

Asthma Over the Age of 65: All's Well That Ends Well



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Overall Purpose/Goal: To provide excellent reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

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List of Design Committee Members: Alan P. Baptist, MD, MPH, and Paula J. Busse, MD (authors); Michael Schatz, MD, MS (editor)

Learning objectives:

1. To understand the epidemiology of older patients with asthma.
2. To recognize the pathophysiologic changes in the innate and immune system in older patients with asthma.
3. To understand the challenges of diagnosing and treating older patients with asthma.

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Asthma in older adults (often classified as those 65 years or older) is relatively common, underdiagnosed, and suboptimally treated. It is an important health problem, as the population of the United States continues to age. Unfortunately, asthma morbidity and mortality rates are highest in this age group. Alterations in the innate and adaptive immune responses occur with aging, and contribute to pathophysiologic differences and subsequent treatment challenges. The symptoms of asthma may

differ from those in younger populations, and often include fatigue. There are unique factors that can complicate asthma management among older adults, including comorbidities, menopause, caregiver roles, and depression. Pharmacologic therapies are often not as effective as in younger populations, and may have greater side effects. Spirometry, peak flow measurements, and asthma education are typically underused, and may contribute to delays in diagnosis as well as worse outcomes. There are specific strategies that health care providers can take to improve the care of older adults with asthma. © 2018 American Academy of Allergy, Asthma & Immunology (*J Allergy Clin Immunol Pract* 2018;6:764-73)

Key words: Asthma; Older adults; Elderly; Spirometry; Immunosenescence; Depression; Menopause; Education; Asthma COPD overlap syndrome

INTRODUCTION

To many, there is the belief that asthma occurs in childhood and resolves over time. However, studies show that a significant number of people first develop asthma at a relatively older age, and that it can persist throughout the lifespan. Understanding asthma in older adults is critical to health care providers and researchers, as the number of those older than 65 years in the

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Abbreviations used

ACO- Asthma COPD overlap
CAM- Complementary and alternative medicine
COPD- Chronic obstructive pulmonary disease
HRT- Hormone replacement therapy
ICS- Inhaled corticosteroid
LOA- Late-onset asthma
OR- Odds ratio

United States is projected to increase to 85 million individuals by the year 2045, a 77% increase since 2015 (Figure 1).¹ In addition, by 2030, the percent of older adults will increase to 20% of the total population, and therefore those who manage adult asthma will likely have many patients older than 65 years. This review covers unique features of asthma in older adults, discusses challenges of diagnostic and management strategies, and highlights areas in which further research is needed to address knowledge gaps.

EPIDEMIOLOGY

Accurate data on the prevalence of asthma in older adults can be difficult to obtain. In part, this is because many asthma trials specifically exclude individuals older than 65 years. In addition, in the older adult with respiratory symptoms, often times those with a minimal, remote, or even nonexistent smoking history are misdiagnosed as having chronic obstructive pulmonary disease (COPD) rather than asthma,^{2,3} even though data suggest that approximately 20 pack-years are typically required to develop COPD.⁴ A 2015 Centers for Disease Control and Prevention survey found that among adults, the prevalence of asthma is highest in those aged 45 to 64 years, with 8.4% having a current diagnosis of asthma.⁵ This was the same prevalence as the overall rate for children aged 0 to 18 years. Therefore, asthma remains a common chronic disease across all ages.

Results of the Centers for Disease Control and Prevention Asthma Call Back Survey (~900,000 individuals) did find that the assumption of asthma typically beginning in childhood is often, but not always, true.⁶ Among all children, asthma incidence was 12.5 per 1000. However, new cases of asthma occurred frequently at any age. In adults older than 18 years, the greatest incidence rate was in those aged 55 to 64 years (4.6 per 1000). In those older than 65 years, the incidence rate was 3.1 per 1000. More recently, Baptist et al⁷ reported that among 180 patients older than 55 years with persistent asthma, 46% were diagnosed after the age of 40 years.⁷ Taken together, these data indicate that asthma is common in those older than 65 years, and that many cases begin later in life.

There appear to be clinical differences between those who develop asthma in childhood, adolescence, or young adulthood (termed “long-standing asthma”) and those who develop asthma after the age of 40 years (termed “late-onset asthma,” or LOA). Those with LOA are more likely to have frequent symptoms, less atopy, and a decreased response to standard inhaled corticosteroids and beta-agonists,^{8,9} though some authors have suggested that those with long-standing asthma may in fact have worsened outcomes.¹⁰ Recent cluster analyses of older adults have been published, and will help to clarify these issues as well as identify specific phenotypes that may respond preferentially to one treatment over another.^{7,11}

What does seem clear is that older adults have some of the highest asthma morbidity and mortality rates. For example, as shown in Figure 2, the mortality rate from asthma steadily increases with age.¹² In addition, studies of severe asthma have shown that older adults may have a more difficult-to-control phenotype than younger populations, with decreased responsiveness to standard medications.^{7,13,14} Of those presenting to the emergency department for asthma, adults 65 years or older have the highest rate who subsequently require hospitalization (~25% admission rate compared with 7.9% for all ages) and longest length of stay.¹⁵ It is important to note that asthma is frequently underdiagnosed, and therefore these numbers may be underestimations.

IMMUNOSENESCENCE

With increasing age, there are alterations in both the innate and adaptive immune responses, which likely impact the pathology, and consequently, the treatment, of asthma in older adults. Two distinct alterations of aging in the innate and adaptive immune responses have been described and can occur simultaneously. One, “immunosenescence,” is a “blunted” response after a pathogenic threat or tissue injury. However, despite an inability to proliferate, some senescent cells remain alive, functioning at an altered capacity. This results in the second process, “inflammaging,” an increased low-grade basal systemic inflammation (eg, IL-1- β , IL-6, and TNF- α) in the absence of an overt infection.¹⁶ The mechanisms of immunosenescence and inflammaging are the consequence of both “random” (eg, environmental exposures, accumulation of reactive oxygen species from metabolic activity, and mutagenesis) and “regulated” (eg, genetic) events.¹⁷

The possible impacts of immunosenescence and inflammaging on asthma are briefly outlined in Table I. Collectively, alterations in innate and adaptive cells likely have several clinical implications including decreasing the response to vaccinations and increasing rates of infections, which in turn may exacerbate asthma, or play a role in the inception of LOA.¹⁸ Furthermore, older patients with asthma may have altered airway and systemic inflammation (ie, higher neutrophils with increased IL-6, IL-8, C-reactive protein) resembling changes seen in a phenotype of severe asthma in younger patients, which is often less responsive to corticosteroid treatment.¹⁹⁻²¹

SYMPTOMS AND DIAGNOSIS

Many of the asthma symptoms common in younger patients (eg, intermittent chest tightness, nocturnal wheezing, and dyspnea) are present in older patients. However, there are important considerations. Older adults frequently note fatigue as a principal symptom, even in the absence of typical asthma manifestations.²² Dyspnea is commonly associated with other chronic disorders in older patients (eg, heart failure, other lung diseases, and anemia); therefore, asthma as the cause of these symptoms may be overlooked. Furthermore, some older patients may limit their activity to avoid becoming dyspneic, or attribute it to aging itself. Older adults may have a decreased perception of dyspnea even with significant airflow obstruction.^{23,24} As smoking can induce symptoms of wheeze, cough, and sputum production, asthma may be confused with COPD. Prominent gastroesophageal reflux disease may present with a chronic cough, hoarseness, and

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