CT

*Gwaltney JM Jr. et al. Computed tomographic study of the common cold. N Engl J Med 1994;330:25-30.*

# Acute **Bacterial** Rhinosinusitis: Burden of disease

- 32 Million office visits
- 1 Million ER visits
- 20 Million cases annually
- 73 Million work/school days lost
- $3.5 Billion annual expenditures

- US Figures

# Pathophysiology





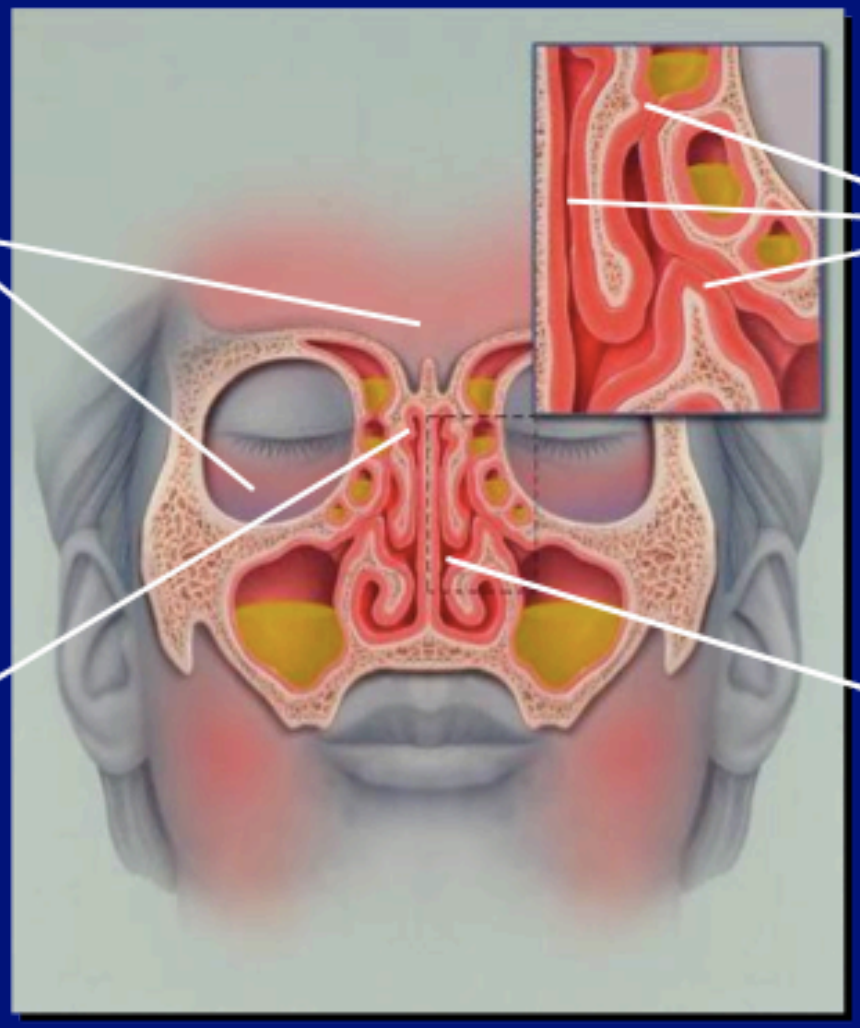
Mucosal inflammation & edema

Ciliary Dysfunction

Sinus ostium obstruction

# Acute Rhinosinusitis: Definition

## Sudden onset of 2 or more of the major symptoms



Facial pain/ pressure

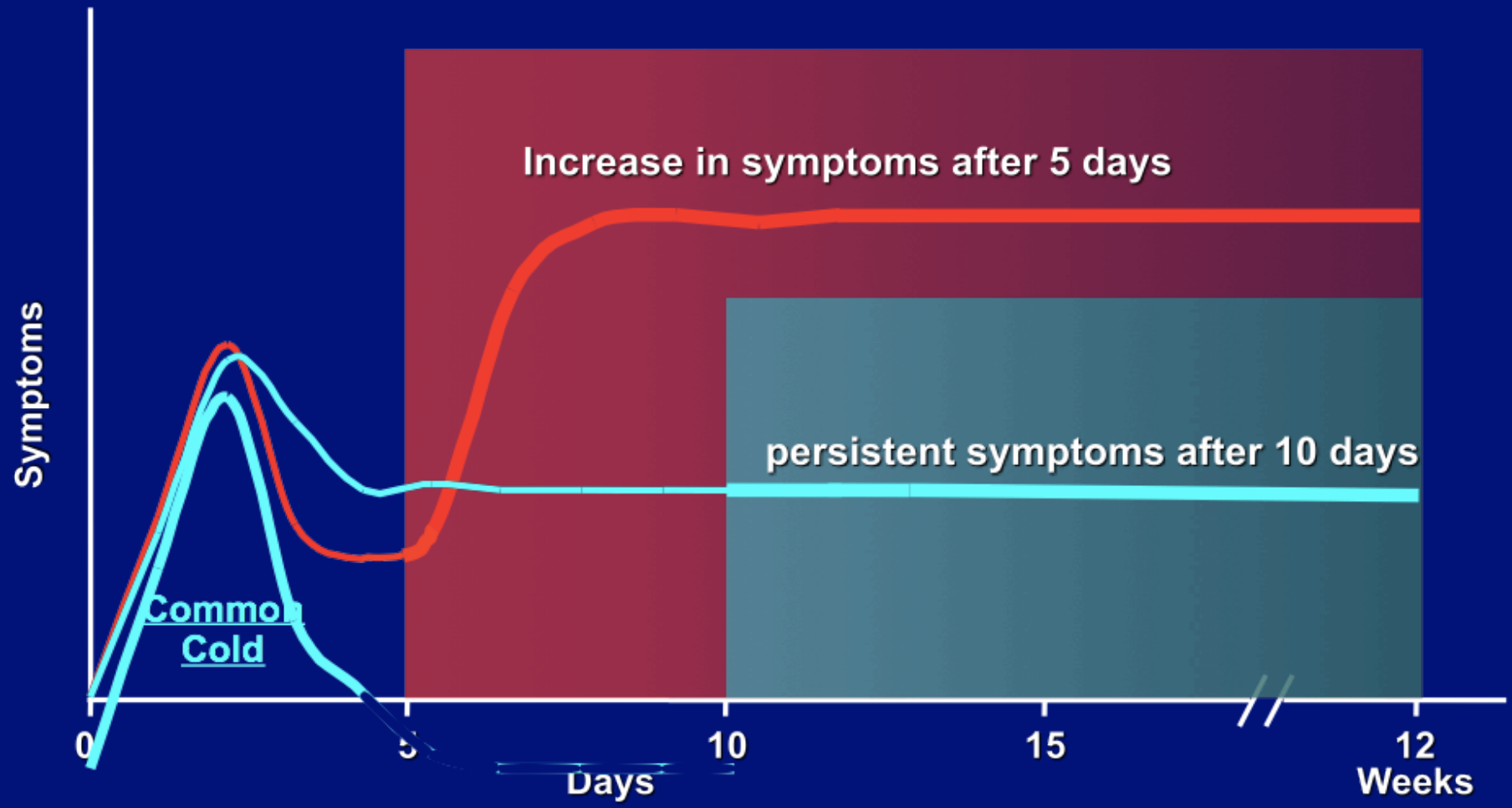
Nasal congestion/ blockage

Reduction/ loss of smell

Anterior discharge/ postnasal drip

Fokkens et al. EP3OS Guidelines. *Rhinol Suppl.* 2005;18:1.

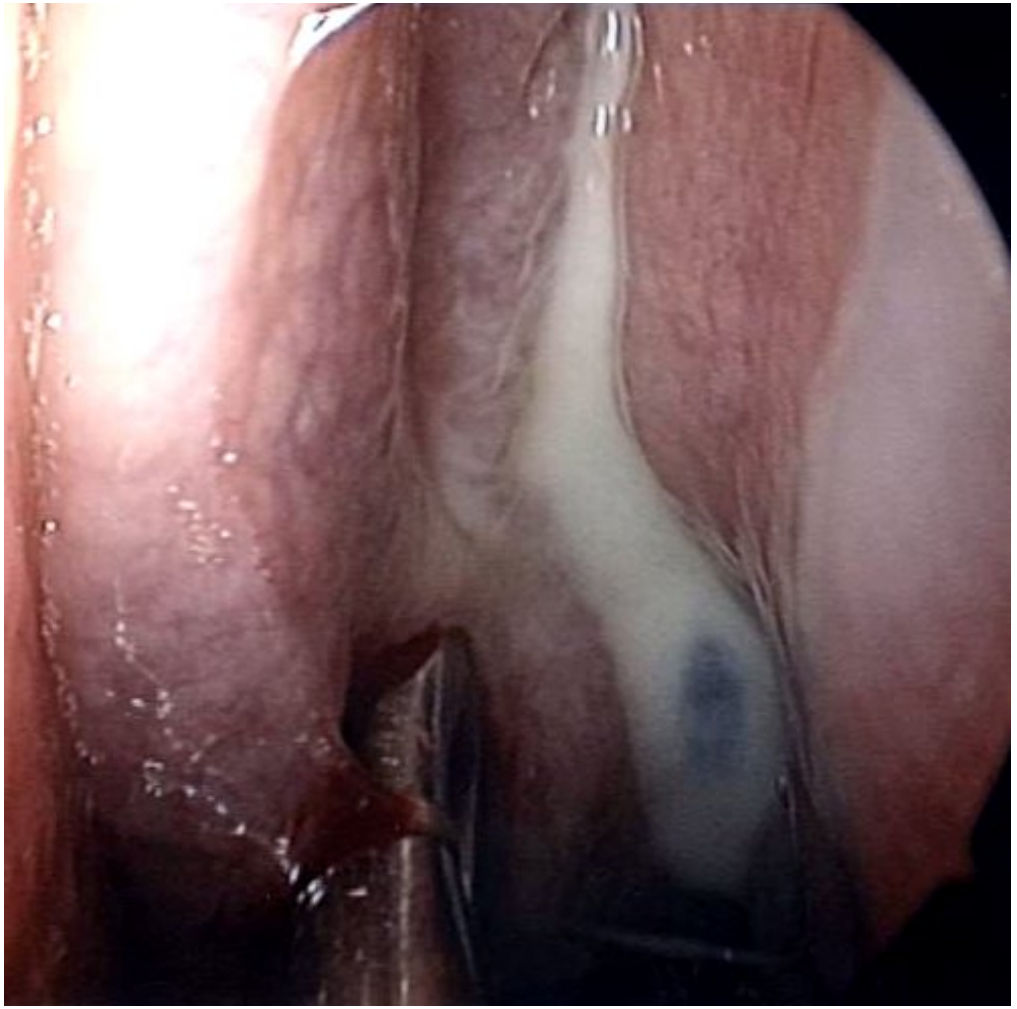
# Acute Rhinosinusitis: Evolution




Adapted from Fokkens et al. EP3OS Guidelines. *Rhinol Suppl.* 2005;18:1.

# Physical Exam

- **Pus from middle meatus**
- **Otoscope with short wide speculum**



# Physical Exam

# Imaging: Sinus films





- Not necessary
- Findings:
  - Air-fluid level
  - Complete opacification / clouding
  - Mucosal thickening NOT specific

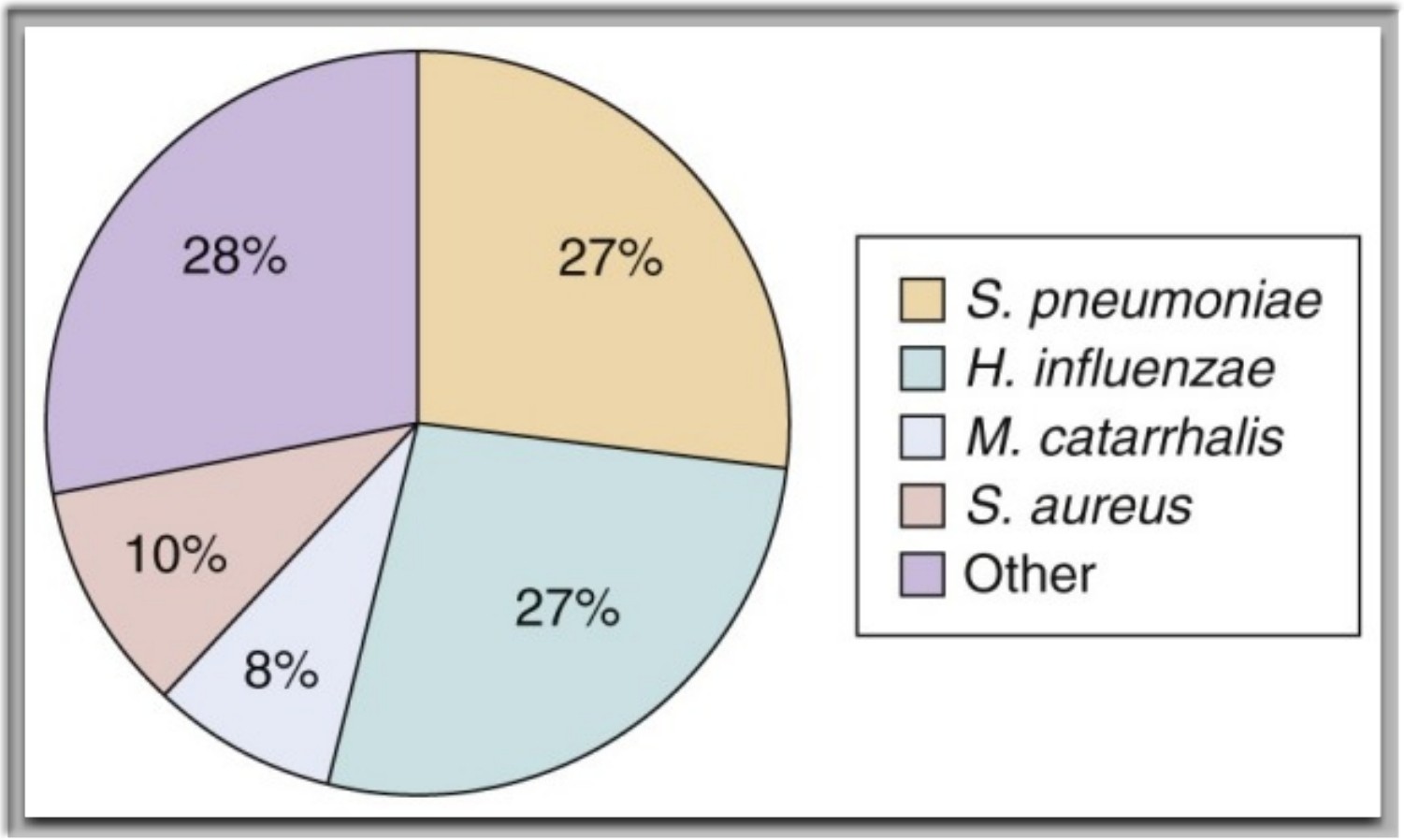
# Opacification

# Air Fluid Level

# Imaging: Sinus CT

- Provides greater detail of nasal and sinus anatomy
- No role in the diagnosis of non-complicated acute sinusitis

# Bacteriology




Payne SC, Benninger MS. Staphylococcus aureus is a major pathogen in acute bacterial rhinosinusitis: a meta-analysis. Clin Infect Dis. 2007;45:e121-e127







# Recommendations for ARS

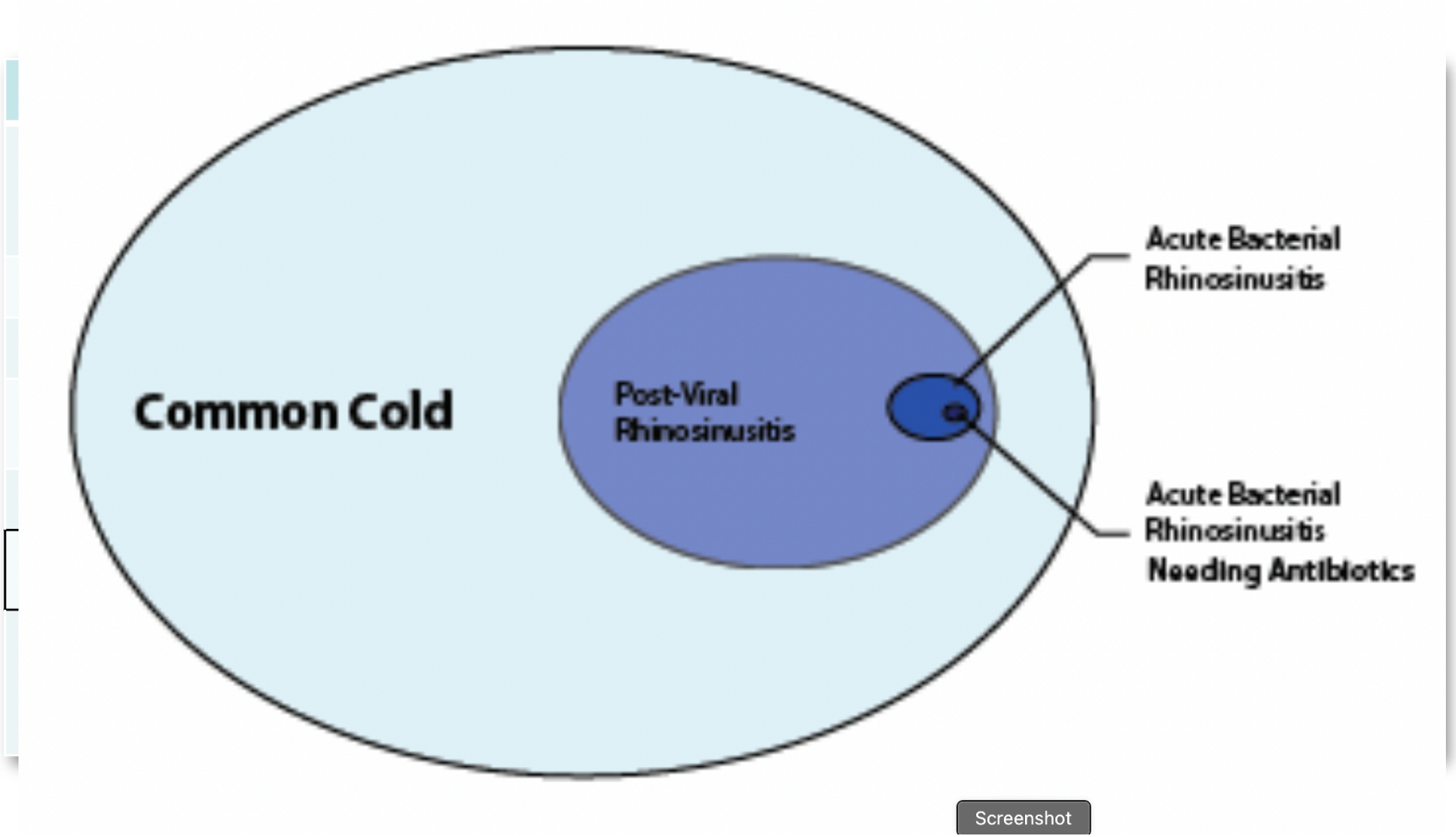
# ABRS: Definition and Diagnosis





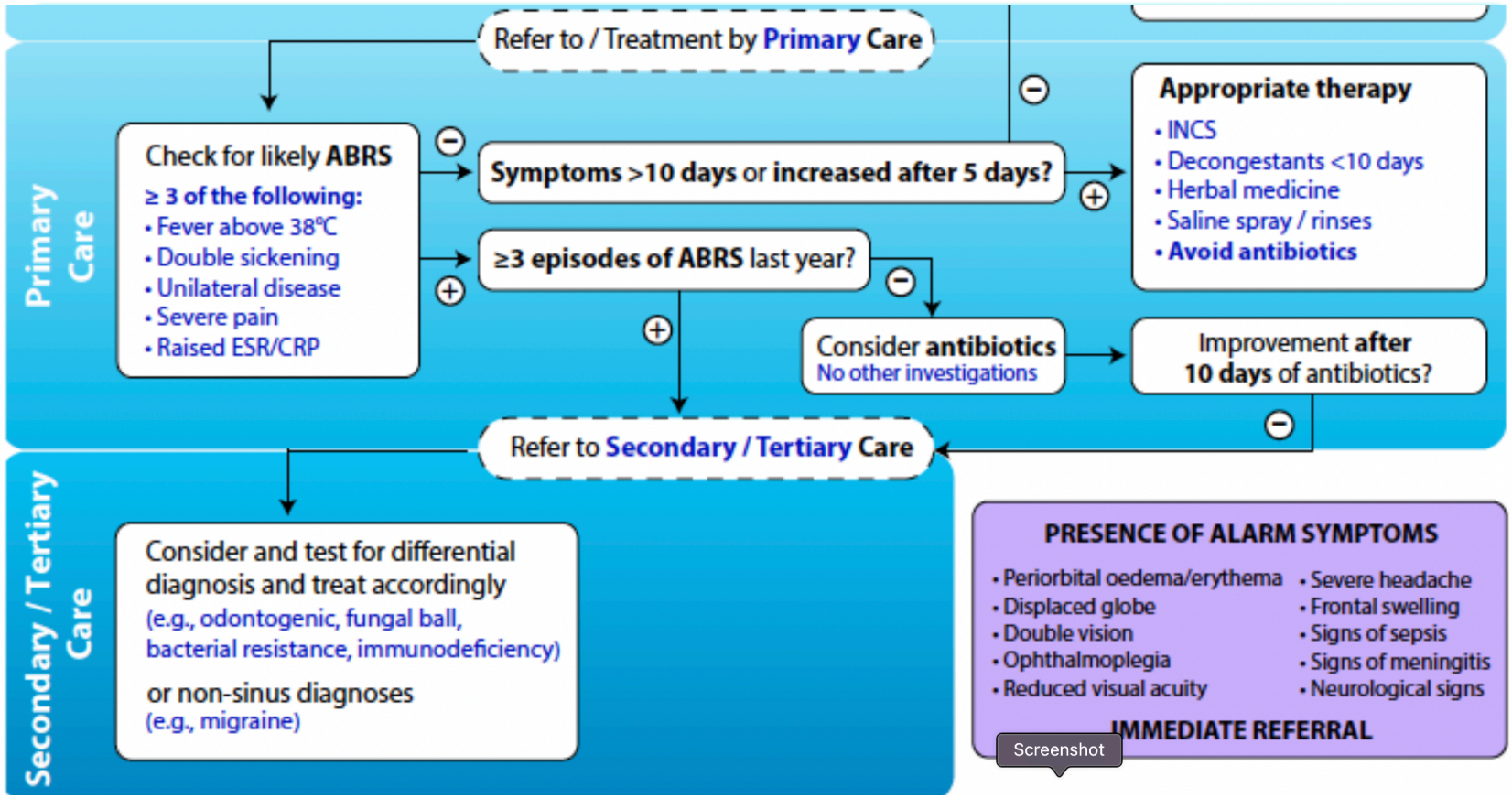
- Based on history and physical examination
- ABRS is a bacterial infection of the paranasal sinuses characterized by:
  - Symptom duration > 7 days
  - Length of episode < 4 weeks
  - Major symptoms (PODDS)
    - Facial **P**ain/**P**ressure/fullness
    - Nasal **O**bstruction
    - Nasal purulent **D**ischarge/postnasal **D**ischarge
    - Hyposmia/anosmia (**S**mell)
- Diagnosis requires the presence of ≥ 2 **PODS** and symptom duration of > 7 days without improvement

# When to Order an Antibiotic?




Screenshot

# EPOS 2020: Care pathways for acute rhinosinusitis (ARS)




EPOS 2020

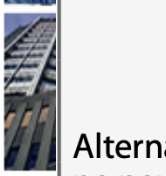
# Symptomatic Treatment

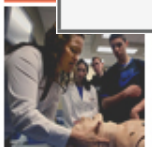
- **Useful whether viral or bacterial rhinosinusitis**
- Oral decongestants
  - Symptomatic relief of pain
- Topical decongestants (<5 days!)
  - Relieve obstruction; help sleep, breathing
- Nasal irrigation
- Anti-inflammatory agents
- Intranasal steroids as adjunctive therapy
  - Concurrent allergic rhinitis
  - Recurrent bouts of ARS

# What about antibiotics?









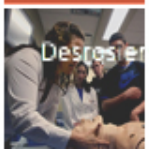
| | Antibiotique[1, 5] | Posologie | Durée recommandée |
|---|---|---|---|
| **ANTIBIOTHÉRAPIE DE 1RE INTENTION** | | | |
| | **Amoxicilline[2]** | 500 mg PO TID | 5 jours |
| ▶ Si suspicion de résistance élevée[3]<br>▶ Patient immunosupprimé<br>▶ Sinusite frontale ou sphénoïdale | **Amoxicilline/Clavulanate[4]** | 500/125 mg PO TID<br>**OU**<br>875/125 mg PO BID | 7 jours |
| ▶ Si antécédent de réaction allergique à un antibiotique de la classe des pénicillines | **Cliquez ici pour consulter l'algorithme spécifique à la rhinosinusite aiguë et vous aider dans le choix de l'antibiothérapie** | | |
| Alternative si une bêta-lactamine[4] ne peut être administrée | **Clarithromycine** | 500 mg PO BID | 7 jours |
| | **Clarithromycine XL** | 1 000 mg PO DIE | 7 jours |
| | **Doxycycline** | 100 mg PO BID | 10 jours |
| | **Triméthoprime-sulfaméthoxazole[3]** | 160/800 mg PO BID | 7 jours |

INESS 2016. https://www.inesss.qc.ca/fileadmin/doc/CDM/UsageOptimal/Guides-serieI/Guide-Rhinosinusite-Adulte.pdf

# Second-line antibiotics







- Presence of risk factors for AB resistance:
  - Previous AB ≤ 3 months
  - Day care exposure
- Risk factors for immunosuppression
- Symptoms suggesting frontal or sphenoid sinusitis
- Failure of first line ABT
- Choices:
  - Amoxicillin/clavulanic acid 875F BID x 10-14d
  - Moxifloxacin 400 mg QD x 10-14d







# COMPLICATIONS

# Complications of Acute Sinusitis







## Orbital complications

- Preseptal cellulitis
- Abscess
- Phlegmona
- Blindness

## Cerebral complications

- Meningitis
- Extradural abscess
- Intradural abscess

## Osteomyelitis

# Red Flags for Urgent Referral







- Systemic toxicity
- Altered mental status
- Severe headache
- Swelling of the orbit or change in visual acuity

# Indications for Surgical intervention

- Severe pain
- Toxic
- Impending complications of sinusitis
- Nonresponse to medical therapy
- Immunocompromised patient

# Choosing Wisely Quality Indicators





| QI | Description |
|---|---|
| 1 | Accurate clinical diagnosis of ABRS is made using signs and symptoms |
| 2 | Nasal culture is not required for diagnosis of ABRS |
| 3 | Uncomplicated ABRS does not require radiographic imaging |
| 4 | Antibiotics may be prescribed for ABRS if disease severely impacts quality of life (QOL)/productivity, the condition worsens, the patient is unable to follow-up, and/or the patient's condition fails to improve by 7 days after ABRS diagnosis |
| 5 | CT scan should be obtained for patients with recurrent ABRS |
| 6 | Amoxicillin for 5-10 days should be used as first line antibiotic therapy for ABRS |
| 7 | Adjunct therapy should be prescribed in individuals with ABRS |

Am J Rhinol Allergy. 2020 Jul;34(4):519-531.






# QUESTIONS?




# CHRONIC RHINOSINUSITIS

# Another typical case…





- 30 yo Female
- PMHX: Asthma
- URTI symptoms 2 years earlier
- Gradually worsening nasal congestion, PND and hyposmia
- RX: Symbicort, Mometasone, Prednisone
- All.: Aspirin, NSAIDs
- Asthma recently getting worse

# Anterior rhinoscopy

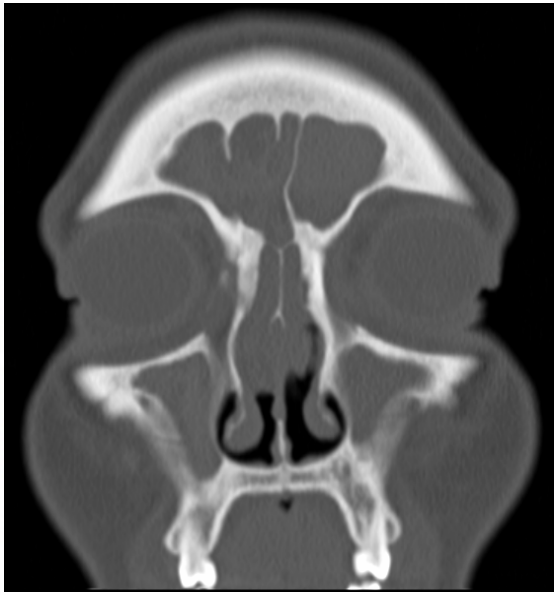
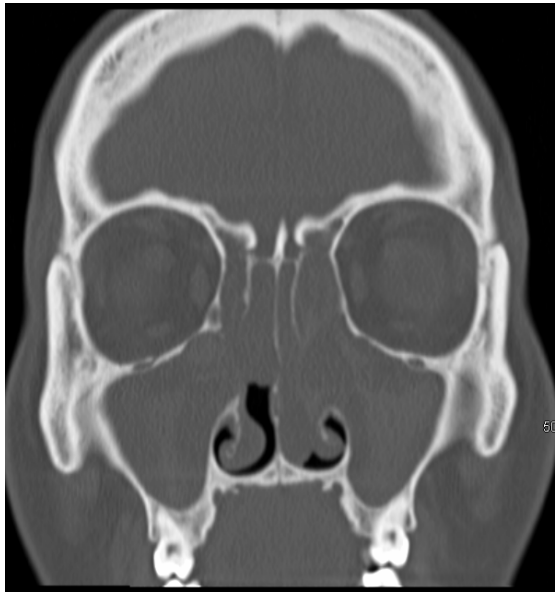
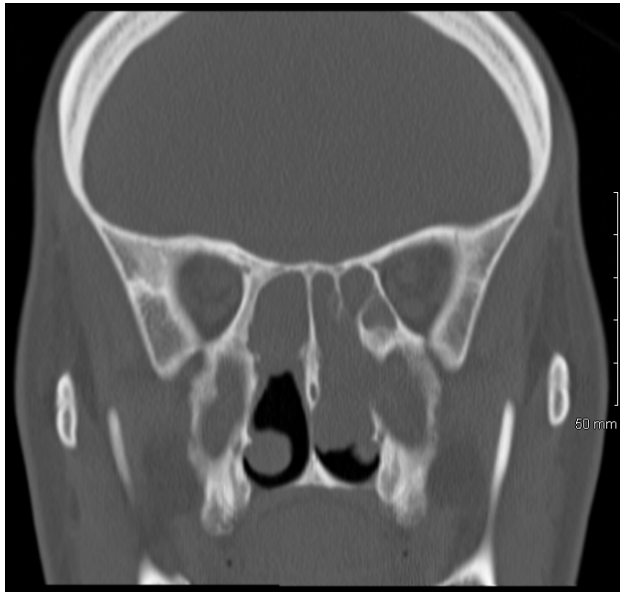






# Imaging

- CT Sinus

# Chronic Rhinosinusitis (CRS)

- 31 million people in the United States each year
- Significantly lower QOL index in measures of bodily pain and social functioning than for CHF, angina, COPD, and back pain
- Significant healthcare cost
- Cause and mechanism of disease unknown*
- No curative treatment
- **Symptom-based, supported by radiology**

# Clinical Manifestations

- Nasal congestion/obstruction
- Nasal discharge

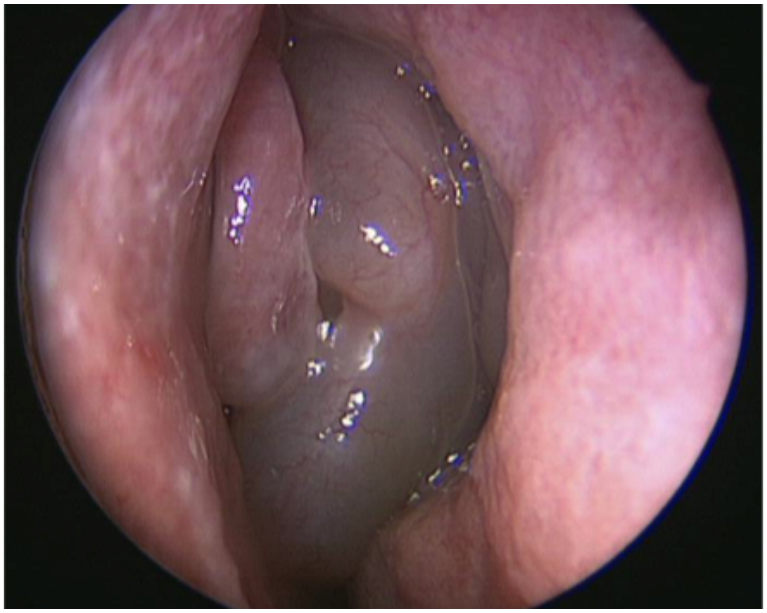
- Anosmia/hyposmia

- Facial pressure or pain

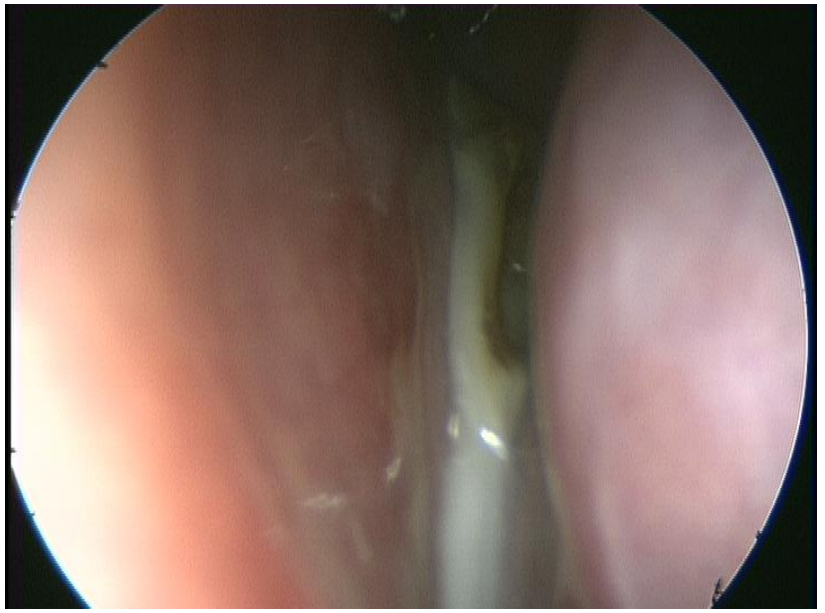
- Lasting >12 weeks
- Diagnosis also requires abnormal endoscopy or CT

# Chronic Rhinosinusitis: Subtypes

**CRSwNP**



**CRSsNP**



# Chronic Rhinosinusitis w/s Polyps





- Symptomatic differences exist between patients with CRSsNP and CRSwNP, summarized below

| Symptom | CRSsNP | CRSwNP |
|---|---|---|
| Facial pain/pressure | Yes | Rarely |
| Facial congestion/fullness | Yes | Yes |
| Nasal obstruction/blockage | Yes | Yes |
| Nasal discharge/purulence/post-nasal discharge | Yes | Yes |
| Hyposmia/anosmia | Rarely | Yes |
| Blood eosinophilia | No | Often |
| Asthma | Rarely | Often |
| Aspirin hypersensitivity | Rarely | Typical |

# CRS Diagnosis

At least **2** or more symptoms of:

- Nasal Blockage / Obstruction / Congestion
- AND/OR
- Nasal Discharge (anterior / posterior nasal drip)

+/- facial pain / pressure

+/- reduction or loss of smell

≥ 12 weeks

No Symptom-Free Intervals
Validated by telephone or interview

Without associated allergic symptoms
Sneezing, watery rhinorrhea, nasal itching, itchy watery eyes

**CRS with Nasal Polyps (CRSwNP)**

bilateral, endoscopically visualized polyps in middle meatus

**CRS without Nasal Polyps (CRSsNP)**

no visible polyps in the middle meatus

# CRS Diagnosis: Examination

- Nasal endoscopy is the preferred method of examination of the middle and superior meatus as well as the nasopharynx and mucociliary drainage pathways
- Anterior rhinoscopy can be done with an otoscope

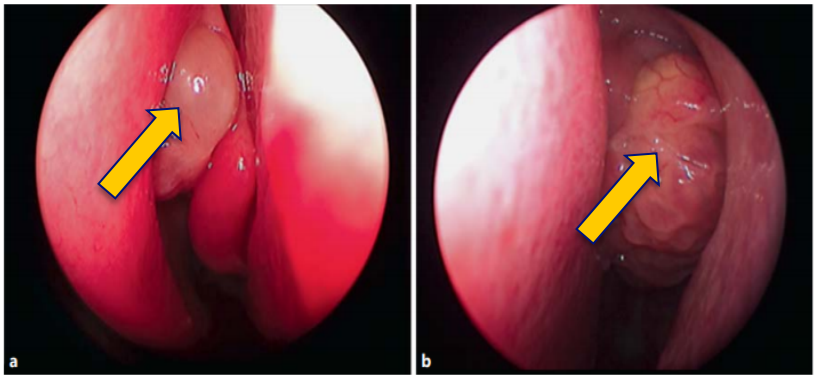



**Figure: Differential diagnosis of nasal polyps.**
**(a) Semi-translucent polyp of the middle meatus.**
**(b) Inverted papilloma characterized by a papillomatous appearance on nasal endoscopy**

Adapted from: Woodworth BA, Poetker DM, Reh DD (eds): Rhinosinusitis with Nasal Polyposis. Adv Otorhinolaryngol. Basel, Karger, 2016;79:1–12



# CRS Diagnosis: Imaging

- CT scanning is the favored modality:
  - Better display of air, bone and soft tissues
  - Extent of polyps and anatomical variations
  - Essential prior to surgical treatment
  - However, a CT scan is not a primary step in diagnosis
- MRI may be considered for unilateral polyps or suspicion of neoplasia

# CT Scoring System for CRS






**Lund–Mackay Sinus CT Grading**

Most widely used tool for analyzing the severity of CRS

Takes into consideration the extent of calcification of each sinus system and of the osteomeatal complex

**Scoring of CRS:**

0: No mucosal thickening

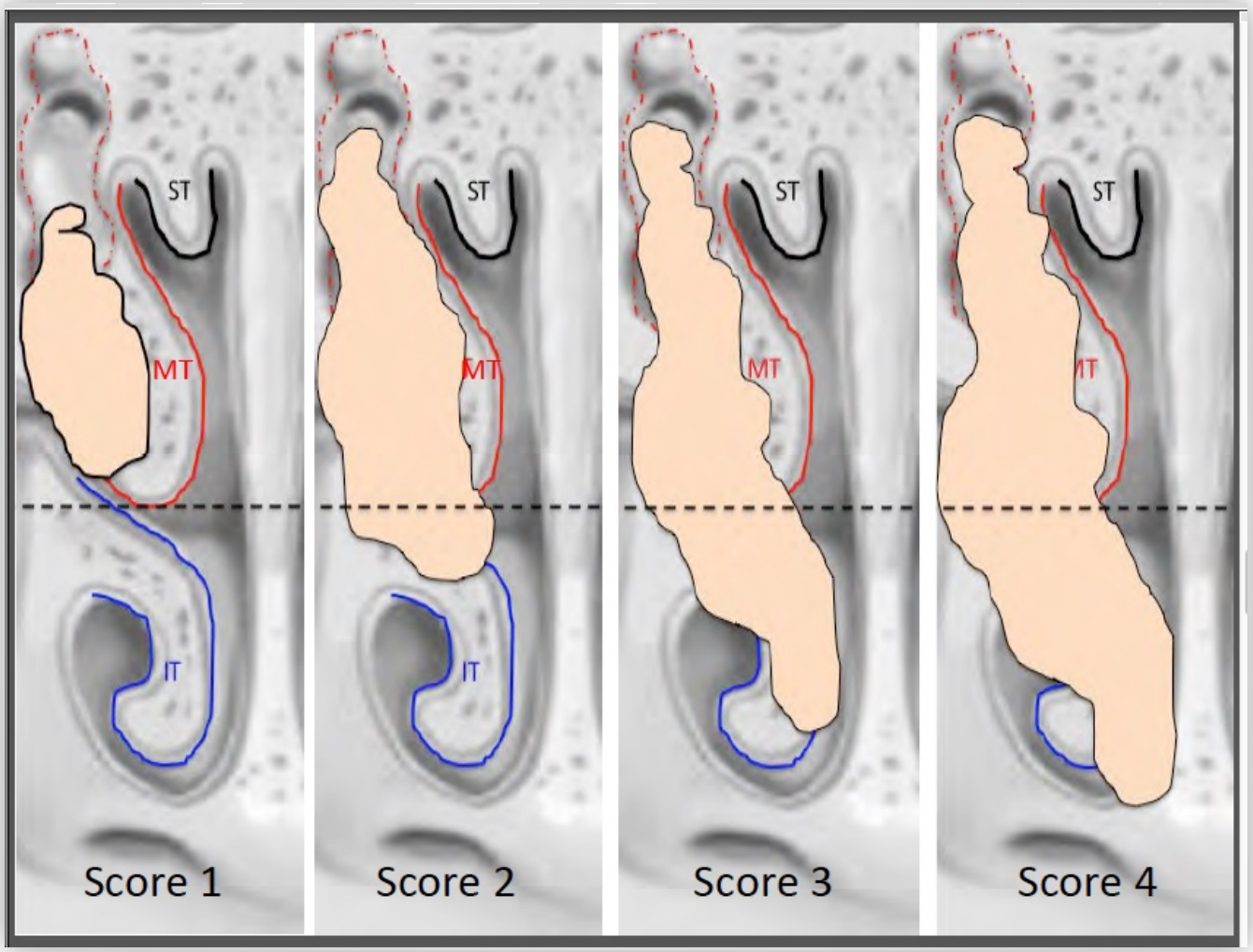
1: Partial opacification

2: Total opacification

The scoring is applied to the maxillary, anterior ethmoid, posterior ethmoid, sphenoid, and frontal sinus on each side

276. Lund VJ and Mackay IS. Rhinology. 1993;31(4):183–184

# Nasal Polyp Size Score



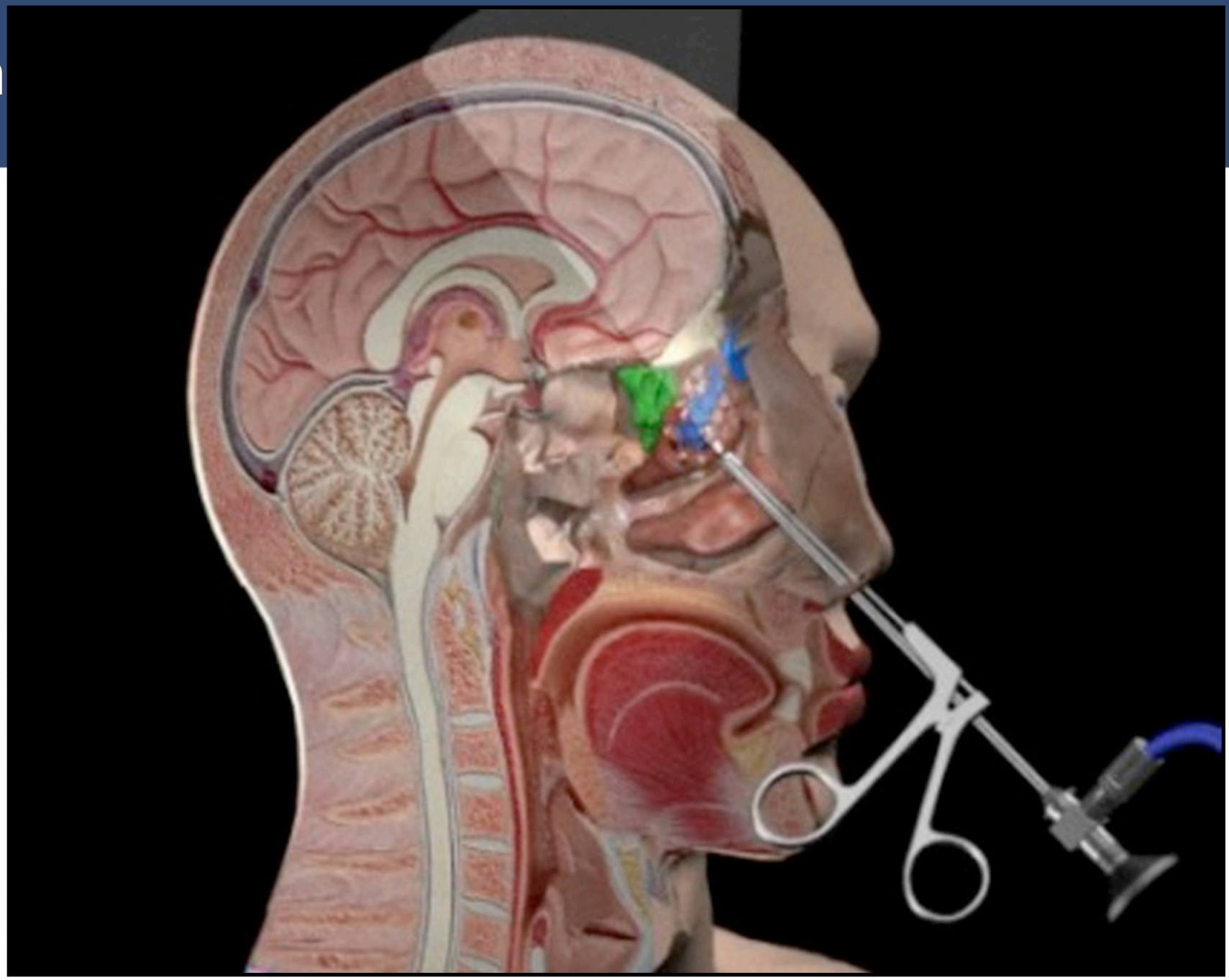
# Nasal Polyps – Points to Remember!

- Unilateral polyps must be further examined to exclude malignancy: Biopsy
- Children with nasal polyps should be tested for cystic fibrosis
- Patients with severe polyps should be tested for aspirin sensitivity, in particular those with recurrent polyps and intrinsic asthma

# Management

- As a chronic condition, CRS should be proactively managed
- Depends on subgroup: Polyp vs. non-polyp
- Treatment options include
  - Saline sprays/irrigation
  - Topical or systemic steroids
  - Antibiotics: second-line OR longterm
  - Surgery for medical failures
  - Now, biologic agents for surgical failures or poor candidates for GA

En

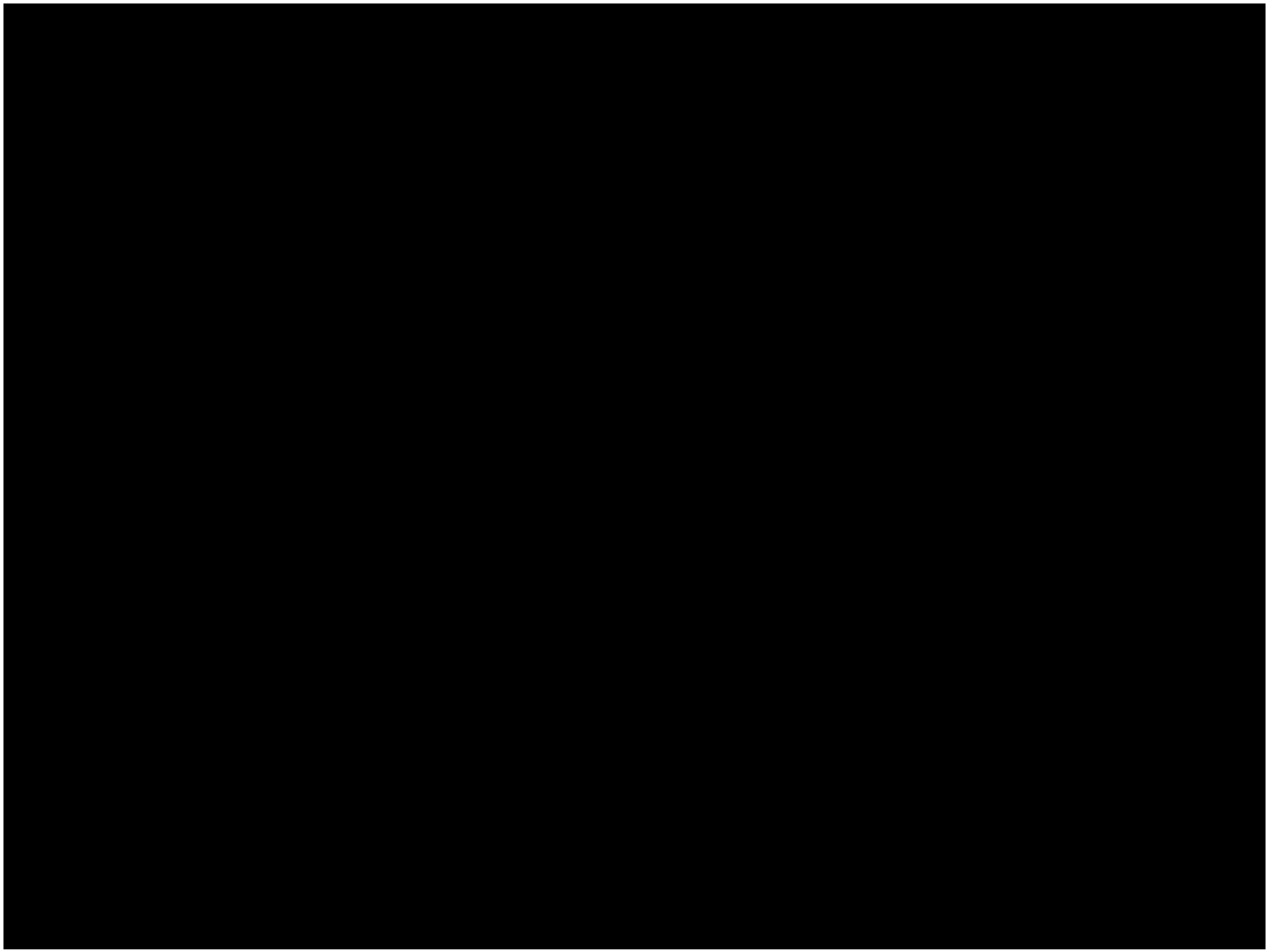


# Removing bony partitions

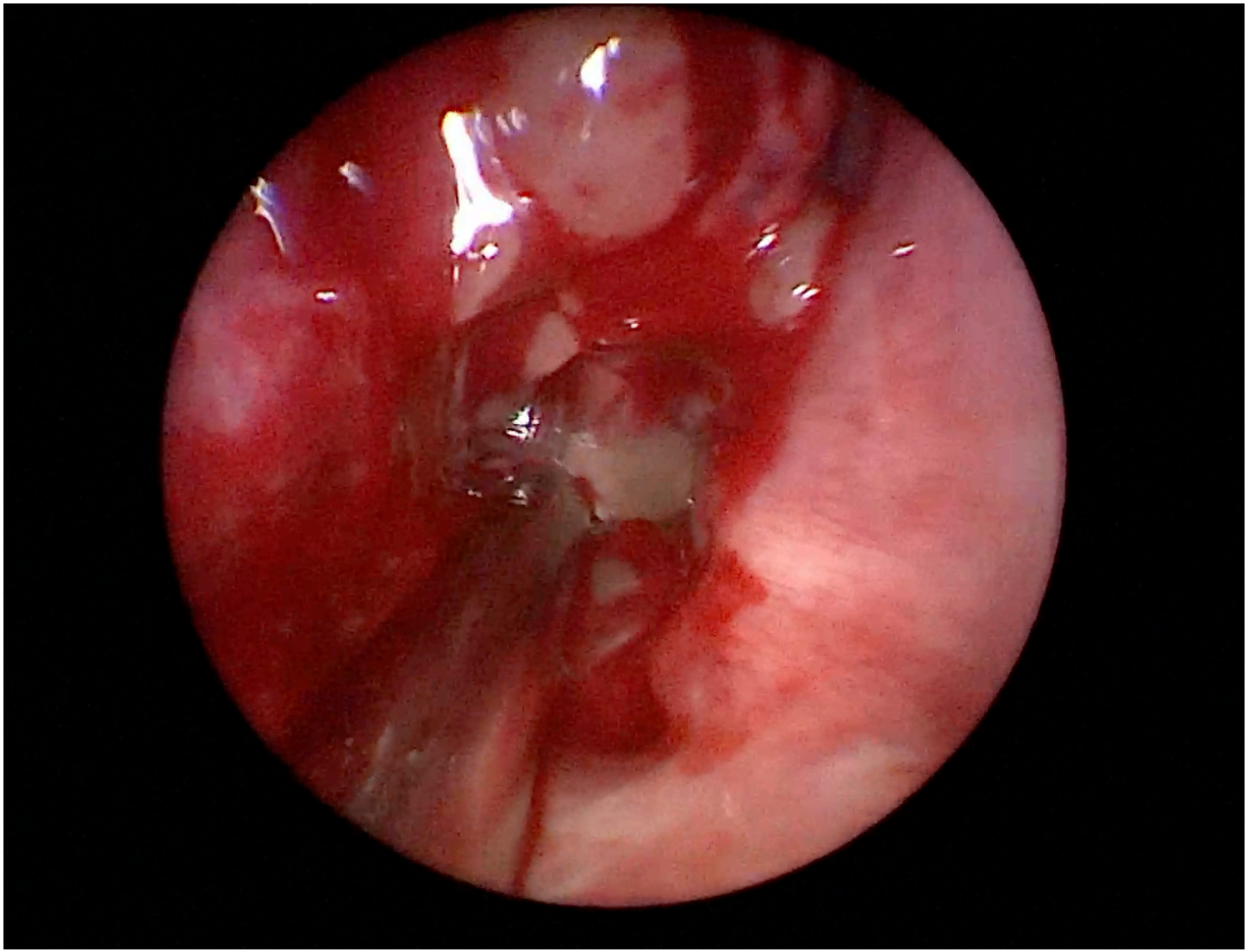








# Debriding nasal polyps

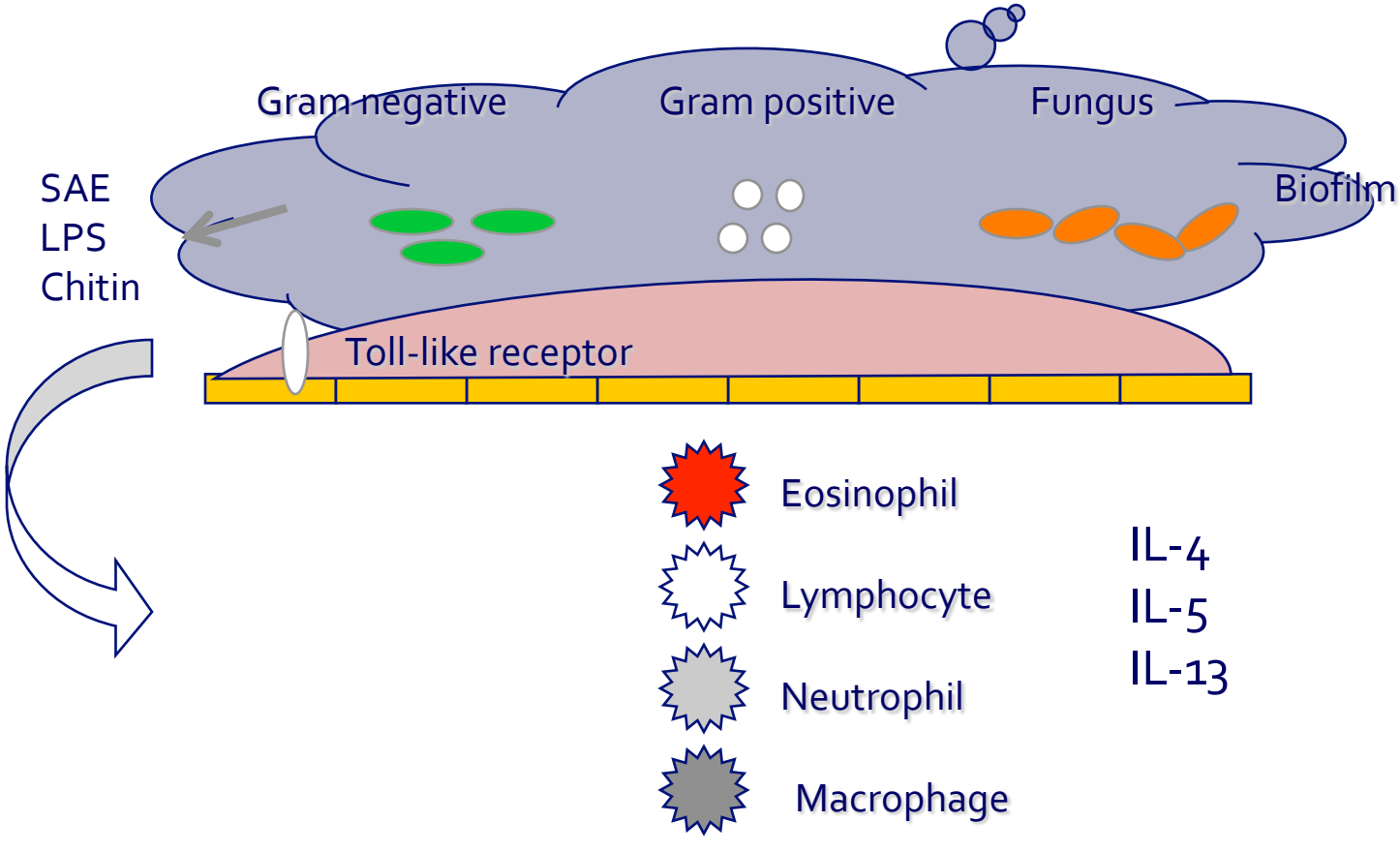


# Current CRS Theories









# United Airways Theory







# UPPER-LOWER AIRWAY INTERACTION

- Natural history of asthma and rhinosinusitis follow a parallel tract

**horizontal relationship**

- Allergic rhinitis/sinusitis appear to affect the course of asthma

**vertical relationship**

# COMMON DISEASES OF UPPER AND LOWER AIRWAYS

- Asthma (allergic)
- ASA triad
- Cystic fibrosis
- Primary ciliary dyskinesia (Kartagener's, Young's)
- Vasculitides (Churg-Strauss, Wegener's)
- Sarcoid, diffuse panbronchiolitis, hypogammaglobulinemia

# UPPER and LOWER AIRWAYS: How are they associated?







- Anatomy and histology
- Physiological relationship
- Immunological similarities

# Management of CRS

**CRS Diagnosis Requires the Presence of at Least 2 Major Symptoms***

| Major Symptoms | | None | Mild Occasional limited episode | Moderate Steady symptoms but easily tolerated | Severe Hard to tolerate and may interfere with activity or sleep |
|---|---|---|---|---|---|
| C | Facial Congestion/fullness | | | | |
| P | Facial Pain/pressure/fullness | | | | |
| O | Nasal Obstruction/blockage | | | | |
| D | Purulent anterior/posterior nasal Drainage | | | | |
| S | Hyposmia/anosmia (Smell) | | | | |

*A diagnosis requires at least 2 CPODS, present for 8 to 12 weeks, plus documented inflammation of the paranasal sinuses or nasal mucosa.

CRS is diagnosed on clinical grounds but must be confirmed with at least 1 objective finding on endoscopy or CT scan.

**Immediately Refer**

- Urgent consultation for
  - individuals with severe pain or swelling of the sinus areas or in immunocompromised patients
  - suspected invasive fungal sinusitis
- Consider referral soon:
  - when failing ≥1 course of maximal medical therapy
  - for ≥4 sinus infections per year

Obtain CT or perform endoscopy

**CRSsNP: ≥2 major symptoms plus all of the following**

Endoscope
- Inflammation (e.g., discolored mucus, edema of middle meatus /ethmoid area
- Absence if polyps in middle meatus
- Purulence originating from the ostiomeatal complex

*or*

CT image
- Rhinosinusitis

**CRSwNP: ≥2 major symptoms plus all of the following**

Endoscope
- Presence of bilateral polyps in middle meatus

CT image
- Bilateral mucosal disease

# Management of CRS

**CRSsNP**

If positive exam, treat with
- INCS
- Antibiotics (2nd line)
- Consider short course of oral steroids
- Consider saline irrigation

If negative exam, assume recurrent sinusitis and treat with INCS or consider alternative diagnoses

+/- specialty assessment

Clinical improvement after 4 weeks?

Yes

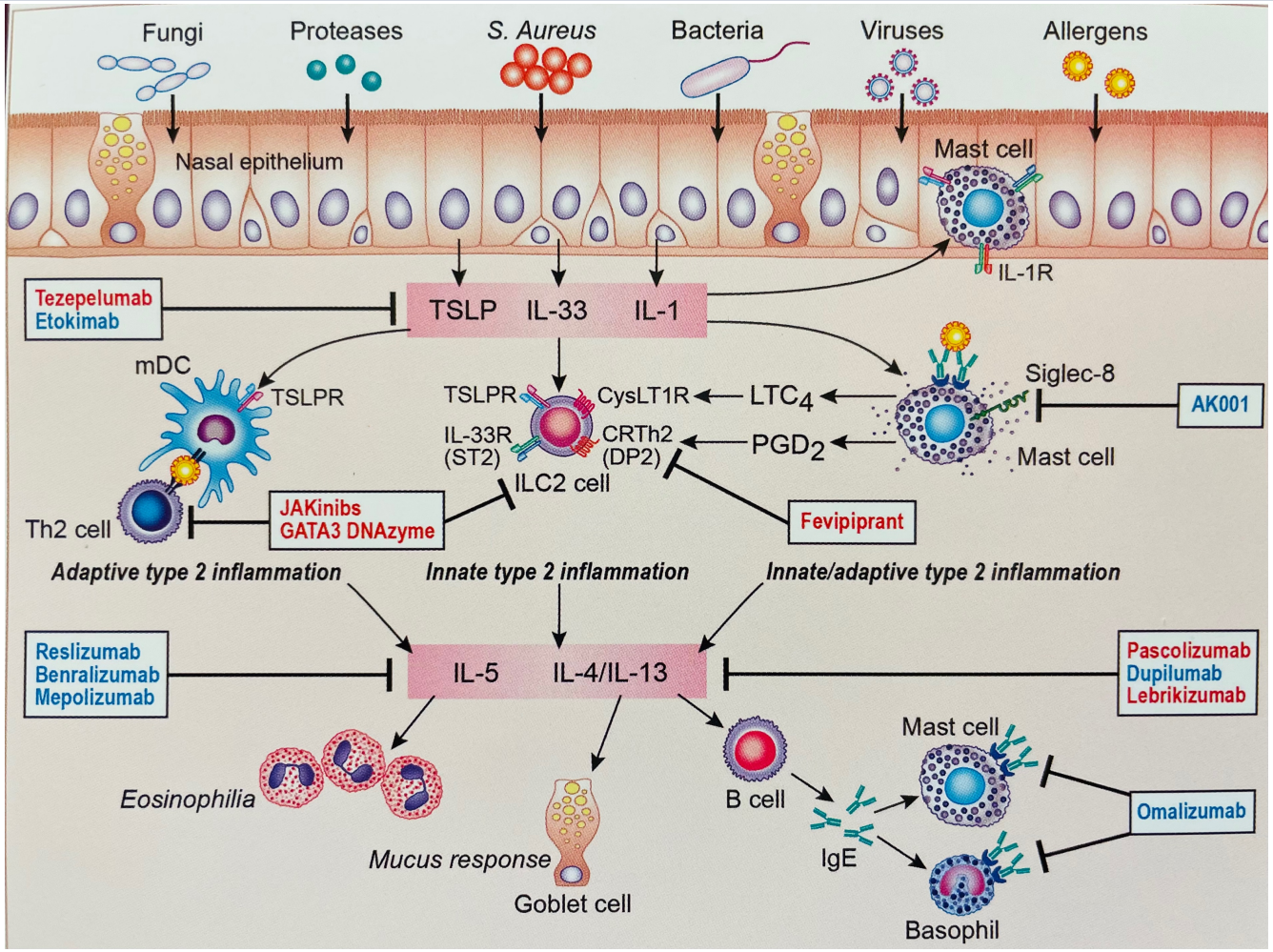
Continue INCS
Consider saline irrigation

No

Refer for surgical evaluation

**Possible alternative diagnoses**
- Allergic fungal rhinosinusitis
- Allergic rhinitis
- Atypical facial pain
- Invasive fungal rhinosinusitis
- Migraine or other headache diagnosis
- Nasal septal deformation
- Nonallergic rhinitis
- Temporomandibular joint dysfunction (TMD)
- Trigeminal neuralgia
- Vasomotor rhinitis

# Therapeutic Targets in CRSwNP




Schneider AL, Schleimer RP, Tan BK. Int Forum Allergy Rhinol. 2021 Aug;11(8): 1220-1234. doi: 10.1002/alr.22787. Epub 2021 Mar 3. PMID: 33660425; PMCID: PMC8316260.

# Pharmacological Treatment of Nasal Polyps

**Humanized monoclonal antibodies**

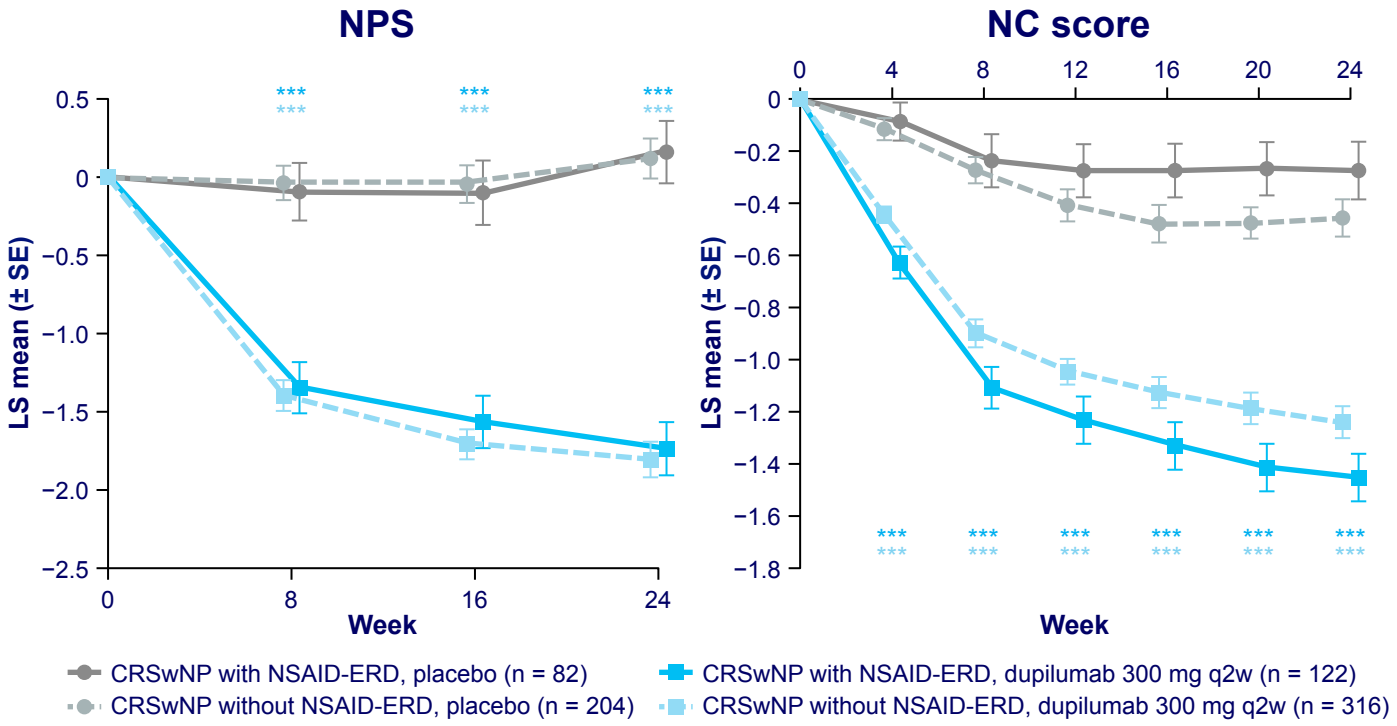
- Dupilumab, a monoclonal antibody targeting the IL-4Rα receptor, has been shown to be effective in patients with nasal polyps by inhibiting the effects of IL-4 and IL-13
- Treatment with mAb therapies may play a role in patients with nasal polyps by suppressing IgE-mediated and eosinophil-mediated inflammation, respectively
- Efficacy of anti-IgE (omalizumab) and anti-IL-5 (mepolizumab, reslizumab) antibodies in CRSwNP has been demonstrated in a number of randomized controlled trials

# Dupilumab





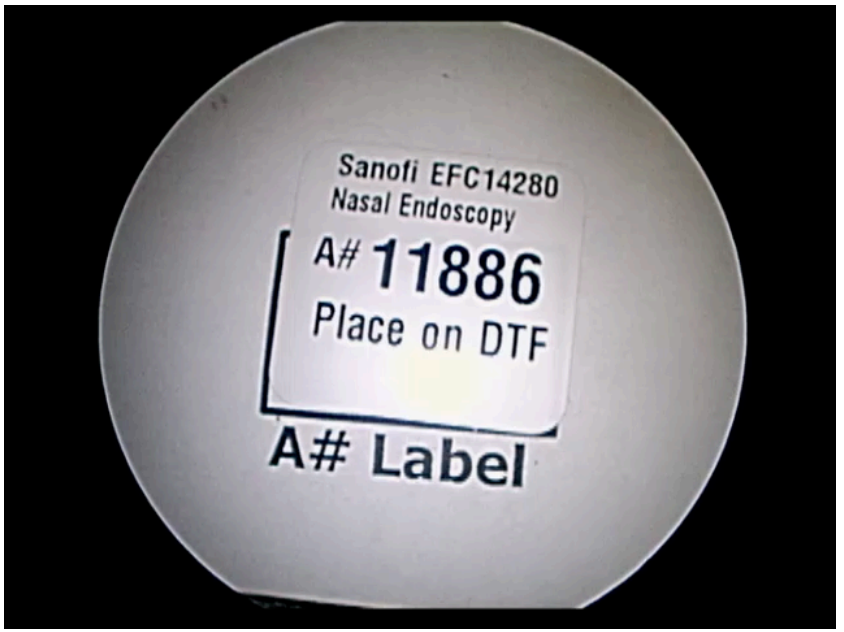
Improvements with dupilumab were noted at the first assessment time point and continued to Week 24




***$P < 0.0001$.

GZCA.DUP.20.06.0234

# Endoscopic Results

# Targeted Therapies for Type 2 Inflammatory Diseases

| Target / Drug / Indication | IL-4R (IL-4/IL-13) | | | IgE | IL-5/-5R | | | IL-13 | | IL-4 | | IL-4 & IL-13 | TSLP | IL-33 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Dupi-lumab | Pitra-kinra | AMG 317 | Oma-lizumab | Mepo-lizumab | Resli-zumab | Benra-lizumab | Tralo-kinumab | Lebri-kizumab | Altra-kincept | Pasco-lizumab | Cytokine Trap | Teze-pelumab | SAR 440340 | Medi-3506 |
| Atopic Dermatitis | ✔ | X | – | Ph2 | X | – | Ph2 | Ph3 | Ph3 | – | – | – | Ph2*‡ | – | Ph2 |
| **Asthma** | ✔ | X | X | ✔ | ✔ | ✔ | ✔ | X | X | X | X | X | Ph3 | Ph2 | Ph2 |
| **CRSwNP** | ✔ | – | – | ✔ | ✔ | Ph3† | Ph3 | – | – | – | – | – | Ph3 | – | – |
| COPD | Ph3 | – | – | – | Ph3 | – | Ph3 | – | X | – | – | – | Ph2 | Ph3 | Ph2 |
| Allergic Rhinitis | Ph2 | – | – | Ph3 | – | – | – | – | – | – | – | – | – | – | – |
| Eosinophilic Esophagitis | Ph3 | – | – | Ph2* | Ph2* | Ph2/3* | Ph3 | – | – | – | – | – | – | – | – |

- **– Not published. X=Investigation terminated. Check mark=approved.**
- * No longer in development due to no efficacy observed or failure to meet primary endpoint.
- †Study was in CRS with or without NP, based on inclusion criteria.
- ‡The phase 2a ALLEVIAD/NCT02525094 trial with tezepelumab failed to reach the primary endpoint of EASI-50 at week 12. However, a subsequent phase 2b trial, NCT03809663, is ongoing and due to complete in 2021. **Slide is not intended to be a comparison of safety or efficacy across diseases listed.** References available upon request.

Updated February 19, 2021.

# Nasal Polyps Treatment – Summary

- Different guidelines for CRSwNP have taken into consideration different criteria, including degree of control and disease severity, for recommending therapeutic options in these patients
- Irrespective of the criteria considered, initial management included nasal saline irrigation, INCS, short course of oral steroids and/or culture-based antibiotics (mainly doxycycline)
- Patients who did not show improvement with the above treatment regimen should be further evaluated for underlying risk factors or other comorbidities including cystic fibrosis, aspirin sensitivity, allergy and asthma
- Individualized therapy should be considered; e.g., oral antihistamines should be considered in allergic patients, biologic agents, and antifungal agents in patients with positive fungal culture.

# Quality Indicators

1. CRS is diagnosed on clinical grounds and must be confirmed with at least 1 objective finding on endoscopy or CT scan
2. Differentiation was made between CRSwNP and CRSsNP
3. The preferred means of radiological imaging modality of the sinuses in CRS is the CT
4. Imaging should always be interpreted in the context of clinical symptomatology because there is a high false-positive rate

5. CRSwNP should be initially managed with topical INCSs and short course of oral steroids
6. Clinicians should not prescribe topical or systemic antifungal therapy for patients with CRS

7. Many adjunct therapies commonly used in CRS have limited evidence to support their use. Saline irrigation is an approach that has consistent evidence of benefiting symptoms of CRS

8. Surgery may be beneficial and indicated for individuals with CRS failing appropriate medical treatment
9. Urgent consultation with the otolaryngologist should be obtained for individuals with severe symptoms of pain or swelling of the sinus areas, or if the patient is immunocompromised
10. Continued use of medical therapy postsurgery is key to success and should be considered for all patients

11. Intravenous and topical antibiotics should not be used for routine cases of CRS

Int Forum Allergy Rhinol. 2018 Dec;8(12):1369-1379.




# SYSTEMIC DISEASES AFFECTING THE NOSE

# Allergic Rhinitis

## Seasonal

histamine

“Runner”: itchiness, sneezing, rhinorrhea

Rx: antihistamines

## Perennial

inflammatory eiconasoids

“Blocker”: nasal obstruction

Rx: nasal steroids




# Typical Environmental Aeroallergens





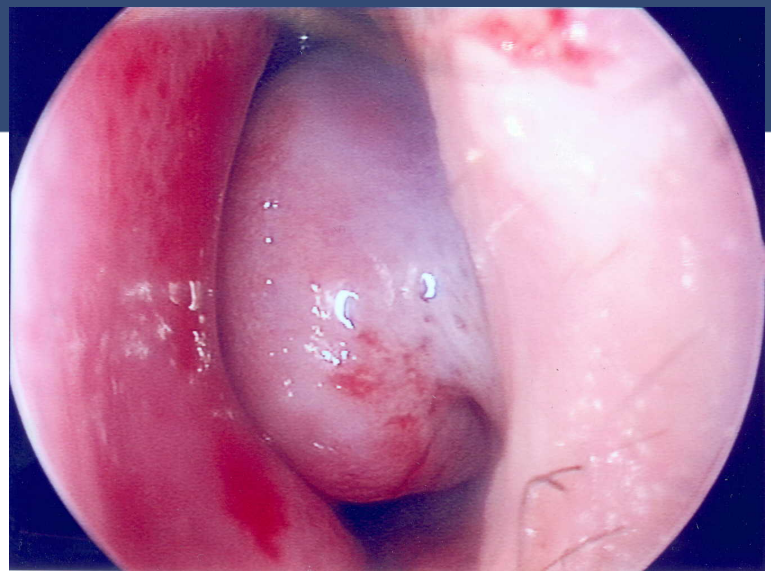
**Seasonal**

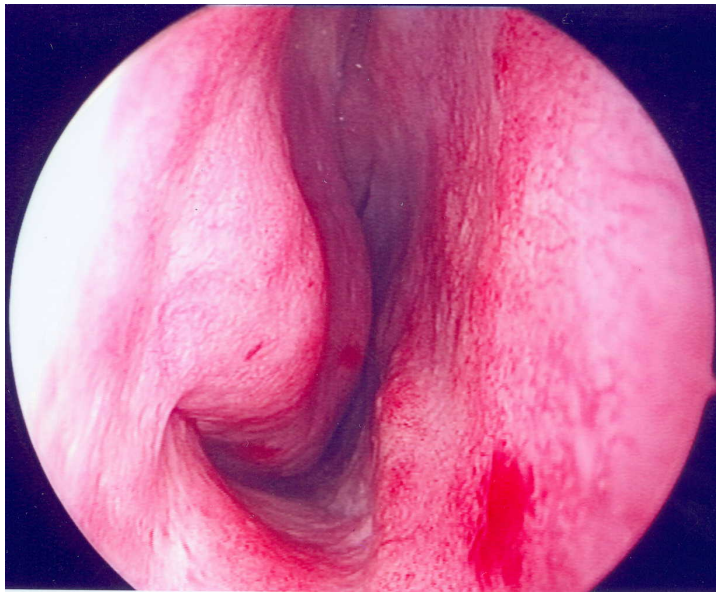
- Tree pollen
- Grass Pollen
- Ragweed Pollen

**Perennial**

- Dust mite
- Mold
- Cockroach
- Animal dander
  - Cat
  - Dog

# Rhinitis





# ARIA Classification - 2009

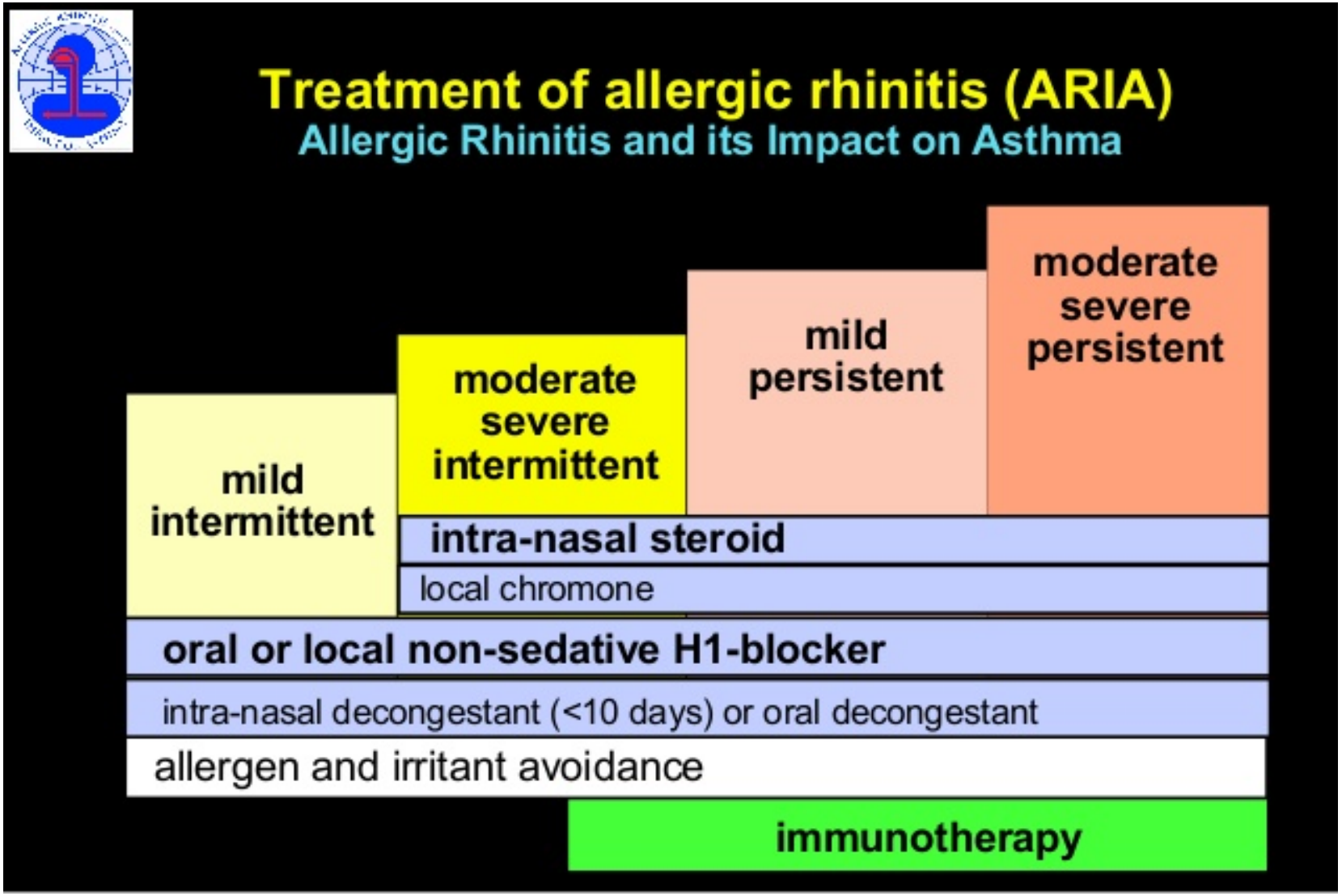
**Intermittent**
Symptoms
<4 days per week
**or** <4 consecutive weeks

**Persistent**
Symptoms
>4 days per week
**and** >4 consecutive weeks

**Mild**
**all** of the following:
1) Normal sleep
2) No impairment of daily activities
3) No impairment of work/school
4) Symptoms present but not troublesome

**Moderate – Severe**
**one or more** of:
1) Disturbed sleep
2) Impairment of daily activities
3) Impairment of work/school
4) Troublesome Symptoms

# ARIA – Treatment Ladder



# Granulomatous Diseases





- Wegener's Granulomatosis
  - Granulomatosis with Polyangiitis (GPA)
- Churg-Strauss
  - Eosinophilic Granulomatosis with Polyangiitis (EGPA)
- Sarcoidosis

# Wegener's Granulomatosis (GPA)

- Triad of:
  - 1) Upper & lower resp tract necotizing granulomas
  - 2) Focal glomerulonephritis
  - 3) Systemic vasculitis
- Unknown etiology - ?Autoimmune
- Pneumonitis, chronic sinusitis, mucosal ulceration URT, renal disease

# Wegener's Granulomatosis (GPA)





- Nasal invovement common, >75%
- Epistaxis, chronic sinusitis
- Labs: cANCA
  - Sensitivity = 65-90%
  - Specificity = 85-98%
- Diagnosis often not made until post-op path

# Churg-Strauss Syndrome (EGPA)

- Diagnosis by 4/6 Criteria:
  - Asthma
  - Nonfixed pulmonary infiltrates
  - Eosinophilia >10%
  - Extravascular eosinophilia
  - Sinus abnormality
  - Neuropathy
- Tests: CBC, ESR, CRP, pANCA (+ in 70%), biopsy

# Other Causes of Sinus Symptoms






**Think out here!**

**Neuralgia**

The Box

**Dental Origin**

**Migraine equivalent / Atypical facial pain**







# THANK YOU