

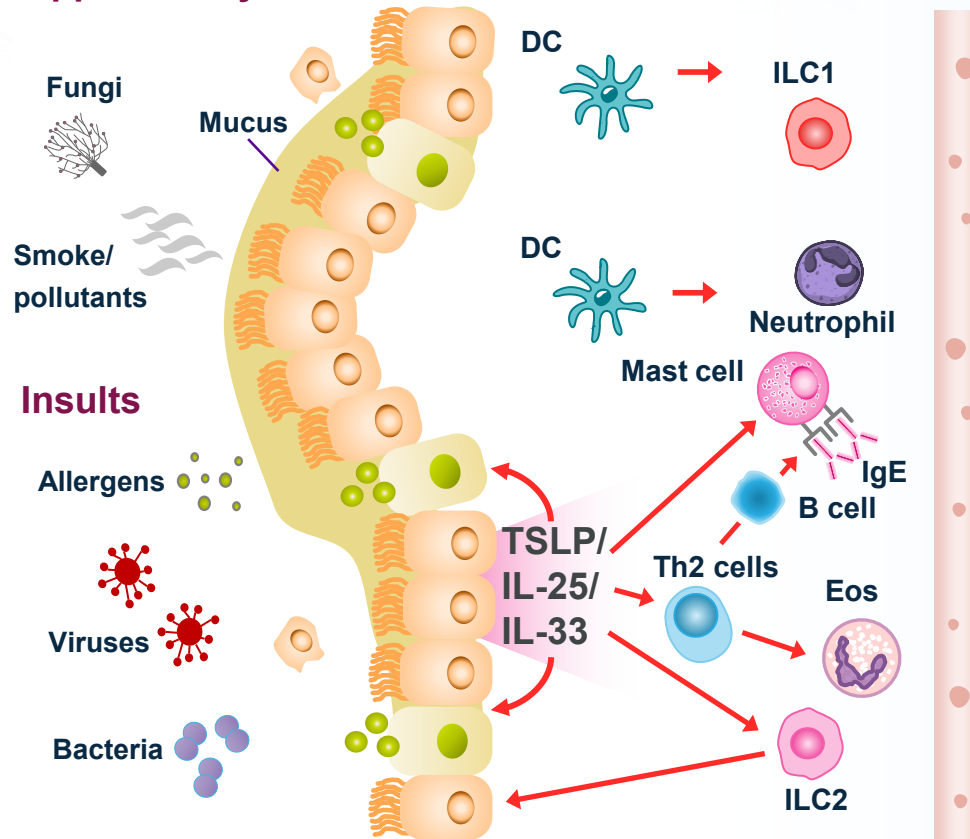
From epithelial dysfunction to remission

Giorgia Carlotta Pipolo
University of Milan, Italy



Upper and lower airways diseases have heterogeneous and overlapping inflammatory pathways:¹⁻¹¹ CRSwNP

Upper airway



Disease pathology²

- Chronic inflammation
- Nasal remodelling
- Nasal polyp formation

CT scans



Endoscopy¹³



Clinical manifestations may include²

- Exacerbations
- Nasal symptoms (rhinorrhoea, nasal congestion, olfactory dysfunction)
- Need for surgery
- Sleep disturbance

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CT image courtesy of Professor Claire Hopkins; used with permission. Endoscopy image from Canevari FR, et al. *Front Allergy* 2023;4:1237131. Licenced under CC BY 4.0 from: <https://creativecommons.org/licenses/by/4.0/>. Accessed August 2026.

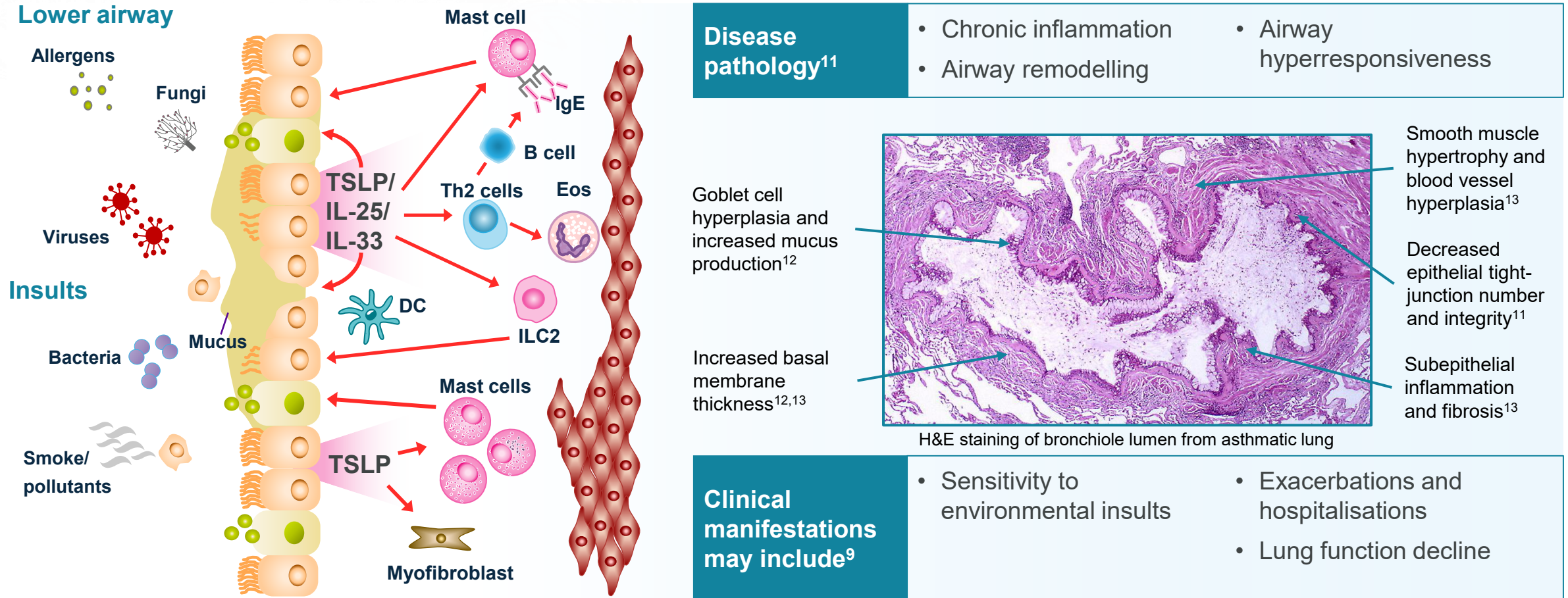
CT, computed tomography; CRSwNP, chronic rhinosinusitis with nasal polyps; DC, dendritic cell; Eos, eosinophil(s); IgE, immunoglobulin E; ILC, innate lymphoid cell; Th, T helper; TSLP, thymic stromal lymphopoietin.

1. Calderon AA, et al. *Eur Respir Rev*. 2023;32(167):220144; 2. Fokkens WJ, et al. *Rhinology*. 2020;58(suppl. S29):1-464; 3. Staudacher AG, et al. *Ann Allergy Asthma Immunol*. 2020;124(4):318-25; 4. Caminati M, et al. *Allergy*. 2024;79(5):1134-45; 5. Yli ACA, et al. *Allergy*. 2018;73(10):1964-78; 6. Fokkens W and Reitsma S. *Otolaryngol Clin North Am*. 2023;56(1):1-10; 7. Brightling C and Greening N. *Eur Respir J*. 2019;54(2):1900651; 8. Bousquet J, et al. *Nat Rev Dis Primers*. 2020;6(1):95; 9. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. <https://ginasthma.org/wp-content/uploads/2026/05/GINA-2026-Strategy-Report-WMS.pdf>. 2026. Accessed August 2026; 10. Roan F, et al. *J Clin Invest*. 2019;129(4):1441-51; 11. Kato A. *Allergol Int*. 2015;64(2):121-30; 12. Schleimer RP. *Annu Rev Pathol*. 2017;12:331-57; 13. Canevari FR, et al. *Front Allergy*. 2023;4:1237131.

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Upper and lower airways diseases have heterogeneous and overlapping inflammatory pathways:¹⁻¹⁰ asthma



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Refer to Caminati M et al. *Allergy*. 2024;79(5):1134–45. Licenced under CC BY-NC 4.0 from: <https://creativecommons.org/licenses/by-nc/4.0/>. Accessed August 2026. Histology image from Asthma Case 103 by Atlas of Pulmonary Pathology.

https://www.flickr.com/photos/pulmonary_pathology/3705143121. Accessed August 2026. Licenced under CC BY-SA 2.0. <https://creativecommons.org/licenses/by-sa/2.0/>. Accessed August 2026.

DC, dendritic cell; Eos, eosinophil(s); FeNO, fractional exhaled nitric oxide; H&E, hematoxylin and eosin; IgE, immunoglobulin E; ILC, innate lymphoid cell; Th, T helper; TSLP, thymic stromal lymphopoietin.

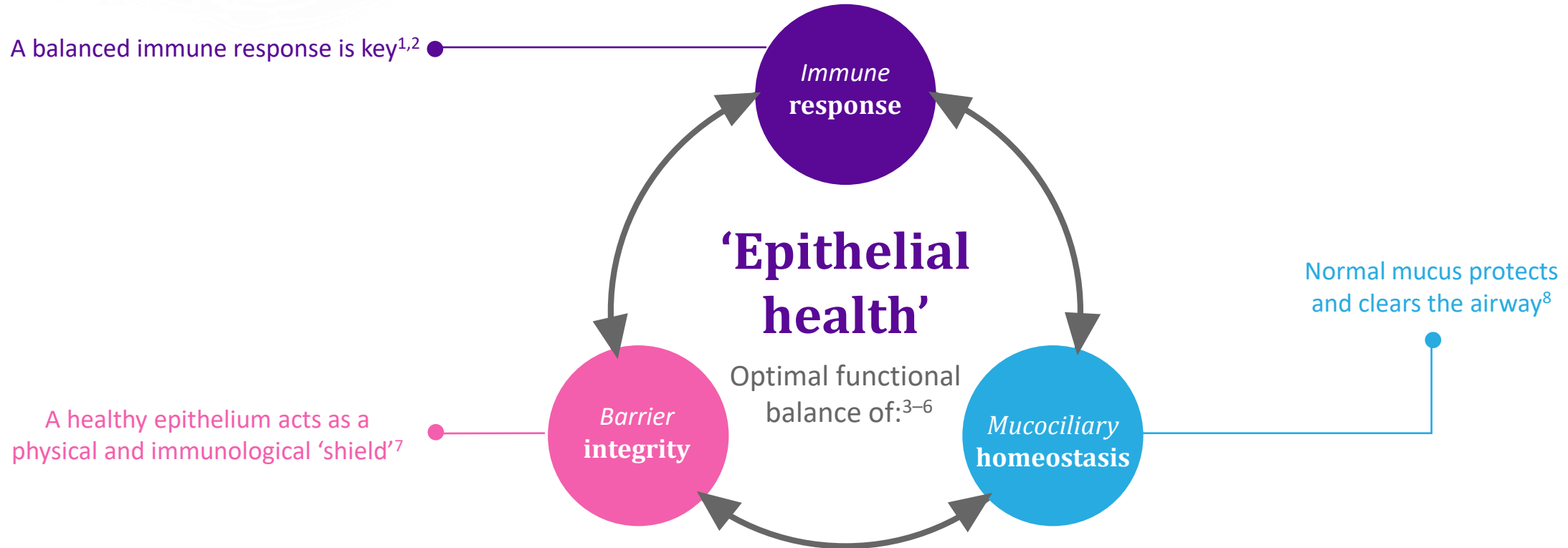
1. Calderon AA, et al. *Eur Respir Rev*. 2023;32(167):220144; 2. Fokkens WJ, et al. *Rhinology*. 2020;58(suppl. S29):1-464; 3. Staudacher AG, et al. *Ann Allergy Asthma Immunol*. 2020;124(4):318–25; 4. Caminati M, et al. *Allergy*. 2024;79(5):1134–45; 5. Yli ACA, et al. *Allergy*. 2018;73(10):1964–78; 6. Fokkens W and Reitsma S. *Otolaryngol Clin North Am*. 2023;56(1):1–10; 7. Brightling C and Greening N. *Eur Respir J*. 2019;54(2):1900651; 8. Bousquet J, et al. *Nat Rev Dis Primers*. 2020;6(1):95; 9. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. <https://ginasthma.org/wp-content/uploads/2026/05/GINA-2026-Strategy-Report-WMS.pdf>. 2026. Accessed August 2026; 10. Roan F, et al. *J Clin Invest*. 2019;129(4):1441–51; 11. Bartemes KR and Kita H. *Clin Immunol*. 2012;143(3):222–35; 12. Holgate ST. *Immunol Rev*. 2011;242(1):205–19; 13. Cohen L, et al. *Am J Respir Crit Care Med*. 2007;176(2):138–45.

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'Epithelial health' refers to the optimal structural integrity and functional balance of the airway epithelial layer

'Epithelial health' is maintained through three core domains

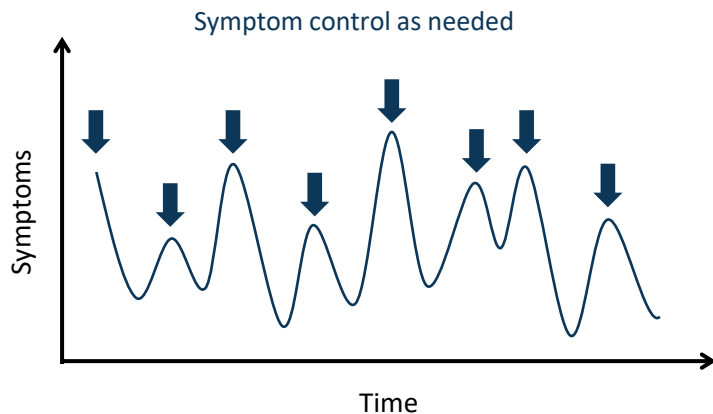


Restoring epithelial health may be a critical step towards clinical remission and disease modification

Greater understanding of airway disease mechanisms is transforming treatment goals in asthma and CRSwNP^{1,2}

Traditional management

Reactive disease control



'One size fits all', reactive treatment:^{1,2}

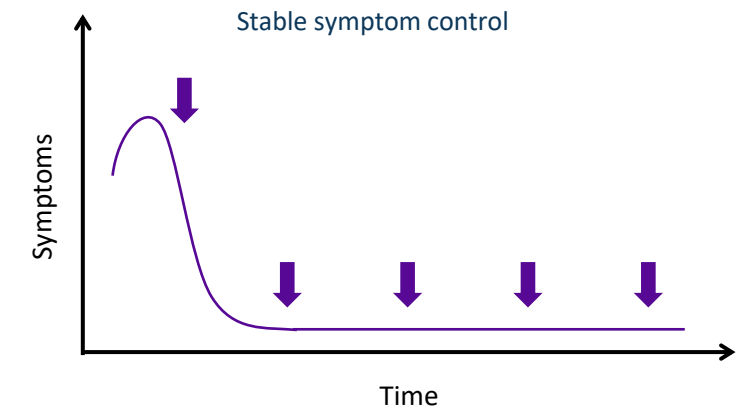
- Recurrent acute therapy
- Aimed to relieve symptoms
- Associated with major adverse effects

Increasing understanding of airway disease pathophysiology¹⁻⁷



Evolving biologic era

Targeted and proactive management



Individualised, proactive prevention:

- 'Treat to target'¹
- Aims for disease modification and remission¹
- May reduce reliance on recurrent acute therapy⁷

CRSwNP, chronic rhinosinusitis with nasal polyps.

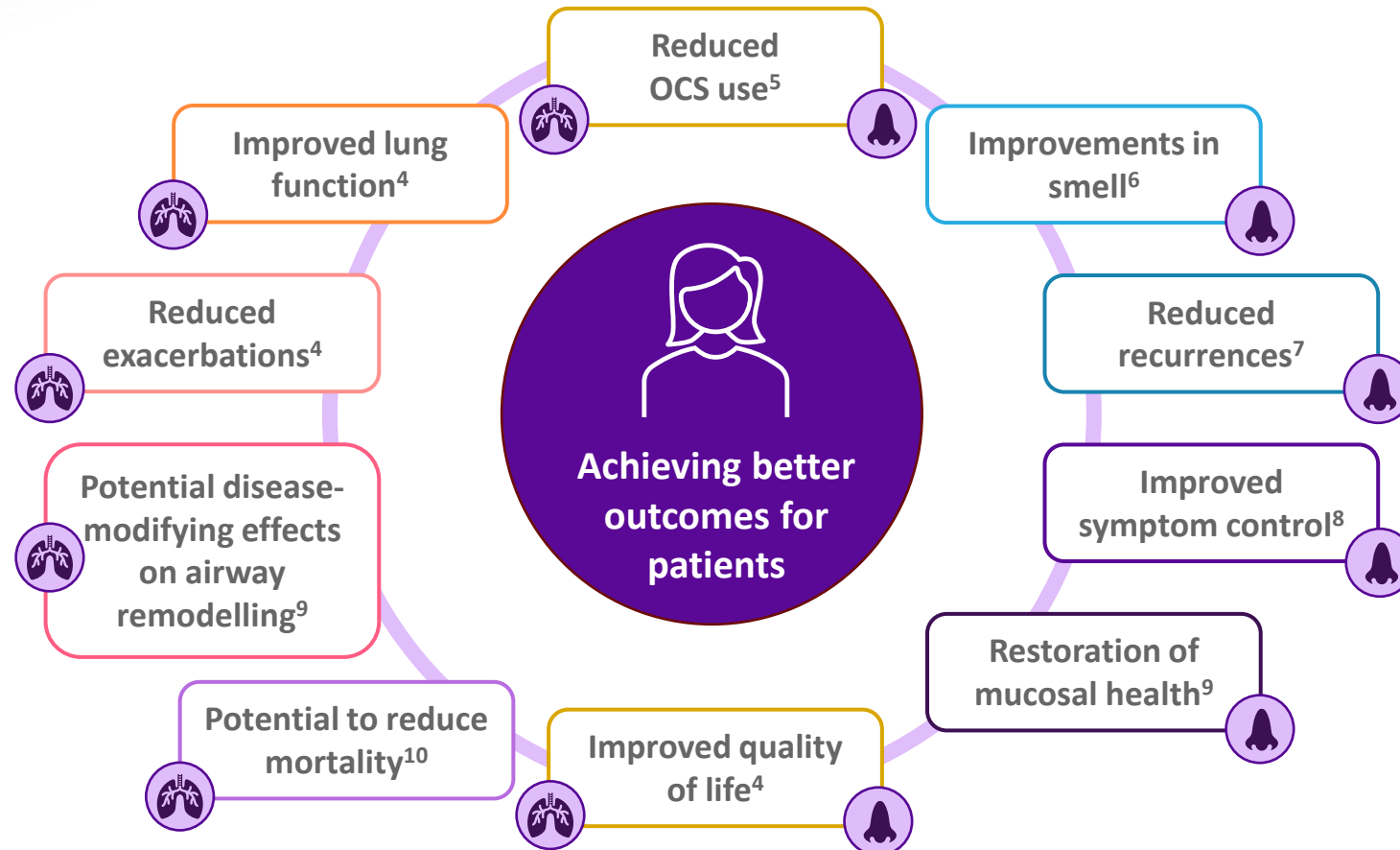
1. Lommatzsch M, et al. *Lancet*. 2022;399(10335):1664–8; 2. Stevens WW, et al. *J Allergy Clin Immunol Pract*. 2016;4(4):565–72; 3. Howell I, et al. *J Exp Med*. 2023;220(7):e20221212; 4. Woodruff PG, et al. *Am J Respir Crit Care Med*. 2009;180(5):388–95; 5. Wenzel SE. *Nat Med*. 2012;18(5):716–25; 6. Miller RL, et al. *J Allergy Clin Immunol*. 2021;148(6):1430–41; 7. Hellings PW, et al. *Allergy*. 2024;79(5):1123–33.

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Advances in biologic therapies are redefining treatment goals towards remission in airway disease¹⁻³

Biologic therapies targeting key inflammatory pathways have improved outcomes across airway diseases, making sustained disease control and clinical remission increasingly achievable goals¹⁻³



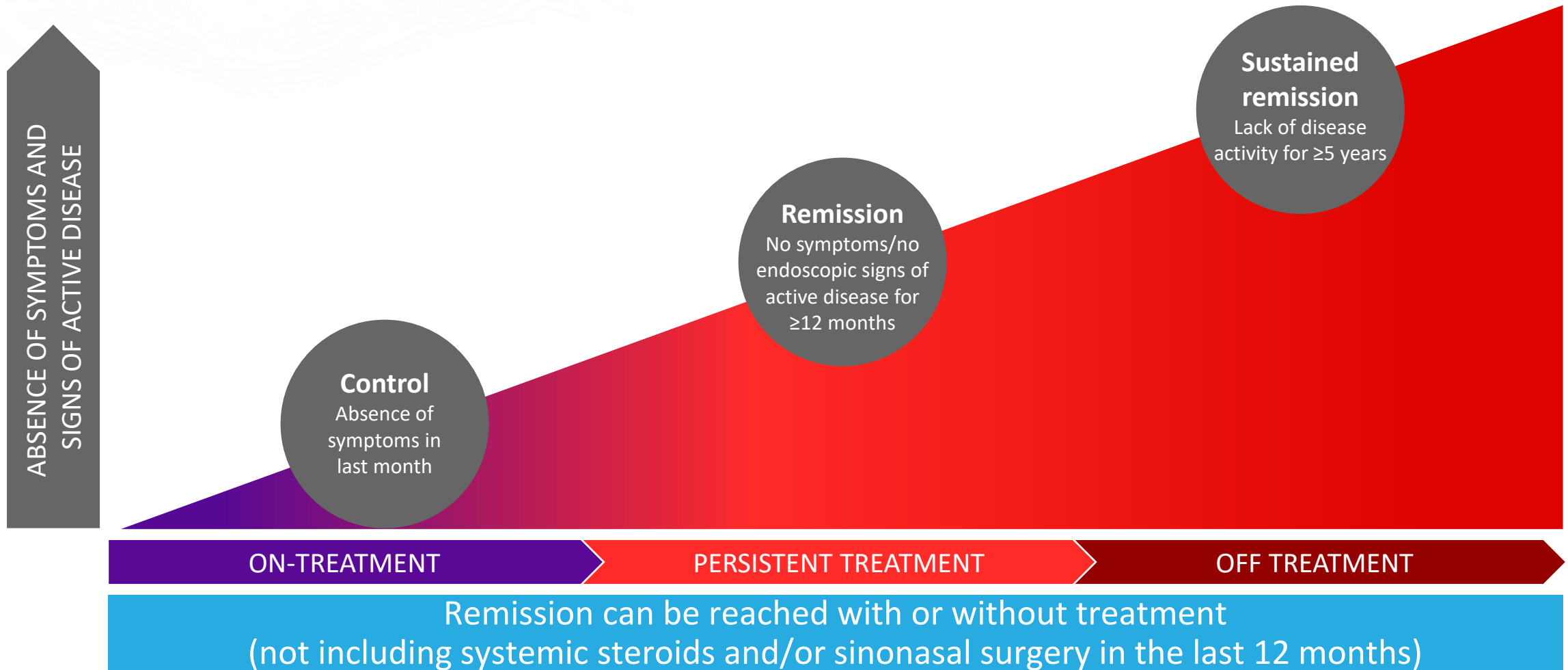
OCS, oral corticosteroids.

1. Lommatzsch M, et al. *Lancet*. 2022;399(10335):1664–8; 2. Hellings PW, et al. *Allergy*. 2024;79(5):1123–33; 3. McDowell PJ, et al. *Eur Respir J*. 2023;62(6):2300819; 4. Carr TF, et al. *Adv Ther*. 2024;41(7):2987–90; 5. Wechsler ME, et al. *Lancet Respir Med*. 2022;10(7):650–60; 6. Tanase MI, et al. *Cureus*. 2025;17(1):e77804; 7. Patel GB and Peters AT. *Ear Nose Throat J*. 2021;100(1):44–7; 8. Pavord I, et al. *J Allergy Clin Immunol*. 2025;156(3S):S15–S19; 9. Varricchi G, et al. *Allergy*. 2022;77(12):3538–52; 10. Caminati M, et al. *World Allergy Organ J*. 2021;14(2):100502

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Moving from disease control to remission and sustained remission in airway diseases



Refer to Fokkens WJ, et al. *Rhinology*. 2024;62(3):287–98. Some language has been amended.

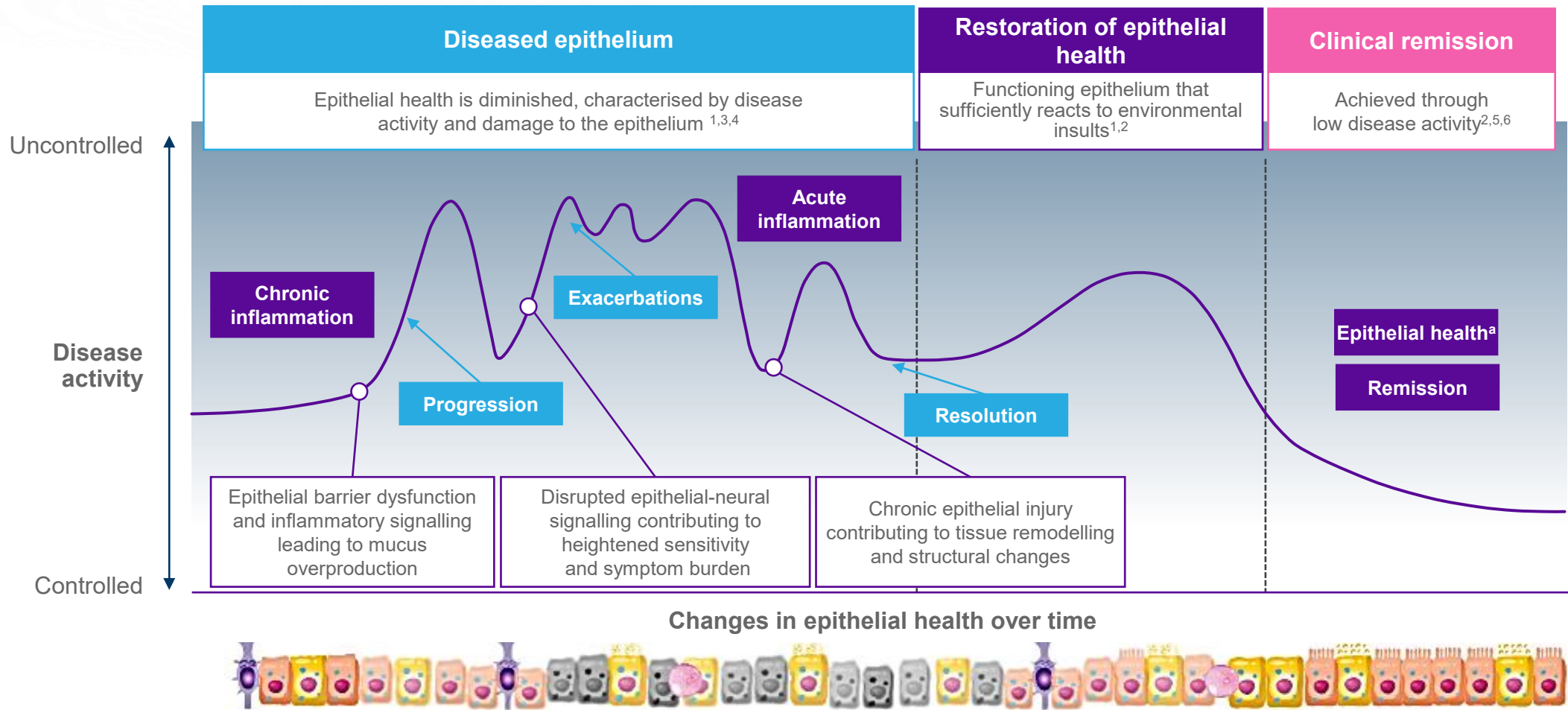
EPOS, European Position Paper on Rhinosinusitis and Nasal Polyps; EUFOREA, European Forum for Research and Education in Allergy and Airway Diseases.

Fokkens WJ, et al. *Rhinology*. 2024;62(3):287–98.

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Restoring epithelial health may be a critical step in achieving remission^{1,2}



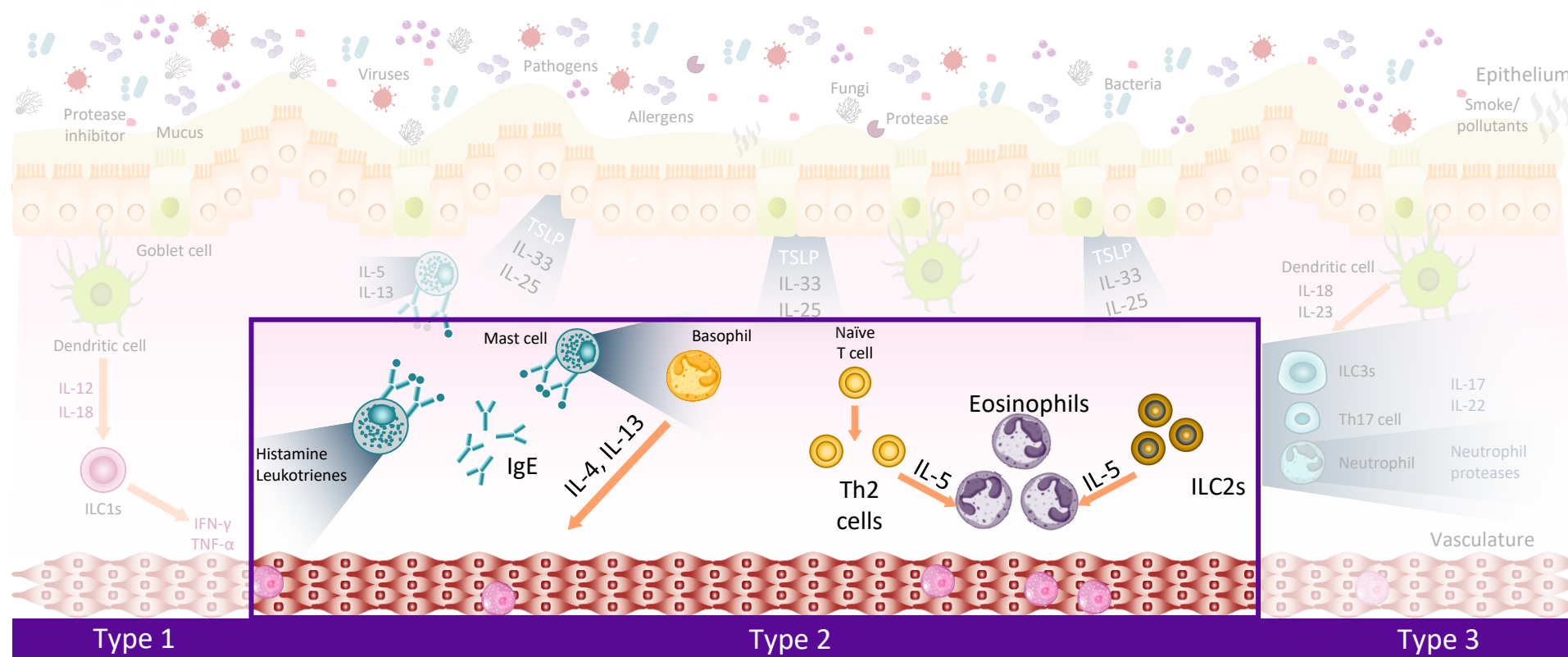
^aThe extent to which epithelial health is restored in remission is still to be fully elucidated;^{2,7} however, it has been proposed that normalisation of underlying pathology, including epithelial function, is essential for complete remission.^{2,8}

1. Russell RJ, et al. *Eur Respir J.* 2024;63(4):2301397; 2. Brightling CE, et al. *Eur Respir Rev.* 2024;33:240221; 3. Heijink IH, et al. *Allergy.* 2020;75:1902–17; 4. Porsbjerg C, et al. *Lancet.* 2023;401:858–73; 5. Vatrella A, Maglio A. *Expert Rev Respir Med.* 2025;19:1–5; 6. Fokkens WJ, et al. *Rhinol.* 2024;62(3):287–98; 7. Carpaij OA, et al. *Pharmacol Ther.* 2019;201:8–24; 8. Thomas D, et al. *Eur Respir J.* 2022;60:2102583.

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Targeting downstream inflammatory pathways has improved patient outcomes, while highlighting the complexity of residual inflammation¹⁻⁴



Refer to Caminati M, et al. *Allergy*. 2024;79(5):1134–45.

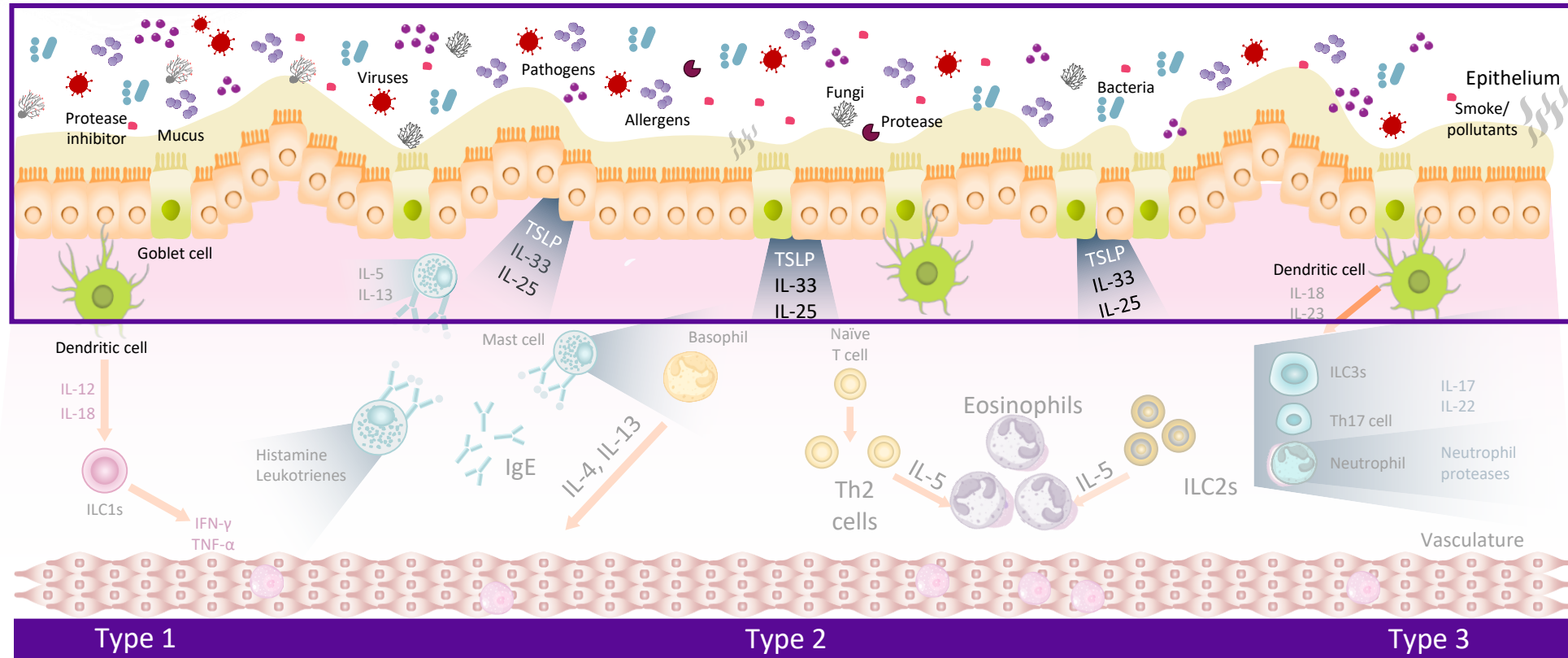
CRSwNP, chronic rhinosinusitis with nasal polyps; IFN- γ , interferon gamma; IgE, immunoglobulin E; IL, interleukin; ILC, innate lymphoid cell; T1, type 1; T2, type 2; T3, type 3; Th, T helper; TNF- α , tumour necrosis factor alpha; TSLP, thymic stromal lymphopoietin.

1. Porsbjerg CM, et al. *Eur Respir J*. 2020;56(5):2000260; 2. Caminati M, et al. *Allergy*. 2024;79(5):1134–45; 3. Fokkens WJ, et al. *Rhinol*. 2020;58(Suppl. S29):1–464; 4. Walsh GM. *Antibodies (Basel)*. 2025;14(4):101.

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Targeting upstream epithelial cytokines potentially offers an opportunity to address multiple inflammation pathways^{1,2}



Refer to Caminati M, et al. *Allergy*. 2024;79(5):1134–45.³

CRSwNP, chronic rhinosinusitis with nasal polyps; IFN- γ , interferon gamma; IgE, immunoglobulin E; IL, interleukin; ILC, innate lymphoid cell; Th, T helper; TNF- α , tumour necrosis factor alpha; TSLP, thymic stromal lymphopoietin.

1. Kato A and Kita H. *Nat Rev Immunol*. 2025;25(8):569–87; 2. Hellings PW and Steelant B. *J Allergy Clin Immunol*. 2020;145(6):1499–509; 3. Caminati M, et al. *Allergy*. 2024;79(5):1134–45.

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Patient case: persistent CRSwNP burden despite controlled asthma

38-year-old man with CRSwNP and severe asthma

Clinical context

- Asthma since childhood; CRSwNP diagnosed at 25 years of age
- House dust mite allergy
- Prior high-dose OCS exposure
- Osteoporosis diagnosed following vertebral fracture
- Switch to multidisciplinary approach in 2018, leading to initiation of anti-IL-5 for severe asthma
- 2019: sinus surgery for CRSwNP

Condensed clinical journey

2018 Uncontrolled severe asthma despite high-dose OCS; anti-IL-5 started

2019 Asthma controlled; CRSwNP uncontrolled for parts of the year; sinus surgery

2024 Asthma controlled, but CRSwNP recurrence on anti-IL-5

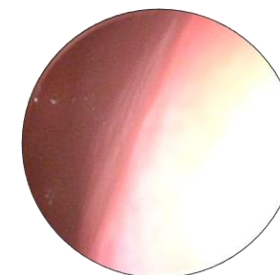
2025 Switch to anti-TSLP; reassessed 6 months later

CRSwNP recurrence while asthma appears controlled

	2024: on anti-IL-5		6 months after switch
	Before		After
Nasal obstruction (VAS)	7	→	2
Rhinorrhoea (VAS)	8	→	3
Nasal polyp score	5	→	2
Smell test	9/16	→	13/16
Frontal headache (VAS)	2	→	2
SNOT-22	45	→	16
ACT	23	→	24
FeNO	48 ppb	→	35 ppb
FEV ₁	4.58L 106%	→	4.0L
FVC	5.48L 98%	→	4.68L

Clinical question: is 'control' sufficient when CRSwNP continues to recur?

Upper airway findings



Endoscopy at recurrence



Endoscopy after 6 months



CT: osteitis and incomplete ethmoidectomy noted

Patient-relevant change

- Sleep improved
- Smell returned, with renewed appreciation of food
- Able to participate in sports again

Key message: In patients with united airways disease, assessment of clinical remission should encompass asthma, sinonasal signs and symptoms, and everyday quality of life.

Actual patient case provided by Dr Pipolo. Individual results may vary – please consult the relevant SmPC for further information. Maintenance inhaler regimen is unknown. The endoscopy videos were obtained from Dr Pipolo's clinic and are used with the patient's consent.

ACT, Asthma Control Test; CRSwNP, chronic sinusitis with nasal polyps; CT, computed tomography; EoS, eosinophil; FeNO, fractional exhaled nitric oxide; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; IgE, immunoglobulin E; IL, interleukin; NPS, nasal polyp score; SNOT-22, Sino-Nasal Outcome Test; TSLP, thymic stromal lymphopoietin; VAS, visual analogue scale.

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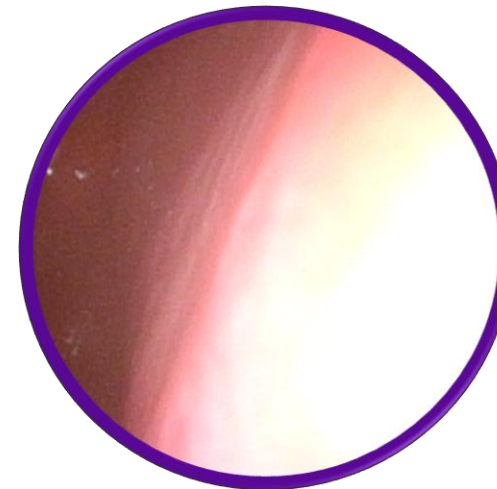
- ❖ The goal of the ENT and pulmonologist is not only control but remission^{1,2}
- ❖ Addressing epithelial dysfunction and restoring immune balance requires a multifaceted approach, including targeting upstream epithelial alarmins and downstream inflammatory cytokines^{3–5}
- ❖ Sustained modulation of the inflammatory cascade may help address the persistent inflammation associated with epithelial dysfunction^{3,4}
- ❖ Clinicians assess remission through objective measures, while patients experience it through sustained improvements in symptoms and quality of life²
- ❖ Multidisciplinary management is essential to assess and address each patient's disease and comorbidities^{6,7}

Review > [Expert Opin Biol Ther.](#) 2026 Apr;26(4):407–414.
doi: 10.1080/14712598.2026.2651314. Epub 2026 Mar 26.

Dual clinical remission in severe asthma and chronic rhinosinusitis with nasal polyps: a comparative review of biologic therapies

Carlo Lombardi ¹, Francesco Menzella ²

Endoscopy at recurrence



Endoscopy after 6 months



The endoscopy videos were obtained from Dr Pipolo's clinic and are used with the patient's consent.

ENT, otolaryngologist

1. Menzies-Gow A, et al. *J Allergy Clin Immunol.* 2020;145(3):757–65; 2. Fokkens WJ, et al. *Rhinology.* 2024;62(3):287–98; 3. Brightling CE, et al. *Eur Respir Rev.* 2024;33:240221; 4. Russell RJ, et al. *Eur Respir J.* 2024;63(4):2301397; 5. Caminati M, et al. *Allergy.* 2024;79:1134–45; 6. Porsbjerg C, et al. *Lancet.* 2023;401:858–73; 7. Fokkens WJ, et al. *Rhinology.* 2020;58(2):82–111.

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