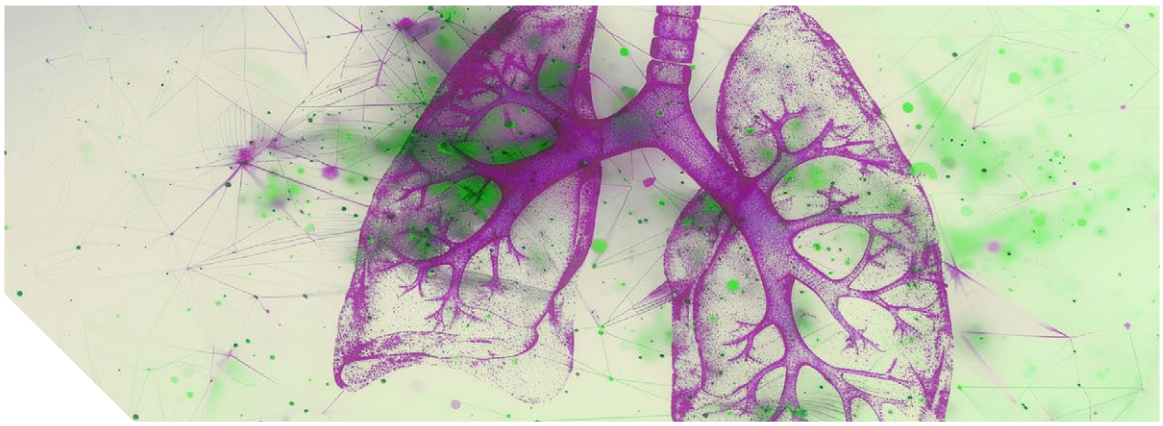
Why controlling inflammation may be the core of treatment in asthma

Despite decades of advances, asthma continues to affect over 260 million individuals globally, making it one of the most common non-communicable diseases (NCDs) worldwide and the leading chronic condition in children.[1,2,3]



Inflammation drives the disease

Chronic airway inflammation is the main pathophysiological driver of asthma symptoms (cough, wheeze, chest tightness, and shortness of breath), exacerbations, and long-term airway remodelling. These manifestations arise from the interaction between environmental and immunological triggers and the immune and structural cells of the airway mucosa.

The inflammatory cascade is initiated by antigen-presenting cells (APCs), which, along with other immune cells like eosinophils and neutrophils, release key cytokines such as IL-4, IL-5, and IL-13. High IL-4 levels sustain the immune response by promoting T and B cells interaction, enabling IgE production and mast cell activation. Basophils further contribute by inducing cytokine release, which perpetuates inflammation.

Additionally, epithelial-derived cytokines like IL-33 and thymic stromal lymphopoietin (TSLP) further amplify airway inflammation by enhancing both eosinophilic and non-eosinophilic pathways.[4,5,6]

Continuous APC and T cell interaction maintains the chronic inflammatory state, resulting in bronchial smooth muscle hypertrophy, fibrosis, increased mucus secretion, basement membrane thickening, and goblet cell hyperplasia, which are all considered hallmarks of airway remodelling.[5,7]

Airway remodelling correlates with disease severity and duration and is a major obstacle to remission. Histopathological evidence shows that basement membrane thickening does not fully resolve during remission, indicating that although inflammation can decrease, structural changes persist and leave patients vulnerable to disease recurrence, highlighting the importance of adequate early inflammation control.[5,8,9]

Controlling inflammation as treatment goal

Asthma therapy is typically adjusted in a stepwise fashion, increasing medication until asthma is controlled, then decreasing medication, when possible, to minimize adverse effects, particularly those related to long-term exposure to high doses of inhaled/oral corticosteroids.[9]

National and international guidelines advise initiating pharmacologic therapy based on the frequency and severity of symptoms, history of exacerbations requiring systemic corticosteroids, and results of lung function measurement (asthma severity), and subsequently adjusting therapy up or down, as needed, according to a stepwise approach, to achieve good asthma control.[9]

Current asthma management approach focuses not only on the best possible long-term symptom control (few/no asthma symptoms, no sleep disturbances due to asthma and unimpaired physical activity) but also on minimizing long-term risk of asthma-related mortality, exacerbations, persistent airflow limitation and side-effects treatment.[9,10]

Global Initiative for Asthma 2025 (GINA) International guidelines emphasize inhaled corticosteroid (ICS) treatments taken daily or when needed, as the cornerstone of long-term symptom control and exacerbations reduction.[9,11]

However, despite advances and variety in pharmacological treatment, achieving long-term remission, defined as sustained absence of symptoms, inflammation, and exacerbations, remains elusive.[5,12]

Strategic inflammation control: beyond corticosteroids

LTRAs (leukotriene receptor antagonists) offer a complementary non-steroidal option that targets cysteinyl leukotriene pathways (CysLT1) involved in bronchoconstriction, mucus production, vascular permeability, and airway remodelling. This makes LTRAs an alternative controller for patients unable to use ICS or in specific situations such as elderly patients, aspirin-exacerbated respiratory disease (AERD), obesity-related asthma, allergic rhinitis, smoking-related asthma, or viral-induced wheezing episodes.[9,13,14]

In addition, biologic therapies have significantly improved asthma outcomes. Monoclonal antibodies targeting the Interleukin-5 receptor, IL-4/IL-13, and TSLP, have demonstrated effectiveness in reducing exacerbations, improving lung function, and decreasing dependence on oral corticosteroids (OCS) in patients with severe steroid-resistant disease.[9]

Together, this broad range of therapeutic options reinforces the idea that targeting airway inflammation remains the central key to achieving better long-term asthma control and patient outcomes.

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