

EDITORIAL

Clinical & Experimental Allergy

Asthma in the elderly . . . Their time is right now

This editorial discusses the findings in the paper by Vale-Pereira et al. [12] pp. 490–496.

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Asthma is considered to be a problem of children and young adults but has more recently been recognized as a growing clinical problem in the elderly. Between 4% and 13% of adults older than 65 years are diagnosed with asthma [1]. Asthma in an older adult is the result either of childhood asthma that is long-lasting, or resurgence of quiescent childhood-onset asthma or late onset disease. In general, asthma in older adults is characterized by less IgE-mediated processes and more frequently by irreversible airway obstruction [2], due to airway remodelling and, sometimes, co-existing COPD and/or bronchiectasis. Thus an accelerated decline in lung function occurs in elderly asthmatics, mainly due to airway remodelling, especially in the small airways from inflammation that characterizes asthma. Compared with the general population, elderly asthmatics are more likely to die of lung diseases, presumably due to respiratory tract infections, especially those with poor socio-economic status [3]. However, older asthmatics are often excluded from asthma research protocols and very little research specifically targets this population.

The pathogenesis of the asthma phenotype in elderly asthmatics is poorly understood. Studies in the past decade have focused on the roles of innate and adaptive immunity in this phenotype. The aging process affects the innate and adaptive immune processes by a phenomenon known as immunosenescence, which increases the susceptibility of elderly asthmatics to develop or exacerbate airway inflammation. Studies in older asthmatics have shown age related changes in innate immunity including lung epithelial cell senescence, increased airway neutrophilia, decreased eosinophil function and decreased levels of cytotoxic natural killer (NK) cells and macrophages [4, 5]. Age related changes in adaptive immunity include

decreased dendritic cell function and a chronic pro-inflammatory state characterized by increased levels of IL-1, IL-6 and TNF- α [6, 7]. Studies showing a decrease in IFN- γ /IL-4 and IFN- γ /IL-10 after stimulation of NK T cells in older asthmatics support the notion of a transition to a greater T-helper type 2 (Th2) response with aging [8, 9]. Th17 cells may also be implicated in the pathogenesis of late onset asthma [10, 11].

Regulatory T (Treg) cells suppress effector functions of T cell subsets including Th1, Th2 and Th17. Natural Treg cells express the transcription factor forkhead box protein 3 (FoxP3) and mediate suppression mainly through cell contact. Most studies suggest a protective role of Treg cells in asthma with aging. In the current issue of *Clinical & Experimental Allergy*, Vale-Pereira et al. [12] examine expression of FoxP3 as well as T-bet and GATA-3 (important for Th1 and Th2 differentiation from naïve T cells respectively), in asthmatics aged > 65 years and compare them to age-matched healthy individuals. Peripheral blood mononuclear cells were isolated and stimulated in vitro using anti CD3/anti CD28, mRNA was isolated and FoxP3, T-bet and GATA3 were measured by real-time PCR. The study demonstrated that elderly asthmatics had lower FoxP3 mRNA expression in PBMC which supports the idea of decreased immune tolerance by Treg cells in the elderly asthmatics and hence favours a sustained inflammatory process. Asthmatics also had a lower T-bet/GATA-3 ratio and increased IgE, which are also found in chronic asthma. As controls were age-matched, the pro-inflammatory state found in these elderly asthmatics was above and beyond that due to the immunosenescence effect alone.

The past decade has seen a major attempt to understand asthma in terms of specific phenotypes, which has significantly improved our understanding about the diverse nature of asthma. Specific asthma phenotypes may benefit from specific therapeutic strategies. Studies into the nature of asthma in the elderly are clearly insufficient in number and in scope. Just as the post war 'baby-boomer' population boost has led to particular socio-economic

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challenges in our current age, the asthma epidemic of the 1980s and 1990s will almost certainly leave a legacy of increased rates of asthma and asthma complexity in the elderly starting in the next decade. We should be ready for it. This paper by Vale-Pereira and colleagues is a step in the right direction and examines mechanistically the nature of the inflammatory response in elderly asthmatics. We should revisit this phenotype of asthma at the clinical,

physiological and pathological level and try to include such populations in our clinical trials. Another area that should be studied is the role of small airways in this phenotype taking in consideration the accelerated decline in peripheral airways function in the elderly population, this is particularly true given the development of newly formulated drugs that can deposit in the small airways [13, 14].

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