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Review Article

Asthma: Current Concepts in Pathogenesis, Precision Medicine and Emerging Therapeutic Strategies

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Abstract

Objectives: To review current concepts in asthma pathogenesis, phenotypes, endotypes, precision medicine, biologic therapies, and emerging therapeutic strategies, with emphasis on recent advances in personalized asthma management.

Data Sources: Peer-reviewed articles were identified through searches of PubMed, Scopus, Web of Science, and Google Scholar, together with relevant international asthma guidelines.

Study Selection: Relevant original research articles, systematic reviews, meta-analyses, and international clinical guidelines were selected based on their relevance to asthma pathogenesis, biomarkers, precision medicine, biologic therapies, and emerging therapeutic strategies.

Summary of Contents: Asthma is a heterogeneous chronic inflammatory airway disease resulting from complex interactions among genetic susceptibility, environmental exposures, epithelial dysfunction, and dysregulated immune responses. Advances in the understanding of asthma phenotypes and endotypes have facilitated biomarker-guided treatment and precision medicine. Targeted biologic therapies directed against immunoglobulin E, interleukin (IL)-5, IL-4/IL-13, and thymic stromal lymphopoietin have significantly improved outcomes in severe type 2 asthma. Emerging approaches, including treatable traits, omics technologies, pharmacogenomics, artificial intelligence, smart inhalers, nanomedicine, gene- and RNA-based therapies, and digital health, are further transforming individualized asthma care.

Conclusion: Precision medicine has substantially improved asthma management through biomarker-guided therapeutic selection and targeted biologic therapy. Future research should focus on reliable biomarkers, disease-modifying therapies, non-type 2 asthma, equitable access to advanced treatments, and strategies to achieve long-term remission and disease prevention.

Keywords: Asthma; Pathogenesis; Precision medicine; Biologic therapy; Phenotypes; Endotypes; Biomarkers; Emerging therapies.

1. Introduction

Asthma is a long-term inflammatory condition affecting the airways, marked by repeated episodes of wheezing, coughing, chest tightness, and difficulty breathing. These symptoms are associated with variable expiratory airflow limitation and increased airway responsiveness. Although airflow obstruction is usually reversible, persistent airway inflammation can lead to airway remodeling and progressive loss of lung function. Asthma is now recognized as a heterogeneous disease with distinct clinical features and biological mechanisms influenced by genetic factors, environmental exposures, and abnormal immune responses [1,2].

Asthma remains one of the most common chronic respiratory diseases worldwide, affecting people of all ages and imposing a substantial public health burden. According to the Global Burden of Disease 2019 study, approximately 262 million people were living with asthma globally. Although age-standardized incidence and mortality rates have declined, the overall number of affected individuals continues to increase because of population growth, urbanization, environmental pollution, and lifestyle changes [3].

Asthma significantly impairs quality of life and increases healthcare utilization through recurrent exacerbations, emergency department visits, hospitalizations, and long-term medication use. Severe asthma accounts for a disproportionate share of healthcare costs and is associated with corticosteroid-related adverse effects and multiple comorbidities, including allergic rhinitis, chronic rhinosinusitis, obesity, gastroesophageal reflux disease, anxiety, and depression [1–3].

Recent advances have improved the understanding of asthma pathogenesis and management. Recognition of

T2-high and T2-low inflammatory endotypes has led to the development of targeted biologic therapies against IgE, IL-5, IL-4/IL-13, and thymic stromal lymphopoietin (TSLP). Biomarker-guided treatment, precision medicine, digital health technologies, and artificial intelligence are further advancing individualized asthma care and improving patient outcomes [1,2].

2. Pathogenesis

Asthma is a complicated and varied condition that arises from the interaction of genetic predisposition, environmental exposures, airway epithelial dysfunction, and abnormal immune responses. It is not a single condition but a group of inflammatory disorders with distinct cellular and molecular mechanisms. Ongoing airway inflammation leads to airway hyperresponsiveness, excess mucus production, structural remodeling, and variable airflow obstruction, producing the characteristic symptoms of asthma [1,4].

2.1 Airway inflammation

Airway inflammation is a major characteristic of asthma and involves eosinophils, mast cells, T lymphocytes, dendritic cells, macrophages, neutrophils, airway epithelial cells, fibroblasts, and airway smooth muscle cells. The airway epithelium acts as both a physical barrier and an active immune organ, recognizing allergens, pathogens, pollutants, and irritants. Epithelial injury releases alarmins, particularly thymic stromal lymphopoietin (TSLP), IL-25, and IL-33, which activate dendritic cells and innate lymphoid cells (ILC2s), leading to persistent airway inflammation and asthma exacerbations [4–].

2.2 Type 2 (T2) immunity

Type 2 inflammation is the predominant immune pathway in approximately 50–70% of asthma cases, particularly allergic and eosinophilic asthma. Airway epithelial alarmins activate dendritic cells and $CD4^+$ T cells, promoting differentiation into Th2 cells that produce IL-4, IL-5, and IL-13. These cytokines stimulate IgE production, eosinophil survival, mucus hypersecretion, airway hyperresponsiveness, and subepithelial fibrosis. ILC2s further amplify type 2 inflammation, and these pathways are targeted by biologic therapies against IgE, IL-5, IL-4/IL-13, and TSLP [4–7].

2.3 Non-type 2 (Non-T2) asthma

About one-third of patients have non-T2 asthma, characterized by neutrophilic or paucigranulocytic airway inflammation. It is associated with smoking, obesity, respiratory infections, occupational exposures, and pollution. Th1- and Th17-mediated immune responses increase IFN-γ, IL-17A, IL-17F, IL-6, and TNF-α, contributing to persistent airway inflammation, corticosteroid resistance, and severe disease. Unlike T2-high asthma, validated biomarkers and targeted biologic therapies remain limited [4,5,8].

2.4 Airway remodeling

Persistent inflammation leads to airway remodeling, including epithelial damage, goblet-cell and mucus-gland hyperplasia, basement membrane thickening, airway smooth-muscle hypertrophy and hyperplasia, angiogenesis, and extracellular matrix deposition. Key mediators include transforming growth factor-β (TGF-β), matrix metalloproteinases, fibroblasts, myofibroblasts, and airway smooth muscle cells. These structural changes reduce airway elasticity, narrow the airway lumen, and contribute to progressive lung-function decline and persistent airflow limitation [4,9,10].

2.5 Bronchial hyperresponsiveness

Bronchial hyperresponsiveness is a hallmark of asthma in which the airways respond excessively to allergens, methacholine, histamine, cold air, exercise, viral infections, and environmental irritants. It results from persistent airway inflammation, airway smooth-muscle dysfunction, neural abnormalities, epithelial injury, mucus plugging, and airway remodeling. Increased airway smooth-muscle contractility and structural airway changes cause exaggerated bronchoconstriction, allowing bronchial hyperresponsiveness to persist even when symptoms improve [9–11].

3. Genetics and Environmental Factors

Asthma is caused by a combination of genetic and environmental factors that interact over a person's lifetime. Genetics alone do not fully account for the growing number of people affected by the disease. Environmental factors, especially during fetal development and early childhood, interact with genetic and epigenetic factors to influence asthma development, severity, and treatment response. Certain genetic variations can change how the body reacts to allergens, pollution, infections, and other exposures, resulting in long-term inflammation and airway changes [12,13].

3.1 Genetic susceptibility

Genome-wide association studies have identified over 100 genetic regions associated with asthma, demonstrating its polygenic nature. One of the strongest associations is the chromosome 17q12–21 region containing ORMDL3 and GSDMB, which is linked to childhood-onset asthma. Other important genes include IL33, IL1RL1, TSLP, HLA-DQ, IL4, IL13, IL4R, ADAM33, STAT6, and FCER1A**.** These genes regulate epithelial barrier function, innate immunity, type 2 inflammation, IgE production, eosinophilic inflammation, and airway remodeling. No single gene causes asthma; instead, the disease results from multiple genetic risk factors interacting with environmental influences [12–15].

3.2 Epigenetics

Epigenetic mechanisms regulate gene expression without altering the DNA sequence. Major mechanisms include DNA methylation, histone modification, and microRNAs. Prenatal tobacco smoke exposure, air pollution, maternal diet, microbes, and respiratory viral infections can produce long-lasting changes in immune development and airway function. MicroRNAs including miR-21, miR-155, miR-126, and miR-146a regulate inflammatory cytokines, eosinophilic inflammation, and airway remodeling. Since epigenetic changes are

potentially reversible, they represent promising therapeutic targets [13,16,17].

3.3 Allergens

Exposure to aeroallergens is a major environmental factor in allergic asthma. Common allergens include house dust mites, pollens, molds, cockroach allergens, animal dander, and fungal spores. In genetically susceptible individuals, allergen exposure activates airway epithelial cells and dendritic cells, leading to Th2 cytokine production (IL-4, IL-5, and IL-13), IgE production, eosinophilic inflammation, mucus secretion, and airway hyperresponsiveness. Persistent allergen exposure contributes to chronic airway inflammation and airway remodeling [12–14,18].

3.4 Air pollution

Ambient and indoor air pollution contribute to both asthma development and exacerbation. Major pollutants include $PM_{2.5}$, PM_{10}, ozone, nitrogen dioxide, sulfur dioxide, volatile organic compounds, and traffic-related pollutants. These pollutants induce oxidative stress, epithelial injury, innate immune activation, and airway inflammation. Long-term exposure is associated with impaired lung growth, reduced lung function, increased asthma incidence, and more frequent exacerbations. Climate change further increases exposure to airborne allergens and wildfire-related particulate matter [12,19,20].

3.5 Smoking

Active and passive smoking are major risk factors for asthma development, poor disease control, accelerated lung-function decline, and corticosteroid resistance. Cigarette smoke damages the airway epithelium, impairs mucociliary clearance, increases oxidative stress, and promotes airway inflammation. Maternal smoking during pregnancy is associated with impaired fetal lung development, altered immune maturation, early-life wheezing, and increased childhood asthma risk [13,20,21].

3.6 Occupational exposure

Occupational asthma results from exposure to workplace allergens or irritants. High-molecular-weight allergens such as flour, latex, animal proteins, and enzymes usually induce IgE-mediated asthma, whereas low-molecular-weight chemicals including isocyanates, formaldehyde, persulfates, and metal salts can cause immune-mediated or irritant-induced asthma. Early recognition and removal from exposure remain the most effective strategies for preventing permanent airway damage and improving outcomes [22,23].

4. Phenotypes and Endotypes

Asthma shows wide variation in symptoms, inflammation types, responses to treatment, and long-term outcomes. Phenotypes are based on observable clinical features, whereas endotypes are defined by specific biological mechanisms. Combining phenotype and endotype information supports more accurate diagnosis and personalized treatment, particularly with biologic drugs targeting specific disease pathways [24,25].

4.1 Allergic asthma

Allergic asthma is the most common type, particularly in children and young adults. It involves sensitization to allergens such as house dust mites, pollen, mold, animal dander, and cockroach proteins. Patients often have elevated allergen-specific IgE and positive skin-prick tests. Type 2 inflammation is driven by Th2 cells and ILC2s, which release IL-4, IL-5, and IL-13, leading to IgE production, eosinophilic inflammation, mucus secretion, and airway hyperresponsiveness. Most patients respond to inhaled corticosteroids, while severe cases may benefit from anti-IgE therapy [24–27].

4.2 Non-allergic asthma

Non-allergic asthma occurs without clear allergen sensitization and usually begins in adulthood. Airway epithelial damage, viral infections, environmental toxins, and altered innate immune responses may contribute. Patients often show neutrophilic or paucigranulocytic inflammation and may respond less effectively to inhaled corticosteroids. The absence of reliable biomarkers and targeted therapies makes management more difficult [24,25,28].

4.3 Eosinophilic asthma

Eosinophilic asthma is a T2-high phenotype characterized by persistent eosinophilic airway inflammation. Blood eosinophils, sputum eosinophils, FeNO, and serum periostin may help identify this phenotype. IL-5 promotes eosinophil development and survival, while IL-4 and IL-13 contribute to airway inflammation and remodeling. Patients frequently experience severe exacerbations but may respond well to biologics targeting IL-5, IL-5 receptor-α, IL-4 receptor-α, or TSLP [25–27,29].

4.4 Neutrophilic asthma

Neutrophilic asthma is a non-T2 phenotype characterized by increased airway neutrophils and Th1- and Th17-associated cytokines, including IFN-γ, IL-17, IL-6, and TNF-α. It is associated with smoking, chronic respiratory infections, occupational exposure, obesity, and corticosteroid-resistant severe asthma. Neutrophilic inflammation contributes to persistent inflammation, mucus production, tissue injury, and fixed airflow limitation. Specific approved therapies remain limited [24,28,30].

4.5 Obesity-associated asthma

Obesity-associated asthma is linked to more severe symptoms, impaired lung function, reduced quality of life, and poorer response to inhaled corticosteroids. Contributing mechanisms include altered lung mechanics, systemic inflammation, adipokine imbalance, oxidative stress, insulin resistance, and metabolic dysfunction. Leptin, adiponectin, IL-6, and TNF-α may worsen airway inflammation. Weight reduction through lifestyle changes, medication, or bariatric surgery can improve asthma control and lung function [24,31,32].

4.6 Exercise-induced asthma

Exercise-induced bronchoconstriction is temporary airway narrowing during or shortly after physical activity. Rapid breathing cools and dries the airways, triggering mast-cell activation and release of histamine, leukotrienes, and prostaglandins. Symptoms include cough, wheeze, breathlessness, chest tightness, and reduced exercise performance. Diagnosis requires exercise or bronchial provocation testing. Management includes controlling underlying asthma, pre-exercise reliever therapy, inhaled corticosteroids, leukotriene antagonists, and warm-up exercises [24,33,34].

Table 1. Major Asthma Phenotypes and Endotypes

Phenotype	Underlying endotype	Predominant inflammatory cells	Key biomarkers	Response to therapy
Allergic asthma	T2-high	Eosinophils, Th2 cells	IgE, FeNO, eosinophils	ICS, anti-IgE
Eosinophilic asthma	T2-high	Eosinophils	Blood eosinophils, FeNO	Anti-IL-5, Dupilumab
Non-allergic asthma	Mixed	Neutrophils/paucigranulocytic	No reliable biomarker	Variable
Neutrophilic asthma	Non-T2	Neutrophils	IL-17 (research)	Poor ICS response
Obesity-associated	Mixed	Low-grade systemic inflammation	BMI, IL-6	Weight reduction
Exercise-induced	Variable	Mast cells	Exercise challenge	ICS + SABA

5. Diagnosis

Asthma is diagnosed by looking at both common symptoms and clear signs of changes in airflow when someone exhales.Since asthma symptoms can change and might not be present during a medical checkup, it is recommended to use objective lung function tests to confirm the diagnosis whenever possible.Accurately identifying asthma is essential to avoid both missing the condition and giving the wrong diagnosis, which could lead to improper treatment or delays in recognizing other lung problems.Current guidelines stress the value of combining physical examinations with lung function tests and biomarkers to ensure a correct diagnosis and provide personalized care [35–37].

5.1 Clinical features

Asthma commonly involves repeated episodes of wheezing, difficulty breathing, a feeling of tightness in the chest, and coughing. These symptoms can vary in how severe they are and how often they occur. They often get worse at night or in the early morning and can be brought on by factors such as exposure to allergens, viral infections affecting the respiratory system, physical activity, cold air, tobacco smoke, workplace irritants, or emotional stress. A history of personal or family allergies, such as allergic rhinitis, eczema, or food allergies, can make asthma more likely. During a physical exam, a doctor might hear wheezing when someone exhales, notice longer exhalations, or observe the use of extra muscles to breathe during flare-ups. Between asthma attacks, the exam may show no signs of the condition [35–38].

5.2 Spirometry

Spirometry is the main test used to confirm asthma and evaluate the seriousness of airflow blockage. This test measures the amount of air exhaled forcefully in one second (FEV_1), the total amount of air exhaled forcefully after a deep breath (FVC), and the ratio of FEV_1 to FVC. A lower FEV_1/FVC ratio than the normal range or below 0.75 to 0.80 in adults, depending on their age, suggests airflow obstruction. Since asthma-related airflow blockage can change, spirometry results may be normal when symptoms are not present. Therefore, the test might need to be repeated when symptoms are present or after stopping bronchodilator medications [35–37,3].

5.3 Bronchodilator reversibility testing

Demonstration of reversible airflow blockage after using a short-acting bronchodilator is an important sign that helps confirm asthma. This test involves doing a spirometry test again about 10 to 15 minutes after inhaling 200 to 400 micrograms of salbutamol. A positive response is when the FEV_1 value increases by more than 12% and at least 200 milliliters compared to the initial measurement in adults. A normal response does not rule out asthma, especially in patients using inhaled corticosteroids or when there are no symptoms present [35–37].

5.4 Peak expiratory flow (PEF)

Peak expiratory flow measurement is a straightforward and cost-effective way to evaluate variable airflow limitation, especially in primary care and areas with limited resources. Patients use a portable peak flow meter to track their morning and evening PEF readings for at least two weeks. An average daily difference of more than about 10% in adults is generally considered to suggest variable airflow obstruction. Continuous monitoring of PEF is especially helpful in suspected occupational asthma and when spirometry is unavailable or normal despite ongoing symptoms [35–37].

5.5 Fractional exhaled nitric oxide (FeNO)

Fractional exhaled nitric oxide is a non-invasive marker of type 2 airway inflammation. Higher levels of FeNO are linked to eosinophilic inflammation and a better response to corticosteroid medicines. In adults, FeNO levels of 50 parts per billion or more usually indicate eosinophilic airway inflammation, while levels below 25 ppb suggest a lower likelihood of significant type 2 inflammation. The overall clinical situation should be considered when interpreting these results [35,40,41].

5.6 Biomarkers

The growing understanding that asthma varies among individuals has increased the use of biomarkers to characterize the disease and guide personalized treatment. Peripheral blood eosinophil count helps identify patients likely to respond to inhaled corticosteroids and biologic treatments targeting IL-5, IL-4/IL-13, and TSLP. Sputum eosinophil analysis is considered the best method for assessing airway eosinophilia but is limited by procedural complexity and poor availability. Total serum immunoglobulin E helps identify allergic asthma and patients who may benefit from anti-IgE therapy. Allergen-specific IgE testing helps determine relevant sensitization. Emerging biomarkers such as serum periostin and eosinophil-derived neurotoxin are not widely used because of limited standardization and variable accuracy [40–43].

6. Pharmacological Management

6.1 Reliever medications

Reliever medications provide rapid bronchodilation during acute asthma symptoms. Short-acting β_2-agonists (SABAs), including salbutamol and terbutaline, stimulate β_2 receptors, producing bronchodilation within minutes. However, SABA monotherapy is associated with increased exacerbations, hospitalization, and asthma-related mortality because it does not address underlying airway inflammation [44–46].

Current guidelines recommend low-dose ICS–formoterol as the preferred reliever for most adolescents and adults because it provides both rapid bronchodilation and anti-inflammatory effects, reducing severe exacerbations more effectively than SABA alone. Patients using SABA should also receive ICS-containing therapy [44–46].

6.2 Controller medications

Controller medications are taken regularly to suppress airway inflammation, reduce bronchial hyperresponsiveness, prevent exacerbations, and improve long-term asthma control. Treatment should be adjusted according to symptom control while ensuring correct inhaler technique, medication adherence, and management of comorbidities [44,45].

Major controller therapies include inhaled corticosteroids, long-acting β_2-agonists, long-acting muscarinic antagonists, leukotriene receptor antagonists, biologics, and oral corticosteroids in selected patients [44–46].

6.3 Inhaled corticosteroids (ICS)

Inhaled corticosteroids are the cornerstone of asthma treatment and the most effective anti-inflammatory therapy for persistent asthma. They reduce airway inflammation, eosinophilic infiltration, mast-cell activation, and airway hyperresponsiveness, thereby improving symptom control, lung function, and reducing exacerbations and asthma-related mortality [45–47].

Common ICS agents include budesonide, beclomethasone dipropionate, fluticasone propionate, fluticasone furoate, mometasone furoate, and ciclesonide. Common adverse effects include oral candidiasis, dysphonia, and throat irritation, while prolonged high-dose therapy may rarely cause systemic adverse effects such as adrenal suppression, osteoporosis, cataracts, glaucoma, skin bruising, and growth suppression in children [45–47].

6.4 Long-acting β_2-agonists (LABA)

Long-acting β_2-agonists provide bronchodilation for 12–24 hours. Common agents include formoterol, salmeterol, indacaterol, olodaterol, and vilanterol. Formoterol has a rapid onset and can be used with ICS as maintenance and reliever therapy, whereas salmeterol should not be used for acute symptom relief [45–48].

LABAs should never be used as monotherapy because they increase the risk of severe exacerbations and asthma-related mortality. Combination ICS/LABA inhalers improve symptom control, lung function, and reduce exacerbations compared with ICS alone [45,48].

6.5 Long-acting muscarinic antagonists (LAMA)

Long-acting muscarinic antagonists block M_3 receptors to reduce acetylcholine-mediated bronchoconstriction. Tiotropium is recommended as add-on therapy for patients with uncontrolled asthma despite medium- or high-dose ICS/LABA treatment. It modestly improves lung function and reduces exacerbations without significantly increasing adverse effects [44,49].

6.6 Leukotriene receptor antagonists (LTRAs)

Leukotriene receptor antagonists inhibit cysteinyl leukotriene receptors, reducing bronchoconstriction, mucus production, vascular permeability, and eosinophilic inflammation. Montelukast is the most commonly used agent, while zafirlukast is prescribed less frequently. LTRAs are less effective than ICS but may benefit patients with mild asthma, aspirin-exacerbated respiratory disease, exercise-induced bronchoconstriction, allergic rhinitis, or ICS intolerance [45,50].

6.7 Theophylline

Theophylline is a methylxanthine bronchodilator that inhibits phosphodiesterases, antagonizes adenosine receptors, and has modest anti-inflammatory activity. Its use has declined because of limited efficacy, a narrow therapeutic index, multiple drug interactions, and

adverse effects including nausea, vomiting, arrhythmias, and seizures [45,51].

6.8 Oral corticosteroids

Oral corticosteroids remain essential for moderate-to-severe acute asthma exacerbations by rapidly suppressing airway inflammation and reducing hospitalization and relapse. Prednisolone or prednisone for 5–7 days is usually sufficient for most acute exacerbations [44–46].

Long-term maintenance oral corticosteroid therapy should be avoided because of cumulative adverse effects, including osteoporosis, diabetes mellitus, hypertension, cataracts, glaucoma, adrenal suppression, obesity, infections, mood disorders, and cardiovascular disease. The availability of biologic therapies has substantially reduced the need for chronic oral corticosteroid treatment in severe asthma [45,52].

7. Biologic Therapy

Biologic therapies have transformed the treatment of severe asthma by targeting specific immune pathways responsible for persistent airway inflammation. They are recommended for patients whose asthma remains uncontrolled despite optimized high-dose inhaled corticosteroid–long-acting β_2-agonist therapy with good adherence, correct inhaler technique, and appropriate management of comorbidities. Current biologics mainly target type 2 inflammation by inhibiting IgE, IL-5, the IL-5 receptor, IL-4/IL-13 signalling, or thymic stromal lymphopoietin (TSLP). These therapies reduce severe exacerbations, oral corticosteroid use, and improve symptom control, lung function, and quality of life [53,54].

7.1 Mechanisms

Biologic agents are monoclonal antibodies that target specific cytokines or receptors involved in asthma. Omalizumab binds free IgE, reducing allergic inflammation. Mepolizumab and reslizumab inhibit IL-5, decreasing eosinophil survival, while benralizumab targets IL-5 receptor-α, resulting in eosinophil depletion [53-56].

Dupilumab blocks IL-4 receptor-α, inhibiting IL-4 and IL-13 signalling, thereby reducing IgE production, eosinophilic inflammation, mucus secretion, and airway hyperresponsiveness. Tezepelumab targets TSLP, blocking multiple upstream inflammatory pathways and demonstrating efficacy across a broader range of severe asthma phenotypes [53,54,57].

7.2 Indications

Biologic therapy should be considered only after confirming severe asthma and excluding causes of poor control such as poor adherence, incorrect inhaler technique, continued exposure to triggers, and unmanaged comorbidities. It is indicated for patients with frequent severe exacerbations, persistent symptoms, impaired lung function, or maintenance oral corticosteroid dependence despite optimized therapy [53,54].

Treatment selection depends on inflammatory phenotype, biomarkers, exacerbation history, age, and comorbidities. Omalizumab is indicated for severe allergic asthma, anti-IL-5 or anti-IL-5 receptor therapies for severe eosinophilic asthma, dupilumab for type 2 asthma with elevated eosinophils or FeNO, and tezepelumab for a broader spectrum of severe asthma [53,54].

7.3 Prediction of response

No single biomarker accurately predicts response to biologic therapy. Blood eosinophil count, FeNO, serum IgE, allergen sensitization, exacerbation history, oral corticosteroid use, age at onset, and type 2 comorbidities help guide treatment selection. Higher eosinophil counts predict better responses to anti-IL-5, anti-IL-5 receptor, dupilumab, and tezepelumab, whereas elevated FeNO predicts improved response to dupilumab and tezepelumab. Appropriate IgE levels with allergic sensitization support the use of omalizumab [53,58].

Clinical features such as nasal polyposis, adult-onset asthma, frequent exacerbations, corticosteroid dependence, and atopic dermatitis further assist biologic selection. Because eligibility often overlaps, treatment should be individualized using shared decision-making [53,54].

7.4 Monitoring

Treatment response should be assessed after approximately 4–6 months by evaluating exacerbation frequency, symptom control, lung function, reliever use, oral corticosteroid requirement, quality of life, and adverse effects. Biomarkers may support assessment but should not replace clinical outcomes [53,54].

A favourable response includes fewer exacerbations, improved symptom control and lung function, reduced corticosteroid use, and decreased healthcare utilization. In patients with inadequate response, adherence, comorbidities, persistent trigger exposure, and biologic selection should be reassessed, and switching to another biologic may be considered. Concurrent use of multiple biologics is not routinely recommended because of limited evidence, high cost, and uncertain long-term safety [53,54].

Safety monitoring varies by agent. Injection-site reactions and hypersensitivity may occur with all biologics. Omalizumab rarely causes anaphylaxis, dupilumab may cause transient eosinophilia or conjunctivitis, and anti-IL-5 therapies are generally well tolerated. Background controller therapy should initially be continued, with gradual reduction of corticosteroids when clinically appropriate.

7.5 Current biologics

7.5.1 Omalizumab

Omalizumab is a humanized monoclonal antibody that targets IgE and is used to treat severe allergic asthma.It works by lowering the amount of free IgE in the blood and reducing the number of IgE receptors on mast cells and basophils, which helps prevent their activation.This

treatment can decrease the frequency of asthma flare-ups and may help lower the need for corticosteroids in suitable patients.The level of IgE in the blood is used to decide if a patient is eligible for this treatment, but it does not always predict how well a patient will respond once treatment begins [53,59].

7.5.2 Mepolizumab

Mepolizumab is a subcutaneously administered monoclonal antibody that targets IL-5 and is used to treat severe eosinophilic asthma.It helps reduce asthma flare-ups, improves control of asthma symptoms, and lowers the need for long-term use of oral corticosteroids.The benefits of this treatment are often more pronounced in patients who have higher levels of eosinophils in their blood or who have had frequent flare-ups in the past [53,60].

7.5.3 Reslizumab

Reslizumab is an intravenously administered monoclonal antibody that targets IL-5 and is approved for use in certain adults with severe eosinophilic asthma.It helps reduce the frequency of asthma flare-ups and improves breathing, especially in patients with high levels of eosinophils.Since it is given intravenously and requires dosing based on weight, and it has a rare but possible risk of causing anaphylaxis, it may not be as commonly used compared to subcutaneous treatments [53,61].

7.5.4 Benralizumab

Benralizumab targets the IL-5 receptor-α and works by rapidly decreasing eosinophil levels through a process called antibody-dependent cell-mediated cytotoxicity.It helps reduce asthma flare-ups and lowers the need for oral corticosteroids.It also has a convenient dosing schedule once the initial treatment phase is completed.It is particularly useful for patients with severe eosinophilic asthma who experience frequent flare-ups or have a reliance on corticosteroids [53,62].

7.5.6 Dupilumab

Dupilumab is a monoclonal antibody that blocks the signals of two inflammatory proteins, IL-4 and IL-13, by targeting the IL-4 receptor-α.It helps reduce asthma flare-ups, improves lung function, and allows for a decrease in the use of oral corticosteroids in patients with type 2 high asthma.It is also effective for treating atopic dermatitis and chronic rhinosinusitis with nasal polyps, making it helpful for patients who have these conditions as well.Some patients may experience a temporary rise in eosinophil levels, and rare cases of eosinophil-related complications should be monitored closely, especially if symptoms indicate a more widespread disease [53,63].

7.5.7 Tezepelumab

Tezepelumab targets TSLP, suppressing multiple upstream inflammatory pathways. Clinical studies have demonstrated reduced exacerbations across a broad range of severe asthma phenotypes, including patients with lower eosinophil counts, although greater benefit is observed in those with higher blood eosinophils and FeNO levels. Its upstream mechanism makes it an important option for patients who do not fit the traditional allergic or eosinophilic asthma phenotypes [53,57].

7.5.8 Depemokimab

Depemokimab is an ultra-long-acting anti-IL-5 monoclonal antibody developed for severe eosinophilic asthma. Phase III studies have evaluated dosing every six months, potentially improving treatment adherence and reducing treatment burden. Its regulatory approval varies between countries, and current approval status should be verified before manuscript submission.

Table 2. Approved Biologic Therapies

Biologic	Target	Asthma phenotype	Key biomarker	Route	Dosing
Omalizumab	IgE	Allergic	IgE	SC	Every 2–4 weeks
Mepolizumab	IL-5	Eosinophilic	Eosinophils	SC	Every 4 weeks
Reslizumab	IL-5	Eosinophilic	Eosinophils	IV	Every 4 weeks
Benralizumab	IL-5Rα	Eosinophilic	Eosinophils	SC	Every 8 weeks*
Dupilumab	IL-4Rα	T2-high	FeNO, eosinophils	SC	Every 2 weeks
Tezepelumab	TSLP	Broad severe asthma	None required	SC	Every 4 weeks
Depemokimab†	IL-5	Eosinophilic	Eosinophils	SC	Every 6 months

8. Precision Medicine

Precision medicine individualizes asthma management according to each patient's biological, clinical, environmental, and behavioral characteristics rather than applying a uniform treatment strategy. It integrates phenotypes, endotypes, biomarkers, treatable traits, patient preferences, and long-term outcomes to optimize treatment selection [64,65].

8.1 Treatable Traits

The treatable-traits approach identifies measurable and modifiable characteristics within pulmonary, extrapulmonary, and behavioral domains. Pulmonary traits include type 2 inflammation, airflow limitation,

mucus hypersecretion, and recurrent exacerbations; extrapulmonary traits include allergic rhinitis, chronic rhinosinusitis, obesity, gastroesophageal reflux disease, obstructive sleep apnea, anxiety, and depression; behavioral traits include poor adherence, incorrect inhaler technique, smoking, allergen exposure, and poor self-management [64,65].

Identifying and treating these traits can improve asthma control while avoiding unnecessary escalation of therapy.

8.2 Biomarkers

Key biomarkers for type 2 asthma include blood eosinophils, sputum eosinophils, fractional exhaled nitric oxide (FeNO), total IgE, and allergen-specific IgE. These biomarkers guide biologic selection and assessment of type 2 inflammation but should always be interpreted alongside clinical features and treatment history. Reliable biomarkers for non-type 2 asthma remain limited.

8.3 Personalized Therapy

Personalized therapy combines guideline-based management with phenotype-directed treatment. Patients with type 2 asthma generally respond well to corticosteroids and biologics guided by eosinophil counts, FeNO, IgE levels, and comorbidities, whereas non-type 2 asthma requires management of alternative mechanisms such as smoking, obesity, infections, occupational exposures, and poor adherence. Treatment decisions should also consider inhaler selection, patient preferences, health literacy, treatment availability, and cost, with the goal of achieving sustained disease control, preventing exacerbations, preserving lung function, and minimizing corticosteroid exposure.

8.4 Omics

Omics technologies—such as genomics, transcriptomics, proteomics, metabolomics, and microbiomics—help identify molecular patterns linked to asthma subtypes and how patients respond to treatment. Combining data from multiple omics fields may enhance the ability to group patients and provide more precise treatments.However, the use of these technologies is currently limited due to their high cost, technical complexity, and the need for further validation outside research settings [66].

8.5 Pharmacogenomics

Pharmacogenomics explores how genetic differences affect how individuals respond to drugs.Certain genetic variations in genes such as ADRB2, GLCCI1, CRHR1, TBX21, FCER2, ALOX5, and LTC4S have been linked to how well people respond to β_2-agonists, corticosteroids, and leukotriene modifiers (67,68).However, genetic testing for asthma management is not yet recommended for regular clinical use because the current evidence is not strong enough.

9. Emerging Therapies

Current biologics have improved the treatment of severe type 2 asthma, but there are still unmet medical needs in non-type 2 asthma, airway remodeling, resistance to corticosteroids, and disease prevention.New therapies are being developed to target epithelial alarmins, new cytokines, gene regulation, nanotechnology, and digital health solutions.

9.1 TSLP Inhibitors

TSLP is an upstream epithelial alarmin that starts type 2 inflammation. Tezepelumab has shown that blocking TSLP can reduce asthma flare-ups in various patient groups.Future research will explore whether using these inhibitors early can stop airway remodeling and slow disease progression [57].

9.2 IL-33 Inhibitors

IL-33 triggers inflammation by acting on the ST2 receptor in multiple immune cells.Drugs like itepekimab and astegolimab have shown promising results, but more large-scale trials are needed to understand their role and who would benefit most from them [69,70].

9.3 IL-25 Inhibitors

IL-25 contributes to type 2 inflammation and airway remodeling by activating ILC2s and Th2 cells.The clinical development of these inhibitors is still in early stages, and more studies are necessary to assess their therapeutic potential.

9.4 CRTH2 Antagonists

CRTH2 antagonists reduce type 2 inflammation by blocking the effects of prostaglandin D_2.While initial studies were encouraging, larger clinical trials did not show enough benefit for these drugs to be used routinely in clinical practice [71].

9.5 Gene Therapy and RNA-Based Treatment

Gene-editing technologies, siRNA, antisense oligonucleotides, and mRNA-based treatments aim to stop specific inflammatory pathways. However, their use in clinical settings is still experimental due to challenges in delivering these treatments effectively into the airways, ensuring safety, and proving long-term effectiveness.

9.6 Nanomedicine

Nanoparticle-based drug delivery systems may improve the targeted delivery of corticosteroids, biologics, and nucleic acids to the lungs, reducing side effects on the rest of the body.However, manufacturing challenges, safety concerns, and regulatory hurdles are currently preventing these systems from being used widely in clinical practice.

9.7 Artificial Intelligence

Artificial intelligence and machine learning could improve the diagnosis, classification, prediction, and treatment of asthma by analyzing clinical data and biomarkers.However, issues like bias, patient privacy, and the ability to apply these tools broadly require further investigation before they can be widely adopted.

9.8 Smart Inhalers

Smart inhalers use electronic sensors to track medication use and patient adherence, helping to tell the difference between poor adherence and actual treatment failure.Their success depends on cost, patient acceptance, and their integration into standard asthma care.

9.9 Digital Health

Digital health tools, including telemedicine, mobile apps, remote spirometry, wearable sensors, and home FeNO monitoring, allow for continuous tracking of asthma and earlier intervention, especially for people in remote areas. These tools should be used to support, rather than replace, traditional methods of asthma care [72].

Table 3. Emerging Therapeutic Targets in Asthma

Target	Example(s)	Mechanism	Development status
TSLP	Tezepelumab	Alarmin inhibition	Approved
IL-33	Itepekimab, Astegolimab	ST2 pathway inhibition	Phase II/III
IL-25	Experimental agents	Type 2 inflammation blockade	Early trials
CRTH2	Fevipiprant	PGD_2 receptor blockade	Limited efficacy
Gene/RNA therapy	siRNA, mRNA	Gene regulation	Experimental
Nanomedicine	Nanoparticles	Targeted pulmonary delivery	Experimental
AI & Digital health	Smart inhalers, ML	Monitoring and prediction	Emerging

10. Future Directions

Future asthma management should focus on disease prevention, disease modification, and long-term remission rather than symptom control alone. Longitudinal studies are needed to understand asthma progression and determine whether early intervention can prevent airway remodeling and irreversible airflow limitation. Birth-cohort studies may identify critical periods for targeting epithelial dysfunction, viral responses, allergen sensitization, and microbiome development to prevent disease onset.

Developing effective therapies for non-type 2 asthma, including neutrophilic and paucigranulocytic phenotypes, remains a major priority. Future research should target epithelial danger signals, inflammasomes, IL-17 pathways, macrophage dysfunction, airway infections, mucus dysregulation, neural mechanisms, and airway remodeling. Therapies capable of reversing airway smooth-muscle hypertrophy, fibrosis, and mucus plugging may provide greater long-term benefit than anti-inflammatory treatment alone.

Biologic therapy should evolve toward precision-based selection using clinical characteristics, biomarkers, comorbidities, and multi-omics data. Comparative-effectiveness studies and standardized definitions of treatment response, remission, and treatment failure are required to optimize biologic use. The optimal treatment duration, switching strategies, dose reduction, discontinuation, and long-term safety of immune modulation remain uncertain.

Asthma remission is emerging as an important therapeutic goal and should include sustained absence of exacerbations, minimal symptoms, preserved lung function, reduced corticosteroid use, and lower treatment burden. Whether biologic therapies modify the natural history of asthma or primarily suppress inflammation remains an important area for future research.

11. Conclusion

Asthma is a varied inflammatory condition affecting the airways, caused by a mix of genetic factors, problems with the airway lining, immune system issues, exposure to environmental factors, and changes in the structure of the airways. Identifying different types of asthma based on their underlying biological and clinical features has changed how the disease is understood, moving from a single diagnosis to a group of distinct conditions with different characteristics. Using biomarkers to guide treatment and focusing on treatable traits help provide a more personalized approach by considering factors such as lung function, other health conditions outside the lungs, and behaviors that affect asthma control.

Despite these advancements, there are still important needs that have not been met, especially in cases of type 2-low asthma, airway remodeling, mucus plugging, resistance to corticosteroids, and unequal access to effective care.New therapies that target alarmins, along with the use of omics technologies, pharmacogenomics, gene-based treatments, nanomedicine, artificial intelligence, smart inhalers, and digital health platforms, could help improve diagnosis and treatment.However, their real-world benefit will rely on thorough testing, affordability, fair access, protection of patient data, and clear evidence of meaningful improvements in outcomes that matter to patients.

The future of asthma care should combine precise biological targeting with thorough clinical evaluation and shared decision-making between patients and healthcare providers. This approach could change the focus of treatment from just controlling symptoms to preventing flare-ups, maintaining lung function,

reducing corticosteroid side effects, slowing disease progression, and achieving long-term remission.

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References

1. Porsbjerg C, Melén E, Lehtimäki L, Shaw DE. Asthma. Lancet. 2023;401(10379):858-873. https://doi.org/10.1016/S0140-6736(22)02125-0 PMid:36682372

2. Jayasooriya SM, Devereux G, Soriano JB, Singh N, Masekela R, Mortimer K, et al. Asthma: epidemiology, risk factors, and opportunities for prevention and treatment. Lancet Respir Med. 2025;13(8):725-738. https://doi.org/10.1016/S2213-2600(24)00383-7 PMid:40684789

3. Wang Z, Li Y, Gao Y, et al. Global, regional, and national burden of asthma and its attributable risk factors from 1990 to 2019: a systematic analysis for the Global Burden of Disease Study 2019. Respir Res. 2023;24:169. https://doi.org/10.1186/s12931-023-02475-6 PMid:37353829 PMCid:PMC10288698

4. Holgate ST, Wenzel S, Postma DS, Weiss ST, Renz H, Sly PD. Asthma. Nat Rev Dis Primers. 2015;1:15025. https://doi.org/10.1038/nrdp.2015.25 PMid:27189668 PMCid:PMC7096989

5. Kato A, Kita H. The immunology of asthma and chronic rhinosinusitis. Nat Rev Immunol. 2025;25(8):569-587. https://doi.org/10.1038/s41577-025-01159-0 PMid:40240657 PMCid:PMC12560183

6. Hammad H, Lambrecht BN. Dendritic cells and epithelial cells: linking innate and adaptive immunity in asthma. Nat Rev Immunol. 2008;8(3):193-204. https://doi.org/10.1038/nri2275 PMid:18301423

7. Camoretti-Mercado B, Lockey RF. Airway smooth muscle pathophysiology in asthma. J Allergy Clin Immunol. 2021;147(6):1983-1995. https://doi.org/10.1016/j.jaci.2021.03.035 PMid:34092351

8. Anderson GP. Endotyping asthma: new insights into key pathogenic mechanisms in a complex, heterogeneous disease. Lancet. 2008;372(9643):1107-1119. https://doi.org/10.1016/S0140-6736(08)61452-X PMid:18805339 PMCid:PMC6549890

9. Joseph C, Tatler AL. Pathobiology of airway remodeling in asthma: the emerging role of integrins. J Asthma Allergy. 2022;15:595-610. https://doi.org/10.2147/JAA.S267222 PMid:35592385 PMCid:PMC9112045

10. Barnes PJ. Immunology of asthma and chronic obstructive pulmonary disease. Nat Rev Immunol. 2008;8(3):183-192. https://doi.org/10.1038/nri2254 PMid:18274560 PMCid:PMC13286889

11. Berend N, Salome CM, King GG. Mechanisms of airway hyperresponsiveness in asthma. Respirology. 2008;13(5):624-631. https://doi.org/10.1111/j.1440-1843.2008.01330.x PMid:18713086

12. Moffatt MF, Gut IG, Demenais F, et al. A large-scale, consortium-based genomewide association study of asthma. N Engl J Med. 2010;363(13):1211-1221. https://doi.org/10.1056/NEJMoa0906312 PMid:20860503

13. Ober C, Yao TC. The genetics of asthma and allergic disease: a 21st century perspective. Immunity. 2011;35(5):646-656.

14. Kabesch M, Tost J. Recent findings in the genetics and epigenetics of asthma and allergy. Semin Immunopathol. 2020;42(1):43-60. https://doi.org/10.1007/s00281-019-00777-w PMid:32060620 PMCid:PMC7066293

15. Yang IV, Schwartz DA. Epigenetic mechanisms and the development of asthma. J Allergy Clin Immunol. 2012;130(6):1243-1255. https://doi.org/10.1016/j.jaci.2012.07.052 PMid:23026498 PMCid:PMC3518374

16. Platts-Mills TAE. The role of allergens in allergic airway disease. J Allergy Clin Immunol. 2015;136(4):845-852.

17. Guarnieri M, Balmes JR. Outdoor air pollution and asthma. Lancet. 2014;383(9928):1581-1592. https://doi.org/10.1016/S0140-6736(14)60617-6 PMid:24792855 PMCid:PMC4465283

18. Huang K, Yang X, Liang F, et al. Long-term exposure to air pollution and asthma: recent advances and future directions. Chest. 2024;165(3):623-636.

19. Polosa R, Thomson NC. Smoking and asthma: dangerous liaisons. Eur Respir J. 2013;41(3):716-726. https://doi.org/10.1183/09031936.00073312 PMid:22903959

20. Tarlo SM, Lemiere C. Occupational asthma. N Engl J Med. 2014;370(7):640-649. https://doi.org/10.1056/NEJMra1301758 PMid:24521110

21. Baur X. A compendium of causative agents of occupational asthma. J Occup Med Toxicol. 2013;8:15. https://doi.org/10.1186/1745-6673-8-15 PMid:23706060 PMCid:PMC3665602

22. Agache I, Akdis CA, Akdis M, et al. EAACI Biologicals Guidelines-recommendations for severe asthma. Allergy. 2021;76(1):14-44. https://doi.org/10.1111/all.14425 PMid:32484954

23. Fahy JV. Type 2 inflammation in asthma-present in most, absent in many. Nat Rev Immunol. 2015;15(1):57-65. https://doi.org/10.1038/nri3786 PMid:25534623

24. Wenzel SE. Asthma phenotypes: the evolution from clinical to molecular approaches. Nat Med. 2012;18(5):716-725. https://doi.org/10.1038/nm.2678 PMid:22561835

25. McGregor MC, Krings JG, Nair P, Castro M. Role of biologics in asthma. Am J Respir Crit Care Med. 2019;199(4):433-445. https://doi.org/10.1164/rccm.201810-1944CI PMid:30525902 PMCid:PMC6835092

26. Brusselle GG, Koppelman GH. Biologic therapies for severe asthma. N Engl J Med. 2022;386(2):157-171. https://doi.org/10.1056/NEJMra2032506 PMid:35020986

27. Ray A, Kolls JK. Neutrophilic inflammation in asthma and association with disease severity. Trends Immunol. 2017;38(12):942-954. https://doi.org/10.1016/j.it.2017.07.003 PMid:28784414 PMCid:PMC5711587

28. Peters U, Dixon AE, Forno E. Obesity and asthma. J Allergy Clin Immunol. 2018;141(4):1169-1179. https://doi.org/10.1016/j.jaci.2018.02.004 PMid:29627041 PMCid:PMC5973542

29. Lugogo N, Kraft M, Dixon AE. Does obesity produce a distinct asthma phenotype? J Appl Physiol (1985). 2010;108(3):729-734. https://doi.org/10.1152/japplphysiol.00845.2009 PMid:19875708 PMCid:PMC2838637

30. Parsons JP, Hallstrand TS, Mastronarde JG, et al. An official American Thoracic Society clinical practice guideline: exercise-induced bronchoconstriction. Am J Respir Crit Care Med. 2013;187(9):1016-1027. https://doi.org/10.1164/rccm.201303-0437ST PMid:23634861 PMCid:PMC10038260

31. Weiler JM, Bonini S, Coifman R, et al. American Academy of Allergy, Asthma & Immunology work group report: exercise-induced asthma. J Allergy Clin Immunol. 2007;119(6):1349-1358. https://doi.org/10.1016/j.jaci.2007.02.041 PMid:17433829

32. Global Initiative for Asthma. Global strategy for asthma management and prevention: 2025 update. Fontana (WI): Global Initiative for Asthma; 2025.

33. Reddel HK, Taylor DR, Bateman ED, et al. An official American Thoracic Society/European Respiratory Society statement: asthma control and exacerbations. Am J Respir Crit Care Med.

2009;180(1):59-99. https://doi.org/10.1164/rccm.200801-060ST PMid:19535666

34. Hekking PWP, Wener RR, Amelink M, et al. The prevalence of severe refractory asthma. J Allergy Clin Immunol. 2015;135(4):896-902. https://doi.org/10.1016/j.jaci.2014.08.042 PMid:25441637

35. Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005;26(5):948-968. https://doi.org/10.1183/09031936.05.00035205 PMid:16264058

36. Khatri SB, Iaccarino JM, Barochia A, et al. Use of fractional exhaled nitric oxide to guide the treatment of asthma: an official American Thoracic Society clinical practice guideline. Am J Respir Crit Care Med. 2021;204(10)-e109. https://doi.org/10.1164/rccm.202109-2093ST PMid:34779751 PMCid:PMC8759314

37. Couillard S, Jackson DJ, Johnston SL, Pavord ID. Biomarkers of type 2 inflammation in asthma: a systematic review and meta-analysis. Eur Respir J. 2022;60(1):2201147.

38. Agache I, Akdis CA, Akdis M, et al. EAACI biologicals guidelines: biomarkers in asthma. Allergy. 2023;78(11):2940-2963.

39. Diamant Z, Vijverberg SJH, Alving K, et al. Toward clinically applicable biomarkers for asthma: an EAACI position paper. Allergy. 2019;74(10):1835-1851. https://doi.org/10.1111/all.13806 PMid:30953574

40. Papi A, Brightling C, Pedersen SE, Reddel HK. Asthma. Lancet. 2018;391(10122):783-800. https://doi.org/10.1016/S0140-6736(17)33311-1 PMid:29273246

41. Beasley R, Holliday M, Reddel HK, et al. Controlled trial of budesonide-formoterol as needed for mild asthma. N Engl J Med. 2019;380(21):2020-2030. https://doi.org/10.1056/NEJMoa1901963 PMid:31112386 PMCid:PMC7332932

42. Barnes PJ. Inhaled corticosteroids. Pharmacol Ther. 2022;237:108166.

43. Cazzola M, Rogliani P, Matera MG. β2-Adrenoceptor agonists: current and future direction. Br J Pharmacol. 2022;179(19):4452-4470.

44. Virchow JC, Kuna P, Paggiaro P, et al. Tiotropium add-on therapy in asthma: a systematic review and meta-analysis. Respir Med. 2019;152:34-42.

45. Israel E, Reddel HK. Severe and difficult-to-treat asthma in adults. N Engl J Med. 2017;377(10):965-976. https://doi.org/10.1056/NEJMra1608969 PMid:28877019

46. Scurek M, et al. A narrative review of theophylline: is there still a place for an old friend? J Thorac Dis. 2024;16(6):4065-4080. https://doi.org/10.21037/jtd-23-1781 PMid:38883616 PMCid:PMC11170423

47. Price DB, Trudo F, Voorham J, et al. Adverse outcomes from initiation of systemic corticosteroids for asthma: long-term observational study. J Asthma Allergy. 2018;11:193-204. https://doi.org/10.2147/JAA.S176026 PMid:30214247 PMCid:PMC6121746

48. Gyawali B, Georas SN, Khurana S. Biologics in severe asthma: a state-of-the-art review. Eur Respir Rev. 2025;34(175):240088. https://doi.org/10.1183/16000617.0088-2024 PMid:39778920 PMCid:PMC11707604

49. Faria N, Costa MI, Fernandes AL, et al. Biologic therapies for severe asthma: current insights and future directions. J Clin Med. 2025;14(9):3153. https://doi.org/10.3390/jcm14093153 PMid:40364184 PMCid:PMC12072268

50. Menzella F, Lusuardi M, Galeone C, Zucchi L. Tailored therapy for severe asthma. Multidiscip Respir Med. 2015;10:1. https://doi.org/10.1186/2049-6958-10-1 PMid:25671117 PMCid:PMC4323120

51. Kolbeck R, Kozhich A, Koike M, et al. MEDI-563, a humanized anti-IL-5 receptor-α monoclonal antibody with enhanced antibody-dependent cell-mediated cytotoxicity function. J Allergy Clin Immunol. 2010;125(6):1344-1353.e2. https://doi.org/10.1016/j.jaci.2010.04.004 PMid:20513525

52. Menzies-Gow A, Corren J, Bourdin A, et al. Tezepelumab in adults and adolescents with severe, uncontrolled asthma. N Engl J Med. 2021;384(19):1800-1809. https://doi.org/10.1056/NEJMoa2034975 PMid:33979488 PMCid:PMC9166326

53. Rattu A, Dixey P, Charles D, et al. Predictors of response to biologics for severe asthma: a systematic review and meta-analysis. Allergy. 2026;81(1):24-55. https://doi.org/10.1111/all.70031 PMid:40956008 PMCid:PMC12773690

54. Hanania NA, Alpan O, Hamilos DL, et al. Omalizumab in severe allergic asthma inadequately controlled with standard therapy. Ann Intern Med. 2011;154(9):573-582. https://doi.org/10.7326/0003-4819-154-9-201105030-00002 PMid:21536936

55. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med. 2014;371(13):1198-1207. https://doi.org/10.1056/NEJMoa1403290 PMid:25199059

56. Castro M, Zangrilli J, Wechsler ME, et al. Reslizumab for inadequately controlled asthma with elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomised, placebo-controlled, phase 3 trials. Lancet Respir Med. 2015;3(5):355-366. https://doi.org/10.1016/S2213-2600(15)00042-9 PMid:25736990

57. Nair P, Wenzel S, Rabe KF, et al. Oral glucocorticoid-sparing effect of benralizumab in severe asthma. N Engl J Med. 2017;376(25):2448-2458. https://doi.org/10.1056/NEJMoa1703501 PMid:28530840

58. Rabe KF, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. N Engl J Med. 2018;378(26):2475-2485. https://doi.org/10.1056/NEJMoa1804093 PMid:29782224

59. Agustí A, Bel E, Thomas M, et al. Treatable traits: toward precision medicine of chronic airway diseases. Eur Respir J. 2016;47(2):410-419. https://doi.org/10.1183/13993003.01359-2015 PMid:26828055

60. McDonald VM, Gibson PG. Treatable traits in asthma: moving beyond diagnostic labels. Med J Aust. 2022;216(7):331-333. https://doi.org/10.5694/mja2.51464 PMid:35342966 PMCid:PMC9313553

61. Yue M, Tran H, Davidson D, et al. Omics approaches in asthma research: challenges and opportunities. J Allergy Clin Immunol Glob. 2024;3:100192. https://doi.org/10.1016/j.pccm.2024.02.002 PMid:39170962 PMCid:PMC11332849

62. Ortega VE, Meyers DA. Pharmacogenetics: implications of race and ethnicity on defining genetic profiles for personalized medicine. J Allergy Clin Immunol. 2014;133(1):16-26. https://doi.org/10.1016/j.jaci.2013.10.040 PMid:24369795 PMCid:PMC3933289

63. Farzan N, Vijverberg SJH, Andiappan AK, et al. Rationale and design of pharmacogenomic studies of asthma treatment response. Pharmacogenomics. 2020;21(9):591-604.

64. Wechsler ME, Ruddy MK, Pavord ID, et al. Efficacy and safety of itepekimab in patients with moderate-to-severe asthma. N Engl J Med. 2021;385(18):1656-1668. https://doi.org/10.1056/NEJMoa2024257 PMid:34706171

65. Kelsen SG, Agache IO, Soong W, et al. Astegolimab, an anti-ST2, in chronic severe asthma: the ZENYATTA randomized clinical trial. J Allergy Clin Immunol. 2021;148(3):790-798. https://doi.org/10.1016/j.jaci.2021.03.044 PMid:33872652

66. Brightling CE, Gaga M, Inoue H, et al. Effectiveness of fevipiprant in reducing exacerbations in patients with severe asthma: the LUSTER-1 and LUSTER-2 randomized clinical trials. Lancet Respir Med. 2021;9(1):43-56. https://doi.org/10.1016/S2213-2600(20)30412-4 PMid:32979986

67. Kaplan A, Cao H, FitzGerald JM, et al. The emerging role of digital health in the management of asthma. Ther Adv Respir Dis. 2023;17:17534666231215235. https://doi.org/10.1177/20406223231209329 PMid:38028951 PMCid:PMC10657529

68. Jackson DJ, Bacharier LB, Gergen PJ, et al. Twice-yearly depemokimab in severe asthma with an eosinophilic phenotype. N Engl J Med. 2024;391:2337-2349. https://doi.org/10.1056/NEJMoa2406673 PMid:39248309

69. Ferreira MAR, Vonk JM, Baurecht H, Marenholz I, Tian C, Hoffman JD, et al. Shared genetic origin of asthma, hay fever and eczema elucidates allergic disease biology. Nat Genet. 2017;49(12):1752-1757. https://doi.org/10.1038/ng.3985 PMid:29083406

70. Haldar P, Pavord ID, Shaw DE, Berry MA, Thomas M, Brightling CE, et al. Cluster analysis and clinical asthma phenotypes. Am J Respir Crit Care Med. 2008;178(3):218-224. https://doi.org/10.1164/rccm.200711-1754OC PMid:18480428

71. Louis R, Satia I, Ojanguren I, Schleich F, Bonini M, Tonia T, et al. European Respiratory Society guidelines for the diagnosis of asthma in adults. Eur Respir J. 2022;60(3):2101585. https://doi.org/10.1183/13993003.01585-2021 PMid:35169025

72. Reddel HK, Bacharier LB, Bateman ED, Brightling CE, Brusselle GG, Buhl R, et al. Global Initiative for Asthma Strategy 2021: executive summary and rationale for key changes. Eur Respir J. 2022;59(1):2102730. https://doi.org/10.1183/13993003.02730-2021 PMid:34667060