

# Type 2 severe asthma: What is the mechanism of disease?



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# The prevalence of type 2 asthma

- Asthma is a heterogenous, prevalent disease that is not fully manageable, and multiple phenotypes are common among patients<sup>1</sup>



In 2016, the Global Burden of Disease study estimated that

**300 million individuals worldwide have asthma,** and many more have uncontrolled disease, putting them at risk of persistent airway inflammation and eventual lung decline<sup>2,3,4</sup>



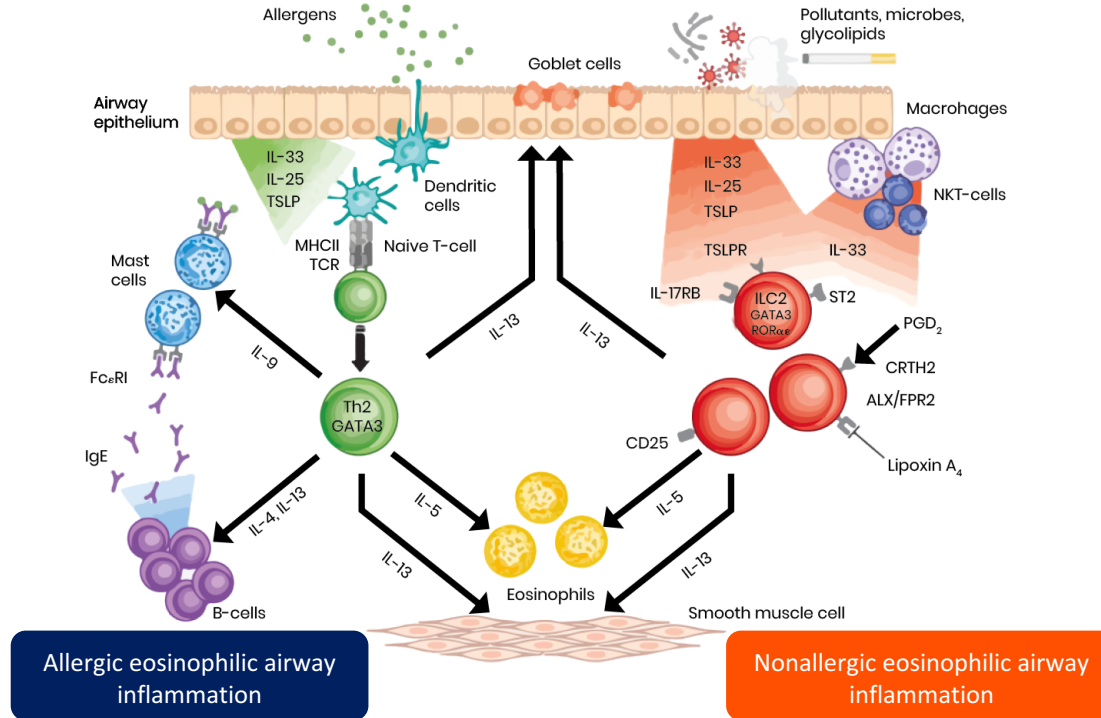
Approximately **50–70% of asthmatic patients have type 2 asthma,** which is characterised by type 2 inflammation<sup>5,6</sup>

This group typically includes<sup>4</sup>

- allergic asthma;**
- exercise-induced asthma; and**
- late-onset eosinophilic asthma**

1. Mc Gregor MC et al. *Am J Respir Crit Care Med* 2019; 199 (4):433–445. 2. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. *Lancet*. 2017;390:1211–59; 3. Naghavi M et al. *Lancet*. 2017;390(10100):1151–210; 4. Canonica GW et al. *EMJ*. 2018;3:24–33; 5. Seys SF et al. *Respir Res*. 2017;18:39; 6. Peters MC et al. *J Allergy Clin Immunol*. 2014;133:388–94.

# Type 2 inflammatory signalling pathways



ALX/FPR, A lipoxin receptor/formyl peptide receptor; CRTH2, chemoattractant receptor-homologous molecule expressed on Th2 cells; FcεR1, Fc-epsilon receptor 1; GATA3, GATA binding protein 3; Ig E, immunoglobulin E; ILC2, group 2 innate lymphoid cell; IL, interleukin; MHC II, major histocompatibility complex class II; NKT, natural killer T; PGD<sub>2</sub>, prostaglandin D<sub>2</sub>; RORα, retinoic acid receptor-related orphan receptor alpha; TCR, T-cell receptor; TSLP, thymic stromal lymphopoietin.  
Lambrecht B, Hammad H. *Nat Immunol.* 2015;16:45–56. Image adapted from: Lambrecht B, Hammad H. *Nat Immunol.* 2015.

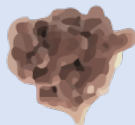
# Overview of the role of type 2 cytokines

Type 2 cytokines drive the recruitment of effector cells (mast cells, basophils and eosinophils) in the inflammatory process of type 2 asthma



**IL-4**

**IL-4 and IL-13** can both trigger airway remodelling



**IL-13**

**IL-13** triggers mucus hypersecretion and airway hyperresponsiveness, as well as inducing chemokines that recruit and retain eosinophils



**IL-5**

**IL-5** modulates the development, maturation and activation of eosinophils, mast cells and basophils

Type 2 cytokines also mediate the switch of **B cell-secreted Igs to IgE**, which has a central role in the inflammatory process

IgE-switched B cell



IgE plasma cell



IgE



# Common co-morbidities in type 2 asthma

- Patients with type 2 asthma can have co-morbidities such as atopic dermatitis and CRSwNP<sup>1</sup>

**CRSwNP is a chronic inflammatory disease of the upper airways**

Symptoms include facial pain/pressure, nasal discharge, nasal obstruction, and decreased sense of smell during chronic inflammation<sup>2</sup>

CRSwNP is mediated by the same **cytokine signalling pathway** as type 2 asthma<sup>2</sup>

The occurrence of CRSwNP in patients with asthma has been associated with **uncontrolled disease and higher asthma scores**, suggesting a worse prognosis for this group<sup>3</sup>

CRSwNP, chronic rhinosinusitis with nasal polyps.

1. Global Initiative for Asthma, 2019. Available at [www.ginasthma.org](http://www.ginasthma.org) (Accessed March 2020); 2. Stevens W et al. *J Allergy Clin Immunol Pract.* 2016;4:565–572;

3. Langdon C, Mullol J. *J Asthma Allergy.* 2016;9:45–53.