

Restoring epithelial health: a step towards clinical remission

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What do we mean by 'epithelial health'?

❁ The term 'epithelial health' encompasses the **holistic ecosystem** of the airway epithelium¹⁻³

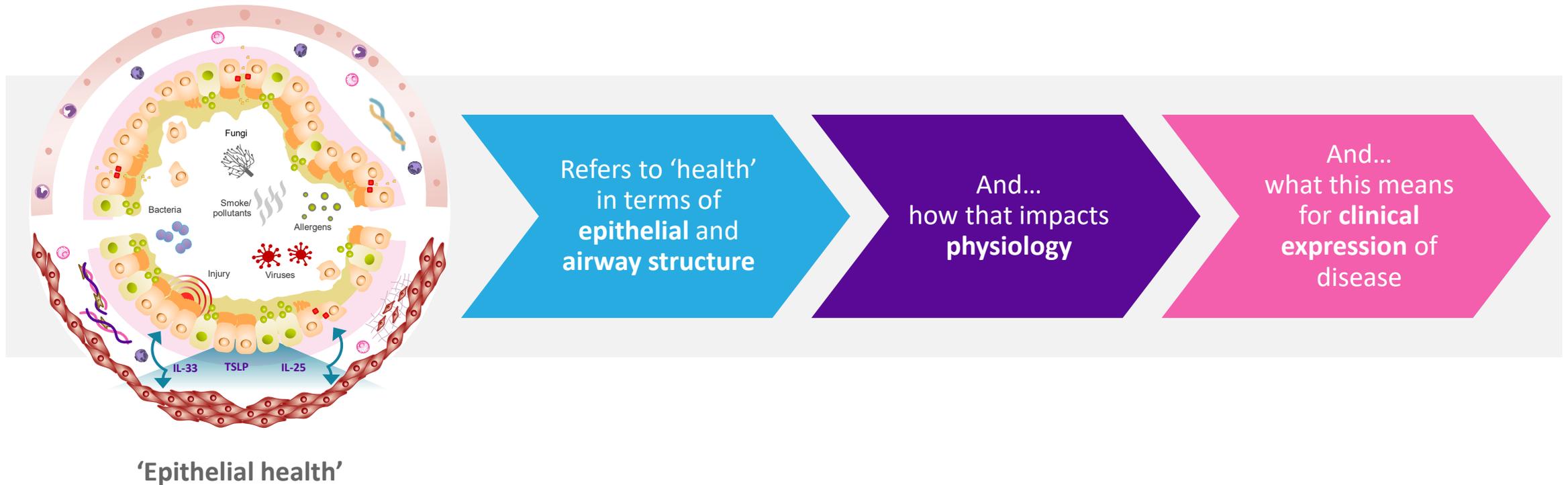


Figure adapted from the Centre of Excellence in Severe Asthma. Severe Asthma Toolkit. 2022. Available from: <https://toolkit.severeasthma.org.au/severe-asthma/pathophysiology/> (Accessed 8 September 2025)

IL, interleukin; TSLP, thymic stromal lymphopoietin

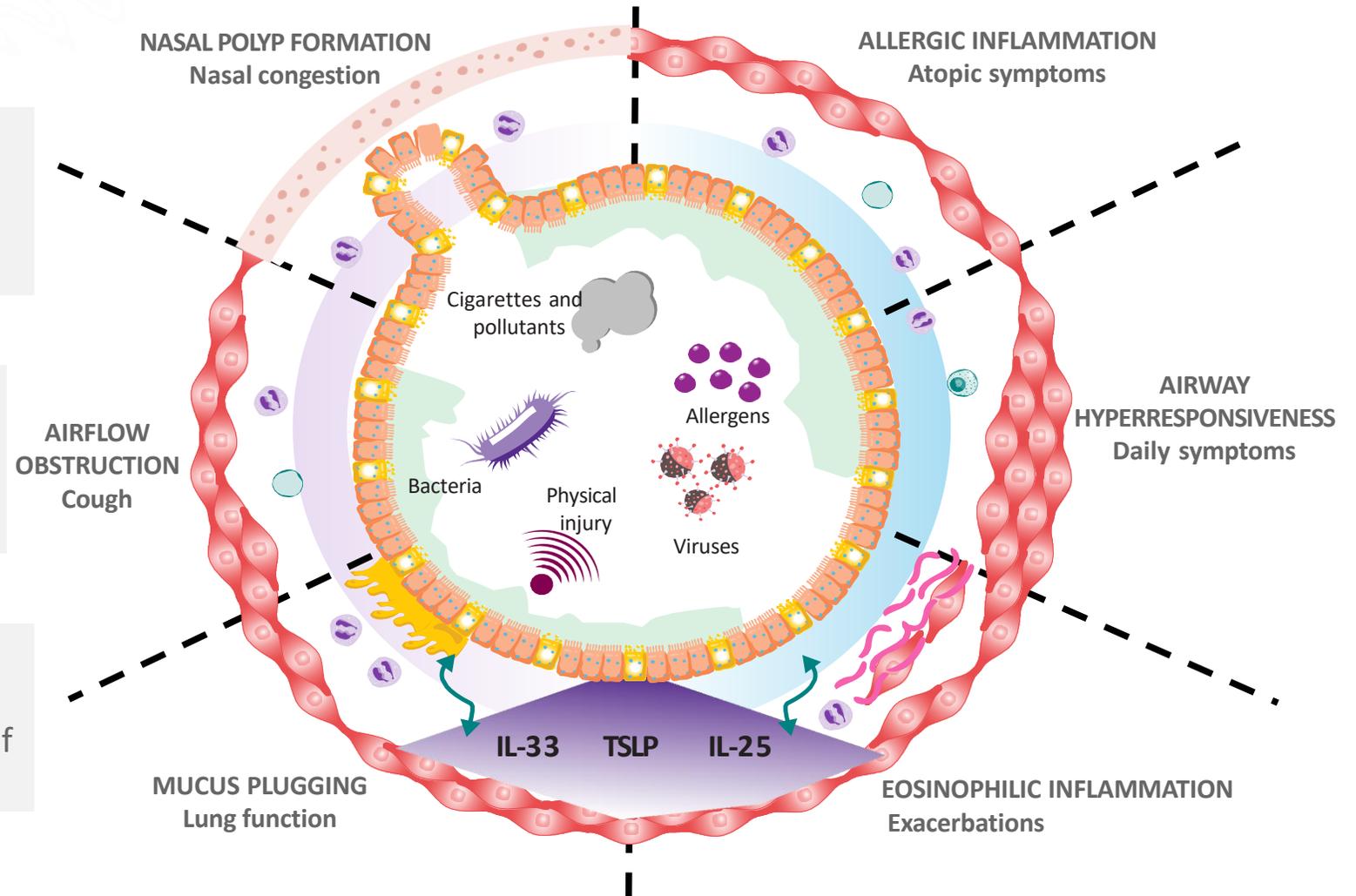
1. Raby KL, et al. Front Immunol 2023;14:1201658; 2. Porsbjerg C, et al. Lancet 2023;401:858–873; 3. Russell RJ, et al. Eur Respir J 2024;63:2301397

Chronic airway diseases can be referred to as 'epithelial-driven diseases': the epithelium is responsible for initiation and amplification of downstream pathways

Epithelial activation is the **critical initiation step** for multiple diseases of the airway, orchestrating complex and overlapping immune pathways¹

Environmental triggers **activate the epithelium** and cause **barrier dysfunction** and **immune hyperresponsiveness**^{1,2}

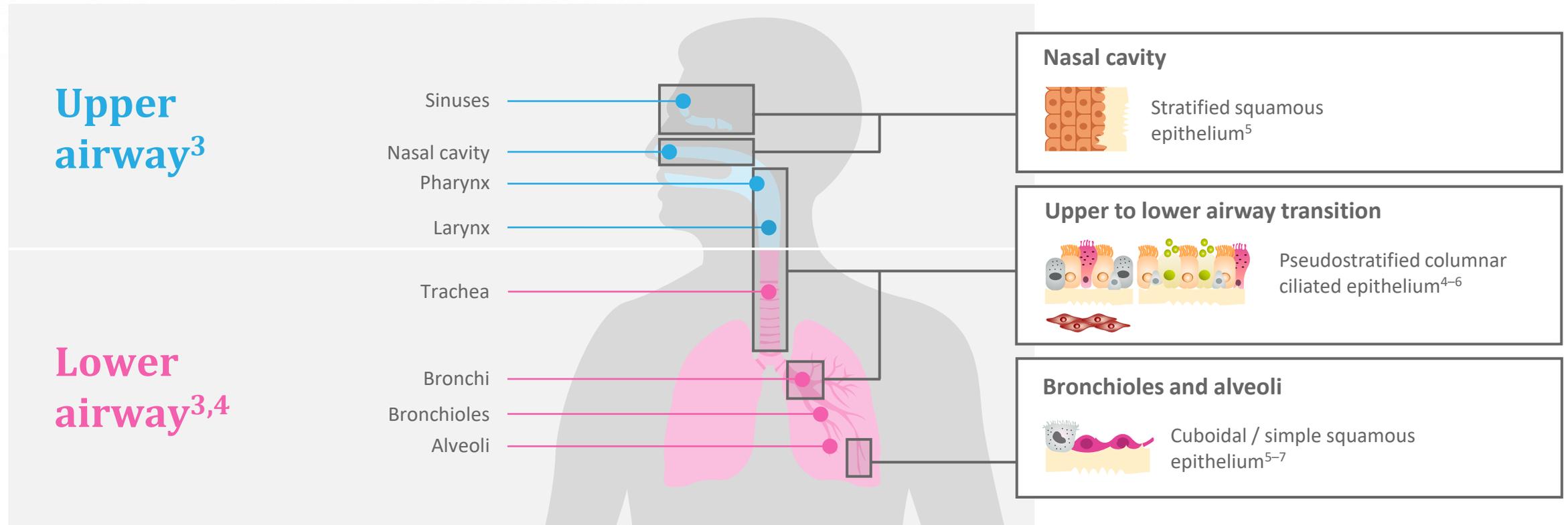
Multiple triggers cause release of **epithelial cytokines** (TSLP, IL-33 and IL-25), which drive inflammatory pathways leading to a variety of clinical manifestations^{3,4}



IL, interleukin; TSLP, thymic stromal lymphopoietin

1. Hellings PW, Steelant B. *J Allergy Clin Immunol* 2020;145:1499–1509; 2. Porsbjerg C, et al. *Lancet* 2023;401:858–873; 3. Roan F, et al. *J Clin Invest* 2019;129:1441–1451; 4. Mitchell PD, O’Byrne PM. *Chest* 2017;151:1338–1344

The epithelium forms a continuous link across the upper and lower airway, acting as the first line of defence from environmental insults^{1,2}



The upper and lower airway epithelium is a physical barrier, environmental sensor and an **immune-functioning organ**, orchestrating overlapping innate and adaptive immune responses against multiple **environmental triggers**^{1,8}
Beyond structural aspects, the upper and lower airways share many **physiological and immunological features**⁹

Figure adapted from Laulajainen-Hongisto A, et al. Front Cell Dev Biol 2020;8:204, Adivitiya, et al. Biology (Basel) 2021;10:95 and Baldassi D, et al. Adv Nanobiomed Res 2021;1:2000111^{5,6,10}

1. Fokkens W, Reitsma S. Otolaryngol Clin North Am 2023;56:1-10; 2. Bartemes KR, Kita H. Clin Immunol 2012;143:222-235; 3. Ball M, et al. Anatomy, airway. In: StatPearls [Internet]. Treasure Island, FL, USA: StatPearls Publishing, 2023; 4. Hewitt RJ, Lloyd CM. Nat Rev Immunol 2021;21:347-362; 5. Adivitiya, et al. Biology (Basel) 2021;10:95; 6. Laulajainen-Hongisto A, et al. Front Cell Dev Biol 2020;8:204; 7. Jakwerth CA, et al. Cells 2022;11:1387; 8. Roan F, et al. J Clin Invest 2019;129:1441-1451; 9. Cho H-J, et al. Rhinology 2021;59:441-450; 10. Baldassi D, et al. Adv Nanobiomed Res 2021;1:2000111

Compromised epithelial health leads to barrier dysfunction, chronic epithelial-driven inflammation and disease¹⁻³

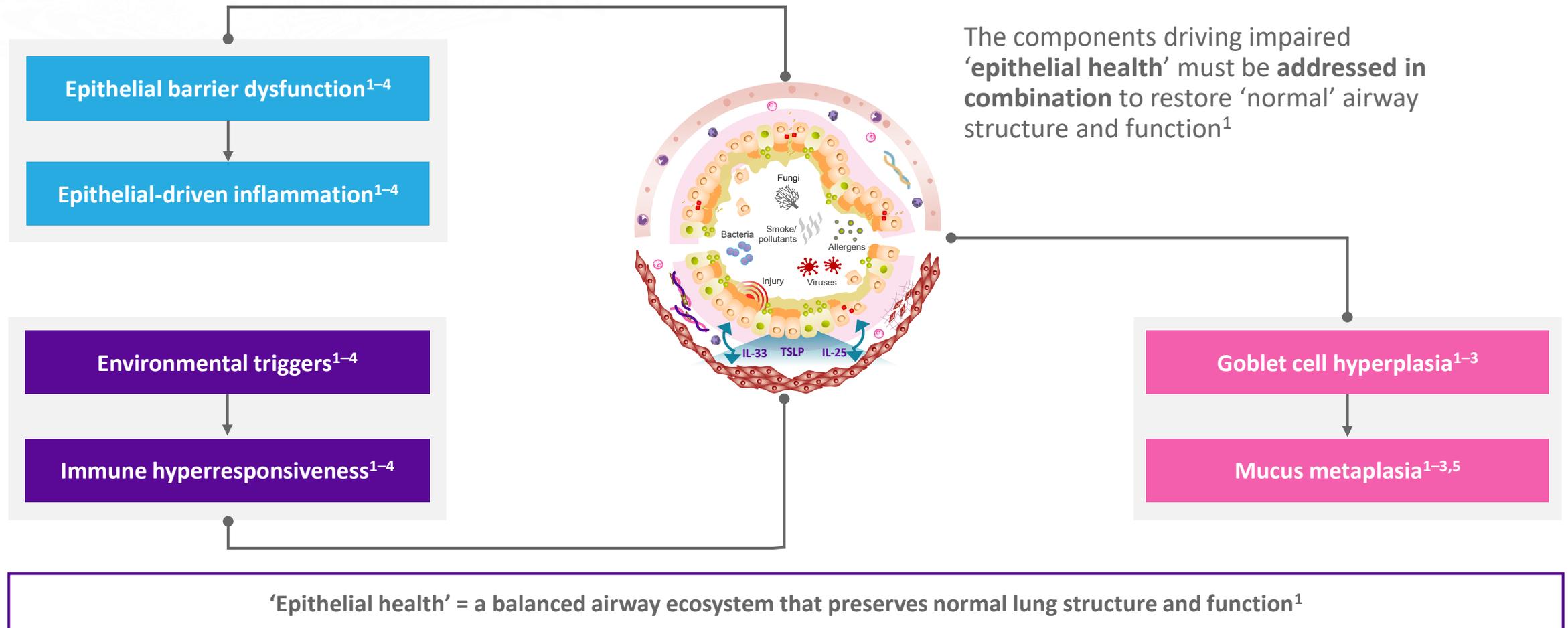


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IL, interleukin; TSLP, thymic stromal lymphopoiectin

1. Russell RJ, et al. Eur Respir J 2024;63:2301397; 2. Porsbjerg C, et al. Lancet 2023;401:858-873; 3. Calvén J, et al. Int J Mol Sci 2020;21:8907; 4. Bousquet J, et al. Nat Rev Dis Primers 2020;6:95;

5. Stolz D, et al. Lancet 2022;400:921-972

Cilia disorientation and loss of cilia in asthma and CRS¹⁻³

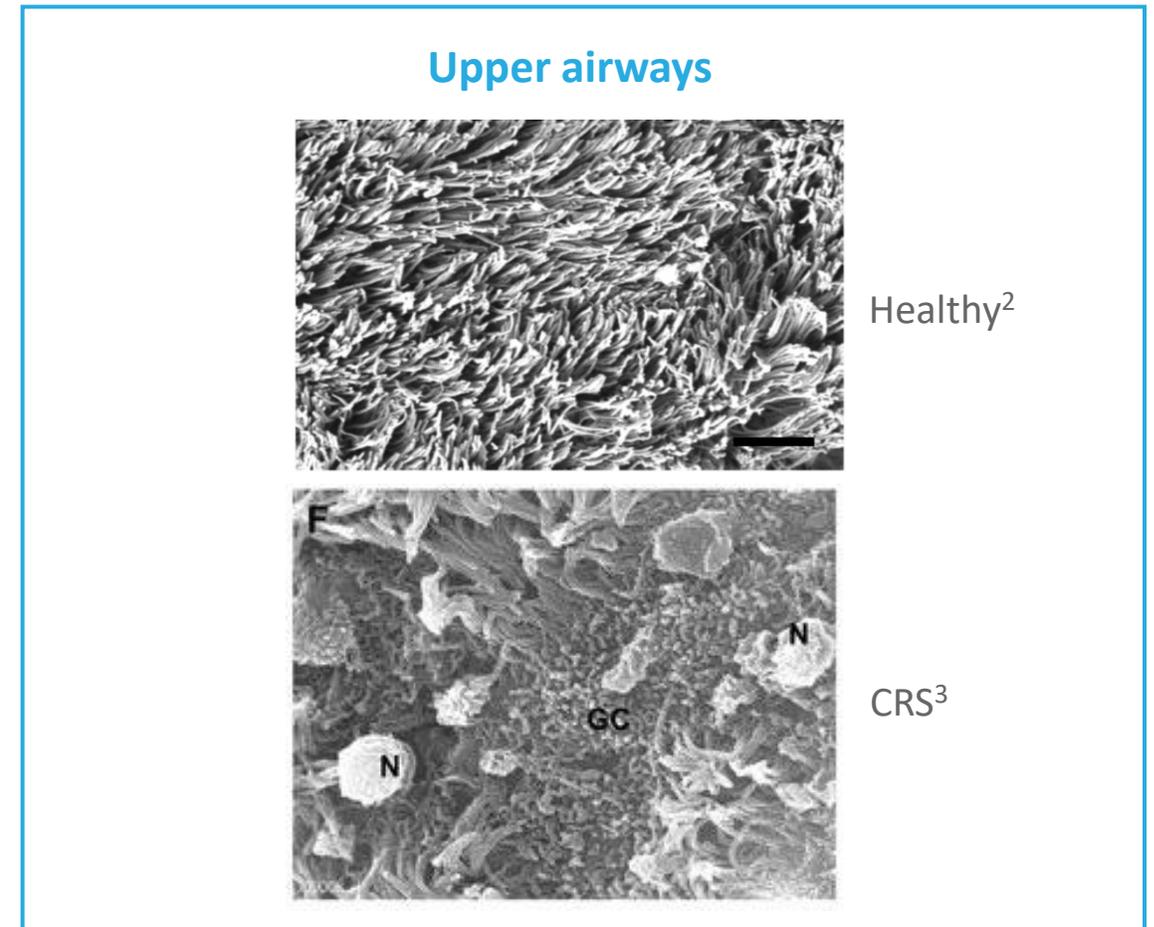
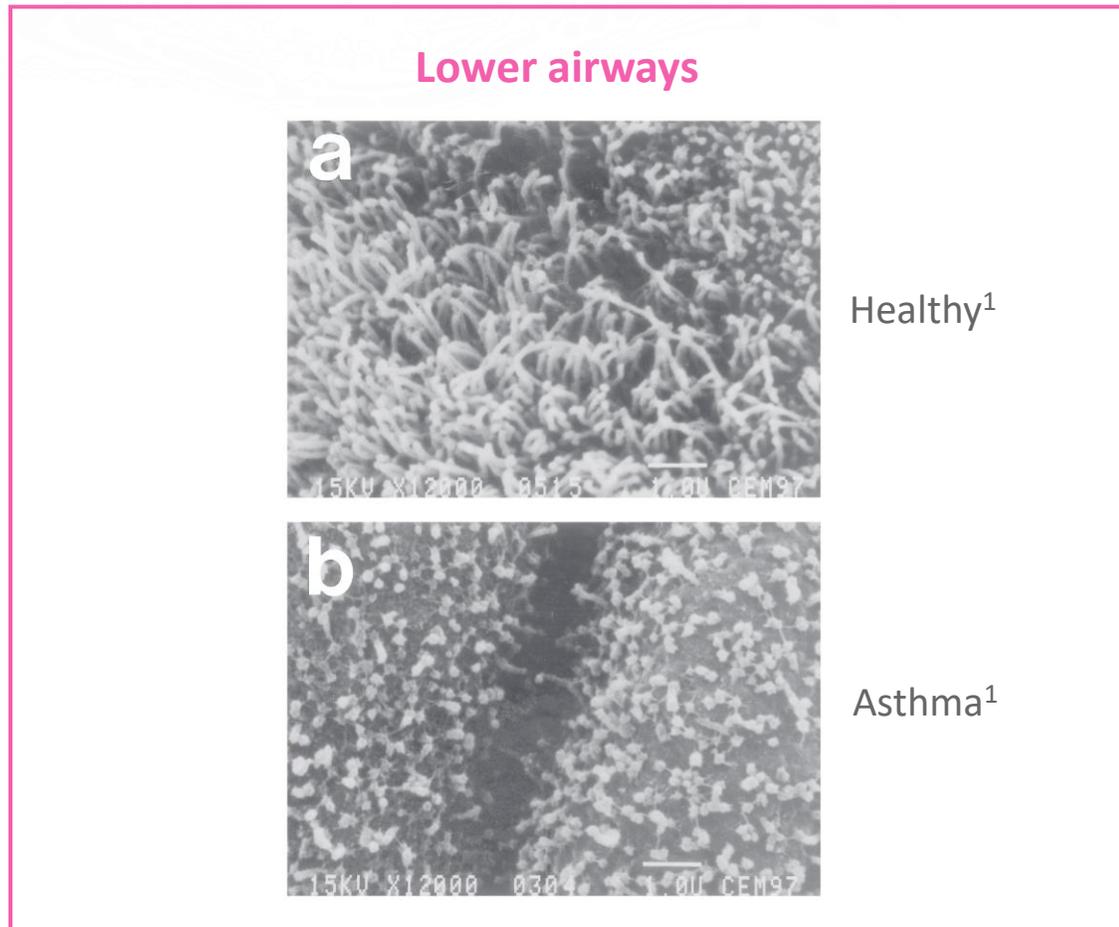


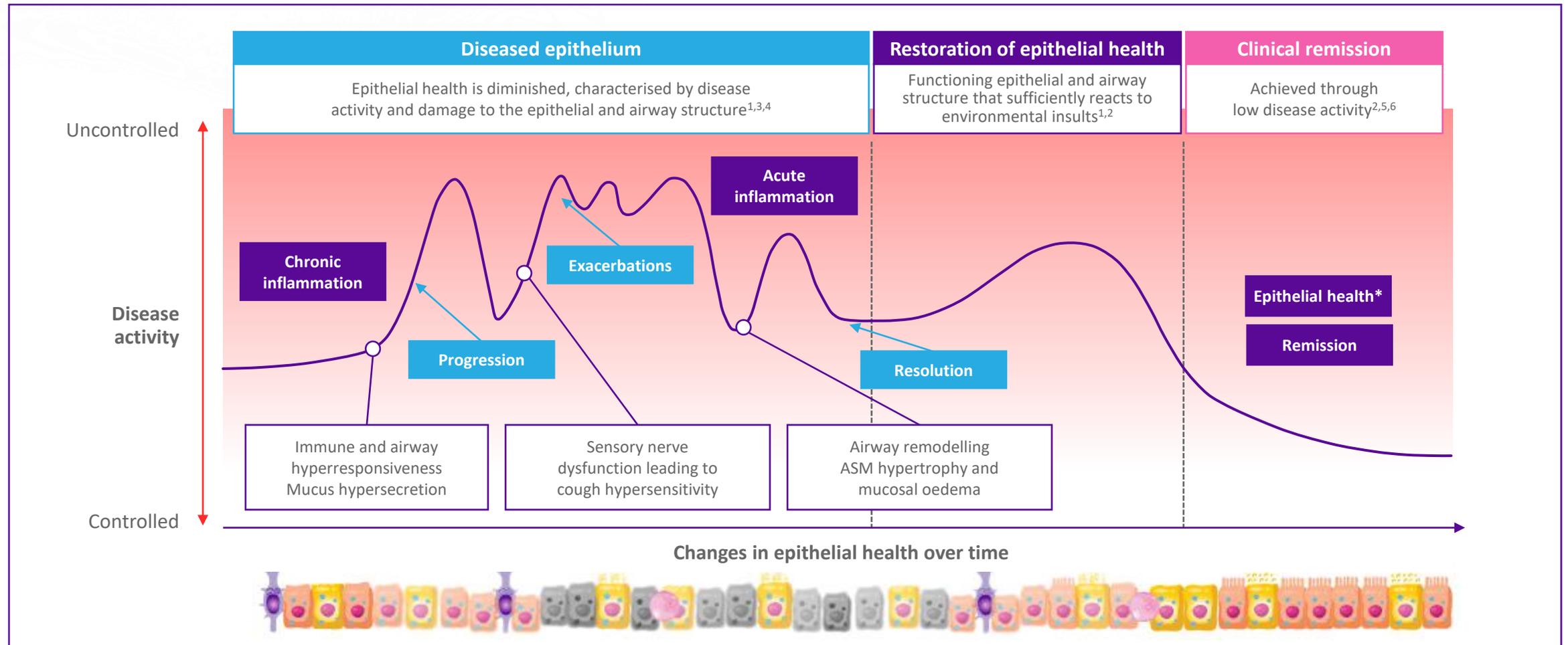
Figure adapted from Paquette JS, et al. *Eur Cell Mater* 2004;7:1–11 (left) licenced under CC BY SA 4.0 from: <https://creativecommons.org/licenses/by-sa/4.0/> (Accessed 8 September 2025), Hirokane S, et al. *Immuno* 2024;4:247–265 (top right) and Jeican II, et al. *J Clin Med* 2021;10:4110 (bottom right) both licenced under CC BY 4.0 from: <https://creativecommons.org/licenses/by/4.0/> (Accessed 8 September 2025)

Figures are from independent publications and are not suitable for direct comparison

CRS, chronic rhinosinusitis; GC, goblet cell; N, neutrophil

1. Paquette JS, et al. *Eur Cells Mater* 2004;7:1–11; 2. Hirokane S, et al. *Immuno* 2024;4:247–265; 3. Jeican II, et al. *J Clin Med* 2021;10:4110

Restoring epithelial health: reducing epithelial inflammation and cycles of epithelial damage could lead to clinical remission^{1,2}



*The 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}

ASM, airway smooth muscle

1. Russell RJ, et al. *Eur Respir J* 2024;63:2301397; 2. Brightling CE, et al. *Eur Respir Rev* 2024;33:240221; 3. Heijink IH, et al. *Allergy* 2020;75:1902–1917; 4. Porsbjerg C, et al. *Lancet* 2023;401:858–873; 5. Vatrella A, Maglio A. *Expert Rev Respir Med* 2025;19:1–5; 6. Fokkens WJ, et al. *Rhinology* 2024;62:287–298; 7. Carpaij OA, et al. *Pharmacol Ther* 2019;201:8–24; 8. Thomas D, et al. *Eur Respir J* 2022;60:2102583

Summary: why is restoring and maintaining epithelial health important?

