Integrated Approach to Pediatric Asthma Allergic Rhinitis and Atopic Multimorbidity

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ABSTRACT

Asthma and allergic diseases are among the most common chronic disorders in childhood and adolescence, producing a substantial burden through recurrent symptoms, school absenteeism, impaired sleep, emergency visits and reduced quality of life. Traditionally, bronchial asthma, allergic rhinitis, atopic dermatitis and food allergy have often been evaluated as separate conditions. However, growing clinical and immunological evidence supports a more integrated concept of "united airway disease" and atopic multimorbidity, in which upper and lower airway inflammation, epithelial barrier dysfunction, type 2 immune responses and environmental exposures interact across childhood. Allergic rhinitis is particularly important because it frequently coexists with asthma, worsens asthma control and may precede lower airway disease. This review summarizes current evidence on the epidemiology, pathophysiology, diagnosis and management of pediatric asthma associated with allergic rhinitis and other allergic disorders. Special attention is given to early-life risk factors, the atopic march, type 2 inflammation, allergen sensitization, air pollution, climate change, diagnostic tools, inhaled corticosteroid-based treatment, allergen immunotherapy and biologic therapy for severe asthma. The review emphasizes that optimal care requires systematic assessment of comorbid allergic rhinitis, inhaler technique, adherence, environmental triggers and individualized risk of exacerbations. Integrated management may improve asthma control, reduce medication burden and prevent disease progression in selected children. Future research should prioritize phenotype-based studies, locally adapted diagnostic algorithms, real-world evidence on biologics and immunotherapy, and prevention strategies targeting environmental and social determinants of pediatric allergic disease.

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Introduction

Asthma is the most frequent chronic respiratory disease in childhood and remains a leading cause of recurrent wheeze, breathlessness, cough, school absenteeism and urgent medical visits. Although many children achieve acceptable disease control with inhaled corticosteroid-based therapy, a considerable proportion continue to experience uncontrolled symptoms or exacerbations because of underdiagnosis, poor adherence, incorrect inhaler technique, continued allergen exposure, air pollution, obesity, viral infections and untreated comorbidities [1,2]. Among these comorbidities, allergic rhinitis is one of the most clinically relevant because it affects the same airway system and shares many immunopathological mechanisms with asthma.

The concept of "united airway disease" proposes that the nose, paranasal sinuses and bronchi form a continuous inflammatory unit rather than independent organs. This concept is especially important in children, in whom allergic rhinitis, recurrent wheeze, atopic dermatitis and food allergy may develop sequentially or together as part of atopic multimorbidity [3,4]. In clinical practice, a child with asthma frequently has nasal obstruction, sneezing, rhinorrhea, postnasal drip or sleep disturbance; however, these symptoms may be overlooked if the physician focuses only on lower airway symptoms. Failure to treat allergic rhinitis may contribute to poor asthma control, persistent cough and increased rescue medication use.

This review discusses pediatric asthma and allergic diseases from an integrated perspective. The proposed topic is: United Airway Disease in Children: Integrating Asthma, Allergic Rhinitis and Atopic Multimorbidity. The aim is to summarize modern evidence on epidemiology, pathophysiology, diagnosis and management, and to identify practical research directions suitable for pediatric internal medicine.

Epidemiology and clinical burden

The global burden of childhood asthma remains substantial, although prevalence varies widely by region, urbanization, socioeconomic status and diagnostic access. The Global Asthma Network has shown that asthma

symptoms remain common among school-aged children and adolescents, with many children having symptoms without a formal diagnosis or adequate treatment [2,5]. This underdiagnosis is particularly important in low- and middle-income settings, where access to spirometry, inhaled corticosteroids, allergy testing and asthma education may be limited.

Allergic rhinitis is also highly prevalent in childhood and adolescence. It may appear as seasonal disease associated with pollen exposure or as perennial disease caused by house dust mite, molds, animal dander or indoor allergens. Although allergic rhinitis is sometimes considered a mild condition, its consequences include impaired sleep, daytime fatigue, poor school performance, irritability, mouth breathing, recurrent cough and increased healthcare use [3,6]. When allergic rhinitis coexists with asthma, the combined burden is greater than either disease alone.

Atopic dermatitis and food allergy also contribute to the pediatric allergic disease spectrum. The traditional "atopic march" describes a sequence in which atopic dermatitis and food allergy appear in infancy, followed later by allergic rhinitis and asthma. However, current evidence suggests that allergic disease progression is not always linear. Many children show overlapping phenotypes, remission, recurrence or persistent multimorbidity rather than a single predictable pathway [4]. Therefore, the term "atopic multimorbidity" may better reflect real clinical patterns.

Environmental change is also reshaping the epidemiology of asthma and allergic disease. Urbanization, traffic-related air pollution, indoor pollution, tobacco smoke exposure, reduced biodiversity, climate-related changes in pollen seasons and respiratory viral infections may all influence asthma development and exacerbations [7,8]. These factors are especially relevant in children because their lungs and immune systems are still developing, they breathe more air per kilogram of body weight than adults and they may have limited control over their environment.

Pathophysiology: from type 2 inflammation to united airway disease

Pediatric asthma is heterogeneous, but allergic or type 2-high asthma is one of the most common phenotypes in school-age children. This phenotype is characterized by allergen sensitization, eosinophilic airway inflammation, increased immunoglobulin E, elevated fractional exhaled nitric oxide in some patients, and responsiveness to inhaled corticosteroids [1,9]. Key cytokines include interleukin-4, interleukin-5 and interleukin-13, which promote IgE production, eosinophil activation, mucus hypersecretion, airway hyperresponsiveness and epithelial remodeling.

The united airway model is based on the anatomical and immunological continuity between the upper and lower respiratory tract. The nasal mucosa and bronchial mucosa are exposed to similar allergens and pollutants. In sensitized children, allergen exposure in the nose may trigger systemic inflammatory responses that influence bronchial reactivity. Similarly, bronchial inflammation may coexist with nasal inflammation even when nasal symptoms are mild. This explains why allergic rhinitis is not only a comorbidity but also a potential marker of asthma risk and severity [3,10].

Epithelial barrier dysfunction is another central mechanism. The airway and skin epithelium act as the first defense against allergens, pathogens and pollutants. Damage to epithelial barriers through genetic susceptibility, viral infection, pollutants, detergents, tobacco smoke or microbiome disruption may increase allergen penetration and immune activation [4,7]. In early childhood, skin barrier dysfunction in atopic dermatitis may promote sensitization to food and aeroallergens, while airway epithelial dysfunction may support allergic rhinitis and asthma development.

The microbiome also influences immune maturation. Reduced microbial diversity, early antibiotic exposure, cesarean delivery, limited exposure to natural environments and dietary changes have been associated with altered immune tolerance. Although causality is complex, these observations support the idea that allergic disease results from interactions between genes, epithelial barriers, immune responses and environmental exposures rather than a single cause.

Clinical phenotypes and risk factors

Children with asthma and allergic disease can present with several overlapping phenotypes. Preschool children often have recurrent viral-induced wheeze, and not all of them develop persistent asthma. Risk increases when wheeze occurs without colds, when there is eczema, allergic rhinitis, parental asthma, eosinophilia or sensitization to aeroallergens [1]. In school-age children, asthma is more likely to show reversible airflow limitation and association with allergic sensitization.

Allergic rhinitis-associated asthma is a common phenotype. These children may have sneezing, nasal obstruction, itchy nose, watery rhinorrhea, allergic conjunctivitis, postnasal drip and nocturnal cough. Nasal obstruction may cause mouth breathing, snoring and sleep fragmentation. In some cases, cough attributed to asthma may partly result from rhinitis and postnasal drip. Therefore, assessment of nasal symptoms is essential in any child with persistent asthma symptoms [3,6].

Severe asthma in children is less common than mild or moderate asthma, but it carries a disproportionate burden. Before labeling a child as having severe asthma, clinicians must exclude poor adherence, incorrect inhaler technique, wrong diagnosis, continued allergen exposure, passive smoking, obesity, chronic rhinosinusitis, gastroesophageal reflux, dysfunctional breathing and psychosocial factors [9]. True severe asthma often requires specialist evaluation and

may be eligible for biologic therapy when type 2 inflammation is demonstrated.

Important risk factors for pediatric asthma and allergic disease include family history of atopy, early atopic dermatitis, food allergy, allergic rhinitis, prematurity, tobacco smoke, indoor dampness, mold exposure, traffic-related pollution, obesity, low physical activity, viral lower respiratory infections and socioeconomic disadvantage [4,7,8]. Some exposures have complex effects. For example, contact with diverse microbial environments may be protective in some rural settings, while indoor dampness and pollution increase respiratory risk.

Diagnosis and assessment

Diagnosis of pediatric asthma should be based on a combination of characteristic symptom patterns, objective evidence of variable airflow limitation when feasible, and exclusion of alternative diagnoses. Typical symptoms include recurrent wheeze, cough, shortness of breath and chest tightness that vary over time and worsen with exercise, viral infections, allergens, cold air, laughter or nighttime exposure [1]. In children older than five years, spirometry with bronchodilator reversibility is recommended when available. Peak expiratory flow variability, bronchial challenge testing and FeNO may provide additional information in selected cases [1,11].

FeNO is particularly useful as a noninvasive marker of type 2 airway inflammation, but it should not be interpreted in isolation. FeNO can be elevated in allergic rhinitis and atopy even without asthma, and low FeNO does not exclude asthma, especially in non-type 2 disease or after corticosteroid use [11]. Blood eosinophils, total IgE and allergen-specific IgE can support phenotyping, but they also require clinical correlation.

Assessment of allergic rhinitis should include timing of symptoms, seasonality, exposure triggers, sleep disturbance, school impairment and response to previous therapy. Physical examination may show pale or edematous nasal mucosa, allergic salute, nasal crease, mouth breathing or allergic conjunctivitis. Skin prick testing or serum specific IgE can help identify relevant allergens, particularly when environmental control or allergen immunotherapy is being considered [3,6].

An integrated pediatric assessment should also include asthma control, exacerbation history, emergency visits, oral corticosteroid use, inhaler technique, adherence, medication access, environmental exposures, growth parameters and comorbid allergic disease. Validated questionnaires such as childhood asthma control tools and rhinitis quality-of-life instruments can standardize evaluation in research and clinical practice.

Integrated management

The cornerstone of pediatric asthma management is anti-inflammatory therapy, usually with inhaled corticosteroids. Current strategies emphasize that asthma treatment should reduce both symptoms and future risk, particularly the risk of severe exacerbations [1]. For many children, low-dose inhaled corticosteroids provide effective control. Depending on age, severity and local guideline recommendations, treatment may include daily inhaled corticosteroids, maintenance-and-reliever therapy using inhaled corticosteroid-formoterol, leukotriene receptor antagonists, or step-up therapy with long-acting bronchodilators under appropriate supervision [1,11].

However, asthma control cannot be optimized if allergic rhinitis is ignored. Intranasal corticosteroids are among the most effective treatments for moderate-to-severe allergic rhinitis, particularly nasal obstruction. Second-generation oral or intranasal antihistamines help sneezing, itching and rhinorrhea. Saline irrigation, allergen avoidance and education may support symptom control. Treating allergic rhinitis can improve sleep and may reduce lower airway symptoms in children with united airway disease [3,6].

Environmental control should be individualized. General advice without identifying relevant exposures often has limited effectiveness. If a child is sensitized to house dust mite and has perennial symptoms, practical measures may include mattress and pillow covers, washing bedding, reducing indoor humidity and minimizing dust reservoirs. For mold exposure, remediation of dampness is more important than symptomatic treatment alone. Tobacco smoke exposure should be eliminated. Air pollution reduction requires both household-level and public-health measures [7,8].

Education is a major therapeutic intervention. Families should understand the difference between controller and reliever medication, correct inhaler technique, spacer use, written asthma action plans, recognition of exacerbation signs and the importance of adherence. Many cases of “difficult asthma” improve after correcting inhaler technique and adherence. In research settings, documenting inhaler technique and adherence is essential because these factors strongly influence outcomes.

Allergen immunotherapy and disease modification

Allergen immunotherapy is important because it targets the underlying allergic mechanism rather than only suppressing symptoms. Subcutaneous and sublingual immunotherapy can reduce symptoms and medication needs in selected children with IgE-mediated allergic rhinitis, particularly when symptoms remain significant despite pharmacotherapy and allergen avoidance [12,13]. In children with allergic rhinitis caused by grass or birch pollen, a three-year course of allergen immunotherapy may reduce the risk of developing asthma for a period after treatment completion [13].

In asthma, immunotherapy should be used carefully. It is generally considered for children with controlled allergic asthma and clinically relevant sensitization. Uncontrolled or severe asthma is a contraindication because of the increased risk of systemic reactions. Therefore, patient selection, asthma stability and specialist supervision are essential [12]. Component-resolved diagnostics may improve selection by distinguishing genuine sensitization from cross-reactivity, although access may be limited in many clinical settings.

For pediatric research, allergen immunotherapy offers several relevant questions: which children benefit most, how local allergen profiles influence response, whether immunotherapy reduces exacerbations, and how adherence differs between subcutaneous and sublingual routes. Real-world studies are particularly valuable because randomized controlled trials may not fully represent daily clinical conditions.

Biologic therapy for severe pediatric asthma

Biologic therapy has changed the management of severe type 2 asthma. Agents targeting IgE, interleukin-5, interleukin-5 receptor or interleukin-4 receptor pathways can reduce exacerbations and improve control in selected children and adolescents with severe asthma [9,14]. Omalizumab is used for allergic IgE-mediated asthma, while mepolizumab and other anti-IL-5 pathway therapies target eosinophilic inflammation. Dupilumab blocks IL-4/IL-13 signaling and is relevant for type 2 asthma, especially when comorbid atopic dermatitis or chronic rhinosinusitis is present [9,14].

Before biologic therapy is started, the diagnosis must be confirmed, modifiable factors must be addressed and biomarkers should be assessed. Biologics are expensive and require long-term monitoring, so they should be reserved for children with true severe asthma after optimization of standard care. Research priorities include predictors of response, long-term safety, cost-effectiveness, growth outcomes, steroid-sparing effects and access in low-resource settings.

Prevention and public-health implications

Prevention of pediatric asthma and allergic disease is challenging because risk factors operate from pregnancy through adolescence. Avoidance of tobacco smoke, reduction of indoor and outdoor air pollution, breastfeeding support, rational antibiotic use, healthy diet, physical activity and obesity prevention are reasonable public-health measures, although the strength of evidence varies across interventions [7,8]. For children who already have allergic rhinitis, early recognition and adequate treatment may reduce symptom burden and possibly modify lower airway risk in selected groups.

Climate change is increasingly relevant. Longer pollen seasons, higher pollen allergenicity, heat exposure, wildfires, dust storms and air pollution may worsen respiratory symptoms in children [8]. Pediatric asthma strategies should therefore include school-based action plans, air-quality alerts, protection during high-pollen periods and community-level pollution reduction.

Research gaps and future directions

Several gaps remain in pediatric asthma and allergic disease research. First, many studies still separate asthma, rhinitis, eczema and food allergy, although children frequently present with multimorbidity. Future studies should use integrated phenotyping that includes upper airway symptoms, skin disease, food allergy, biomarkers, lung function and environmental exposures. Second, more data are needed from low- and middle-income countries, where underdiagnosis and undertreatment are common. Third, practical diagnostic algorithms are required for settings without spirometry or allergy testing.

Fourth, real-world evidence is needed on adherence, inhaler technique, school-based interventions, allergen immunotherapy and biologics. Fifth, prevention studies should examine combined interventions, including environmental control, nutrition, microbiome-related factors and early treatment of allergic rhinitis. Finally, locally adapted research is needed because allergen profiles, pollution patterns, housing conditions and healthcare access differ widely between regions.

Conclusion

Pediatric asthma and allergic diseases should increasingly be understood as interconnected disorders rather than isolated diagnoses. The united airway concept highlights the close relationship between allergic rhinitis and asthma, while atopic multimorbidity explains the overlap among eczema, food allergy, rhinitis and lower airway disease. Clinically, every child with asthma should be evaluated for allergic rhinitis and other atopic conditions, and every child with persistent allergic rhinitis should be assessed for lower airway symptoms. Effective management requires anti-inflammatory asthma therapy, treatment of rhinitis, environmental control, education, adherence monitoring and individualized escalation. Allergen immunotherapy and biologic therapy offer disease-modifying and phenotype-specific options for selected children. Future research should focus on integrated phenotypes, prevention, real-world effectiveness and equitable access to diagnosis and treatment.

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