Allergic inflammatory response consists of both early and late phase reactions. The inflammatory mediators are involved in both phase responses. These mediators are associated with the development of symptoms in patients with allergic disease. The early-phase response is primarily caused by the release of preformed mediators (e.g., histamine, tryptase and bradykinin). During the late-phase response, patients experience a recurrence of early-phase symptoms. Histamine has been recognized as a major mediator producing allergic reactions. A new potent H1-receptor antagonist possesses greater affinity and avidity for H1 receptors. In vitro and in vivo data have demonstrated that a new-generation of H1-receptor antagonist, attenuates numerous critical pathways of the allergic inflammatory response. These anti-inflammatory properties may contribute to its efficacy in patients with allergic rhinitis, allergy-induced asthma, and other related allergic conditions.

An immune cascade of allergic conditions are the interactions between numerous cell types and inflammatory mediators. These allergic responses have three distinct phases: sensitization, early-phase responses, and late-phase responses. The sensitization phase begins with the production of allergen-specific IgE antibodies that bind to the surfaces of mast cells and basophils, causing degranulation and subsequent mediator release. During the early-phase reaction, preformed inflammatory mediators (e.g., tryptase, eosinophil chemotactic factor), in addition to histamine, and newly synthesized molecules (e.g., PGD2, LTC4, platelet-activating factor, bradykinin), are released from mast cells and basophils. About half of all patients who exhibit an early-phase allergic response experience a late-phase inflammatory reaction approximately 4–24 hours following allergen exposure. This late-phase response is characterized by endothelial cell activation and release of inflammatory cytokines (e.g., IL-3, IL-4, IL-5, IL-6, IL-8, IL-13, TNF-α and granulocyte-macrophage colony-stimulating factor) with an intense influx of inflammatory granulocytes – predominantly eosinophils, along with basophils, neutrophils, and lymphocytes – into the affected tissues. Especially, eosinophils secrete several substances that promote the chronic late-phase inflammatory reaction.

The clinical significance of the anti-allergic and anti-inflammatory properties of antihistamines is an interesting area of research. Antihistamines have demonstrated clinical efficacy against symptoms of allergic illness. Many second-generation antihistamines (e.g., loratadine, fexofenadine, cetirizine) have proven anti-inflammatory properties, including down-regulation of cell adhesion molecule expression and inhibition of cytokine production. A newer antihistamine, desloratadine has demonstrated its efficacy for the treatment of allergic rhinitis. It causes a significant reduction in classic symptoms typically attributed to histamine (e.g., sneezing, rhinorrhea), and also has effectively reduced nasal congestion. Therefore this drug might target both early and late phase mediators of the allergic cascade. Anthes et al. showed that the association of desloratadine with the H1 receptor was significantly greater than other antihistamines. The slow dissociation from the receptor and noncompetitive antagonism suggests that desloratadine may be a pseudoirreversible antagonist of the human histamine H1 receptor. Terfenadine, another antihistamine, can inhibit antigen-induced histamine release from sensitized guinea pig lung and rat peritoneal mast cells and ketotifen can also inhibit antigen-induced histamine release from human sensitized basophils correlating with an increase in intracellular cAMP levels which prevents intracellular calcium mobilization.

This new antihistamine, desloratadine, can inhibit the release of preformed histamine from human mast cells and basophils induced by both IgE-dependent and IgE-independent mechanisms. Desloratadine can also inhibit IgE-mediated histamine release from leucocytes in a concentration-dependent manner. The intercellular adhesion system plays a pivotal role in the accumulation of inflammatory cells at the site of an allergic reaction. Desloratadine can down-regulate cell adhesion molecule expression (i.e., ICAM-1 and P-selectin) in vitro. Agrawal has evaluated the effects of desloratadine on the chemotaxis, adhesion, and superoxide production of human blood eosinophils in vitro. Desloratadine can down-regulate platelet-activating factor - induced chemotaxis by up to 36%. To compared the suppression of IL-6, IL-8, IL-3, TNF-α, and GM-CSF secretion from stimulated human mast cells incubated with various antihistamines. Desloratadine was almost as effective as dexamethasone and more potent than cetirizine in inhibiting cytokine secretion. Therefore, this new antihistamine affects several phenomena of allergic
inflammation, including mediator release, cellular activation and adhesion molecule expression. In clinical trials of desloratadine, Cyr et al. showed that in a four-week, randomized, double-blind study, 45 symptomatic patients with seasonal allergic rhinitis randomly received desloratadine or placebo daily. Peripheral blood eosinophil and basophil progenitors declined significantly in patients who were administered the placebo compared with desloratadine, suggesting an increased eosinophil influx into the nasal mucosa following placebo treatment. In children with respiratory allergy, Rossi et al. provided data about upper and lower airway symptom improvement after a 4-week treatment with desloratadine syrup. Desloratadine can reduce nasal symptoms, including nasal obstruction. In children with coexisting asthma and/or conjunctivitis, desloratadine also induced a significant improvement of asthma and eye symptoms and a reduction of the need for rescue bronchodilators.

Our knowledge of the mechanisms underlying the allergic reaction has increased rapidly and has revealed a complex network of cells, mediators and inflammatory responses. This helps to form the proposed strategy for the treatment of allergic diseases. Histamines always play an important role in the production of allergic reactions. The new antihistamines represent the first line of treatment of these conditions, especially in nose, conjunctiva, skin and the respiratory tract. They can modulate various inflammatory reactions besides their H1-receptor antagonism. The aim of new antihistamine treatments are to reduce the symptoms of allergic inflammatory response which means to improve the quality of life or, the health-related quality of life of our allergic patients.

REFERENCES