Asthma Comorbidities

Allergic / Immune Comorbidities

- Allergic rhinitis (AR): Present in up to 80% of asthmatic children; worsens asthma control, increases ED visits/hospitalizations, and predicts lung function decline.
- Both conditions share type 2 inflammation with eosinophils and IgE-mediated pathways. Nasal inflammation can trigger bronchoconstriction via neural reflexes, and shared aeroallergen sensitization contributes to disease overlap.
- Treatment: Inhaled corticosteroids (ICS) and second-generation antihistamines reduce exacerbations. Allergen avoidance and immunotherapy may also help.Treating AR improves asthma outcomes.

- Food allergy (FA) :The association is more intense when the food hypersensitivity is persistent or starts early in life. FA was associated with worse morbidity, greater severity, and poorer asthma control. Several publications have shown that FA can be a risk factor for life-threatening asthma,and asthma also seems to be a risk factor for severe anaphylaxis in children with food allergy. FA may be a relevant clinical marker for severe atopic asthma.

- Anaphylaxis:Global anaphylaxis guidelines agree that severe/uncontrolled asthma is a risk factor for severe anaphylactic reactions and a criterion to be considered for the hospitalization of these children. Asthma has been considered a significant risk factor for fatal anaphylactic reactions in children.

- Atopic dermatitis (AD): Early-onset AD is associated with asthma and allergic multimorbidity; however, most children with AD will not develop asthma. AD severity is an important risk factor. In children,severe versus mild-moderate AD was associated with a higher lifetime prevalence of asthma (36.9% vs 24.3) and a prevalence of severe asthma (36.1%vs 5.5%).
- ABPA and fungal sensitizations: Rates of fungal sensitization in pediatric asthma range from 12 to 50%. ABPA may manifest as difficult-to-treat asthma and may progress to bronchiectasis, pulmonary fibrosis, or lung collapse.

- Multiple sensitizations: Sensitization to multiple aeroallergens, especially in early life, is important not only in the inception of asthma but also as determinant of disease severity.
- Chronic rhinosinusitis (CRS):Associated with difficult-to-control asthma;Chronic rhinosinusitis has an estimated prevalence around 5%, and is less frequent in children than adults.Chronic rhinosinusitis diagnosis in children requires at least 2 out of 4 cardinal symptoms: nasal obstruction, nasal congestion or discharge, facial pain, and cough, which must be present for at least 12 weeks. ; treatment improves asthma control.

- Eosinophilic esophagitis (EoE): Active EoE was found associated with severe asthma and deterioration of pulmonary function tests.
- Besides food allergens, other inhaled and subsequently swallowed environmental allergens may contribute to EoE through triggering mucosal histologic changes. Another possible mechanism is that a local airway or a more systemic response, is followed by trafficking of eosinophils into the esophagus. An interesting link between EoE and asthma is that, often the only way to deliver systemic corticosteroids to the esophagus, is using asthma medications. Both oral viscous budesonide and fluticasone administered by metered-dose inhaler (MDI) induce and maintain remission in EoE in children.More recently, it has been shown that dupilumab can be used in patients with multiple atopic diseases and it effectively induces symptomatic and histologic remission of EoE

Mechanical / Airway Comorbidities

- Vocal cord dysfunction (VCD) / Inducible laryngeal obstruction (ILO):Mimics asthma; coexistence increases exacerbations and medication overuse. It is caused by paradoxical adduction of vocal cords during inspiration leading to airflow obstruction and symptoms mimicking asthma. Often triggered by GERD, rhinitis, irritants, or exercise.
- Treatment:Speech therapy is first-line. Behavioral techniques, inspiratory muscle training, and in some cases antimuscarinics or supraglottoplasty are used.

- Obstructive sleep apnea (OSA):Prevalence up to 2/3 of asthmatic children (20× higher than general pediatric population). Linked to poor control, exacerbations, ICU admissions. It worsens asthma control and severity through mechanisms such as airway hyperresponsiveness due to increased vagal tone and oxidative stress from intermittent hypoxia/reoxygenation.
- Treatment:Leukotriene receptor antagonists, intranasal steroids, reduced exposure to allergens and pollutants, and weight loss in obesity, can significantly help in OSA control. Adenotonsillectomy, results in improved asthma control in patients suffering from OSA. Continuous positive airway pressure (CPAP)may be indicated.

- Gastroesophageal reflux disease (GERD):Highly prevalent in asthmatics (up to 70% in some studies). Bidirectional relationship but causality unclear; PPIs generally not effective for asthma control. Mechanisms include microaspiration of gastric contents, vagal reflex-induced bronchoconstriction, and epithelial inflammation/remodeling.
- Treatment:Symptomatic GERD should be treated with PPIs, though results for asthma improvement are inconsistent. Surgery evidence is limited. Avoid unnecessary PPI use if asymptomatic.

- # Metabolic / Systemic Comorbidities

- Obesity & metabolic disturbances: Increases asthma incidence (20% in overweight, 40% in obese children). Mechanisms include systemic inflammation (adipokines, TNF-α, IL-6), altered immune polarization (M1/M2 macrophages), mechanical restriction of lungs, and steroid resistance.Leads to more exacerbations, worse QoL, and reduced responsiveness to ICS/bronchodilators. overweight and obesity were underdiagnosed and undertreated in children hospitalized for asthma. Pediatricians and general practitioners should be vigilant for obesity signs. Therapeutic strategies, such as family-based interventions for lifestyle approaches, aiming at prevention of obesity and are recommended in countries with increased prevalence.
- Cardiovascular disease (CVD): Evidence suggests a complex interplay between asthma and cardiovascular disease (CVD), indicating
- a comorbid relationship.Evidence in adults suggests higher risk of CHD and stroke, but pediatric data are inconclusive. At least 2 recent meta-analyses have confirmed the increased risk of CVD in patients with asthma.116,117 Although the outcomes refer to adult age, this increased risk supports the need for early prevention and control efforts.

- Psychiatric & Neurodevelopmental Comorbidities

- Anxiety & depression:More frequent in asthmatic children, linked to poor asthma self-management and uncontrolled asthma.
- ADHD:Associated with lower adherence and increased visits.
- Parental anxiety:Higher in families of children with poorly controlled asthma.