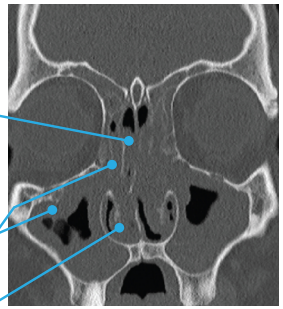
# The burden of chronic rhinosinusitis with nasal polyps

## CRS is an inflammatory condition of the upper airways[1]



CT image of a patient with severe CRSwNP[5]

**Estimates of global CRS prevalence vary: >10%** of the population has been estimated to have CRS based on symptomatic or objective evidence, while the presence of both has produced estimates of **<5%**.[1]

**CRS with nasal polyps (CRSwNP)** represents **18–30%** of all cases of CRS.[1-3]

CRSwNP is characterized by the presence of nasal polyps and chronic sinonasal inflammation, which can result in symptoms such as:[4]


Nasal congestion


Nasal discharge


Facial pain/pressure


Impaired sense of smell

**CRSwNP is characterized by a decreased quality of life, and it places a significant psychological and social burden on patients[6,7]**


Quality of life can be further reduced for patients with CRSwNP and comorbid asthma.[8]

## CRSwNP represents heterogeneous, and often overlapping, endotypes[9]

CRSwNP can be divided into **three endotypes** based on the inflammatory profiles associated with **specific immune cells**, **cytokines**, and **dominant clinical features**:[10]

| Type 1 | Type 2 | Type 3 |
|---|---|---|
| **IFN-γ and IL-12**[10] | **IL-4, IL-5, and IL-13**[10] | **IL-17 and IL-22**[10] |
| **ILC1, NK cells, Th1 cells, CD8+ T cells, and M1 macrophages**[10] | **ILC2, eosinophils, basophils, mast cells, Th2 cells, and M2 macrophages**[10] | **ILC3, neutrophils, and Th17 cells**[10] |
| **Headache and facial pain**[9] | **Loss of sense of smell and comorbid asthma**[9-11] | **Purulent rhinorrhea**[9-11] |

- In the US, Europe and Australia, **Type 2** was the most common endotype of CRSwNP.[10]
- Many patients with CRSwNP have a **mixed endotype**, and ~9% have **no clear endotype**.[9,11a]

## Despite medication and surgery, many patients with CRSwNP have uncontrolled disease[15]


In a survey of **437 physicians**, **70%** reported that **OCS** provide only **temporary symptom relief** in CRSwNP.[16]


**38% of patients** (n=125) experienced **polyp recurrence** 12 months after medical therapy and sinus surgery.[15c]


**~80% of patients** with CRSwNP (n=212) experienced **inadequately controlled symptoms** within 3 to 5 years after surgery.[17d]

## CRSwNP is frequently associated with asthma[8]

**Up to 56%** of patients with **CRSwNP** have **comorbid asthma**[33b]

**8–21%** of patients with severe asthma have a history of nasal polyps[12,13]

In asthmatic patients, comorbid CRSwNP is associated with increased exacerbation frequency, increased symptom severity, and reduced quality of life.[8,14]

### Did you know?[18]

- **NPS** is often used as a primary outcome in clinical trials for CRSwNP.
- NPS uses endoscopy to assess **polyp size** in each nostril, ranging from 0 to 4.
- Total NPS is the sum of the scores for each nostril (0–8); **higher scores indicate more severe disease**.

[a]Patients without a clear endotype are defined as those expressing biomarkers below detection thresholds;[9,11] [b]Range: 5–56%;[33] [c]Medical therapy included, but was not limited to, at least one course of either topical corticosteroids or a course of OCS therapy and at least one course of broad-spectrum or culture-directed antibiotics;[15] [d]Control was assessed using mean total VAS, SNOT-22, and SF-36 scores in patients with CRSwNP 3–5 years after FESS.[17]

CRS, chronic rhinosinusitis; CRSwNP, chronic rhinosinusitis with nasal polyps; CT, computed tomography; EMT, epithelial-mesenchymal transition; FESS, functional endoscopic sinus surgery; IFN, interferon; IL, interleukin; ILC, innate lymphoid cell; NK, natural killer; NPS, nasal polyp score; OCS, oral corticosteroid(s); PRR, pattern recognition receptor; SF-36, Short Form 36-item Health Survey; SNOT-22, Sino-Nasal Outcome Test-22; Th, T helper; tPA, tissue plasminogen activator; TSLP, thymic stromal lymphopoietin; VAS, visual analog scale.

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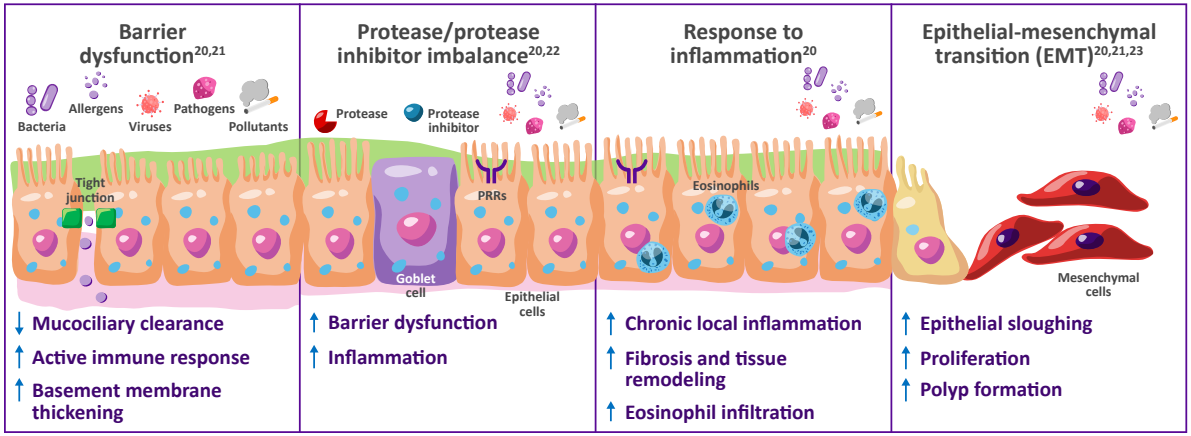
# The central role of the epithelium in CRSwNP

## The nasal epithelium is significantly altered in CRSwNP and plays a critical role in the disease[19]




## Role of epithelial cytokines in CRSwNP

Epithelial cytokines are released in response to environmental irritants, such as allergens, pathogens, and pollutants.[26]

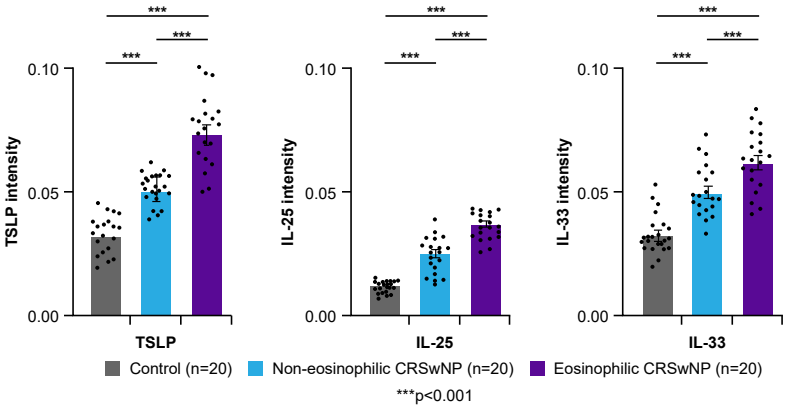
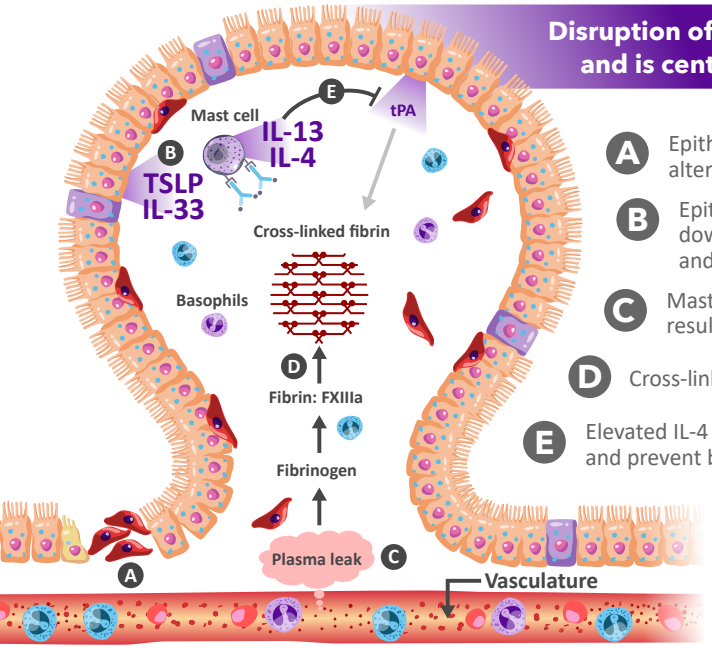



Figure adapted from Zhang M, et al. *Int Immunopharmacol*. 2023;121:110559

**TSLP**, **IL-25**, and **IL-33** are increased in nasal mucosal epithelial tissue from patients with CRSwNP compared with controls, with the highest levels observed in eosinophilic CRSwNP.[26]

**TSLP, the TSLP receptor, and the IL-33 receptor correlated with increased disease severity and Type 2 inflammation[27]**




### Disruption of the epithelium augments inflammation and is central to nasal polyp formation:*

**A** Epithelial damage triggers EMT; mesenchymal cells alter inflammatory and remodeling processes.[23,24]

**B** Epithelial cytokines TSLP and IL-33 drive multiple downstream processes, including mast cell activation and production of IL-4, IL-5, and IL-13.[20]

**C** Mast cells and basophils drive mucosal edema, resulting in plasma leakage.[20]

**D** Cross-linked fibrin forms a dense mesh and promotes edema.[20,22]

**E** Elevated IL-4 and IL-13 suppress the expression of tPA and prevent breakdown of fibrin.[20,25]

### Did you know?

CRSwNP and asthma share similar features of **airway remodeling and inflammation**.[28,29]

Fibrosis and matrix deposition[28] | Impaired mucociliary clearance[28] | Immune cell infiltration[28] | Epithelial cytokine production[29] | Impaired epithelial integrity[28]

Their shared pathophysiology and frequent co-occurrence support the concept of **united airways disease**, in which the upper and lower airways are linked anatomically, histologically, and immunologically.[30-32]

*The role of IL-25 in nasal polyp formation requires further elucidation.

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