Nasal Polyps: Epidemiology, burden of illness and pathophysiology

Russell Settipane, MD

Clinical Professor of Medicine

The Warren Alpert Medical School of Brown University

Disclosures

- Speaker – AbbVie, AstraZeneca, BioCryst, Boehringer Ingelheim, Genentech, GlaxoSmithKline, Grifols, Pharming, Regeneron, Shire
- Advisory Board – AbbVie, Aimmune, AstraZeneca, BioCryst, DBV Technologies, GlaxoSmithKline, Grifols, Pfizer, Regeneron, Sanofi
- Independent Contractor – AstraZeneca, BioCryst, Genentech, GlaxoSmithKline, Regeneron, Teva

Objectives

Participants should be able to:

- Discuss the differential diagnosis, epidemiology and underlying pathophysiology of nasal polyps
- Describe theories regarding the etiology of nasal polyps

CRS: Definition and Phenotypes

- Sinonasal inflammation ≥ 12 weeks
- Characterized by at least 2 symptoms: congestion, drainage, facial pressure, olfactory dysfunction
- Should be supported by objective endoscopic or CT evidence of polyps, purulence or edema (EPOS 2012)
- Phenotypes:
  - CRSsNP ~ 80%
  - CRSwNP ~ 20%
    - Eosinophilic vs. noneosinophilic

Fokkens WJ, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2012. *Rhinol Suppl*. 2012;23:1-298.

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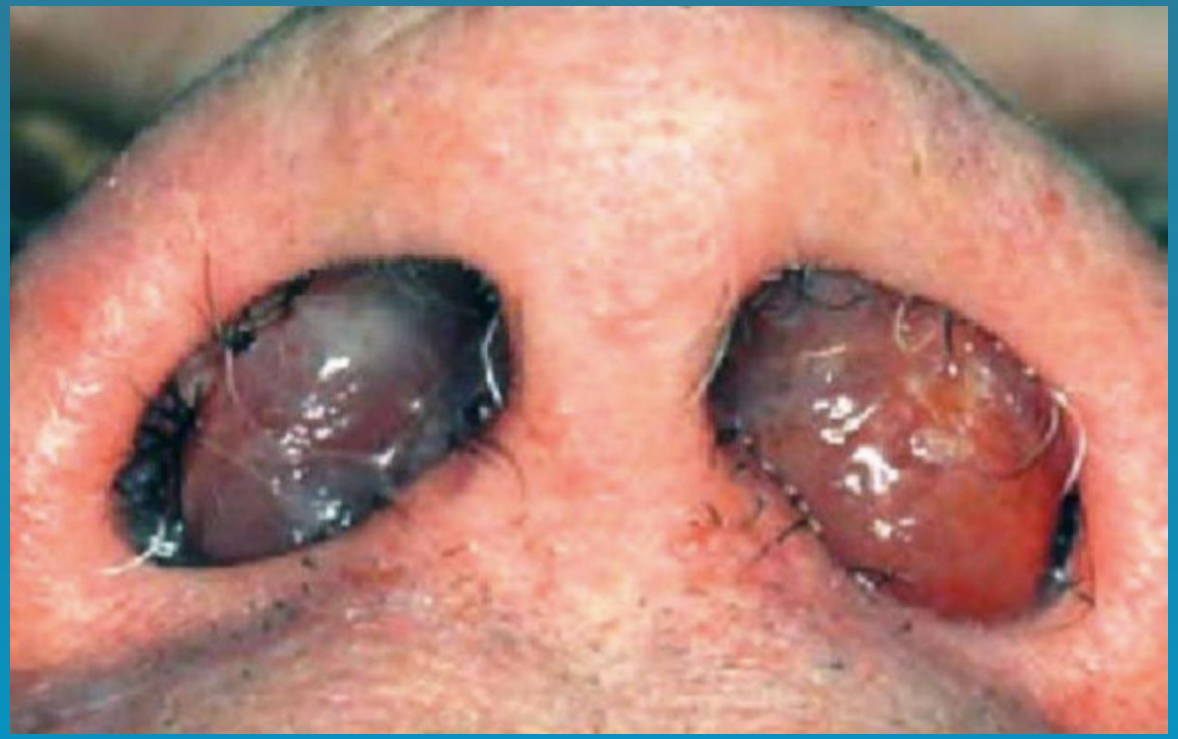
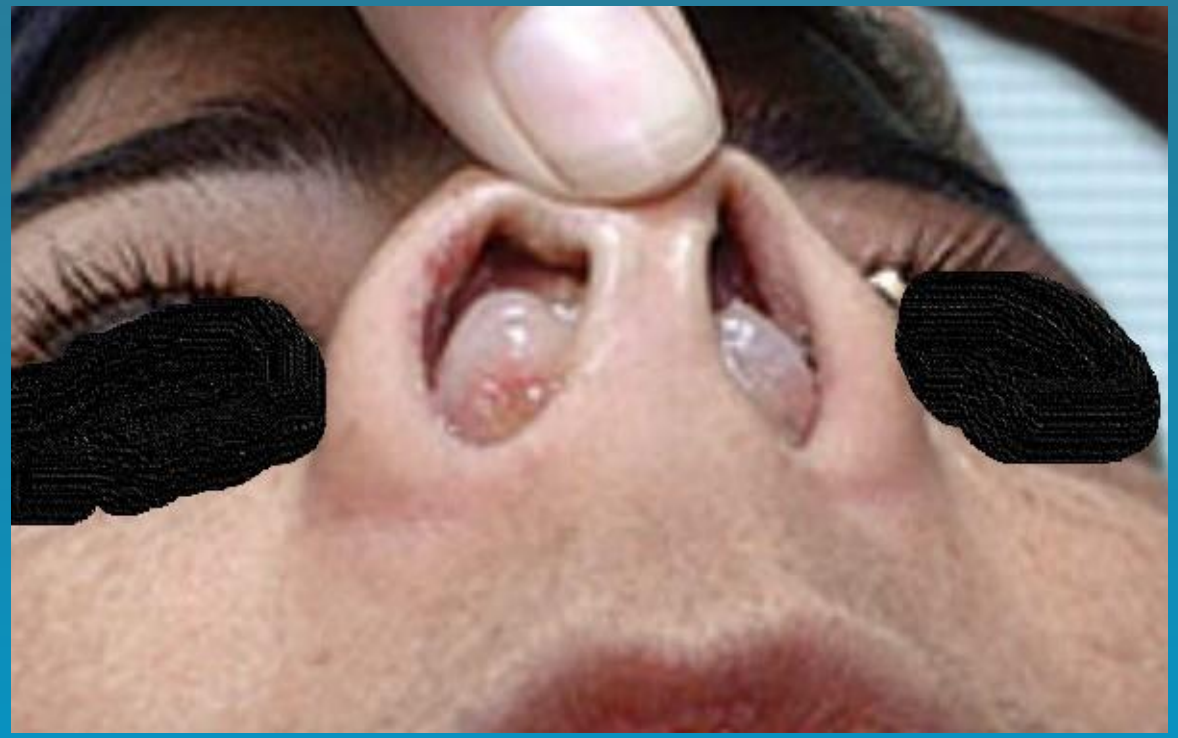
CRS: Definition and Phenotypes

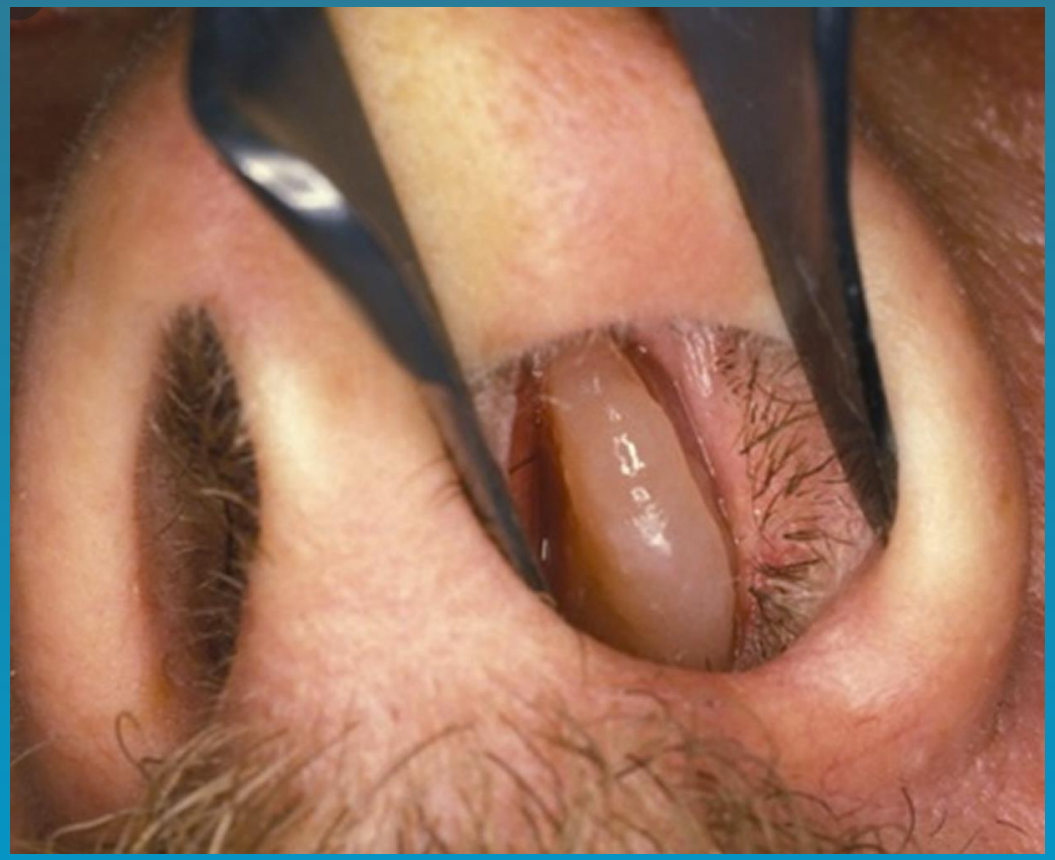
Is nasal endoscopy or CT really necessary for the diagnosis of CRSwNP?



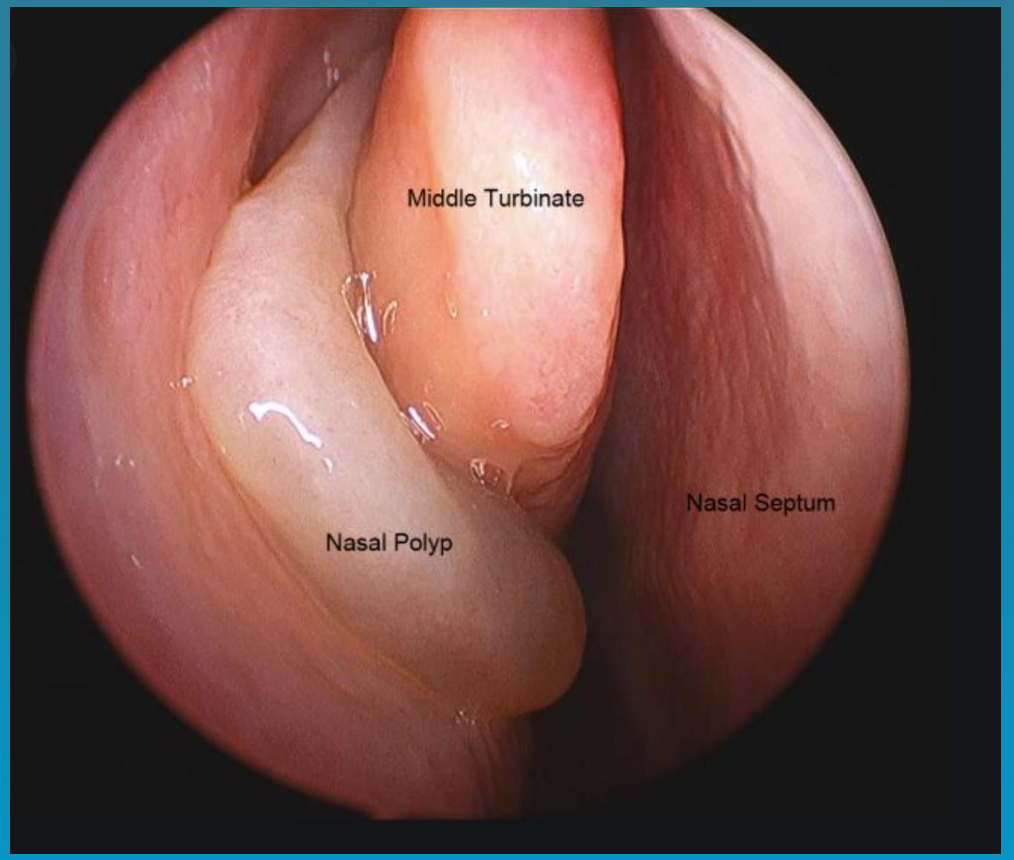


CRS: Definition and Phenotypes

The diagnosis can simply be made anterior rhinoscopy



ANTERIOR RHINOSCOPY



NASAL ENDOSCOPY

Characteristics of CRSwNP on physical exam

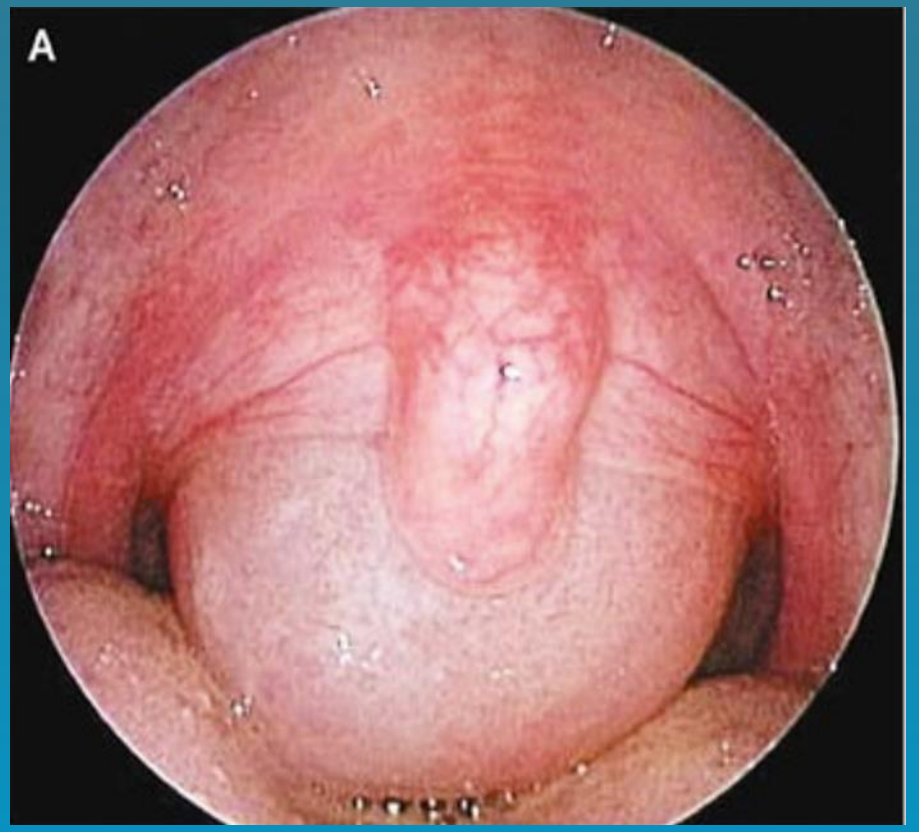
- Large polyps are often visible with anterior rhinoscopy
- Usually bilateral
- Smaller polyps may require nasal endoscopy or imaging
- Translucent, yellowish-gray to white, glistening masses
- Gelatinous
- Lack sensation
- Swollen nasal turbinates are sometimes mistaken for nasal polyps, but turbinates are pink in color, similar in appearance to the rest of the nasal mucosa, and very sensitive to touch

CRSwNP: Definition and Phenotypes

- Nasal Polyp
  - Hypertrophied
  - Edematous
  - Pedunculated
  - Mucosa
  - Prolapsing out of nose or paranasal cavity
  - Originate from the mucosa of the sinus outlets
    - ostia, clefts, and recesses of the ostiomeatal complex
- Phenotypes of nasal polyps
  - Antrochoanal
  - CRSwNP (eosinophilic)
  - CRSwNP (noneosinophilic)
  - NP associated with specific diseases (CF, PCD, Young's, etc)

Antrochoanal polyp

- A 19-year-old man with a 6-month history of snoring, a sensation of having a foreign body in his mouth, dysphagia and foul-smelling breath
- PE: a mass in the oropharynx that was pushing the soft palate forward



Lee J, Chou Y. N Engl J Med 2010;362:2113-2113.

The NEW ENGLAND JOURNAL of MEDICINE

Antrochoanal vs. CRSwNP

	Antrochoanal	CRSwNP
Age	Children	Adult
Inflammatory	No	Yes
Number	Single	Multiple
Occurrence	Unilateral	Bilateral
Shape	Pear-like*	Grape-like
Growth direction	Backward	Forward
Recurrence	uncommon	Common

*** Half in the maxillary antrum, ½ in the nose, extruding into the nasopharynx**

DIFFERENTIAL DIAGNOSIS of NASAL POLYPS: MALIGNANT LESIONS

Epithelial

- Squamous cell carcinoma
- Adenocarcinoma
- Adenoid cystic carcinoma
- Acinic cell carcinoma
- Mucoepidermoid carcinoma
- Olfactory neuroblastoma
- Malignant melanoma
- Metastatic tumors
- Undifferentiated carcinoma

Mesenchymal Tumors

- Lymphoreticular
  - Lymphoma
  - plasmacytoma
- Rhabdomyosarcoma
- Chondrosarcoma
- Ewing's Sarcoma

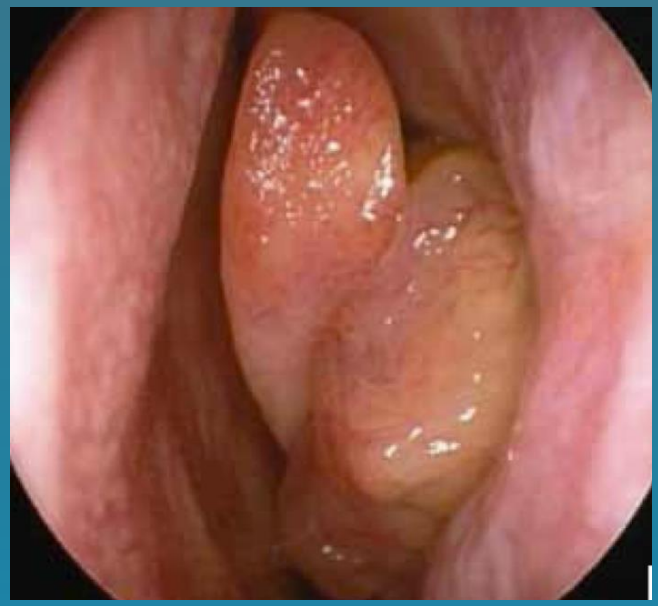
Bernstein JM. The immunohistopathology and pathophysiology of nasal polyps.(The differential diagnosis of nasal polyps). In Nasal polyps: Epidemiology, pathogenesis and treatment. Settipane GA, Lund VJ, Bernstein JM, Tos M (Eds). Providence:OceanSide Pubications, 1997. 85-95.

DIFFERENTIAL DIAGNOSIS of NASAL MASS in CHILDREN

- *Congenital*
  - Encephalocoele
  - Glioma
  - Dermoid cyst
  - Nasolacrimal duct cyst
  - *Neoplasia*
- *Benign*
  - Raniopharyngioma
  - Haemangioma
  - Neurofibroma
- *Malignant*
  - Rhabdomyosarcoma

Bernstein JM. The immunohistopathology and pathophysiology of nasal polyps.(The differential diagnosis of nasal polyps). In Nasal polyps: Epidemiology, pathogenesis and treatment. Settipane GA, Lund VJ, Bernstein JM, Tos M (Eds). Providence:OceanSide Pubications, 1997. 85-95.

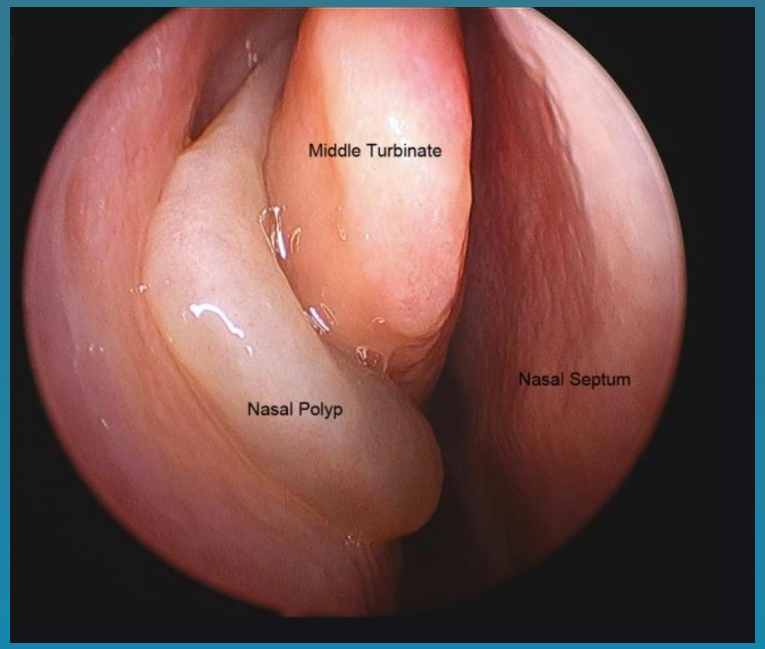
DIFFERENTIAL DIAGNOSIS of NASAL POLYPS: BENIGN LESIONS

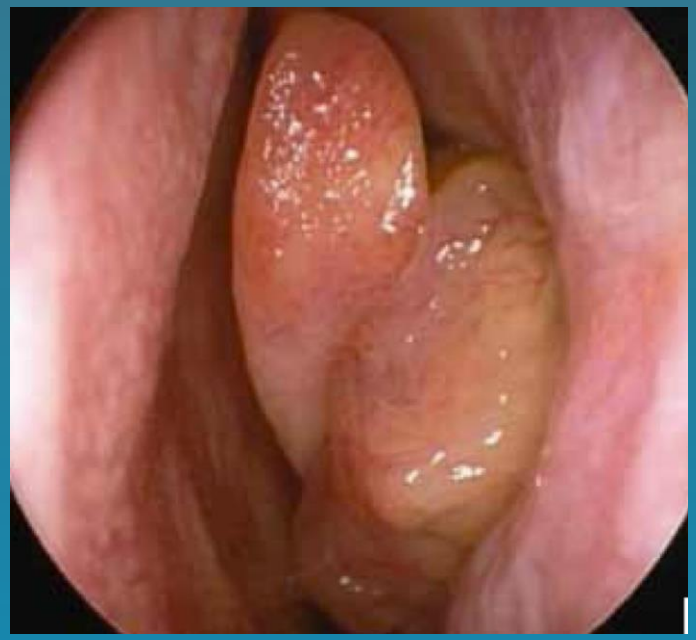


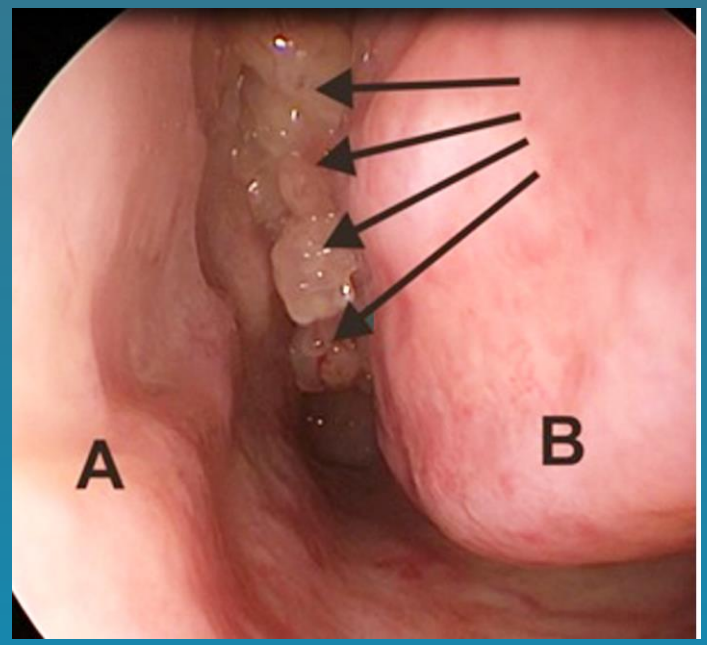
- Anatomic
  - Concha bullosa
- Tumors
  - Epithelial
    - Papilloma—inverted, everted, cylindric
    - Minor salivary—pleomorphic adenoma,
  - Mesenchymal
    - Neurogenic— meningioma, schwannoma, neurofibroma
    - Vascular— haemangioma, angiofibroma
    - Fibro-osseous— ossifying fibroma Muscular— leiomyoma, angioleiomyoma
- Granulomatous/Inflammatory
  - GPA (formerly Wegener's granulomatosis)
  - Sarcoidosis
  - Chrohn's

Bernstein JM. The immunohistopathology and pathophysiology of nasal polyps.(The differential diagnosis of nasal polyps). In Nasal polyps: Epidemiology, pathogenesis and treatment. Settipane GA, Lund VJ, Bernstein JM, Tos M (Eds). Providence: OceanSide Pubications, 1997. 85-95.

CRSwNP vs Inverted Papilloma







- Bilateral and multiple
- Smooth & grape-like
- yellowish-gray to white
- Translucent/ glistening
- Gelatinous / pliable

Unilateral (99%) and single

Wart-like irregular surface

Pink to gray / Firm texture

10-15% malignant transformation

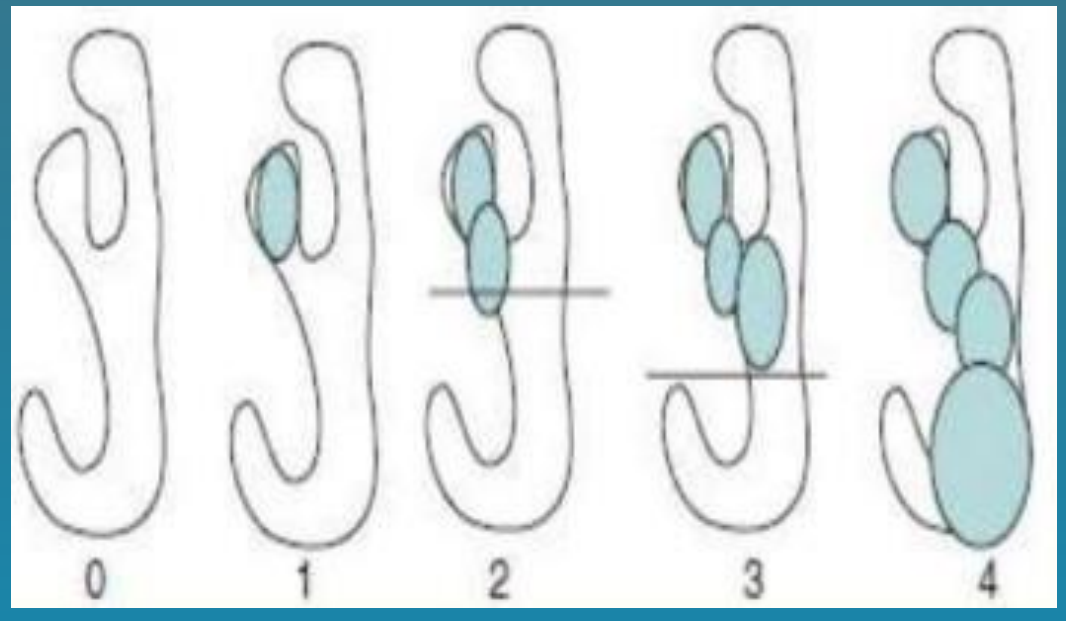
Epistaxis

CRSwNP: Definition and Phenotypes

- For both adults and children, CRSwNP is diagnosed when nasal polyps (NPs) can be visualized in the nose and/or middle meati, in the context of appropriate symptoms
- Symptoms (relating to polyp size and sinus involvement):
  - Congestion (blockage)
  - Hyposmia
- Disease burden assessed by objective and subjective measures

Burden assessed by objective and subjective measures

- Nasal polyp scoring system
  - 0-4 per nostril
- Nasal congestion score (0-3)
- TNSS (0-12)
- Sinus CT Lund-McKay score (0-24)
- SNOT-22 (0-110)
- SF-36
- UPSIT (UPenn Smell ID Test) score
- Nasal airflow (PnIF)



Lund–Mackey system.

Sinus	Right sinus	Left sinus
Frontal	0–2	0–2
Anterior ethmoids	0–2	0–2
Posterior ethmoids	0–2	0–2
Maxillary	0–2	0–2
Sphenoid	0–2	0–2
Ostiomeatal complex	0 or 2	0 or 2

For the sinuses: 0 = no inflammation; 1 = partial inflammation; 2 = 100% inflammation.
For the ostiomeatal complex: 0 = not occluded; 2 = occluded.
Maximum total score: 24.

CRS: Economic burden - considerable

- Direct costs: diagnostic tests, medical and surgical therapies
- Indirect: Lost and reduced school and work productivity
- Detrimental impact on physical and emotional health
- US estimates of the direct and indirect costs: $13 and 60 billion annually

DeConde AS, Soler ZM. Am J Rhinol Allergy 2016; 30:134.
Caulley L et al. J Allergy Clin Immunol 2015; 136:1517.
Smith KA, Orlandi RR, Rudmik L. Laryngoscope 2015; 125:1547.

Burden CRSwNP: recurrence rate and co-morbidities

- Wide variations reported in revision ESS rates for CRSwNP
- Following PRISMA guidelines, a systematic review and meta-analysis was performed on studies that reported **revision surgery data** for CRSwNP patients
- 45 studies with 34,220 subjects were meta-analyzed
- Overall revision rate of 18.6% (95% CI = 14%-24%)
- Mean revision rate of 16.2% over a weighted mean follow-up of 89.6 months
- Factors associated with increased revision rates included:
  - allergic fungal rhinosinusitis (28.7%)
  - AERD (27.2%)
  - asthma (22.6%)
  - prior polypectomy (26.0%)
  - publication prior to 2008 (22.7%)
- Conclusion: Long-term ESS revision rates are approximately 14% to 24%

Loftus CA, et al. Revision surgery rates in CRSwNP: meta-analysis of risk factors. Int Forum Allergy Rhinol. 2020;10:199-207.

Burden CRSwNP: Revision rates vs. Recurrence rates

- 40% of patients experience recurrence < 18 months post sinus surgery
- Prospective, multicenter cohort of adult patients undergoing ESS for medically recalcitrant CRSwNP
- 363 CRSwNP patients having undergone ESS involving polypectomy
- All patients had at least 6 months of postoperative endoscopy examinations
- NP recurrence
  - 35% after 6 months post-ESS
  - 38% after 12 months post-ESS
  - 40% after 18 months post-ESS
- A 40% recurrence rate was also reported by Settipane, GA in 167 post surgical patients (1987)

DeConde AS, et al. Prevalence of polyp recurrence after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. Laryngoscope. 2017;127:550-555.

Settipane GA et al. Asthma and Nasal polyps. In Myers E, ed. New dimensions in Otlolaryngology, Head and Neck Surgery. Amsterdam: Excerpta Medica, 1987, 499-500.

EPIDEMIOLOGY of NASAL POLYPS

- Nasal polyps affect 1-4% of the general population
- By nasal endoscopy:
  - **2.7%** in a Swedish cohort
  - **2.6%** (28,912 subjects) reported in the Korean NHANES (2008-2012)
- By autopsy:
  - **26% - 42% of autopsy specimens have NP**
- Occur in all races
- Male predominance
- More common after age 40
- Childhood presentation (<age 16-20) is rare (Consider dx of CF)
- CRSwNP closely linked with dx asthma

Settipane RA, Peters AT, Chiu AG. Nasal polyps. Am J Rhinol Allergy. 2013;27:S20-5.

Johansson L,et al. Prevalence of nasal polyps. *Ann Otol Rhinol Laryngol*. 2003;112:625-629.

Ahn JC, et al. Prevalence and risk factors of CRS: Korean NHANES 2008-2012. *JAMA Otolaryngol Head Neck Surg*. 2016;142:162-167.

Bateman ND et al. Nasal polyps: still more questions than answers. J Laryngol Otol. 2003;117:1-9.

Settipane GA. Epidemiology of nasal polyps. Allergy Asthma Proc. 1996;17:231-6.

Burden: Nasal Polyp – Asthma Association

- 10-15% of adults with asthma (> 40 y.o.) have polyps
- 40-67% of pts with CRSwNP have comorbid asthma
- Correlation exists between the inflammatory profiles of nasal and bronchial biopsies in patients with CRSwNP
  - NP: upregulation of IL-4, IL-5, IL-13, MCP-4, local IgE, eotaxin
- In severe asthma, correlation exists between the extent of sinus disease and sputum eos, peripheral blood eos and eNO
- NP patients with comorbid asthma have more severe NP disease –
  - high rates of NP recurrence and higher rates of OCS dependence
- Asthma with NP is more difficult to control, more exacerbation prone, with increased airway obstruction and eosinophilic inflammation

Håkansson K. Airway inflammation in chronic rhinosinusitis with nasal polyps and asthma: the united airways concept further supported. PLoS One 2015;10: e0127228.

Larsen K. The clinical relationship of nasal polyps to asthma. Allergy Asthma Proc 1996;17:243-9.

Burden: NP usually occur in the setting of underlying local or systemic disease

- CRS – up to 1/3 are associated with NP
- Allergic fungal sinusitis (AFS)
- Aspirin exacerbated respiratory disease (AERD)
- Churg-Strauss Syndrome
- Cystic Fibrosis
- Primary ciliary dyskinesia (Kartagener syndrome)
- Asthma
- Young's Syndrome (azoospermia, sinopulmonary infections)

Settipane RA, Peters AT, Chiu AG. Nasal polyps. Am J Rhinol Allergy. 2013;27 Suppl 1:S20-5.

CONDITIONS ASSOCIATED WITH NASAL POLYPS

Condition	Prevalence
AERD	15-23%
Adult asthma	7%
IgE mediated	5%
Non-IgE mediated	13%
CRS in Adults	33%
Rhinitis	
Nonallergic rhinitis	5%
Allergic rhinitis	1.5%
Childhood asthma/sinusitis	0.1%

Condition	Prevalence
Cystic fibrosis	
Children	10%
Adults	50%
EGPA (Churg-Strauss syndrome)	50%
Allergic fungal sinusitis (AFS)	66-100%
Primary ciliary dyskinesia (Kartagener's)	40%
Young's syndrome (azoospermia)	?

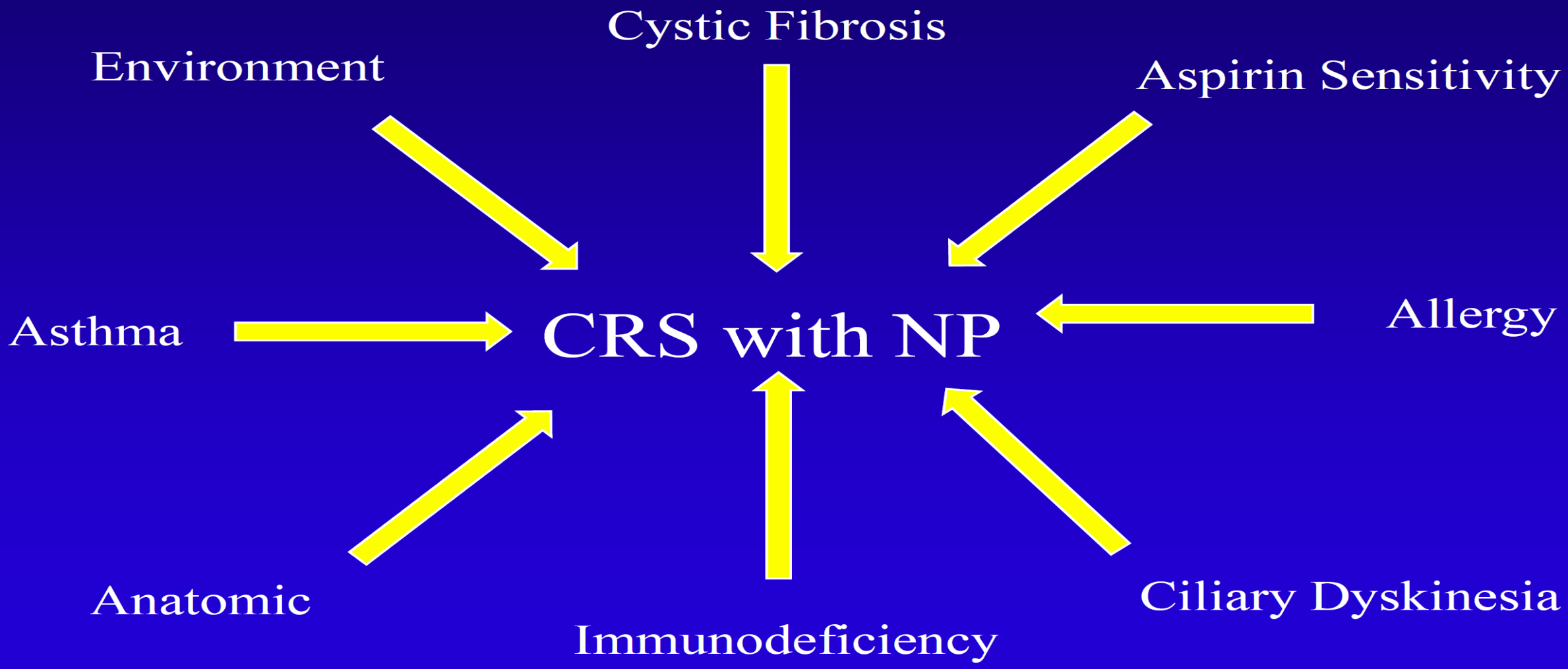
Settipane RA, Peters AT, Chiu AG. Nasal polyps. Am J Rhinol Allergy. 2013;27 Suppl 1:S20-5.

Role of allergy in sinonasal disease

- Observed association between increased levels of total IgE, specific IgE, and eosinophilic inflammation in NPs
- May be relevant to NP pathophysiology
- Despite high local levels of tissue IgE, the role of environmental allergy in CRSwNP remains unclear
- Prevalence of NP in AR is comparable to that seen in the normal population
- When atopy is present in NP, worse QoL and a higher incidence of asthma
- The presence of specific IgE to staphylococcal enterotoxins A and B also points to a possible role of bacterial superantigens
- Omalizumab clinical efficacy in the treatment of NP supports the importance and functionality of local IgE

Settipane RA, Borish L, Peters AT. Determining the role of allergy in sinonasal disease. Am J Rhinol Allergy. 2013;27 :S56-8.
Settipane GA. Nasal polyps and immunoglobulin E (IgE). Allergy Asthma Proc. 1996;17:269-73.
Bachert C et al. Total and specific IgE in nasal polyps is related to local eosinophilic inflammation. JACI. 2001;107:607-14.
Helman SN et al. The Role of Allergic Rhinitis in CRS. *Immunol Allergy Clin North Am*. 2020;40:201-214.

Factors Associated with the Development of CRS with NP



HISTOPATHOLOGY OF NASAL POLYPS

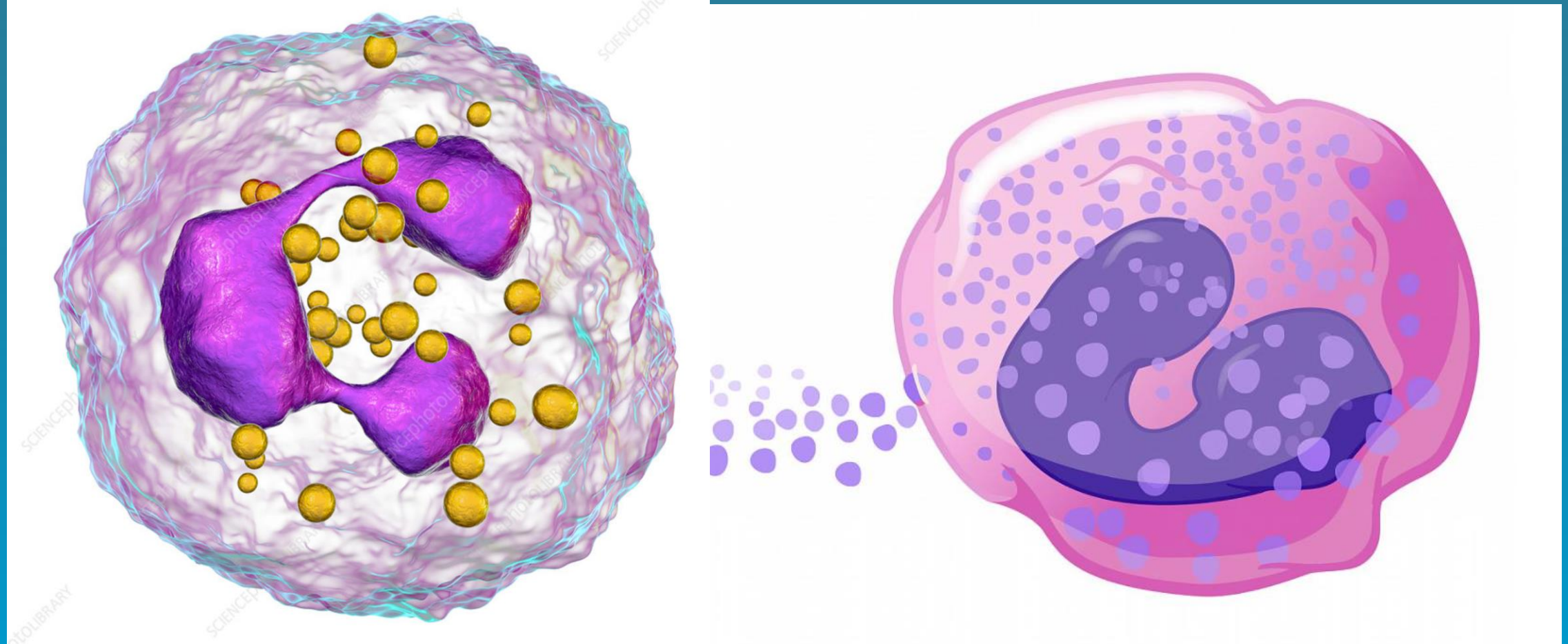
- Biopsy of mucosal tissue characteristically shows edematous tissue and a paucity of submucosal glands and stromal fibrosis
- Mixed infiltrates of eosinophils > mononuclear cells
- US and Europe: NP are accompanied by an eosinophilic infiltrate in approximately 80% of cases
- Asia: NP are more likely to be associated with a noneosinophilic or neutrophilic infiltrate and Th1 and/or Th17 cytokine skewing
- A very low rate of AERD has been observed in Chinese patients with CRSwNP
- Neutrophilic inflammation is also seen in NP found in cystic fibrosis

Nasal Polyps: T1 vs. T2 inflammation

Cystic Fibrosis, Ciliary Dyskinesia, Immunodeficiency

Eosinophilic Mucin Rhinosinusitis

Allergic Fungal Sinusitis

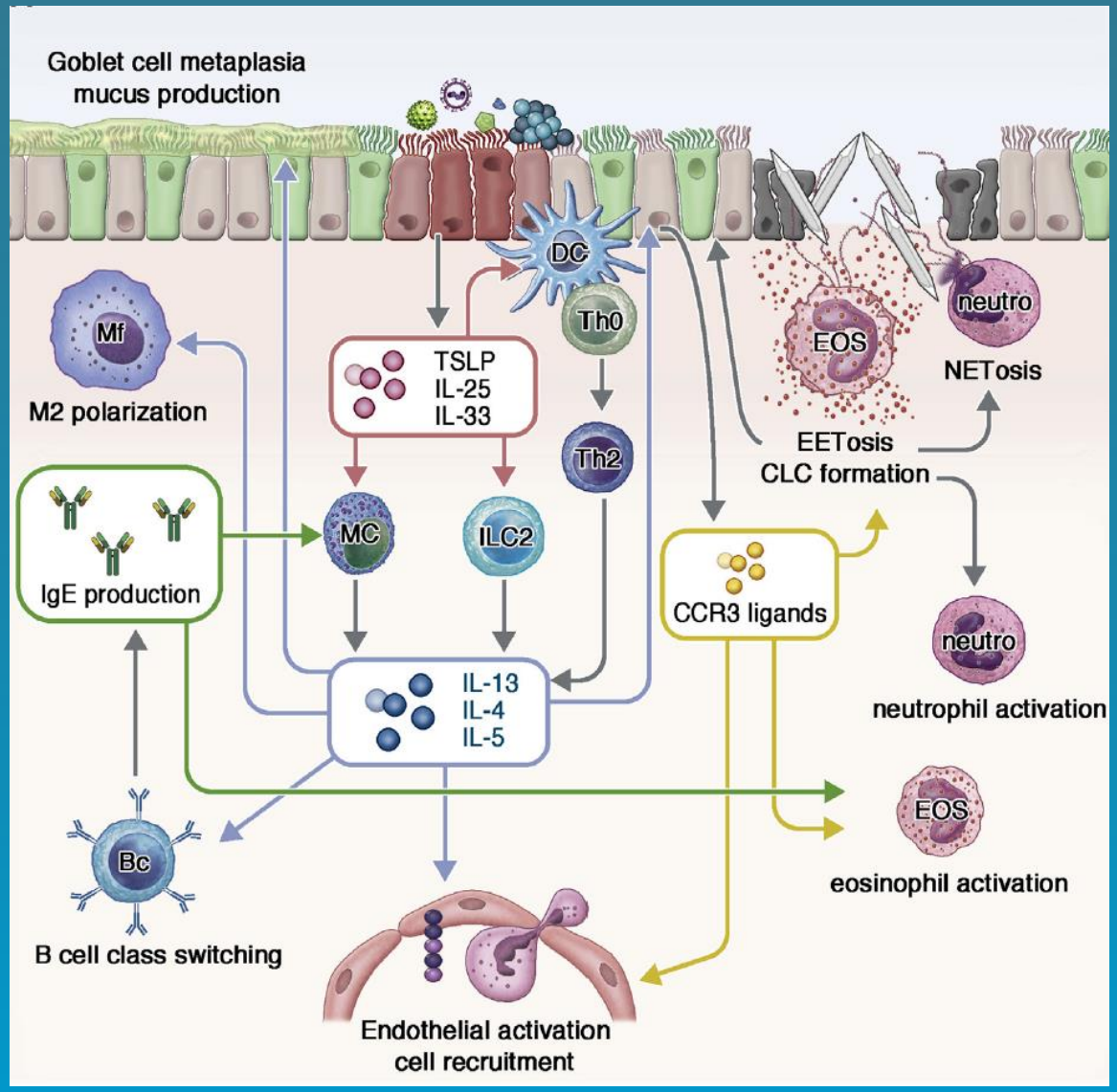


Nasal Polyps: T1 vs. T2 inflammation

- 85% of NP in Western countries have T2 eosinophilic inflammation
- Similar cytokine profile to asthma with significant elevations of:
  - Key cytokines: IL-4, IL-5, IL-13,
  - Type 2 chemokines: ECP, eotaxin, TARC, MCP-4
  - High levels of local IgE and profound tissue eosinophilia
  - ILC2, macrophages, and mast cells have also been detected in NP biopsies
- An alternative inflammatory profile mediated by Th1 and/or Th17 cells is more common in Asian populations with either CRSwNP or CRSsNP

Batra PS et al. Laryngoscope 113:1703-1706 (2003)

Cytokines in Type 2 immune reactions

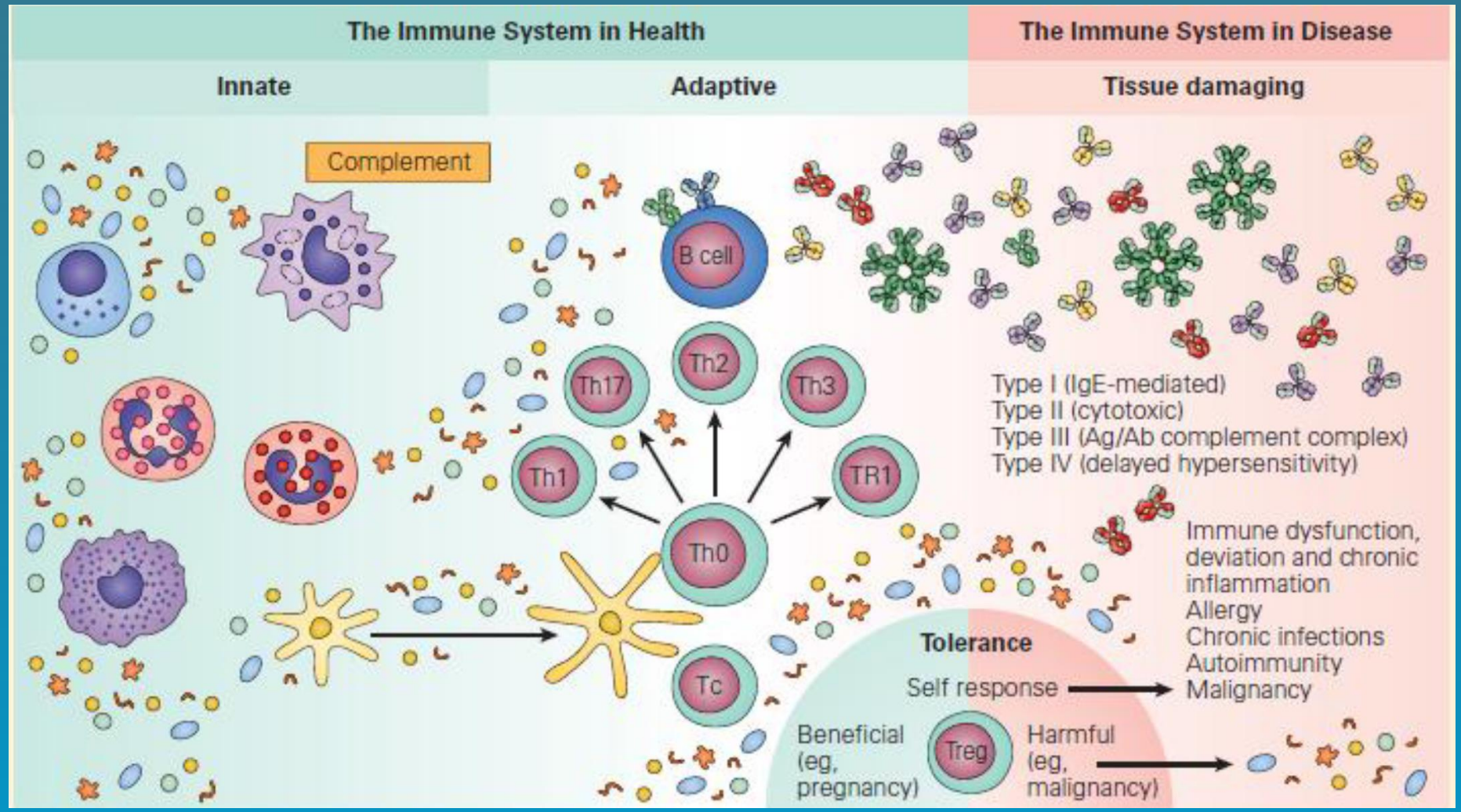


Pathophysiology of NP

- Type 2 inflammation
- Evidence of localized allergic hyper-responsiveness to colonizing *Staphylococcus aureus*
- The "staphylococcal superantigen hypothesis"
  - Local production of specific IgE antibodies against staphylococcal enterotoxins
  - Enterotoxins act as superantigens → broadly activate T lymphocytes
  - Patients with CRS without NP do not appear to produce IgE to staphylococcal enterotoxins

Settipane RA, Peters AT, Chiu AG. Nasal polyps. Am J Rhinol Allergy. 2013;27 Suppl 1:S20-5.

Development of NP: Interaction of innate and adaptive immunity with epithelial remodeling



Bellanti JA. Immunology IV. I Care Press, Bethesda MD, 2012

Development of NP: Interaction of innate and adaptive immunity with epithelial remodeling

Epithelial Cell Changes

- Injury caused by pathogens, proteases, and irritants
- Reduced cell adhesion and tight junction proteins
- Epithelial-mesenchymal transition
- Goblet cell hyperplasia
- Extracellular matrix degradation
- Fibrin deposition
- Tissue edema

Epithelial Response

- Production of Th2-cytokines (IL-25, IL-33) and TSLP
- TSLP amplifies the T2 inflammatory response
- Activates type 2 ILC2s, mast cells and the release of type 2 cytokines (IL-5 and IL-13)
- IL-4 and IL-13 may perpetuate barrier dysfunction by stimulating expression of TSLP

Laidlaw TM et al. Chronic Rhinosinusitis with Nasal Polyps and Asthma. JACIP. 2021;9:1133-1141.

Endotyping of CRS based on biomarkers

ENDOTYPING

- Type 2 vs. non-type 2 immune reactions
- Type 2 (such as IL-4, IL-5, or IL-13)
- Type 1 cytokines (IFNγ)
- Type 3 (IL-17 family)

PHENOTYPING

- CRSwNP associated with –
  - late-onset asthma
  - AERD
  - Allergic fungal rhinosinusitis (AFRS)

Bachert et al. JACIP 2020;8:1514-9

Endotyping of CRS based on biomarkers: 3 Groups

- Non type 2 – (mostly of CRSsNP)
  - comprising type 1 and type 3 immune reactions
- Type 2 - moderate type 2 and severe type 2 (mostly CRSwNP)
  - the severe type demonstrating significantly higher concentrations of inflammatory cytokines compared with the moderate type
  - Biomarkers: blood eosinophils, tissue eosinophils, total serum IgE

Bachert et al. JACIP 2020;8:1514-9

EUFOREA: Severe CRSwNP vs. Uncontrolled CRSwNP

- **Severe CRSwNP –**

"bilateral CRSwNP with a nasal polyp score of at least 4 of 8 points and persistent symptoms (loss of smell and/or taste, nasal obstruction, secretion and/or postnasal drip, and facial pain or pressure) with the need for add-on treatment to supplement intranasal corticosteroids"

"The diagnosis of CRSwNPs therefore demands a nasal endoscopy"

- **Uncontrolled CRSwNP –**

"persistent or recurring despite long-term treatment with INCSs and having received at least 1 course of systemic corticosteroids in the preceding 2 years (or having a medical contraindication or intolerance to systemic corticosteroids) and/or previous sinonasal surgery (unless having a medical contraindication or being unwilling to undergo surgery)

Bachert C, et al. **EUFOREA expert board meeting** on uncontrolled severe chronic rhinosinusitis with nasal polyps (CRSwNP) and biologics: Definitions and management. JACI 2021;147:29-36.

EUFOREA: CRSwNP with comorbid disease

- ‘‘nasal polyp disease with other coexisting type 2 inflammatory diseases such as asthma, N-ERD, atopic dermatitis/eczema, allergic rhinitis, urticaria, food allergy, or eosinophilic esophagitis’’

Bachert C, et al. **EUFOREA expert board meeting** on uncontrolled severe chronic rhinosinusitis with nasal polyps (CRSwNP) and biologics: Definitions and management. JACI 2021;147:29-36.

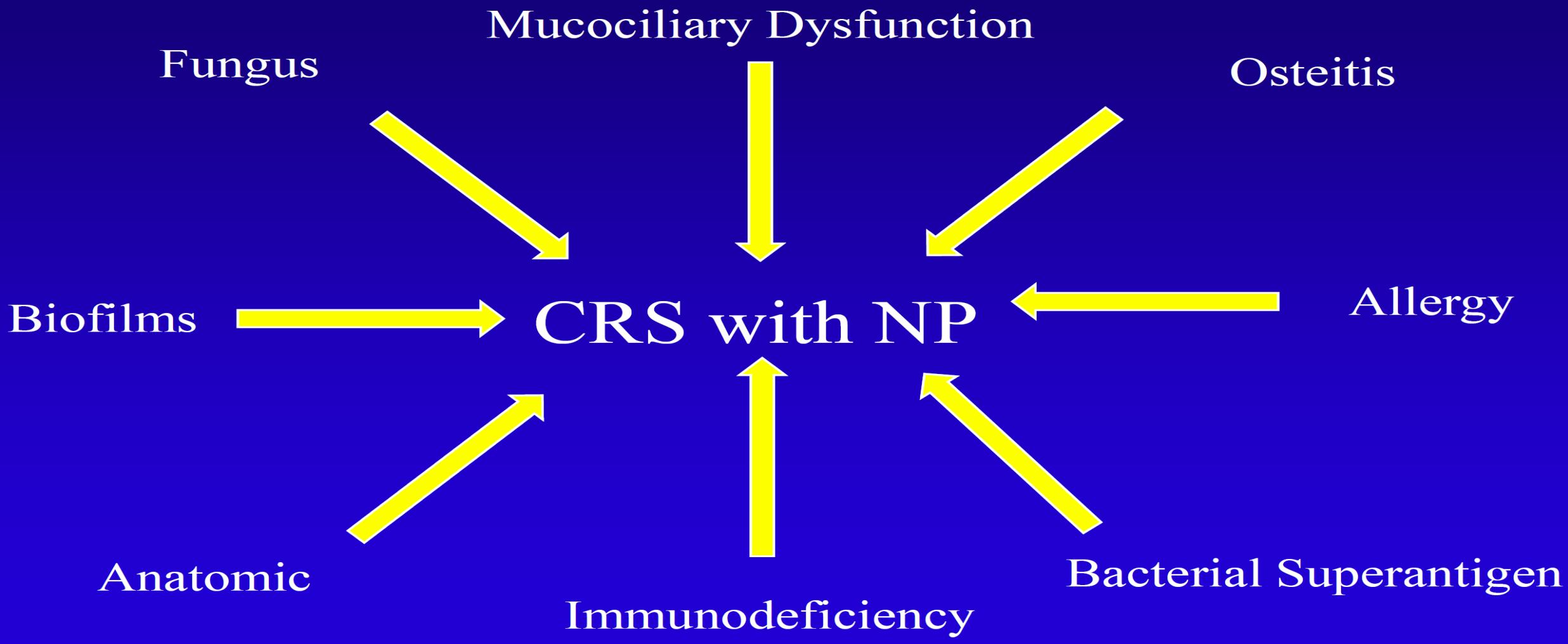
Indicators of T2 inflammation in CRSwNP

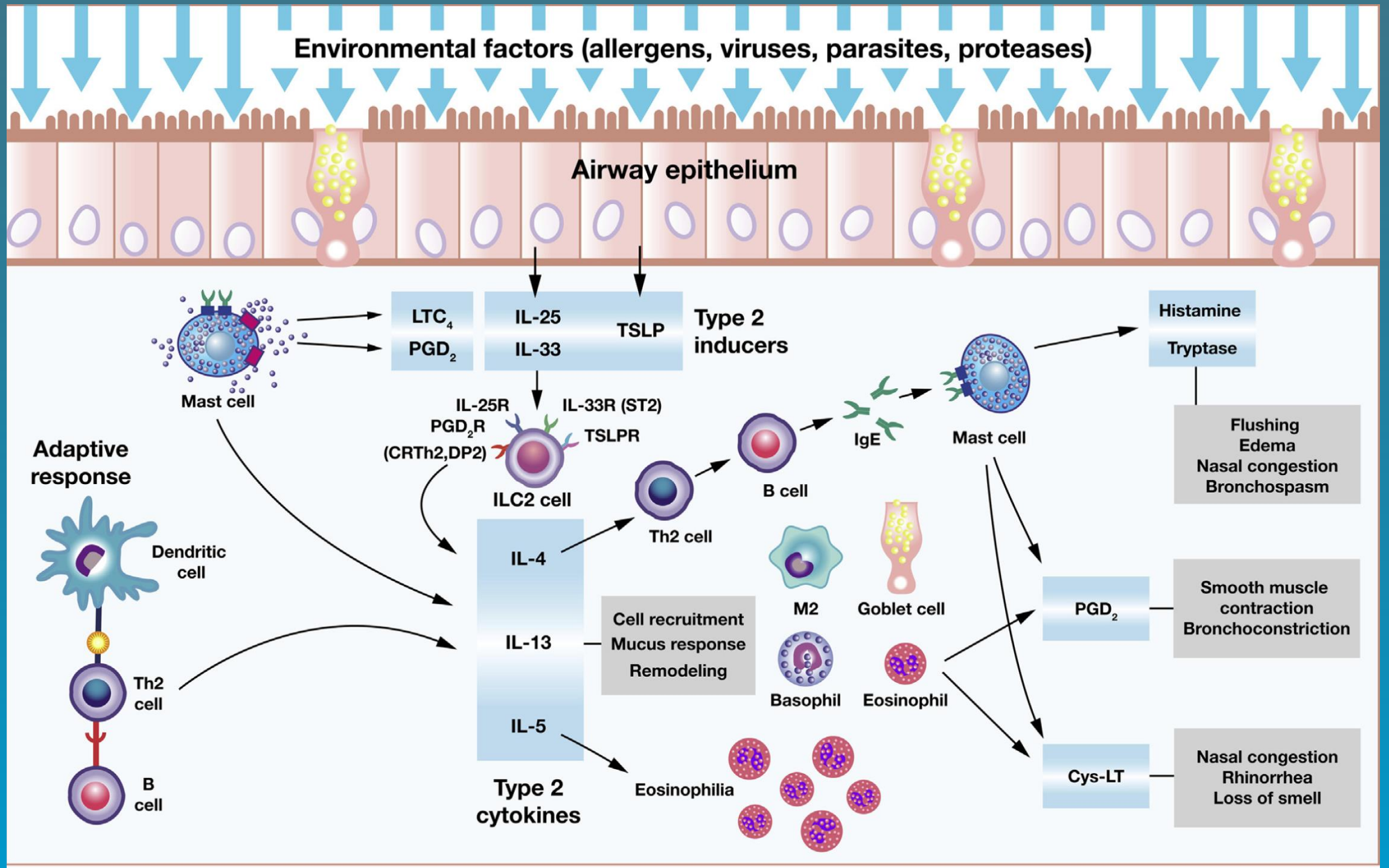
Strong indicators	Possible indicators
Comorbid late-onset asthma	Other type 2 comorbidities, allergy
Former surgery with tissue eosinophilia in histology	One or more surgeries for CRSwNP
Nonsteroidal anti-inflammatory drugs–exacerbated disease	One or more oral GCS courses in last 2 y for CRS
	Blood eosinophils >150/>300 cells/mm^3
	Blood IgE >100/>150 kU/L
SE-IgE positivity	

(Staph aureus enterotoxin-IgE)

Bachert et al. JACIP 2020;8:1514-9

CRS with NP - Etiology




Environmental factors (allergens, viruses, parasites, proteases)
Airway epithelium
LTC4
PGD2
IL-25
IL-33
TSLP
Type 2 inducers
Mast cell
IL-25R
PGD2R
(CRTh2,DP2)
IL-33R (ST2)
TSLPR
ILC2 cell
Adaptive response
Dendritic cell
Th2 cell
B cell
IL-4
IL-13
IL-5
Type 2 cytokines
Th2 cell
B cell
IgE
Mast cell
Histamine
Tryptase
Flushing
Edema
Nasal congestion
Bronchospasm
M2
Goblet cell
Cell recruitment
Mucus response
Remodeling
Basophil
Eosinophil
Eosinophilia
PGD2
Smooth muscle contraction
Bronchoconstriction
Cys-LT
Nasal congestion
Rhinorrhea
Loss of smell

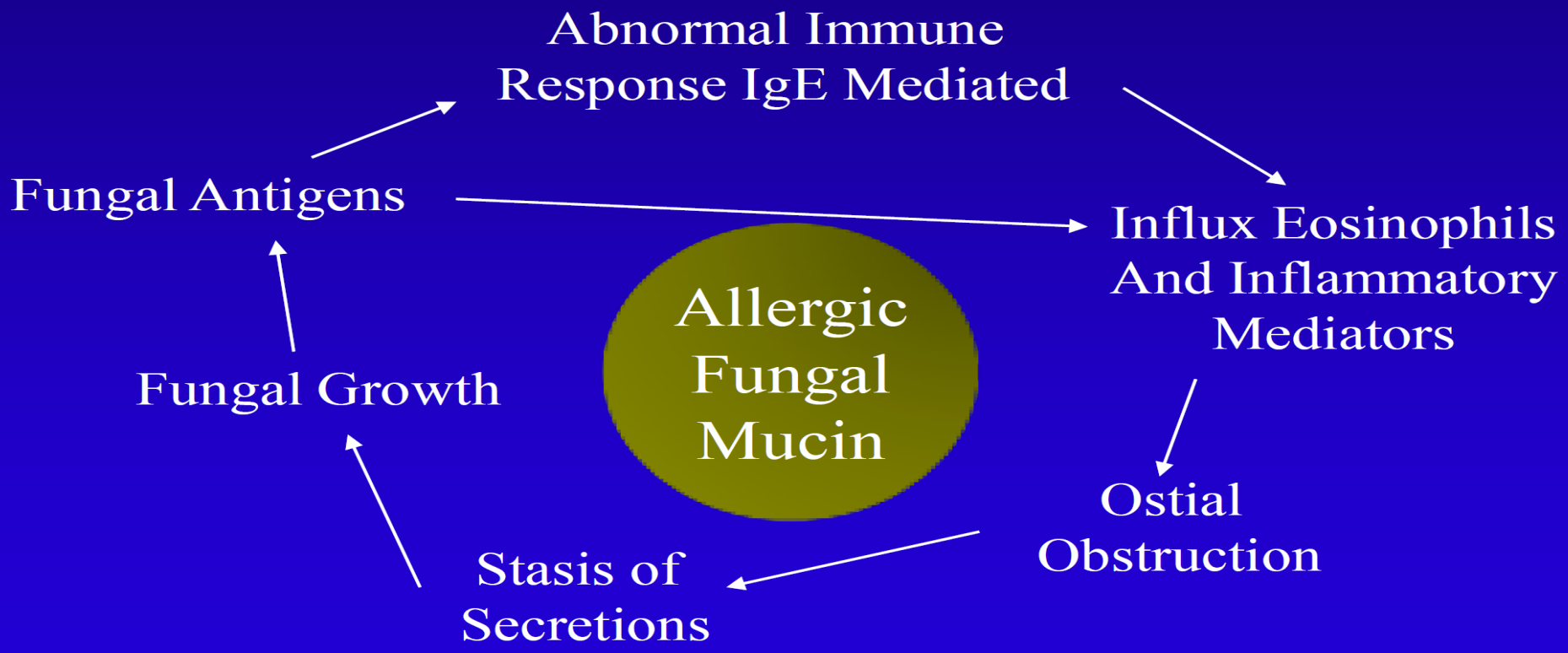
Allergic Fungal Rhinosinusitis

- Prevalence: 2-6% of patients with CRS
- All are atopic (& reactive to fungus-causing AFS)
- Noninvasive fungal-induced inflammation related to type I hypersensitivity
- Dematiaceous fungi most common
  - Alternaria, Bipolaris, Curvularia

Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. Am J Rhinol Allergy. 2013;27:473-8.

Proposed Pathophysiology AFRS

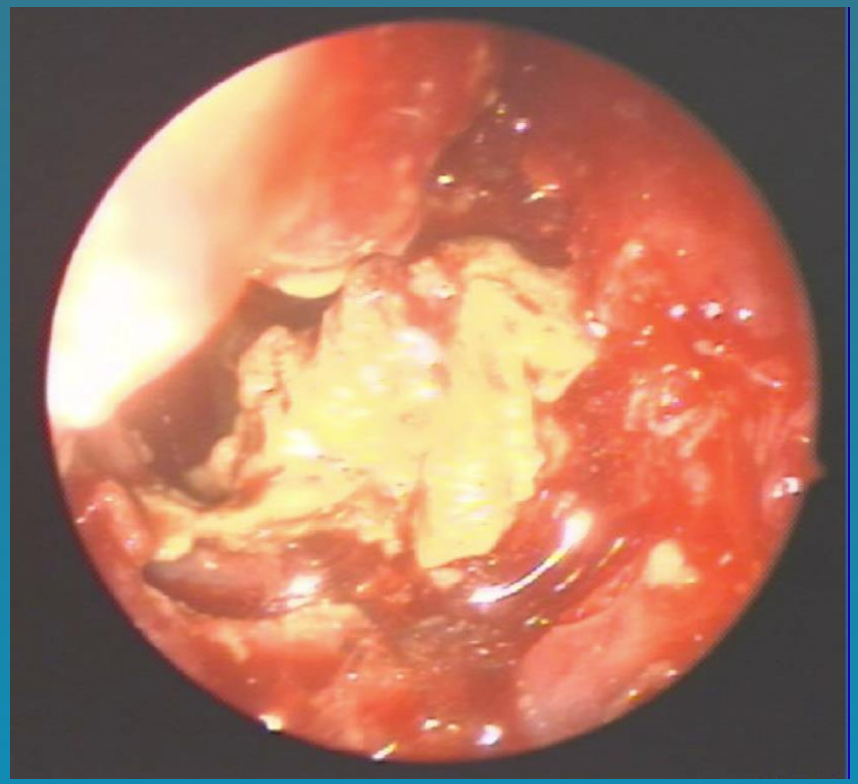
- AFRS is the nasal correlate of ABPA



Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. Am J Rhinol Allergy. 2013;27:473-8.

Clinical Presentation of AFS

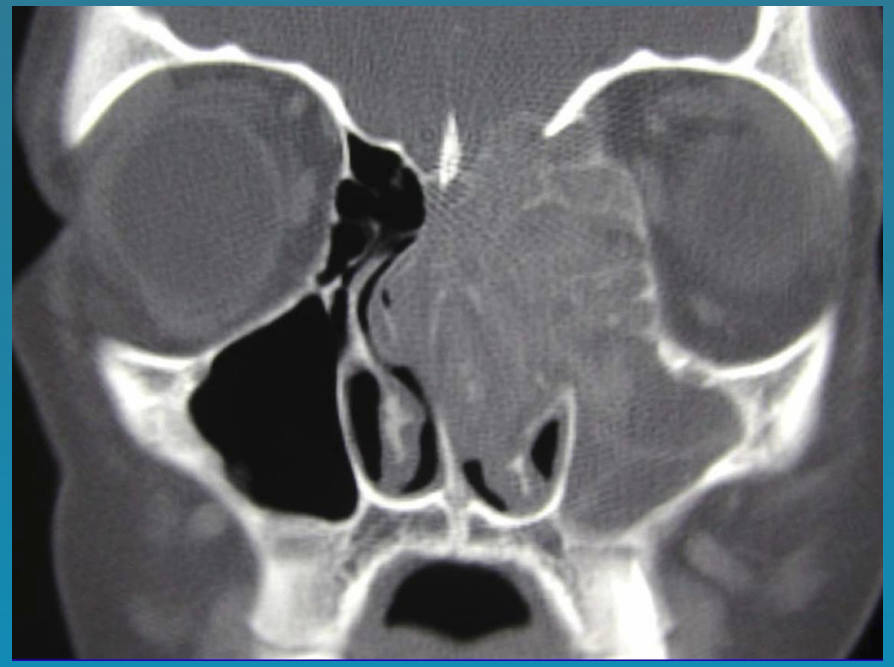
- Nasal congestion
- Nasal polyps
- Allergic fungal mucin
- Bony abnormalities
- Nasal drainage with production of crusts



Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. Am J Rhinol Allergy. 2013;27:473-8.

AFS: CT Findings

- Opacified sinuses
- Unilateral disease
- Bony abnormalities
- Differential density, especially with soft tissue windows



Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. Am J Rhinol Allergy. 2013 Nov-Dec;27(6):473-8.

Laboratory Dx of AFS

- Elevated serum IgE level
- Positive skin tests / serum IgE to fungi
- Allergic Fungal Mucin Fungi on GMS stain
- Eosinophils, Charcot-Leyden crystals on H&E
- Culture - Depending on laboratory 25-100% sensitive

Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. Am J Rhinol Allergy. 2013 Nov-Dec;27(6):473-8.

AFS: Diagnostic Criteria

Major criteria

- Type I Hypersensitivity
- Nasal Polyps
- Characteristic CT scan
- Eosinophilic Mucus
- Fungus on pathology or stain

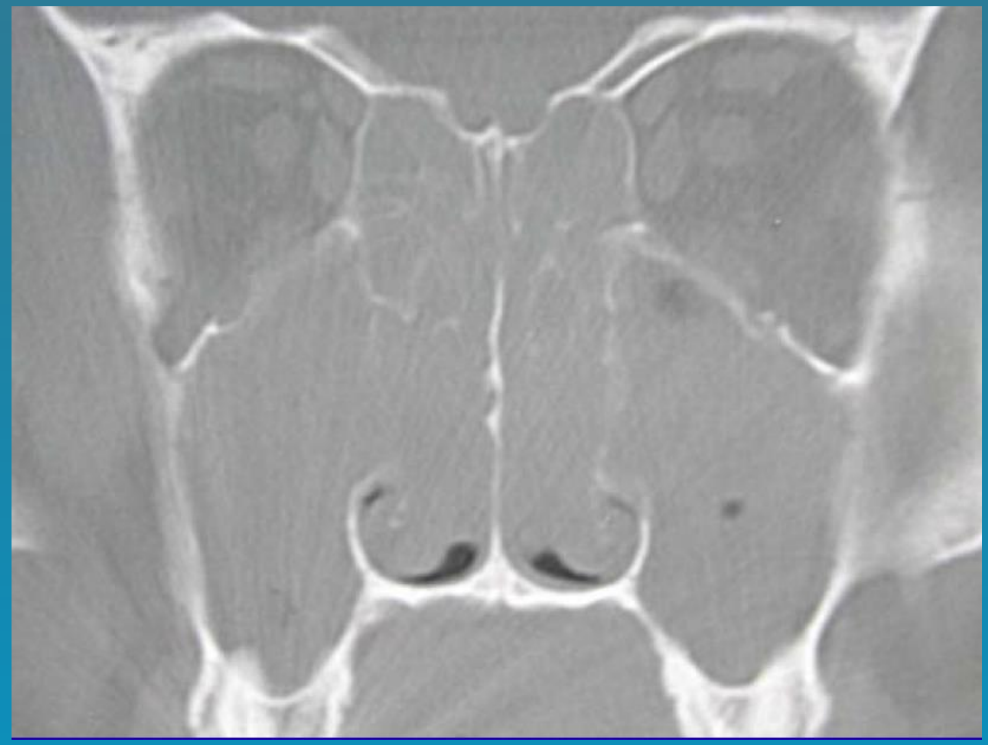
Minor criteria

- Asthma
- Unilateral predominance
- Bone erosion on CT
- Fungal culture
- Charcot-Leyden crystals
- Peripheral eosinophilia

Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. Am J Rhinol Allergy. 2013 Nov-Dec;27(6):473-8.

Eosinophilic CRS: Various forms of CRSwNP

- Eosinophilic inflammatory component, but without all of the AFRS characteristic features
- Polyps may appear similar to those of AFRS
- CT scans bilateral disease - no characteristic hyperdense secretions and less bony erosion into the orbit or skull base



Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. Am J Rhinol Allergy. 2013 Nov-Dec;27(6):473-8.

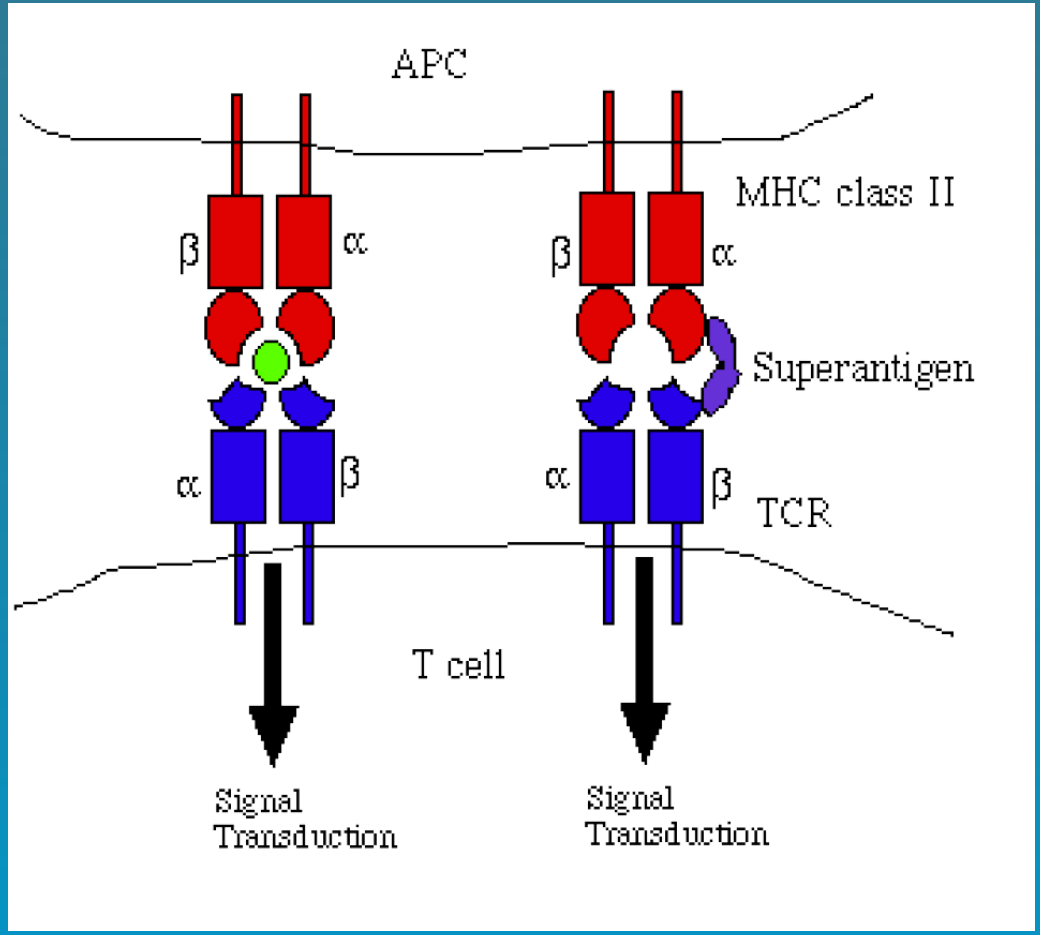
ECRS: N-ERD

- Upregulation of leukotriene production and response
- Leukotrienes increase vascular permeability, inflammatory cell chemotaxis, and smooth muscle constriction
- Produced by eosinophils, mast cells, macrophages, and basophils and found in the nasal secretions of asthmatics

Laidlaw TM et al. Chronic Rhinosinusitis with Nasal Polyps and Asthma. JACIP. 2021;9:1133-1141.

ECRS - Bacterial Superantigen

- Bacteria elicit exotoxins that activate large subpopulations of the T- lymphocyte pool
- Superantigens bind to HLA class II MHC complexes on APCs through TCRs separate from antigen binding sites
- Conventional antigen specificity is bypassed



ECRS - Bacterial Superantigen

- Potential unifying theory for the pathogenesis of many types of ECRS
- Microbial persistence, superantigen production, and host T-lymphocyte response are fundamental components unifying common chronic eosinophilic respiratory mucosal disorders
- Explains how coexisting immune responses, including type 1 hypersensitivity, cellular antigen-specific immune responses, and superantigen-induced T-lymphocyte activation, could contribute to the heterogeneity of the disease
- Evidence of a specific IgE-mediated response to the superantigen
- May act as classic antigens in addition to stimulating nonspecific T-cell activation

Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. Am J Rhinol Allergy. 2013;27:473-8.

Cystic Fibrosis associated Nasal Polyps

- CF patients have a high incidence of nasal polyposis up to 50%
- Non T2 inflammation
- Response to treatment is poor
- Prognosis poor: Numerous surgeries, overall refractory NP
- Children with NP and adult patients with refractory NP and infection (especially with pseudomonas) should be evaluated with a sweat chloride test

Chaaban MR, Walsh EM, Woodworth BA. Epidemiology and differential diagnosis of nasal polyps. Am J Rhinol Allergy. 2013;27:473-8.

Summary

- CRS with NP has a broad impact on QoL and significant economic burden
- The majority of nasal polyps are secondary to eosinophilic inflammation
- Type 2 cytokines including IL-4, IL-5, and IL-13 as well as IgE are expressed in about 80% of CRSwNP mucosal tissue
- Evaluation should include allergy, asthma, and evaluation for N-ERD
- Remember to consider the full ddx and less common etiologies including CF and inverted papilloma