

Challenges of managing asthma in an elderly population

To the Editor Human life expectancy has increased over the past few decades, with the average male now expected to live up to 69.1 years and the average female—up to 73.8 years.¹ Longevity is inevitably associated with further accrual of morbidity, including respiratory ailments. The prevalence of asthma for those over the age of 65 years ranges from 4.5% to 12.7%, with an incident rate of 0.1% according to recent studies.² With a projected 2-fold increase in the elderly population (from approximately 500 million people),³ the most conservative estimate would suggest that there will be 50 million elderly asthmatics. The United States National Surveillance of Asthma report⁴ shows that across the American lifespan, those aged 65 years or older had the largest increase in the prevalence of current asthma, the highest rate of asthma-related deaths, and the second highest rate of asthma-based physician office visits and hospitalizations. Unexpectedly, this age group had the lowest rate of reported asthma attacks in the previous year, as well as emergency department visits for asthma. The most vulnerable older Americans were women, African Americans, Hispanics, and low-income groups. The National Institute of Aging organized a workshop in 2008 to discuss the issues specifically related to the diagnosis and management of asthma in the elderly.⁵ In 2015, the American Thoracic Society organized a second workshop to examine the knowledge gaps, to review the current state-of-the-art in the field, and to identify future areas of research. A rigorous and methodologically sound process led to an informative document that provided key recommendations on the unique pathophysiological features, challenges with the diagnosis and management, and directions for future research.⁶

It has long been recognized that asthma in the elderly population is underperceived, underdiagnosed, and undertreated.^{7,8} In addition to the physiological effects of aging on lung mechanics, such as a reduction in lung elastic recoil, forced expiratory volume in 1 second to forced vital capacity ratio, and respiratory muscle strength, which affect interpretation of pulmonary function tests, the lack of accurate prediction equations to interpret and identify airflow obstruction,

the underutilization of tests such as methacholine tests to identify airway hyperresponsiveness, and the coexistence of comorbidities in the elderly make it very challenging to establish an accurate diagnosis of reversible and variable airflow obstruction that characterizes asthma.⁶ Limited progress has been made in this field over the past 10 years. There has been an increase in the use of computed tomography scans of the thorax and measurements of airway resistance by impulse oscillometry in the elderly,⁹ but they do not seem to have translated into more prompt and frequent identification of asthma. Lower health expectations and declining cognitive impairments may also contribute to poor perception of breathing and underreporting of symptoms that lead to underdiagnosis.⁶

There has been more progress over the past decade in relation to the pathobiology of asthma in the elderly than to strategies for diagnosis. There has been considerable progress in our understanding of the process of “immunosenescence”⁶ and the association of a low-grade, chronic, systemic inflammation with aging, referred to as “inflamm-aging,” characterized by increased interleukin (IL) 1b, IL-6, and tumor necrosis factor α .¹⁰ A number of other processes, including telomere shortening,¹¹ decreased eosinophil degranulation in response to IL-5,¹² increased airway neutrophilia,¹³ or decreased numbers of regulatory T cells,¹⁴ may contribute to an altered inflammatory profile in the airways of elderly asthmatics, which may be a significant determinant of responses to various therapeutic interventions. Both aging and the duration of asthma (that may be mutually related) could potentially lead to alterations in the structural changes in the airway wall, submucosa, and in the smooth muscle layers leading to remodelling, loss of lung function, and impaired treatment responses; some of these features may resemble chronic obstructive pulmonary disease.⁶

The lack of timely and accurate diagnosis and specific immunopathological changes may modulate treatment responses, in addition to the challenges imposed by comorbidities, altered pharmacology and drug metabolism profiles related to aging, drug interactions due to polypharmacy, poor

inhaler techniques, poor access to health care, lack of affordability of medications, and rational or irrational concern for the adverse effects of medications, in particular, corticosteroids and anticholinergic drugs. However, the general principles of asthma management in the elderly should not be different from those in a younger individual. These principles are summarized below:

1 Confirmation of variable airflow obstruction by peak flow variability over time, demonstrating bronchodilator reversibility of 12% to 15% to a short-acting bronchodilator, or airway hyperresponsiveness to a direct (eg, methacholine) or indirect (eg, mannitol) bronchoprovocation.

2 Identification and avoidance of allergen triggers. A careful history of potential exposures to previous occupational or recreational sensitizers, pets, and birds is often helpful.

3 A careful review of medications that may induce eosinophilia or symptoms such as cough that may mimic asthma, or potentially cause dangerous drug interactions, arrhythmias, heart failure, and other comorbidities that may present similarly to asthma. Particular caution should be exercised in those patients who are on cholinomimetics for conditions that are relatively common in the elderly and that may worsen asthma, such as glaucoma (eg, topical pilocarpine), dementia (eg, donepezil), and myasthenia gravis (eg, neostigmine).^{6,15}

4 Identification of both respiratory and nonrespiratory comorbidities such as autoimmune disorders, pulmonary fibrosis, smoker's bronchitis and emphysema, bronchiectasis, and heart failure that may mimic or coexist with asthma.

5 Assessment and identification of cognitive impairment, depression, and physical (including inhaler technique and arthritis or deformities that may prevent the use of inhalers) and economical barriers that may impede successful therapy. This would have bearing on the choice of inhaler therapies.

6 Assessment of airway inflammation to guide therapy. Although in a stable state, the majority of elderly asthmatics may have mild sputum neutrophilia, the principles of inflammometry as applied to younger individuals would be effective for older patients. Eosinophilic inflammation responds to inhaled and oral corticosteroids, and this has been convincingly shown to reduce hospitalization and mortality rates in older patients. Neutrophilic inflammation may be less responsive to steroid therapy. Intense neutrophilia should prompt a search for unrecognized bacterial bronchitis. Elderly patients may be particularly susceptible to the adverse effects and therefore should be carefully monitored for easy bruisability, fluctuating mood, osteoporosis and fractures, cataracts, glaucoma, hypertension, adrenal suppression, diabetes, and the rare complication of avascular necrosis.

7 Short- and long-acting β -agonists and muscarinic antagonists should be used as recommended by guidelines as add-on therapy. However,

the physician and the patient should be aware of potential adverse events that may cause significant discomfort to the elderly patient, such as benign or malignant cardiac arrhythmias, excessive dryness of the mouth, worsening of glaucoma, and prostate obstruction.

8 The prescription of theophylline may cause problems with adverse effects and the potential of interaction with other drugs such as macrolides or anticoagulants that the elderly are likely to be administered.

9 Finally, just as in the younger patient, the elderly should be advised to give up tobacco and other recreational smoking, recommended annual flu vaccinations, and offered pneumococcal vaccination as appropriate.

The workshop⁶ summarized the current state of knowledge and identified key areas of future research that included developing optimal strategies for identifying airflow obstruction in the elderly, establishing normal prediction equations for this age group, elucidating mechanisms of inflammation and deep endotyping of these patients using "omics" platforms and unbiased cluster analyses, and including more elderly patients in clinical trials (from which they are currently excluded) so that specific pharmacotherapies may be developed for this vulnerable patient population.

Author names and affiliations Parameswaran Nair, Terence Ho (Department of Medicine, Division of Respiriology, St Joseph's Healthcare & McMaster University, Hamilton, Ontario, Canada)

Corresponding author Prof. Parameswaran Nair, MD, PhD, Firestone Institute for Respiratory Health, St. Joseph's Healthcare, 50 Charlton Avenue East, Hamilton, Ontario, Canada, L8N 4A6, phone: +1 905 522 1155, e-mail: parames@mcmaster.ca

Conflict of interest The authors declare no conflict of interest.

Acknowledgments Dr. Nair is supported by the Frederick E. Hargreave Teva Innovation Chair in Airway Diseases.

How to cite Nair P, Ho T. Challenges of managing asthma in an elderly population. *Pol Arch Intern Med.* 2017; 127 (4): 291-293. doi:10.20452/pamw.4011

REFERENCES

- 1 World Health Organization. World Health Statistics 2016. Geneva, Switzerland: WHO Press; 2016.
- 2 Ozturk AB, Iliaz S. Challenges in the management of severe allergic asthma in the elderly. *J Asthma Allergy.* 2016; 9: 55-59.
- 3 Kinsella K, Wan H. U.S. Census Bureau, International Population Reports, An Aging World: 2008. Washington, DC: U.S. Government Printing Office; 2009.
- 4 Moorman JE, Akinbami LJ, Bailey CM, et al. National Surveillance of Asthma: United States, 2001-2010. National Center for Health Statistics. *Vital Health Stat.* 2012. 3: 1-58.

- 5 Hanania NA, King MJ, Braman SS, et al. Asthma in the elderly: Current understanding and future research needs – a report of a National Institute on Aging (NIA) workshop. *J Allergy Clin Immunol*. 2011; 128: S4-S24.
- 6 Skloot GS, Busse PJ, Braman SS, et al. An official American Thoracic Society workshop report: Evaluation and management of asthma in the elderly. *Ann AM Thorac Soc*. 2016; 13: 2064-2077.
- 7 Burr M, Charles T, Roy K, Seaton A. Asthma in the elderly: An epidemiological survey. *BMJ*. 1979; 1: 1041-1044.
- 8 Nair P, Hildreth A, Chadha D, et al. Asthma in the elderly: Underperceived, underdiagnosed and undertreated; A community survey. *Respir Med*. 1998; 92: 573-577.
- 9 Inoue H, Niimi A, Takeda T, et al. Pathophysiological characteristics of asthma in the elderly: A comprehensive study. *Ann Allergy Asthma Immunol*. 2014; 113: 527-533.
- 10 Franceschi C, Campisi J. Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. *J Gerontol A Biol Sci Med Sci*. 2014; 69: S4-S9.
- 11 Barnes PJ. Mechanisms of development of multimorbidity in the elderly. *Eur Respir J* 2015; 45: 790-806.
- 12 Mathur SK, Schwantes EA, Jarjour NN, Busse WW. Age-related changes in eosinophil function in human subjects. *Chest*. 2008; 133: 412-419.
- 13 Ducharme ME, Prince P, Hassan N, et al. Expiratory flows and airway inflammation in elderly asthmatic patients. *Respir Med*. 2011; 105: 1284-1289.
- 14 Vale-Pereira S, Todo-Bom A, Gerales L, et al. FoxP3, GATA-3 and T-bet expression in elderly asthma. *Clin Exp Allergy*. 2011; 41: 490-496.
- 15 Khalil D, Hirota J, Nair P. Cholinergics, airway eosinophils and asthma exacerbation in the elderly. *Indian J Chest Dis Allied Sci*. 2011; 53: 59-61.