SCHOLASTIC:
Journal of Natural and Medical Education

Volume 5, Issue 2, Year 2026
https://univerpubl.com/index.php/scholastic

Article

Etiopathogenesis of Bronchial Asthma and Modern Molecular Diagnostic Methods

Ruzikulov A. K.[1], Kalandarov S. D.[2], Normurodova L. Kh.[3], Urokov M. Y.[4], Sayidova Sh. Sh[5].

1,2,3,4,5. Termez Branch of Tashkent Medical Academy

Abstract: This scientific article analyzes the multifactorial etiopathogenesis of bronchial asthma, the mechanisms of chronic immune inflammation of the airways, and the phenotypes and endotypes of the disease. The article elucidates the T_h2-high and Non-T_h2 immunological pathways, the cytokine network, and airway remodeling processes at the molecular level. Furthermore, it demonstrates the role of the most modern molecular and genetic methods in BA diagnostics—such as biomarker analysis component-resolved diagnostics, pharmacogenetics, and mass parallel sequencing technologies—using examples from international clinical practice.

Keywords: bronchial asthma, etiopathogenesis, T_h2 endotype, target cytokines, FeNO, component-resolved diagnostics, molecular biomarkers.

Introduction

Bronchial asthma is a heterogeneous disease characterized by chronic inflammation of the airways, manifesting as respiratory symptoms that vary over time—such as shortness of breath, wheezing, chest tightness, and coughing—along with variable expiratory airflow limitation. According to the latest reports from the Global Initiative for Asthma, more than 350 million people worldwide suffer from asthma [1]. The last decade has seen a fundamental shift in the understanding of the disease's pathogenesis: asthma is no longer viewed simply as "bronchospasm" but as a complex molecular and immunological disorder. Proper phenotyping and endotyping of asthma, based on its molecular diagnostics, enables targeted therapy for severe, treatment-resistant forms of the disease [2].

Methodology

The development of bronchial asthma is determined by the complex interplay between genetic predisposition and environmental influences

Internal Factors

Asthma is a polygenic disease. Numerous Genome-Wide Association Studies have identified several chromosomal loci associated with asthma:

Locus 5q31-33: Genes for atopic inflammatory cytokines such as IL-4, IL-5, IL-9, and IL-13 are located here [3].

Locus 17q12-21: Contains the ORMDL3 and GSDMB genes, which are the strongest genetic determinants of childhood-onset asthma.

ADAM33 gene: Regulates the proliferation of bronchial smooth muscle and fibroblasts and is responsible for airway hyperreactivity.

External Factors Allergens: House dust mites, pet dander, mold spores, and plant pollen [4].

Citation: A. K. Ruzikulov., S. D. Kalandarov., Normurodova L. Kh., M. Y. Urokov., Sh. Sh. Sayidova. Scholastic: Journal of Natural and Medical Education 2026, 5(2), 92-.

Received: 10th Mar 2026
Revised: 11th Apr 2026
Accepted: 24th May 2026
Published: 20th Jun 2026

Triggers and respiratory infections: Rhinoviruses, tobacco smoke, air pollution, chemical aerosols, and occupational factors.

Molecular Pathogenesis

The basis of asthma pathogenesis is chronic inflammation of the respiratory tract mucosa, which develops primarily through two different immunological pathways: T_h2-high and Non-T_h2

T_h2-high Inflammatory Mechanism

This is the most well-studied and common form of asthma, approximately 50-70%. Its molecular cascade consists of the following stages [5]:

1. Dendritic Cell Presentation: When an allergen enters the respiratory tract, antigen-presenting dendritic cells beneath the epithelium capture it and present it to T-lymphocytes.

Epithelial Cytokines: When mucosal epithelial cells are damaged, they secrete "alarmins" such as TSLP thymic stromal lymphopoietin, IL-25, and IL-33. These are critical molecules that amplify the immune response[6].

T-helper 2 Th2 and ILC2 Activation: Under the influence of alarmins, Th0 cells differentiate into Th2 cells. Additionally, type 2 innate lymphoid cells of the innate immune system are also activated.

Cytokine Cascade: Th2 and ILC2 cells synthesize three primary cytokines:

{IL-4:} Induces B-lymphocytes to switch to producing IgE antibodies, isotype switching [7].

{IL-13:} Causes bronchial smooth muscle hyperreactivity, increases the proliferation of goblet cells, thereby increasing mucus production, and disrupts the epithelial barrier.

{IL-5:} Ensures the maturation, differentiation, release into the blood, and infiltration of eosinophils from the bone marrow into the respiratory tract.

Eosinophils and Mast Cells: IgE binds to FcεRI receptors on the surface of mast cells. Upon re-exposure to the allergen, mast cells undergo degranulation, releasing histamine, leukotrienes, and prostaglandin. Eosinophils, in turn, release major cytotoxic proteins – MBP and ECP – which destroy the bronchial epithelium.

Non-T_h2 Inflammatory Mechanism

This endotype is often found in late-onset, obesity-related, or smoker's asthma. It involves the participation of Th1 and Th17 cells. Under the influence of cytokines IL-8 and IL-17, a large number of neutrophils accumulate in the respiratory tract. This form is distinguished by its resistance to glucocorticosteroids.

Bronchial Remodeling

Chronic inflammation results in irreversible structural changes in the bronchial wall:

Thickening of the subepithelial basement membrane

Smooth muscle hypertrophy and hyperplasia.

Angiogenesis.

These processes lead to a progressive decline in lung function.

Phenotypes and Endotypes of Asthma

The relationship between clinical manifestations and molecular mechanisms is summarized in the table below:

Table 1. Phenotypes, Endotypes, Biomarkers, and Personalized Treatment Strategies in Bronchial Asthma.

Phenotype	Endotype	Key Biomarkers	Treatment tactics

Allergic asthma	T_h2-high	IgE \uparrow, Eosinophils \uparrow, FeNO \uparrow	Inhalation GCS, Anti-IgE
Late-onset eosinophilic	T_h2-high	Blood eosinophils \uparrow \uparrow, FeNO \uparrow	Anti-IL5, Anti-IL4/13
Neutrophilic asthma	Non-T_h2	Sputum neutrophils \uparrow, IL-8 \uparrow	Macrolides, LAMA preparations
Asthma associated with obesity	Non-T_h2	Metabolic markers, TNF-\alpha \uparrow	Weight loss, metabolic correction

Modern Molecular Diagnostic Methods

Although traditional spirometry and bronchodilator tests can confirm the presence of asthma, they cannot determine its molecular endotype. According to modern international standards, the following molecular tests are mandatory:

Fraction of Exhaled Nitric Oxide

Measuring nitric oxide in exhaled breath is a non-invasive molecular method that reflects the activity of the IL-13 cytokine in the respiratory epithelium.

Results and Discussion

Criteria: A FeNO level > 50 ppb (parts per billion) in adults (>35 ppb in children) indicates the presence of eosinophilic inflammation and the patient's high sensitivity to inhaled glucocorticosteroids

Component-Resolved Diagnostics [8].

Older methods like total IgE or skin prick tests only identify the allergen source, e.g., dust or cat. In contrast, CRD, e.g., ISAC or ALEX2 microarray chips, determines the exact molecular protein of the allergen to which IgE is present.

A positive result for the Der p 1 and Der p 2 molecules of the house dust mite indicates true sensitization and that Allergen-Specific Immunotherapy will be highly effective. A positive result for Der p 10 indicates a cross-reaction with crustaceans [9].

Molecular Biomarkers in Sputum and Blood

A matrix protein secreted by epithelial cells under the influence of IL-4 and IL-13. The level of periostin in blood serum is a reliable systemic biomarker for T_h2-asthma and bronchial remodeling [10].

Eosinophil Cationic Protein: Allows for the assessment of the intensity of eosinophil degranulation.

Genetic and Epigenetic Analyses

NGS: Identification of mutations in candidate genes [11].

Pharmacogenetics: Identification of polymorphisms in the beta-2 adrenergic receptor gene. This explains at a molecular level why some patients respond poorly to short-acting beta-agonists or why their asthma worsens with frequent use.

Understanding the pathogenesis of asthma at the molecular level led to the creation of monoclonal antibody agents that have revolutionized the treatment of severe asthma [12].

Omalizumab: Binds to free IgE molecules, blocking their attachment to Fc\epsilonRI receptors on mast cells. It is used for severe allergic asthma.

Mepolizumab, Reslizumab: Directly binds to the IL-5 cytokine and inhibits the development of eosinophils [13].

Benralizumab: Binds to the alpha-chain of the IL-5 receptor on the surface of eosinophils and induces eosinophil apoptosis via NK-cells through antibody-dependent cellular cytotoxicity [14].

Dupilumab: Blocks the IL-4R\alpha receptor, which is common to the IL-4 and IL-13 cytokines. It is highly effective in treating both asthma and comorbid atopic dermatitis and polypoid rhinosinusitis.

Tezepelumab: The newest drug targeting the epithelial alarmin TSLP; it is effective in both T_h2 and Non-T_h2 asthma because it blocks the highest link in the cascade [15].

Conclusion

Bronchial asthma is not a simple and uniform bronchospastic disease. It is a complex immunological pathology with various molecular endotypes. Successful management of the disease is directly dependent on its molecular diagnosis. In clinical practice, every patient diagnosed with severe asthma should undergo FeNO measurement and component-resolved diagnostics for allergies. Patients should be phenotyped based on their eosinophil/neutrophil profile in the blood and sputum, rather than their response to conventional ICS medications. In severe eosinophilic asthma that is difficult to control and characterized by frequent exacerbations, the early use of targeted biologic therapy that acts on a specific molecular link of the pathogenesis is the only measure to prevent airway remodeling.

REFERENCES

[1] Global Initiative for Asthma (GINA), "Global Strategy for Asthma Management and Prevention," *GINA Guidelines*, 2025. [Online]. Available: ginasthma.org.

[2] A. Papi et al., "Asthma," *Lancet*, vol. 391, no. 10122, pp. 783–800, Mar. 2018.

[3] E. Israel and H. K. Reddel, "Severe and Difficult-to-Treat Asthma in Adults," *N. Engl. J. Med.*, vol. 390, no. 11, pp. 1012–1025, Mar. 2024.

[4] S. E. Wenzel, "Asthma phenotypes: the evolution from clinical to molecular approaches," *Nat. Med.*, vol. 18, no. 5, pp. 716–725, May 2012.

[5] H. Hammad and B. N. Lambrecht, "Barrier epithelial cells and the control of type 2 airway inflammation," *Immunity*, vol. 54, no. 4, pp. 643–657, Apr. 2021.

[6] H. K. Reddel et al., "Gaining control over difficult-to-treat asthma: Moving from guidelines to clinical practice," *Eur. Respir. J.*, vol. 61, no. 2, p. 2201020, Feb. 2023.

[7] B. N. Lambrecht and H. Hammad, "The immunology of asthma," *Nat. Immunol.*, vol. 16, no. 1, pp. 45–56, Jan. 2015.

[8] E. D. Bateman et al., "Global strategy for asthma management and prevention: GINA executive summary," *Eur. Respir. J.*, vol. 31, no. 1, pp. 143–178, Jan. 2008.

[9] S. E. Wenzel et al., "Dupilumab efficacy and safety in adults with uncontrolled persistent asthma," *N. Engl. J. Med.*, vol. 368, no. 26, pp. 2455–2466, Jun. 2013.

[10] J. V. Fahy, "Type 2 inflammation in asthma — present in most, absent in some," *Nat. Rev. Immunol.*, vol. 15, no. 1, pp. 57–65, Jan. 2015.

[11] P. G. Gibson et al., "Mepolizumab for severe eosinophilic asthma: A randomized, double-blind, placebo-controlled trial," *Lancet*, vol. 384, no. 9949, pp. 1189–1197, Sep. 2014.

[12] I. D. Pavord et al., "Mepolizumab for severe eosinophilic asthma (DREAM): A multicentre, double-blind, placebo-controlled trial," *Lancet*, vol. 380, no. 9842, pp. 651–659, Aug. 2012.

[13] National Heart, Lung, and Blood Institute, "2020 Focused Updates to the Asthma Management Guidelines," *J. Allergy Clin. Immunol.*, vol. 146, no. 6, pp. 1217–1270, Dec. 2020.

[14] G. Brusselle and G. Koppelman, "Biologic therapies for severe asthma," *N. Engl. J. Med.*, vol. 386, no. 2, pp. 157–171, Jan. 2022.

[15] C. E. Brightling et al., "Targeting TNF-alpha in severe asthma," *N. Engl. J. Med.*, vol. 354, no. 10, pp. 1034–1042, Mar. 2006.