The Aging Lung: Implications For Diagnosis and Treatment of Respiratory Illnesses in the Elderly

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Introduction

Respiratory conditions are among the leading causes of morbidity and mortality worldwide. Although they are currently listed as the fifth leading cause of death in Canada, respiratory diseases are predicted to be the third leading cause of mortality by the year 2020, following ischemic heart disease and stroke.[1] Furthermore, since the prevalence of these conditions increases with age, the adverse impact of respiratory illnesses on the Canadian health care system will grow enormously over the next few decades as the overall population ages[2] and treatments for other common conditions, such as ischemic heart disease, stroke and diabetes, improve. A good understanding of the aging process of the respiratory system is clearly needed to formulate better strategies to prevent, diagnose and manage respiratory conditions in Canada.

Why are Respiratory Diseases so Prevalent in the Elderly?

The lungs of elderly persons are subject to a lifetime of exposure to known and unknown harmful agents. Decades may pass before the physical manifestations of cigarette smoke, pollution and other noxious environmental agents become clinically apparent. Furthermore, the respiratory system of an elderly person may have "battle scars" from repeated bouts of upper and lower respiratory tract infections, aspiration pneumonia, hypersensitivity reactions and other acute insults. The accumulated "left-over" damages from these acute episodes may build up over the years to produce functional impairments. Elderly individuals also may have many more comorbid illnesses than their younger counterparts. Comorbidities that affect oxygen delivery—such as congestive heart failure, anemia or cardiac ischemia—frequently exacerbate dyspnea associated with underlying respiratory conditions, and make it more refractory to standard therapy. Finally, as we will discuss further, the pulmonary system ages physiologically, making elderly individuals susceptible to frequent respiratory illnesses.

Physiologic Age-related Changes of the Lung

Lung Parenchymal Changes

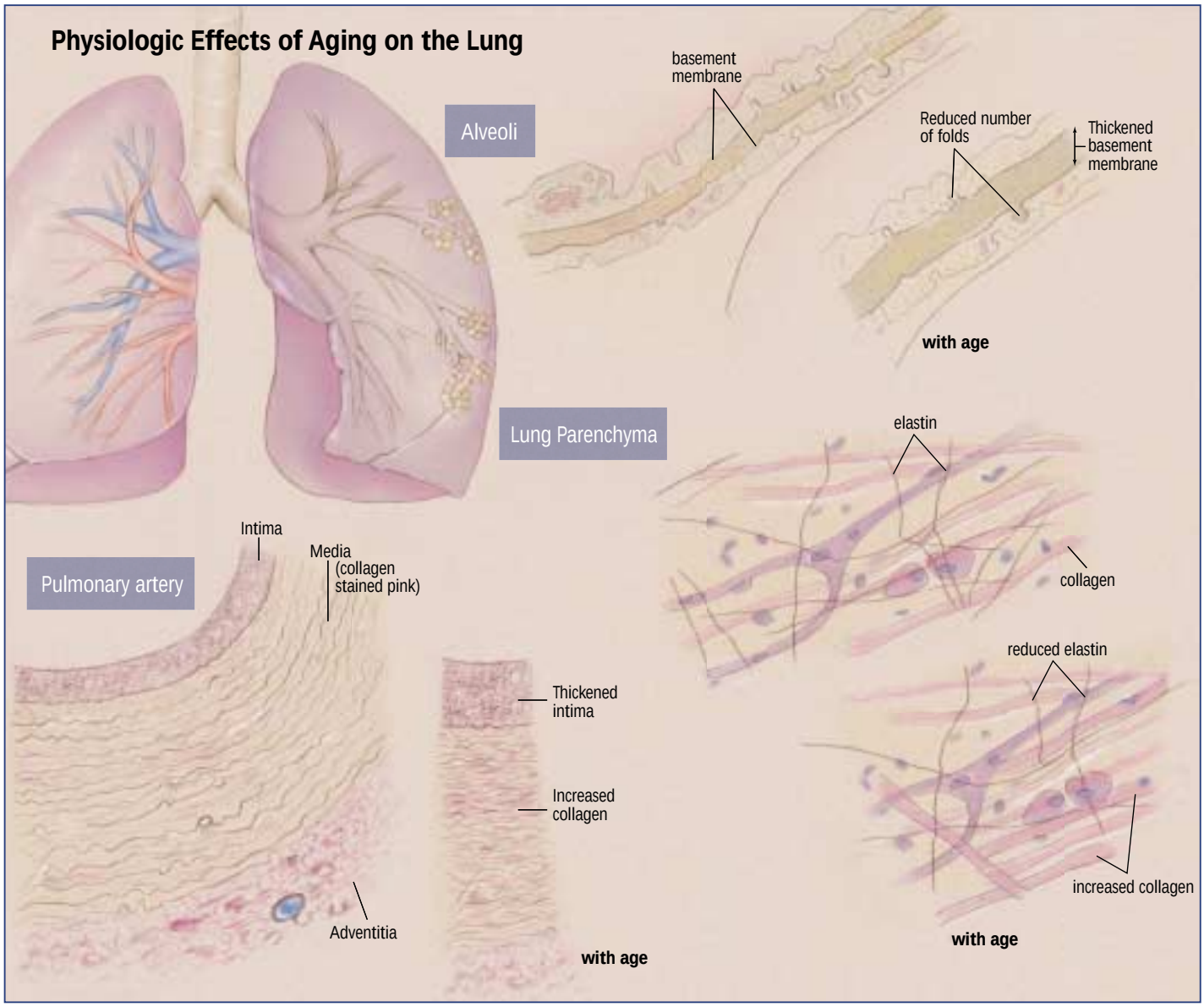
With the aging process, the elastin component of the lung matrix decreases while the amount of type III collagen increases,[3] making the pulmonary system more compliant. Because of this, during respiratory cycles alveolar units can become destabilized, leading to fluid / mucous retention and atelectasis. Alveolar basement membrane also thickens with aging,[4] which reduces diffusion capacity and may result in poor gas exchange (i.e., increased alveolar-arterial oxygen gradient). Indeed, the arterial oxygen tension ($Pa0_2$) decreases with aging independent of any superimposed disease processes such as chronic obstructive pulmonary disease (COPD), pulmonary hypertension or heart failure. Even among elderly individuals without any associated lung disease, the alveolar-arterial oxygen gradient is larger than that observed in the young, healthy population, making it imperative that prediction equations for oxygen tension take into account age-related changes to $Pa0_2$. Carbon dioxide tension, on the other hand, is not materially influenced by age.

Airways

Even in the absence of any material insult or injury to the airways, bronchiolar diameter diminishes significantly after age 40, largely in response to decreased elastin fiber deposition in the supporting connective tissues.[4] Physiologically, this leads to a marked reduction in the "tethering" forces of the surrounding matrix to keep the adjacent airways patent. This can increase airway resistance and promote premature airway closure (Figure 1), and as such, elderly individuals can demonstrate mild airflow obstruction at low lung volumes even in the absence of any disease. Since airway inflammation is not a prominent feature of age-related changes in the airways, corticosteroids and bronchodilators are largely ineffective in reversing mild airflow obstruction associated with aging.

Chest Wall

There are two important components of the chest wall that become adversely affected with the aging process: the bony structures and the respiratory muscles. With bone demineralization and osteoporosis, kyphoscoliotic changes may become apparent in some elderly individuals, which may diminish chest wall expansion and produce lung restriction. Moreover, some may develop significant calcification and fusion of rib-vertebrae joints, which can produce similar physiologic impairments. Although muscle fiber atrophy has not been consistently demonstrated



with aging,[5] there is a progressive loss in muscle fibers after the fifth decade, which probably explains the reduced respiratory muscle strength associated with aging. Because the diaphragm is also involved, additional ventilatory loading (during acute illnesses) can quickly lead to respiratory muscle fatigue and respiratory failure in some elderly individuals.[6]

Ventilatory Responsiveness to Hypercapnia and Hypoxia

Ventilatory responsiveness as well as neural output from central and peripheral chemoreceptors are diminished with aging.[7] The changes are most prominently observed with hypercapnia.[8] Compared to healthy young individuals, elderly persons have a blunted ventilatory response to increases in carbon dioxide. They also have a reduced perception of dyspnea associated with hypercapnia, hypoxia and/or airflow obstruction, which can delay their presentations to health care providers for treatment of respiratory infections.[9] Such delays can markedly increase their risk for arrhythmias, respiratory failure and even sudden deaths.

Paradoxically, during exertion the elderly have a more vigorous ventilatory response to exercise compared to younger individuals, which allows them to reach their ventilatory "ceiling" at lower workloads, thus limiting their overall exercise capacity.[10] Peak oxygen consumption falls because of other age-related physiologic changes, including loss of muscle mass, airflow obstruction and reduced stroke volume.

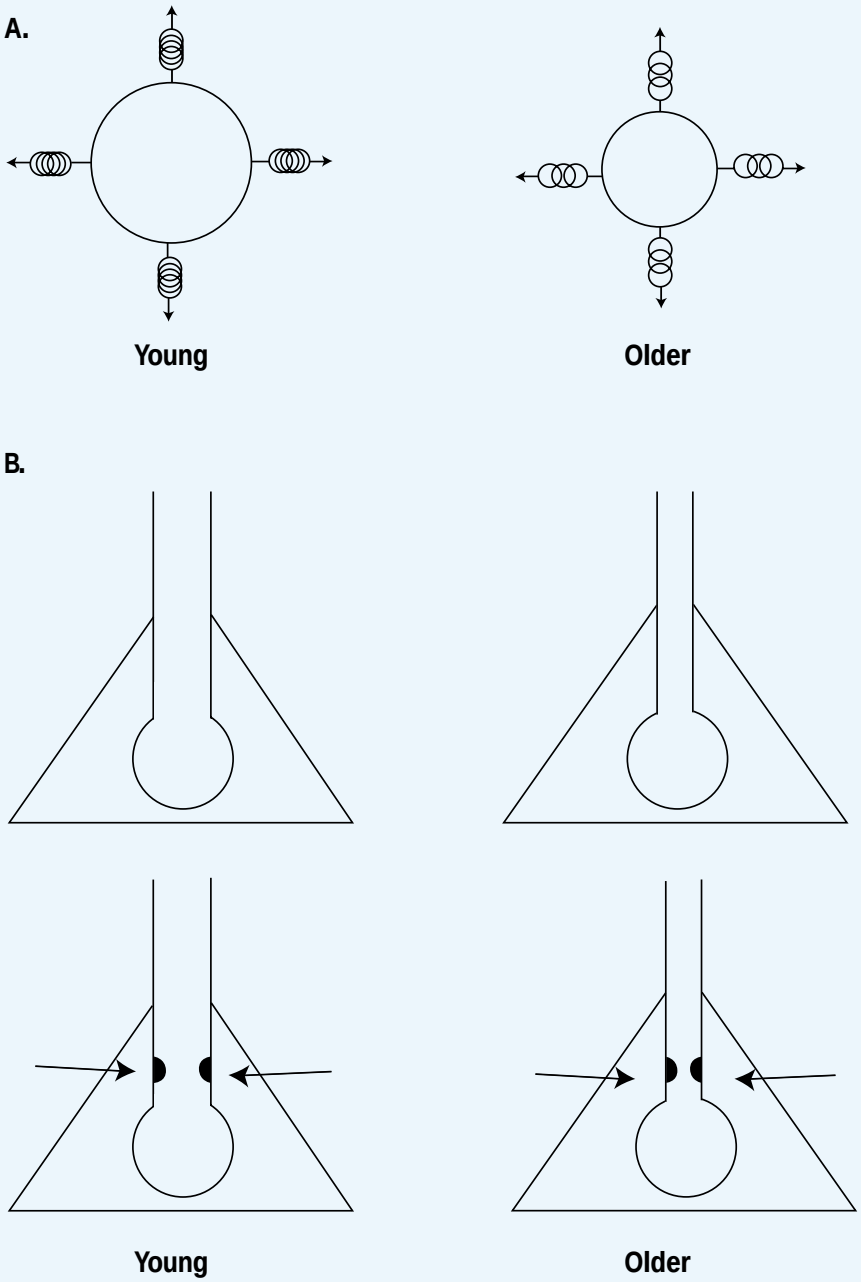
Pulmonary Vasculature

Although the effects of aging on the pulmonary vasculature are not well understood, pulmonary vessels become less distensible and more constricted with aging, principally due to vascular wall remodeling. This may limit the individual's ability to increase cardiac output during exertion.[11] However, age-related changes in the pulmonary circulation usually have minimal impact on cardiac output at rest.[11]

Age-related Changes in Pulmonary Function

There are two directly opposing forces that govern lung expansion and contraction: elastic recoil pressure and expansive force of the chest wall. At end-expiration (or functional residual capacity [FRC]), the recoil pressure of the lung generated by elastic fibers is balanced perfectly by an equal but opposite (expansive) force generated by the chest wall. Because the lung recoil pressure decreases with age due to a reduction in elastic tissues, FRC increases. The residual volume (RV) is the principal component of FRC that is increased. Vital capacity (VC), on the other hand, remains the same or decreases slightly with aging[12] (Figure 2). If FRC exceeds the closing volume (i.e., the lung volume at which airways begin to close), premature airway closure can occur during normal expiration, leading to flow-limitation.

Figure 1



(A) The schematic represents a cross-sectional view of a small airway. Note that reduction of tethering effect reduces the airway diameter. (B) The practical implication of reduced tethering is demonstrated when expiration increases transpulmonary pressure (arrows). Smaller diameter airways are at higher risk of obstructing.

Owing to age-related physiologic changes to the airways, forced expiratory volume in one second (FEV_1), forced vital capacity (FVC) and FEV_1 to FVC ratio also decrease with age. FEV_1 is reduced by approximately 15–30cc / year among non-smoking men and 10–20 cc / year among non-smoking women.[13] The decline in FEV_1 accelerates after age 65 and is further exacerbated by smoking. Inspiratory and expiratory pressures also decrease with age, reflecting the decline in respiratory muscle strength. The reduced surface area and increased thickness of alveolar walls cause a decline in diffusing capacity from midlife at a rate of 2.03mL / min / mmHg per decade in men and 1.47mL / min / mmHg per decade in women.[14]

Impact of Age on Diagnosis of Respiratory Disorders

Obstructive Airway Diseases

Most of the deaths in asthma and COPD are among elderly patients. There is a general under-recognition and under-treatment of these disorders in the elderly, which may, in part, be related to decreased patient perception and reporting of symptoms and to the frequent occurrence of comorbidities that may confound the diagnosis and lead to an under-appreciation of disease severity.[15] Decreased perception of airflow obstruction, hypoxia and hypercapnia may also lead to a significant delay in elderly patients seeking medical care. Even when care is sought, the patients may trivialize the significance of their symptoms, leading to inappropriate management.[15] Whenever possible, clinicians should supplement patient's history with objective measurements of lung function through spirometric testing in order to establish disease severity.

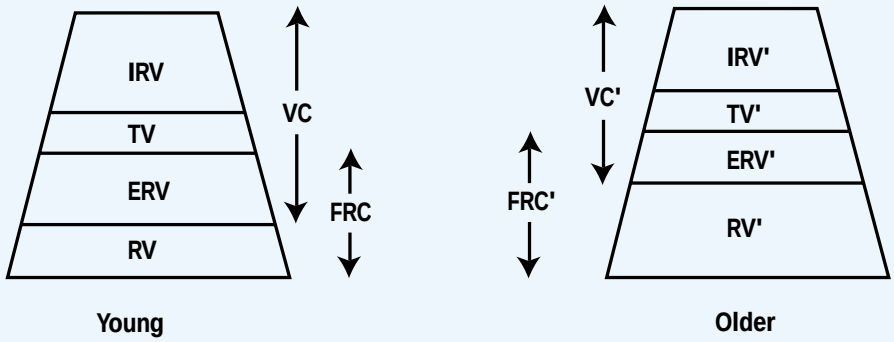
Despite the usefulness of lung function data in the evaluation of elderly individuals with dyspnea or cough, spirometric testing is an underutilized resource in the community. Therefore, the diagnosis of obstructive airway disease is frequently overlooked or missed entirely.[16] In the setting of symptoms (i.e., dyspnea and / or cough), an FEV_1 to FVC ratio of less than 0.70 indicates airflow obstruction. Complete reversal of airflow obstruction with bronchodilators is highly suggestive of asthma. Incomplete reversal, on the other hand, is suggestive of COPD. A clear distinction between asthma and COPD is often difficult in the elderly patient because their symptoms are very similar and, even with "pure" asthma, airflow obstruction is rarely completely reversed. Moreover, unlike younger individuals with asthma, the prevalence of allergy and atopy is low in the elderly population and very few react positively to immediate skin testing or have detectable circulating IgE levels.[15] Bronchoprovocation with methacholine or histamine may be used in cases where the diagnosis of hyper reactive airway disease is ambiguous. Despite important physiologic changes in the airway, bronchial responsiveness remains stable with age.[17]

Pneumonia

The elderly individual is at increased risk of developing pneumonias. The pathophysiology of pneumonia among the elderly is complex. However, it is well known that with aging, immunity wanes.[15] Not only do neutrophils and lymphocytes decrease in number, they also become less functional. Tonically and with antigenic challenge, the production (and release) of cytokines and chemokines diminishes with age, making it difficult for elderly individuals to mount a serious immune response to virulent pathogenic organisms.[18] Immunity is further compromised by a negative nitrogen balance, resulting from poor appetite and cachexia, commonly observed in the frail elderly population.[19] Gag reflex and swallowing mechanism may also be suboptimal in some elderly individuals, making them susceptible to aspiration pneumonias.[19] Those in nursing homes and other long-term care centres have an increased risk of nosocomial pneumonias, which are associated with very poor clinical responses and outcomes.[20]

Figure 2

Age-related Changes in Lung Volumes



IRV: Inspiratory reserve volume; TV: Tidal volume; ERV: Expiratory reserve volume; RV: Residual volume; VC: Vital capacity; FRC: Functional residual capacity.

Impact of Age on Treatment of Respiratory Disorders

Obstructive Airway Diseases

Management of elderly patients with obstructive airway disease should be similar to that of younger patients. Proper education and follow-up are of paramount importance in the elderly. There is a higher rate of adverse reactions in the elderly compared to the non-elderly population due to a variety of factors, including altered drug metabolism, potential for multiple drug interactions and presence of comorbidities. Elderly patients must be followed carefully to monitor for any significant toxic effects related to their pulmonary medications. As well, they should be instructed regularly on the proper use of the inhaler devices. Some elderly patients have poor eyesight or have poor hand to eye coordination; they may also have trouble holding their breath for the required period of time, resulting in suboptimal inhaler use and inadequate delivery of medications to the sites of active disease.[15]

As a general rule, systemic administration of bronchodilators is best avoided in the elderly, as many have co-existing cardiovascular conditions that increase their risk for life-threatening arrhythmias and ischemic events.[21] When theophyllines are used, their levels should be checked regularly. Co-administration of theophyllines with cimetidine, ciprofloxacin, allopurinol and other medications can unintentionally elevate theophylline levels beyond the toxic threshold, leading to nausea, vomiting and in serious cases, seizures and life-threatening arrhythmias.[22]

In many cases, prolonged use of systemic corticosteroids also should be avoided. Many elderly patients have underlying risk factors for diabetes, hypertension, peptic ulcer disease, osteoporosis, cataracts, glaucoma and psychiatric illnesses, all of which can be exacerbated by systemic corticosteroid therapy. If steroids must be used, the lowest possible dose should be employed. Concomitant therapy with a bone-sparing medication such as calcium supplements and / or bisphosphonates should be instituted for at least the duration of their systemic steroid therapy. Inhaled corticosteroids should be used for elderly patients with asthma. They appear to exert a beneficial effect in moderate to severe COPD. Although inhaled corticosteroids have a safer toxicity profile than the systemic formulations, they, nevertheless, can decrease bone mass and increase the risk for cataracts and glau-

coma.[23] It is also important to note that certain commonly used medications, such as topical beta-blocking agents and non-steroidal anti-inflammatories, can exacerbate underlying obstructive airway disease.

Pneumonia

Because pneumonia is a common problem among the elderly, vaccination should be considered. Although elderly individuals have diminished humoral immune responses to vaccines in general, influenza vaccination is still very effective in preventing clinically relevant and severe influenza infections. Accordingly, all individuals 65 years of age and older should receive yearly influenza vaccination, regardless of their clinical status.[24] The clinical efficacy of pneumococcal vaccination is modest. However, it has been demonstrated to be effective in preventing pneumococcal sepsis and possibly reducing lung infections. Elderly patients, and especially those with significant comorbid illnesses, should receive pneumococcal vaccination.

Summary

In summary, because of the physiologic effects of aging on the respiratory system and accumulated exposures to harmful infectious and non-infectious respiratory agents, obstructive airway disease and other respiratory conditions are common in the elderly population. In the presence of dyspnea and / or cough, spirometry should be used to confirm the diagnosis of obstructive airway disease and therapy should be instituted, when necessary. If medications are implemented, the lowest possible dose should be used and their effects need to be carefully followed and monitored. ◆

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