JNP

# Update on Diagnosis and Management of Severe Asthma

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**ABSTRACT**

Patients with severe asthma comprise 5% to 10% of the patient population with asthma, but they use 60% of treatment costs. As a result of high morbidity and mortality rates and frequent health care use, these patients are commonly encountered in primary care settings. Treatment is complex and often requires an interdisciplinary approach to reduce risks, treat comorbidities, optimize medications, and to engage patients in care. Through early diagnosis, patient education, the provision of standard of care asthma management, and close collaboration with specialists, nurse practitioners can facilitate timely and comprehensive treatment that can improve patient outcomes.

**Keywords:** asthma, endotypes, eosinophilic, interdisciplinary approach, phenotypes, severe uncontrolled asthma, targeted biological therapies



Asthma is an increasingly common chronic airway disorder that in 2015 affected 7.8% of the United States population.[1] It occurs more frequently among children, female sex, those with family income below the poverty level, and among multiple race, black, and American Indian or Alaska Native persons.[1,2] Health care encounters for asthma are significant, accounting for 10.5 million primary care appointments in 2012, and 1.6 million emergency department visits during 2013.[1] Mortality rates are equally sobering. In 2015, 219 children and 3,396 adults died of asthma.[1,2] In addition to causing significant morbidity and mortality, asthma is expensive, accounting for an annual cost of $56 billion in 2007 and leading to 10.5 million missed days of school and 14.2 million missed days of work in 2008.[1] Patients who have severe asthma (SA) comprise approximately 5% to 10% of the asthma population; yet, they use 60% of treatment resources, primarily due to high medication use.[1,3,4] The overall expense of caring for these patients exceeds the health care costs of patients with diabetes, stroke, or chronic obstructive pulmonary disease.[4]

As primary care practitioners, nurse practitioners (NPs) provide advanced care to more than 1 million patients yearly.[5] Due to their focus on patient-centered care that emphasizes the patients' overall health care needs and preferences, NPs are well poised to help patients successfully manage the chronic medical and lifestyle issues associated with asthma.[5] When standardized treatment fails and the patient presents with the frequent exacerbations associated with SA, NPs are highly skilled at diagnosing and collaboratively managing these patients within an interdisciplinary team that places the patient at the center.[5]

## EVOLVING DEFINITIONS OF ASTHMA

Asthma is a chronic respiratory disorder characterized by reversible airflow obstruction, bronchial hyperreactivity, and airway inflammation.[6,7] Effective management of asthma can be achieved through the implementation of evidence-based treatment guidelines that focus on symptom control, prevention of exacerbations, and risk reduction.[6,7] Although prevention should be addressed in depth in another article, NPs should pay attention to allergens, such as pollens, dust mites, mold spores, and pet dander, that often lead to poor control.[6,7] Measures to limit exposure include mattress covers, washing bedding weekly, removing carpets and upholstered furniture, frequent cleaning, and reduction of indoor

humidity.[6,7] During high pollen seasons, patients should use air conditioning and limit outdoor activities.[6,7] Strategies to reduce risk factors include weight management, not smoking, and avoidance of occupational triggers.[6,7]

Assessment of asthma control is based on patients' symptoms, frequency of flare ups, and airflow obstruction.[6,7] Patients who have uncontrolled asthma resulting from allergen exposure, comorbidities, or lack of medication adherence need to be distinguished from patients with SA.[4,7] In asthma patients who have dealt with these factors, SA is defined as asthma that requires high-dosed inhaled corticosteroids (ICS), combined with a long-acting $\beta_2$-agonist, a leukotriene modifier, or theophylline for the preceding year or treatment with oral corticosteroids (OCS) for 50% or more of the previous year to prevent it from becoming uncontrolled or that remains uncontrolled despite this therapy.[3,4,7]

Many patients with SA exhibit similar inflammatory and clinical features that can be categorized into specific phenotypes by the shared characteristics related to the interaction between genetic, environmental, and clinical patterns.[8,9] These phenotypes have been identified through objective studies that use cluster analysis to identify subgroups of patients with similar clinical characteristics.[8–11] An additional means of further characterizing phenotypes is by identifying specific biological pathways and pathophysiological mechanisms that can be divided into disease endotypes.[8–11] Some examples of phenotypes include childhood-onset allergic asthma, adult-onset atopic asthma, and eosinophilic asthma.[10,11] Although there is often an overlap between phenotypes and their clinical significance is still under investigation, their discovery has changed the definition of asthma from a singular disorder to one that includes a heterogeneous group of respiratory diseases.[8–11] The ability to identify these phenotypes and endotypes through noninvasive biomarkers is clinically relevant when used to identify and stratify patients who might benefit from targeted treatment options.[8–11]

## PATHOPHYSIOLOGY

Despite their differences, most phenotypes are associated with inflammation of the respiratory tract, which can be categorized by the mechanism of the inflammatory response.[3] Eosinophilic inflammation, which accounts for 50% of patients with SA, is the most common.[12–15] Eosinophils are granulocytes, which under the regulation of cytokines—primarily interleukin (IL) 3, IL-5, and granulocyte macrophage–colony stimulating factor—become activated and infiltrate the airways.[12–16] After activation, eosinophils release cytotoxic and inflammatory mediators that cause airway epithelial damage, mucous hypersecretion, hyperresponsiveness, and airway remodeling.[12–16]

Neutrophilic inflammation represents another common phenotype that is characterized by high levels of neutrophils, which trigger the release of cytokines such as IL-8.[4,8,10] Two additional phenotypes that occur less frequently and are associated with varying degrees of inflammation are mixed neutrophilic and eosinophilic inflammation and paucigranulocytic asthma.[4,8,10] A strong correlation exists between airway inflammation and SA, but the significance of this relationship is unclear.[7,9,10] The underlying pathophysiology of SA is complex and requires further research.[7,10]

## DIAGNOSIS

As a result of the high morbidity rates associated with SA, it represents an uncommon disorder that is frequently encountered in primary care settings because of high utilization, and it often goes unrecognized.[4,7,17] SA is misdiagnosed in as many as 30% to 50% of cases,[17] and as frontline providers, NPs will often be the first to distinguish between SA and uncontrolled asthma, which is the most amenable to treatment.[5] NPs can evaluate the level of asthma control through the use of patient self-assessment questionnaires such as the Asthma Control Test (http://www.asthmacontroltest.com),[18] the Asthma Control Questionnaire (http://www.qoltech.co.uk/acq.html),[19] and the Global Initiative for Asthma asthma control scoring system.[7] These tools measure symptoms such as occurrence of night waking, frequency of rescue inhaler use, and interruption in daytime activities during an interval of 1 to 4 weeks.[7,18,19] In addition, documenting the frequency of asthma exacerbations by monitoring emergency care visits or the use of OCS, or both, 2 times or