Normal ageing of the lung: implications for diagnosis and monitoring of asthma in older people

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ABSTRACT

What we need to know

- Is there an increased loss of elastic recoil over and above that due to ageing alone?
- How do we interpret inflammatory changes in the light of age-related airway inflammation?
- Is there an interaction between perception of airway narrowing and severity or control of disease?
- Are symptom-based action plans appropriate?
- Is control of the disease affected by the distribution of inhaled therapeutic aerosols and dry powder particles?

What we need to do

- Include patients aged 80 years and over in clinical trials.
- Assess functional and inflammatory parameters with appropriate age-matched controls in clinical trials.
- Assess feasibility and efficacy of symptom-based action plans versus those based on objective monitoring.
- Assess the responsiveness of elderly people to currently recommended therapies.

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Elderly people have a functionally decreased reserve of the respiratory system that reduces their capacity for exercise and puts them at increased risk of respiratory failure. There are well documented and important age-related structural and functional changes to the respiratory system that may amplify the effects of obstructive disorders and raise special problems in diagnosing and monitoring asthma in elderly people.

Two of the most important changes involve structures in the chest wall. The first is an age-related increase in the stiffness of the chest wall due to a change in shape, calcification and articulations of the rib cage. The second is a decrease in strength of the respiratory muscles, related to multiple factors, including generalised degenerative changes in muscle, nutritional status and the impact of changes in chest wall configuration on the force generation capacity of the diaphragm. These alterations reduce the capacity for exercise and result in increased oxygen demand by the respiratory muscles at any given level of exercise. Clinical assessment of elderly patients with airway obstruction should be tempered by awareness that older subjects have smaller tidal volumes and higher frequencies of breathing[1] and that there is a marked attenuation in the ventilatory responses to hypoxaemia and hypercapnia.[2]

With increasing age, subtle changes in the connective tissue of the lungs also occur. These include a decrease in elastic fibres and increase in type 3 collagen, together with changes in crosslinking and fibre orientation.[3-5] These changes alter the elastic properties of the lung parenchyma and the airway, with loss of elastic recoil. Structural changes in the lung parenchyma, such as reduced number of alveoli and an increase in the size of alveolar ducts, reduce the alveolar surface area.[6,7] This has important functional consequences for gas exchange, and contributes further to the loss of lung elastic recoil by reducing surface tension because of the increased radii of curvature of the alveolar spaces. There is no evidence of changes in the cells producing surfactant or of the composition of surfactant. The loss of lung elastic recoil, together with increased compliance of the intraparenchymal airway,[8] favours airway closure. There is an age-related increase in the lung volume at which dependent airways close.[9] In elderly people, this may exceed the functional residual capacity, resulting in airway closure during tidal breathing. This is an important mechanism accounting for the increased alveolar–arterial difference for oxygen with age.

As lung elastic recoil transmitted to the airway wall by alveolar attachments is a force tending to keep airways open, it constitutes a load against which airway smooth muscle must contract. Theoretically, loss of elastic recoil would thus make the ageing lung more vulnerable to bronchospastic stimuli, although increased airway responsiveness has not been found in elderly people without asthma.[10] There is a decrease in β_2-receptor function with age[11] that has not been reported for cholinergic receptors.[12] It might, therefore, be expected that anticholinergic agents in the elderly may be relatively more effective bronchodilators than β agonists. However, clinical guidelines at present do not suggest a preference for use of anticholinergic agents in elderly patients with asthma.

As most provoking stimuli in asthma are airborne and most asthma medications are administered by inhalation, it is important to consider whether there are any differences in particle deposition or aerosol distribution in elderly people. There is little information on these issues, although current evidence suggests that age-related changes in aerosol deposition are small.[13] The ability of elderly patients with poor respiratory muscle strength to generate sufficient inspiratory flow to optimise lung deposition from dry powder inhalers has not been systematically studied. On the other hand, there is evidence that mucociliary clearance from the lung is impaired in elderly people, and this may allow inhaled noxious particles or allergens to remain longer in the airway.[14]

There is some evidence that the ageing lung may be subject to chronic low-grade inflammation in the absence of overt lung disease. Bronchoalveolar lavage has demonstrated increased levels of neutrophils, interleukin 8 and neutrophil elastase in the lungs of elderly people.[15,16] These changes are similar in nature, but not in magnitude, to those seen in chronic obstructive pulmonary disease (COPD). Presumably this is related to longstanding exposure to

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atmospheric particles and pollutants, including sidestream ("environmental") tobacco smoke (ie, tobacco smoke produced by burning cigarettes that is not inhaled by the smoker).

Any possible interaction between this underlying inflammation and the inflammatory processes involved in asthma or diagnostic difficulties in the overlap of asthma with COPD remain speculative.

Several other issues may affect asthma monitoring in elderly people. There is some evidence of an age-related blunting of patient perception of airway narrowing. This has been demonstrated with internal resistive loads (methacholine-induced bronchoconstriction)[10] and with added external loads.[17] There is also a reduction in the sensitivity of the cough reflex.[18] This raises a potential problem both with early diagnosis and with symptom-based action plans. Simple objective measures of lung function can generally be performed in elderly patients, but many normal reference values are deficient for people over 80 years of age.

In summary, changes in the structure and function of the respiratory system in elderly people amplify the deleterious effects of a given degree of airway narrowing in asthma. These factors, together with altered perception of airway obstruction, may give rise to a different expression of the disease. This may affect the diagnosis and monitoring of asthma, as well as its differentiation from other obstructive diseases.

Competing interests

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References

1 Krumpe PE, Knudson RJ, Parsons G, Reiser K. The aging respiratory system. *Clin Geriatr Med* 1985; 1: 143-175.
2 Kronenberg R, Drage G. Attenuation of the ventilatory and heart rate responses to hypoxia and hypercapnia with aging in normal men. *J Clin Invest* 1973; 52: 1812-1819.
3 Crapo RO. The aging lung. In: Mahler DA, editor. Pulmonary disease in the elderly patient. New York: Marcel Dekker, 1993: 1-21. (Lung biology in health and disease, Vol. 63.)
4 Verbeken E, Cauberghs M, Mertens I, et al. The senile lung. Comparisons with normal and emphysematous lungs. I. Structural aspects. *Chest* 1992; 101: 793-799.
5 D'Errico A, Scarani P, Colosomo E, et al. Changes in alveolar connective tissue of the aging lung. An immunohistochemical study. *Virchows Archiv A* 1989; 415: 137-144.
6 Thurlbeck W. The internal surface area of non-emphysematous lungs. *Am Rev Respir Dis* 1967; 95: 765-773.
7 Gillooly M, Lamb D. Airspace size in lungs of lifelong nonsmokers: effect of age and sex. *Thorax* 1993; 48: 39-43.
8 Knudson RJ, Clark DF, Kennedy TC, Knudson DE. Effect of aging alone on mechanical properties of the normal adult human lung. *J Appl Physiol* 1977; 43: 1054-1062.
9 Anthonisen NR, Danson J, Robertson PC, Ross WR. Airway closure as a function of age. *Respir Physiol* 1969; 8: 58-65.
10 Connolly MJ, Crowley JJ, Charan NB, et al. Reduced subjective awareness of bronchoconstriction provoked by methacholine in elderly asthmatic and normal subjects as measured on a simple awareness scale. *Thorax* 1992; 47: 410-413.
11 Geokas MC, Lakatta EG, Makinodan T, Timiras PS. The aging process. *Ann Intern Med* 1990; 113: 455-466.
12 Ullah MI, Newman GB, Saunders KB. Influence of age on response to ipratropium bromide and salbutamol in asthma. *Thorax* 1981; 36: 523-529.
13 Bennett WD, Zeman K, Kim C. Variability of fine particle deposition in healthy adults. Effects of age and gender. *Am J Respir Crit Care Med* 1996; 153: 1641-1647.
14 Puchelle E, Zahm JM, Bertrand A. Influence of age on bronchial mucociliary transport. *Scand J Respir Dis* 1979; 60: 307-313.
15 Thompson AB, Scholer SG, Daughton DM, et al. Altered epithelial lining fluid parameters in old normal individuals. *J Gerontol* 1992; 47: M171-M176.
16 Meyer KC, Rosenthal NS, Soergel P, et al. Neutrophils and low-grade inflammation in the seemingly normal lung. *Mech Ageing Dev* 1998; 104: 169-181.
17 Tack M, Altose M, Cherniack N. Effect of aging on the perception of resistive ventilatory loads. *Am Rev Respir Dis* 1982; 126: 463-467.
18 Newnham DM, Hamilton SJC. Sensitivity of the cough reflex in young and elderly subjects. *Age Ageing* 1997; 26: 185-188. ❑