

Asthma and Chronic Obstructive Pulmonary Disease in the Elderly: What is New Under the Sun?



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Seneca (4 BC–65 AD), a Roman philosopher and playwright, was a 60-year-old man when he wrote of his asthma-like breathing difficulty: “I have suffered every kind of unpleasant or dangerous physical complaint but none is worse than this.”¹ Seneca observed that his impaired breathing tended to worsen with age. Although asthma affects older adults to the same extent as children and adolescents, the disease is depicted as a rare entity in the most advanced ages.²

From a clinical perspective, this misconception has consequences if delayed diagnosis postpones proper treatment. Asthma in older individuals poses questions to researchers with regard to understanding pathogenic mechanisms, and it challenges clinicians in terms of the traditional diagnostic approach and therapeutic algorithms that are commonly applied to younger populations. The question is therefore not whether asthma in the elderly is a rare disease,³ but whether *allergic* asthma is a rare entity in the elderly, and how that should impact management.

The immune system undergoes an involution process with increasing age, termed *immunosenescence*; as a consequence, immunoglobulin production, including IgE, decreases, leading to the suggestion that asthma in the elderly has a nonallergic pathogenesis. In assessment of the geriatric respiratory patient, atopy is often not evaluated or ignored.

When defining atopy, increased total IgE levels and positive skin prick test to allergens are used interchangeably. The use of specific IgE (sIgE) toward aeroallergens should be pursued instead of using an arbitrary total IgE level, which may suggest but does not diagnose the origin of symptoms in an individual patient. Finally, the assessment of the allergic component in the elderly could be affected by the incorrect interpretation of skin testing, which could be due to the age-associated reduction in skin reactivity to histamine and allergens.⁴

The current paper reinforces the concept that atopy in the older asthmatic can still play a central role, with potential clinical consequences. For example, the age-related reduction in IgE does not decrease the efficacy of a pharmacological approach with anti-IgE in the severe forms of asthma occurring in older ages, if the patient is otherwise likely to benefit.⁵ Moreover, the allergic reactions in older adults may be worse, because of impairment of other organs to counteract the adverse effects of comorbid conditions. Systemic anaphylactic reactions, let alone influenza, may have consequences in elderly subjects in whom the cardiovascular system is not able to effectively compensate. In this scenario, the assessment of atopy provides the opportunity to act on the environment (removal of allergens) and to modify the natural history of the allergic condition with allergen immunotherapy. Age does not preclude the use of allergen desensitization.

A distinction may be made between asthma occurring for the first time in older ages (late-onset asthma), and asthma that begins in younger ages (early-onset asthma). The definition of late-onset asthma is complicated by the fact that some studies have defined “late” asthma as a disease that first makes its appearance in adulthood. Agondi et al⁶ rightly propose to further dissect the age of onset of asthma, therefore contributing to an alternative but useful way to characterize disease characteristics at different age ranges. In this analysis, the prevalence of atopy tended to be significantly reduced by half in late in life onset as opposed to early in life onset asthma.

In their paper⁶ in this issue of the journal, Agondi et al took the opportunity to investigate the characteristics of patients labeled with the diagnosis of what has come to be called asthma-chronic obstructive pulmonary disease (COPD) overlap syndrome (ACOS). Agondi et al⁶ highlighted the importance of assessing atopy in older asthmatics, focusing on ACOS. Others have come to reject the use of the ACOS diagnosis, suggesting “asthma-COPD overlap” or ACO (*GINA 2017, P 10*). It is proposed that the term ACOS erroneously implies a distinct separate disease.

In a systematic examination of this topic,⁷ the prevalence of allergic sensitization was shown to be lower in the most advanced ages. The current study is in line with this observation. Although there has been great interest in this finding and the appropriate therapeutic response, the published literature in the field suffers from the lack of longitudinal studies to confirm a reduction in the atopic condition with aging, rather than reflecting the elderly’s demographics, and the current study is not an exception. In the study by Agondi et al,⁶ only a small proportion of subjects meet the stringent criteria they adopted for the application of the ACOS label, with little demographic difference from their non-ACOS group. In effect, they support the conclusion of those who reject ACOS as a discreet pathophysiologic entity. The case is increasingly compelling that the

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“overlap” state is no different from other concurrent and interacting but independent common conditions, not a distinct nosologic entity. The concept can be extended to extra-respiratory diseases (eg, cardiovascular diseases) or even physiological abnormalities (eg, obesity).

In most developed countries, approximately 25% of adults with asthma are current cigarette smokers.⁸ Active cigarette smoking in asthmatics is responsible for more severe symptoms, accelerated decline in lung function, greater need for rescue medication, worse indices of health status, and impaired short-term therapeutic response to corticosteroids when compared with never-smokers. This stands in contrast to Agondi et al's findings. They report that “More than 80% of the studied patients had low FEV₁, independent of the group to which they belonged (smokers and ex-smokers, passive smoking and no exposure groups), suggesting that smoke exposure can be less relevant than long-standing asthma.” This flies in the face of extensive data of the damage done by cigarette smoking.⁹ Perhaps the high proportion of patients with abnormal pulmonary function in their series obscures some of the expected differences between smokers and nonsmokers.

Agondi et al remind us that, although atopy is less frequent with increasing age in cross-sectional examination, it is still common. Their subjects dropped from an incidence of atopy of over 72% in the youngest onset cohort to almost 38% in those with onset after age 55, arguably still a meaningful prevalence. Likewise, there was no statistically significant difference in serum total IgE or blood eosinophils between the ACOS and non-ACOS groups. Table 3 of the current paper includes 14 “demographic characteristics” of allergic versus nonallergic patients. Excluding total serum IgE, a marker of atopy, there was only a single statistically significant difference for duration of disease ($P < .001$), which was 44.2 years in the allergic asthma group, and 37.1 years in the nonallergic group, with standard deviations assuring considerable overlap.

Almost 2000 years after Seneca's death, Gross¹⁰ wrote in an editorial that asthma is like love, “We all know what it is but who would trust anybody else's definition?” Still a difficult definition to come by, this concept has evolved to the conclusions of a recent Lancet Commission that advised “Use the term asthma solely as a descriptive label for a collection of symptoms, with no assumption about pathophysiology.”¹¹

In short, the case for ACOS representing a specific pathophysiology as opposed to a descriptor of common diseases presenting commonly is weak. But regardless of the asthma or COPD label, the atopic state should not be overlooked in daily clinical practice when managing elderly patients with chronic obstructive airways disease, no matter what they are called.

Indeed, recent data have suggested benefit for patients with cigarette smoking-associated COPD and an eosinophilic phenotype treated with antieosinophil biologics,¹² including 2 large multicenter studies.¹³

In the context of an approach to chronic respiratory diseases based on “treatable traits” in each patient,¹⁴ atopy could be listed among the most relevant in elderly patients. ACO patients as a group tend to do less well,¹⁵ but they are often excluded from clinical studies because they fail to meet common selection criteria of tobacco use and/or reversibility—or a lack thereof.

More work is needed to better define the phenotypes that can help the clinician and patient select optimal therapy in the elderly chronic respiratory population. For bringing this to our attention, Agondi et al⁶ have done a service.

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