

Sinus Infections, Inflammation and Asthma

آکادمی آسم خدمات تندرستی پایه
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Questions ?

CRS and Asthma

What is role of infections in the airways?

What is role of colonization in the airways?

What is role of impaired epithelium?

What is role of dysregulated immune responses?

KEY POINTS

- ▶ **Rhinosinusitis** is clinically defined as the presence of;
Nasal drainage (anterior or posterior), Nasal congestion, Facial pain/pressure, and/or reduced sense of Smell.
- ▶ **In acute rhinosinusitis**, nasal symptoms last for less than **12 weeks** and inflammation is often secondary to a **viral or bacterial infection**.

KEY POINTS

- ❖ In chronic rhinosinusitis (CRS), nasal symptoms persist for longer than 12 weeks and the inflammation observed is *secondary to*;
 - *Impairments in the epithelial barrier*
 - *Dysregulation of the host immune response*
 - *Potential infections (or colonization) by pathogens.*
- ❖ CRS and asthma have a strong clinical association and share similar pathophysiologic mechanisms in support of the unified airway hypothesis.

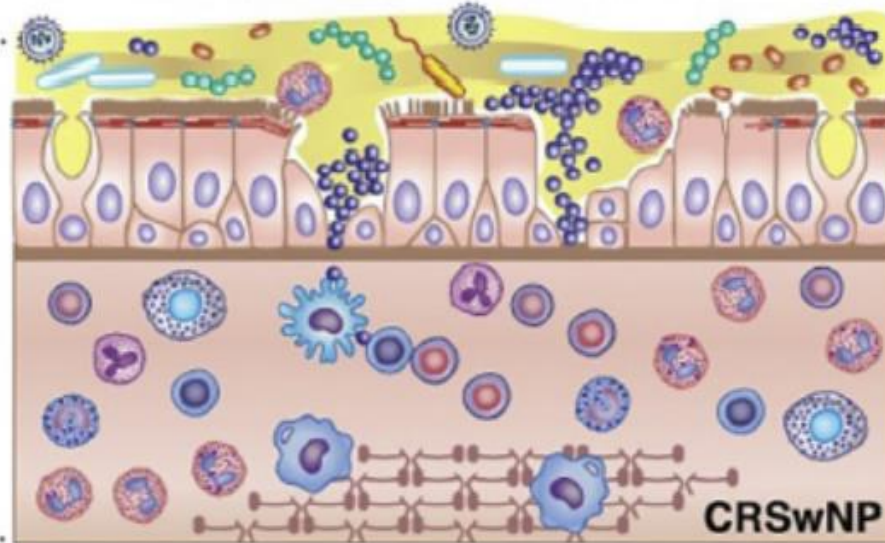
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Bacterial/viral
pathogens
trigger acute
response

ARS

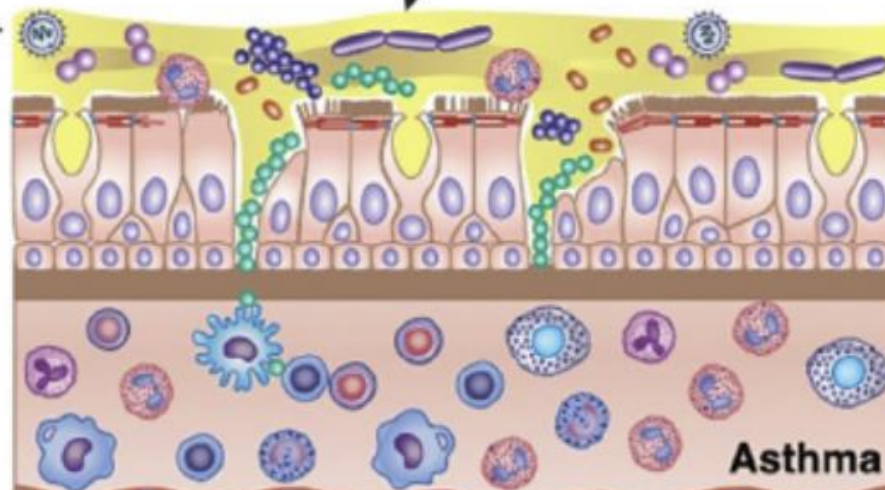
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Barrier defects, immune dysregulation, and pathogens
enable chronic sinonasal/bronchial inflammation



3

Unified airway hypothesis



Unified airway hypothesis

- ▶ The unified airway hypothesis suggests that the nose and lungs are not separate organ systems but instead are part of the same continuum.
- ▶ Inflammation of the upper respiratory tract can affect the lower respiratory tract and vice versa



ACUTE RHINOSINUSITIS

ARS is a clinical diagnosis:
objective confirmation by sinus CT scan or
nasal endoscopy is generally not indicated

Acute rhinosinusitis

- ▶ Acute rhinosinusitis is extremely common. Studies specifying ARS found a disease prevalence of 6% to 15%, with an estimated 0.035% of the population suffering from recurrent episodes
- ▶ in 2015 alone, acute upper respiratory infection (or presumed ARS) was one of the top 20 leading diagnoses for outpatient office visits.

PATHOGENS AND ACUTE RHINOSINUSITIS

- ▶ Certain individuals may be predisposed to rhinosinusitis due to:
 - ❖ allergic rhinitis
 - ❖ atopic disease
 - ❖ smoking history
 - ❖ mechanical obstruction of the sinus ostium
- ▶ The most common viruses isolated in ARS are rhinoviruses and coronaviruses, but RSV, influenza virus, parainfluenza virus, enterovirus, and adenovirus can also be the causes.

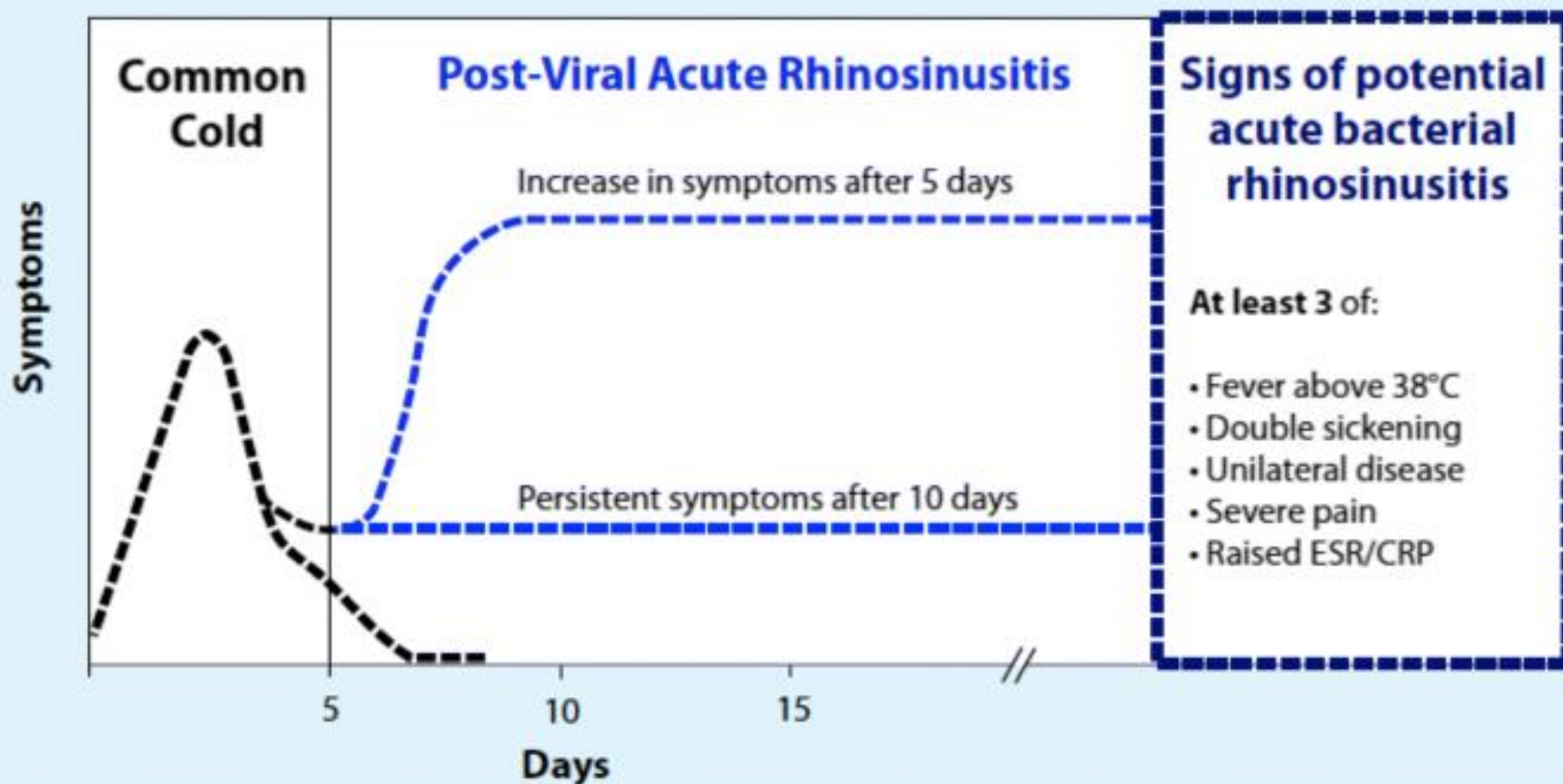
Acute Bacterial Rhinosinusitis

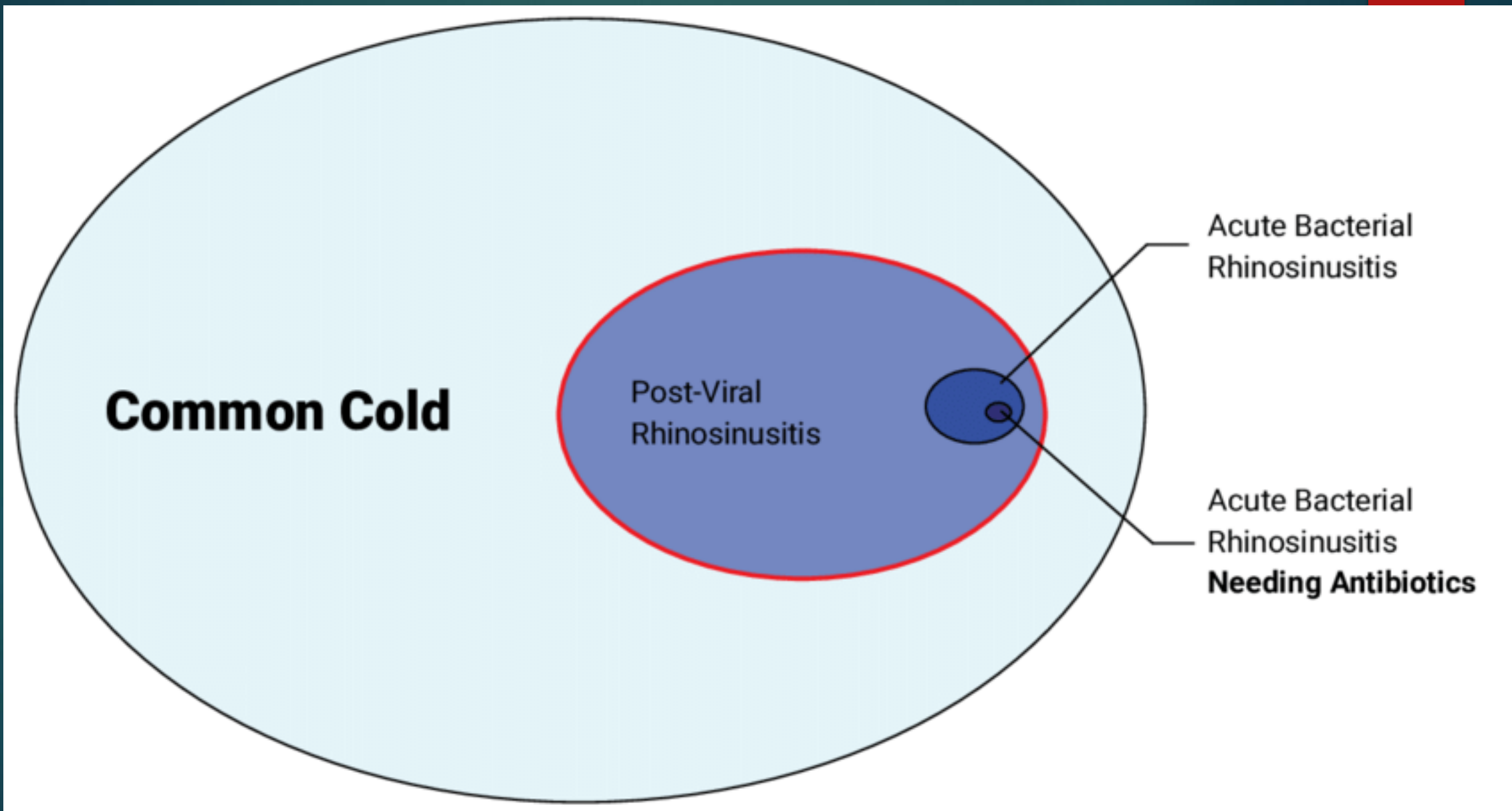
- ▶ If URI/cold symptoms persist for greater than 10 days, or if symptoms initially improve but then worsen again ABRS should be considered.
- ▶ Additional symptoms are persistent purulent nasal drainage, severe facial pain, fever, and dental pain.
- ▶ ABRS generally develops following acute viral rhinosinusitis but overall is not a common occurrence, developing in only 0.5% to 2% of cases



Definition of Acute Rhinosinusitis

Increase in symptoms after 5 days, or persistent symptoms after 10 days
with less than 12 weeks duration





ACUTE RHINOSINUSITIS AND ASTHMA

- ▶ It is well known that acute upper respiratory infections are capable of **exacerbating preexisting asthma**.
- ▶ One episode of ARS **is not** generally associated with **having a higher risk of developing asthma** per se.
- ▶ There are **specific pathogens** associated with ARS that have also been **associated with the development asthma**.

For example, RSV infections in infancy are a risk factor for developing allergic asthma in adolescence

CHRONIC RHINOSINUSITIS

Among patients reporting CRS symptoms, objective evidence of chronic inflammation should be confirmed either by direct visualization with nasal endoscopy or by sinus CT scan

- ▶ A small subset of patients with CRS (20%) also has nasal polyps, which are benign inflammatory outgrowths of the sinonasal mucosa

Is there any similarity between Asthma and CRS?

Epidemiology/burden

- ▶ Using symptom-based criteria, the overall prevalence of **CRS** within a primary care US population was **11.9%**.
- ▶ This is similar to earlier studies in **Europe** that reported the prevalence of CRS to be **10.9%**.

Is there any similarity between Asthma and CRS? epidemiology/burden

- ▶ As a comparison, the lifetime prevalence of asthma in adults was 13.9% according to the 2016 National Health Interview Survey.

Asthma and CRS are prevalent within the US population and can place large socioeconomic and financial burdens on affected patients and the health care system.

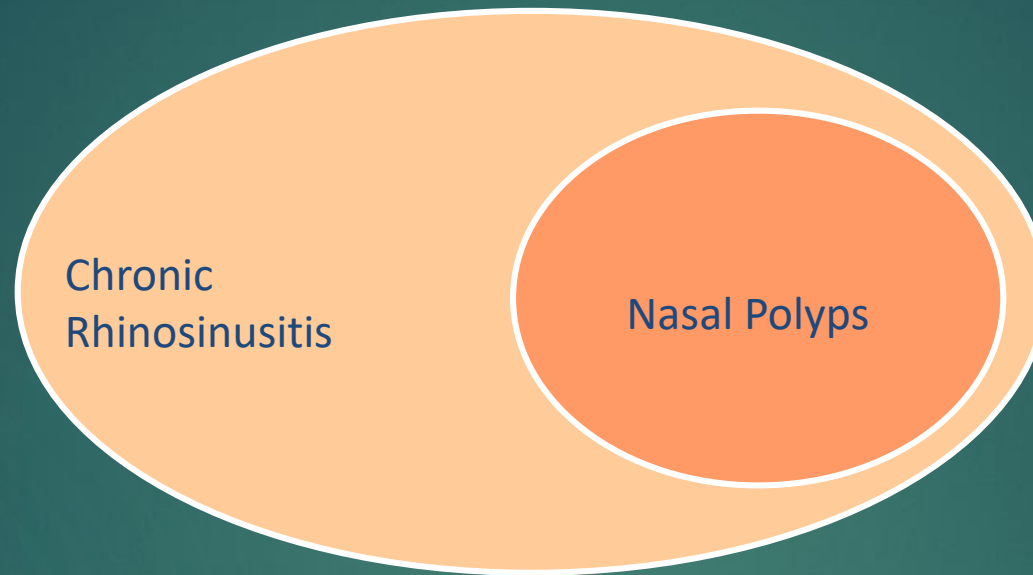
Similarity of nasal polyp/ asthma

PATHOPHYSIOLOGIC OBSERVATIONS

The strongest association between asthma and CRS is observed among patients with CRSwNP

- ▶ Nasal polyps are predominantly characterized by **type 2 inflammation**
- ▶ **Eosinophils** as well as their **granule proteins** (eg, eosinophil cationic protein, eosinophil peroxidase) are elevated in nasal polyps
- ▶ Other type 2 immune cells, including **mast cells**, **basophils**, and group 2 **innate lymphoid cells**, are also increased in nasal polyps
- ▶ Elevated levels of prosurvival and **chemotactic Mediators** such as interleukin **4 (IL-4)**, **IL-5**, **IL-13**, eotaxins, and thymic stromal lymphopoietin

Chronic rhinosinusitis with and without nasal polyps



The spectrum of sinus disease



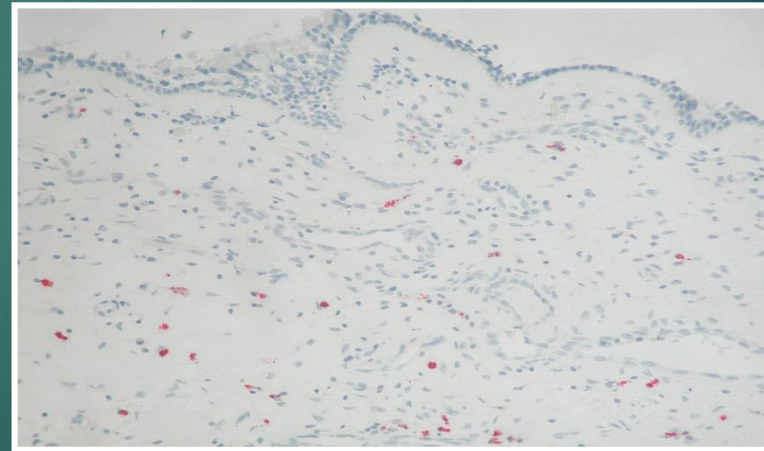
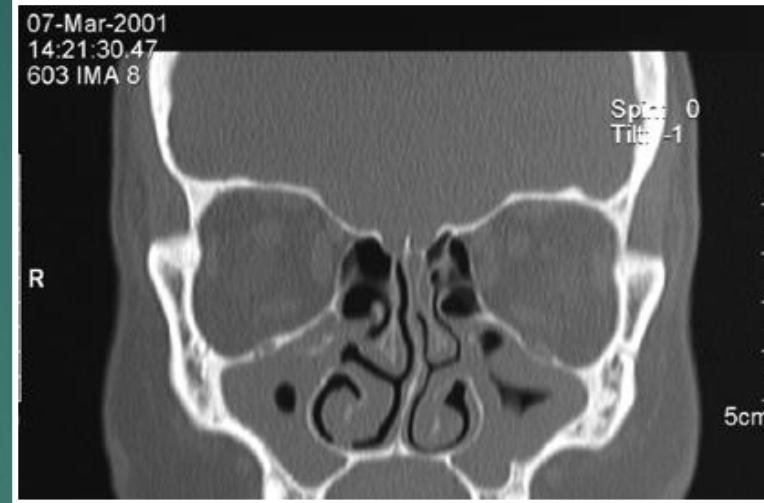
Chronic sinusitis - without nasal polyps

Prevalence of 14.7% in the normal population

Th1 type Inflammation with

- increased $\text{IFN}\gamma$ ↑
- increased $\text{TGF}\beta$ and remodeling

Pathogenic role of infections is unclear



Nasal polyposis

Prevalence approx. 2- 4%

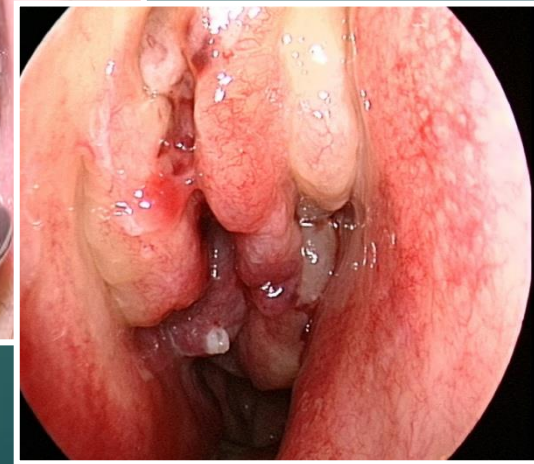
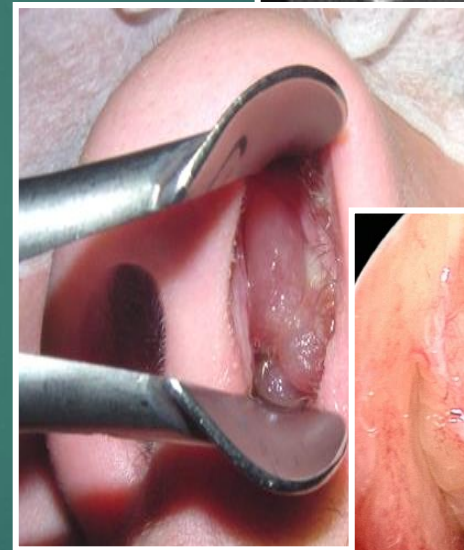
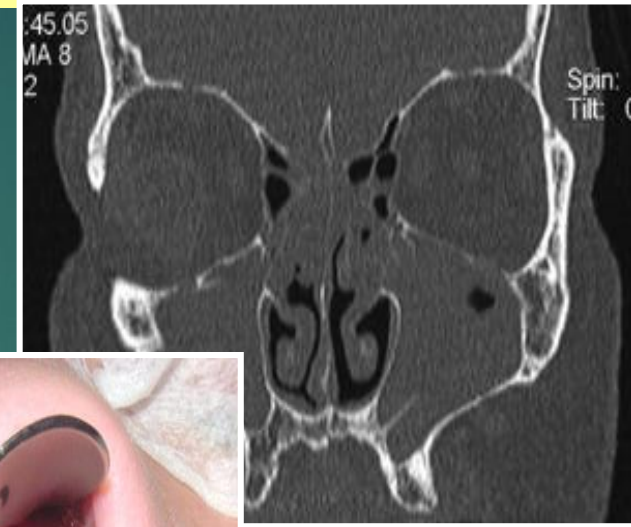
Asthma in approx. 40-65%

Aspirin sensitivity in 10-15%

Mixed cellular infiltrate with
prominent eosinophilia in 90%

Inflammation with

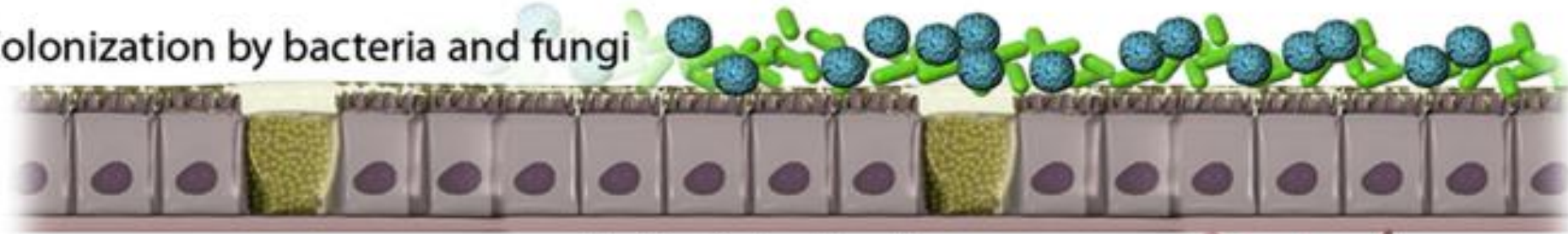
- local IgE production
- increased IL-5, eotaxin, cys-LTs and ECP



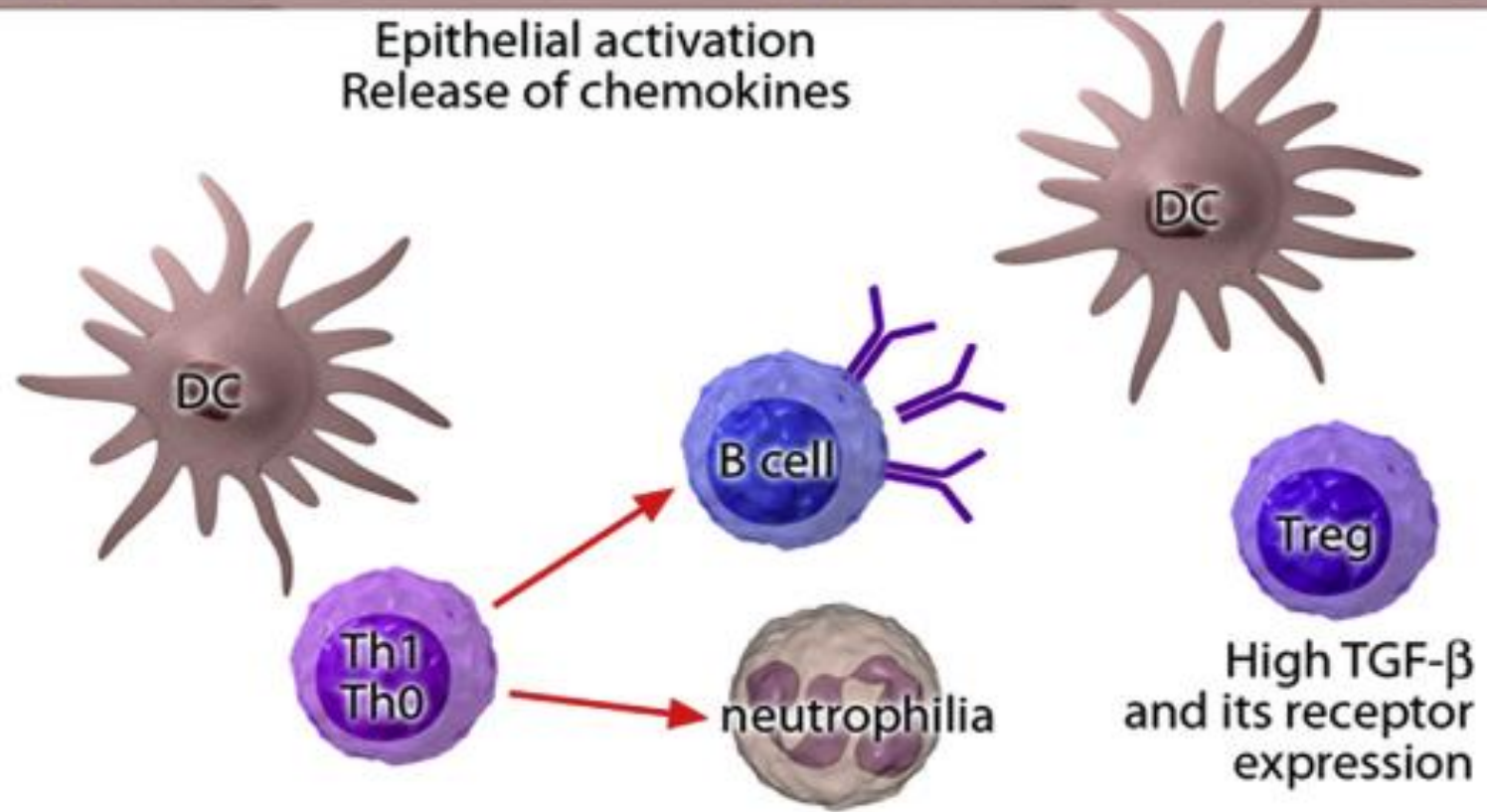
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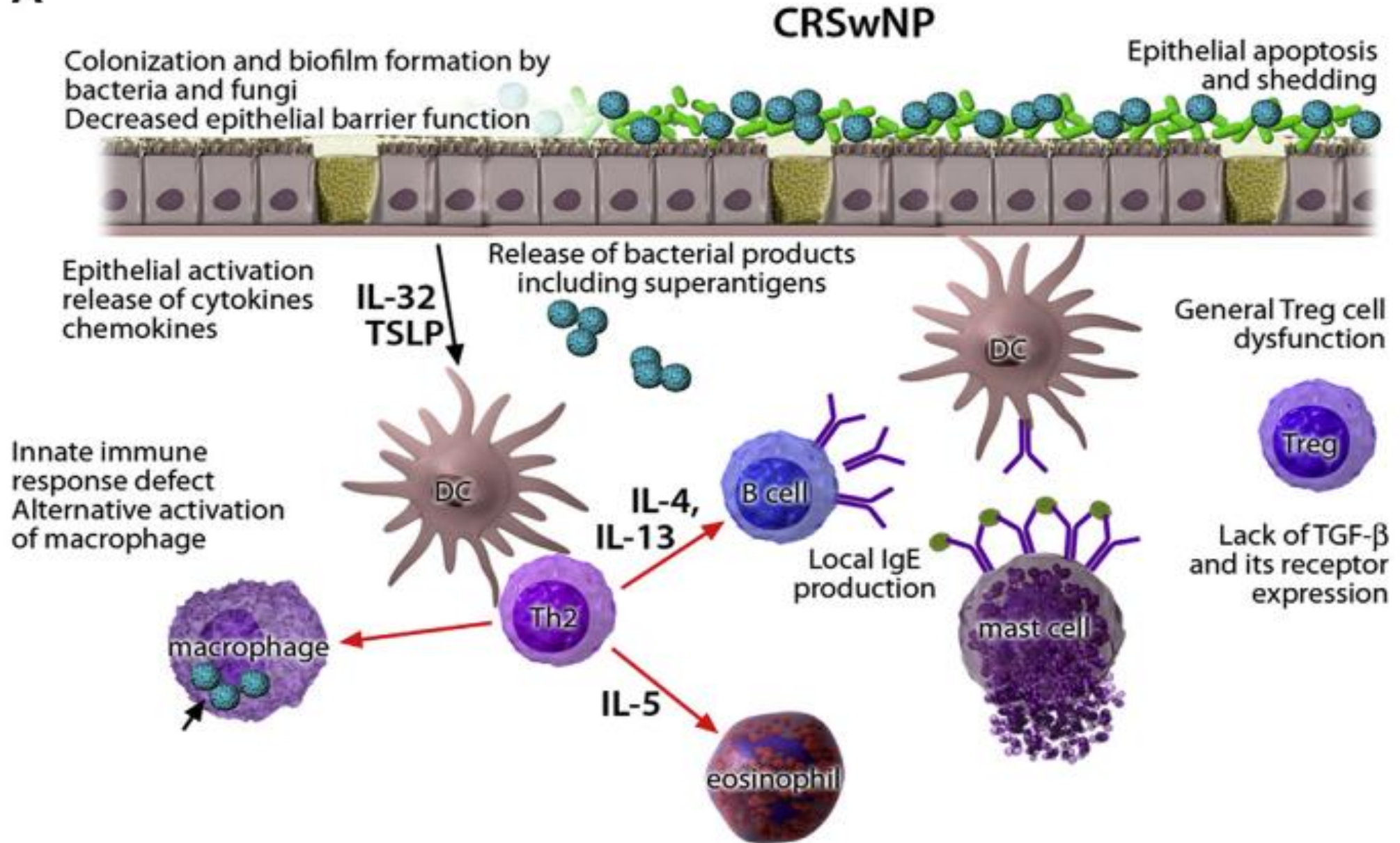
CRSsNP

Colonization by bacteria and fungi



Epithelial activation
Release of chemokines



A

Chronic rhinosinusitis with and without nasal polyps

	<u>Chronic Sinusitis</u>	<u>Nasal Polyposis</u>
Facial pain/pressure	Yes	Sometimes
Facial congestion/fullness	Yes	Yes
Nasal obstruction/blockage	Yes	Yes
Nasal discharge/purulence/postnasal drip	Yes	Yes
Anosmia	Sometimes	Yes
Blood eosinophils	Sometimes	Often
Asthma	Yes	Often
Aspirin exacerbated respiratory disease	Rarely	10% of cases

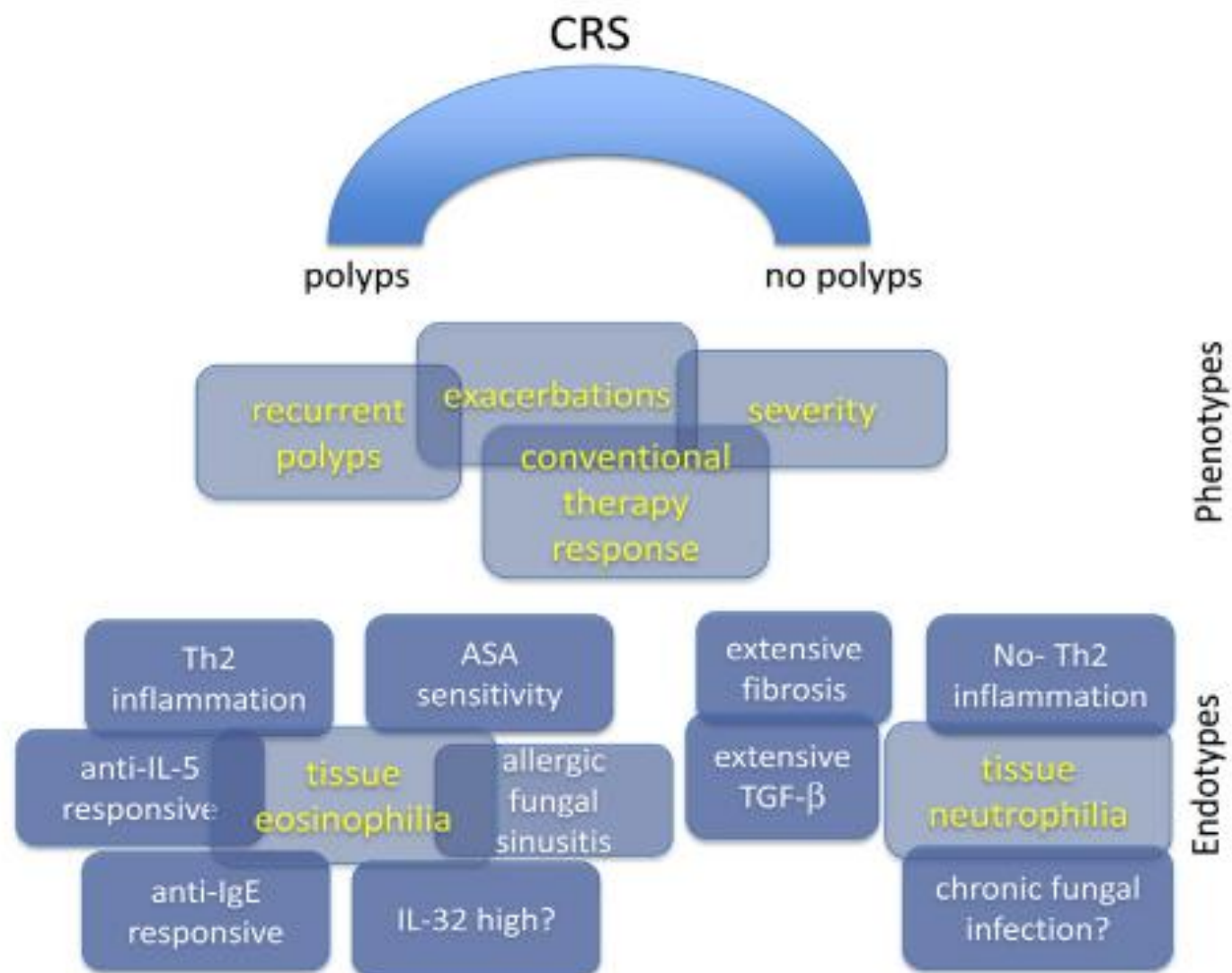


FIG 2. Key phenotypes in relationship to proposed endotypes and their possible associations are shown. ASA, Aspirin.

Ghent Classification of Chronic Rhinosinusitis

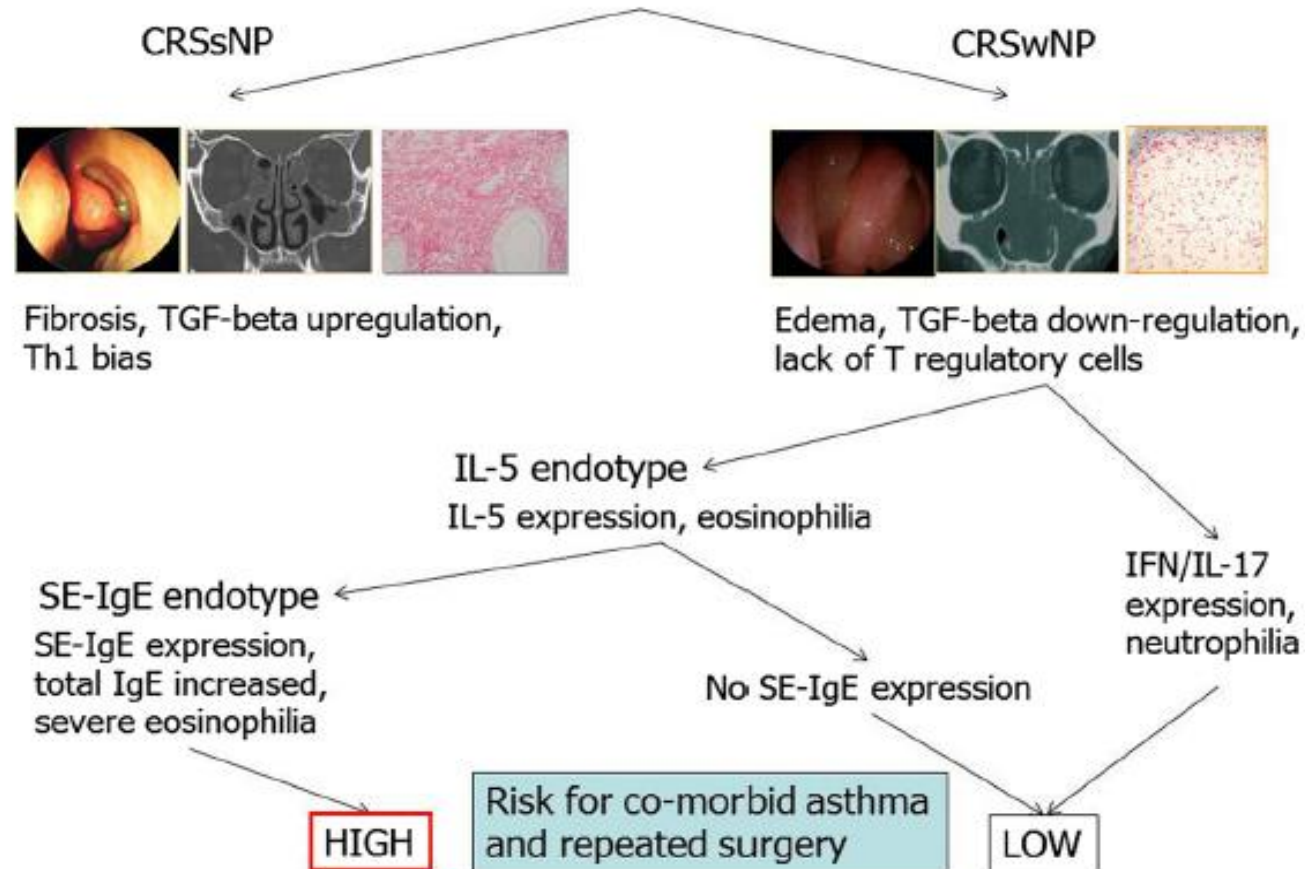


Figure 3 "Pheno- and endotype" CRS. Pheno- and endotyping of CRS based on the recently published findings on asthma comorbidity and recurrence after surgery (Ghent classification of CRS).

