Asthma is a heterogeneous chronic inflammatory lung disease originating from a complex interaction between individual and environmental factors. As consequence of world population ageing an increase of chronic diseases prevalence, including asthma, has been documented. Late-onset asthma may have more complex pathogenic mechanisms other than Th2-mediated pattern. Diagnosis in older subjects is not straightforward as consequence of poor symptoms perception; in adults co-morbidities are associated with different asthma outcomes. A careful assessment and management of all potential concurrent disorders is essential to achieve a better disease control and an adequate response to treatment in elderly asthmatic patients.

Key words: Asthma, Elderly, Late-onset

INTRODUCTION

The ageing of the world’s population is, at least in part, the reason of increased prevalence of several chronic diseases, including asthma and chronic obstructive pulmonary disease. In particular, asthma in the elderly is not a rare disorder and age-related changes in the dyspnea perception and the increasing of associated co-morbidities modify frequently its clinical presentation. Asthma is a heterogeneous chronic inflammatory lung disease originating from a complex interaction between individual and environmental factors. Main characteristics of asthma include bronchial hyper-reactivity, reversible airflow obstruction, and tissue remodeling. The most frequent symptoms in asthmatic patients are recurrent coughing, dyspnea, chest tightness, shortness of breath and sporadic wheezing, which are also common to other respiratory diseases. Exposures, tobacco smoke, exercise and stress; respiratory viruses are a major trigger for acute asthma exacerbations. Diagnosis of asthma is made by a history of variable respiratory symptoms and evidence of variable expiratory airflow limitation. Pulmonary functional tests are essential for diagnosis; additional investigations include skin prick tests, IgE serum levels, FeNO whilst imaging procedures are more relevant for differential diagnosis. As consequence of poor symptoms perception asthma, in the elderly, may be under-diagnosed. Asthma exhibits multiple phenotypes arising from different clinical features and biological pathways including those involved in metabolic dysregulation. In order to obtain effective treatment, it is important to determine the specific type of asthma. Atopic asthma is commonly characterized by type 2 helper T cell (Th2) cytokine-induced eosinophilic inflammations in the airway. Some studies showed a strong link between genetic predisposition and early-onset of asthma.
Allergic asthma commonly starts in youth and may either remit or recur in adulthood 33; it is characterized by mast cell degranulation, amplification goblet cell hyperplasia, thickening of the sub-epithelial basement membrane, and epithelial damage 34. By contrast, non-atopic asthma which exhibit a late disease onset and is prevalent in elderly patients, usually may display high levels of serum and sputum neutrophils 35. Most children with persistent asthma phenotype exhibit current symptoms in adulthood, whilst around half reach remission 36. In asthmatic children who become asymptomatic in adolescence and have a recurrence of asthma in adulthood, the disease may be misclassified as “adult-onset asthma” 37,38.

Compared to childhood-onset asthma, asthma of adult onset is prevalent among nonatopic females and shows a more severe decline in lung function despite a shorter duration of disease 39,40. Indeed, in terms of lung function, non-atopic asthma may be even more detrimental than atopic asthma 35. The adult-onset asthma phenotype is associated with greater corticosteroid resistance when compared with youth’s eosinophilic asthma 41. In addition, elderly patients have low serum immunoglobulin E (IgE) levels due to immunosenescence; therefore, measurement of total serum IgE for clinical asthma diagnosis is less effective 35. Age-related changes in the respiratory system may contribute to clinical features of the disease: reduced diaphragmatic force generation and systemic inflammatory changes may occur in the elderly causing an accelerate functional decline 42.

**EPIDEMIOLOGY**

Asthma causes a significant public health burden and can manifest itself in any age 43. According to the World Health Organization, 4.3% of adults around the globe received a diagnosis of asthma 44.

Adult-onset asthma has become much more prevalent recently and is now an important public health concern due to its severity and lower remission rate 45. The mortality is high in the elderly population 46. Older asthmatic patients typically have more severe symptoms than younger ones requiring emergency treatment or hospital admission 47. Asthma in the elderly can be misdiagnosed or under-diagnosed due to the under-reporting of symptoms, atypical presentation, or age-related factors 48,49. For example, dyspnea, which is one of the most common symptoms in asthmatic patients, can be considered as an age-related reduction in respiratory efficiency. In addition, in older adults, a poor response to bronchodilators, the absence of an atopic history, low skin test sensitivity, and a lack of recognized diagnostic contribute to the under-diagnosis of asthma in the elderly 50-56.

Furthermore, to avoid misdiagnoses, it is important to discriminate asthma from other airway diseases with similar features. For example, it can be difficult to discriminate COPD from asthma in older patients since both diseases are characterized by airway obstruction and dyspnea; a large number of neutrophils are associated with both COPD and non-atopic asthma 57,58. Moreover, owing to a large number of comorbidities in the elderly, it has been observed that asthmatic symptoms in these patients have been wrongly attributed to comorbid conditions such as congestive heart failure, coronary artery disease or chronic bronchitis (Fig. 1) 42,50. Comorbidities, such as obesity and heart disease, can complicate but also complicate asthma and leave it under-diagnosed or difficult to treat 59-61, also because drugs targeting these comorbidities may interfere with asthma medications and exacerbate asthma in the elderly (Fig. 2).

In a study by Pipari et al. 62 current smokers and ex-smokers had a significantly higher risk of developing asthma compared with those who have never smoked. The authors concluded that smoking highly increases the risk of asthma in adulthood.

**PATHOGENESIS AND IMMUNOSENESCENCE**

Increased reactive oxygen species (ROS) levels strongly correlate with the severity of asthma 63. These higher amounts of ROS are largely responsible for the airway inflammation observed in asthma 64. ROS and reactive nitrogen species (RNS) play an important role during airway inflammation (65). ROS/RNS initiate the inflammatory response in the lungs by activating nuclear factor-kappa B (NF-κB), mitogen activated protein kinase (MAPK), activator protein-1 (AP-1), and other transcription factors 65,66. These redox-sensitive transcription factors promote the expression of numerous pro-inflammatory cytokines such as tumor necrosis factor (TNF-α), interleukin (IL)-1, IL-6, and IL-8, which induce the activation of inflammatory cells within the respiratory tract 67. Interestingly, it seems that these inflammatory cells including macrophages, eosinophils, neutrophils, and monocytes are able to generate ROS themselves in order to kill the invading bacteria 68.

In elderly adults, the lower ability of neutrophils to kill invading organisms can be attributed to a decline in their ROS production. For this reason, elderly patients are more predisposed to a variety of infections and diseases. Bacterial stimulation of the immune system is related to
Performing metacholine challenge test is central to clinical disease management, also in elderly asthmatic patients; metacholine BHR seems, indeed, to be very common in old patients, with relevant implications in terms of appropriate treatment. In this regard, significant progress in the management of asthma in the elderly could be made by introducing a test that discriminates between asthma and COPD bronchial hyperresponsiveness through using adenosine 50-monophosphate; a single dose of inhaled fluticasone propionate (1000 mg) on adenosine's AHR has been shown to determine a remarkable reduction in the bronchoconstriction in asthmatic subjects but not in patients with COPD (86).

Finally, the approach to asthmatic patients requires considering the role of Staphilococcus Aureus that seems to be largely implicated in older patients causing more severe symptoms, major airway hyperresponsiveness, and worse control of the disease. For these reasons, specific treatment against SA needs to be considered to improve asthma management in the elderly.

### Table 1: Asthma characteristics in elderly patients

**COMORBIDITIES:**
- COPD
- Chronic Rino-Sinusitis
- Congestive heart failure
- Osteoporosis
- GERD
- Panic disorders

**MAJOR CHARACTERISTICS:**
- No atopy
- Fewer specific symptoms
- Immunosenescence
- Lack of diagnostic criteria
- Tobacco smoking

**Delayed Diagnosis**

**Figure 1.** Asthma characteristics in elderly patients.

**Figure 2.** Diagnostic approach to asthma in older adults.
stimulation of the innate immune system and Th1 and Th17 activation in the adaptive response, it is recognized that bacterial products, such as superantigens, may be related to Th2-mediated inflammation. Staphylococcus aureus (SA) is one of the most frequent human bacterial pathogens producing enterotoxins (SE) that act as toxins as well as superantigens. The prevalence of SE sIgE positivity among asthmatics population varied with study populations, ranging from 14.9% to 79.1%; however, the rates showed trends to increase in older subjects and in more severe asthmatics. In non-asthmatic controls, the rate of SE sensitization also ranged widely, from 3.8% to 41.3%.

Older age is apparently a clinical factor to link asthma and SE sIgE. In older adult asthma, eosinophilic airway inflammation is frequently observed while no serum sIgE is detectable for common inhalant allergens. Some studies hypothesize that Th2 responses to inhaled bacterial antigens may contribute to non-atopic eosinophilic asthma in older adults. Severe asthma is another subtype which is related to SE sIgE, as suggested by two recent case-control studies.

Staphylococcus aureus commonly colonizes the human nasal mucosa, and the enterotoxins there of may provoke chronic rhinosinusitis (CRS) and nasal polyp development. Furthermore, SE-IgE sensitization is independently associated with inadequate outcomes and asthma severity in non-atopic adult patients and with severe eosinophilic asthma in the elderly.

Many clinical trials suggest a potential role of SA superantigens in the persistence and severity of asthma and allergic rhinitis. Bachert et al. show that SE-specific IgE were more commonly found in patients with severe asthma (as assessed by measurement of FEV1, need for inhaled or oral steroid treatment, and serum level of ECP) compared to controls (62% vs 13%, P = 0.01).

Song et al. in their systematic review show that SE sensitization has significant associations with asthma, and in particular, it was suggested to have relationships with the clinical reactivity and severity of asthma. Immunosenescence includes age-related functional declines in the innate and adaptive immune systems. However, the effects on adaptive immunity are more well-known than on innate immunity. Probably, altered immune responses may facilitate the pathogenesis of asthma in the elderly.

**ASTHMA COPD OVERLAP SYNDROME (ACOS)**

Obstructive ventilatory defects are a considerable challenge in elderly patients. Asthma and COPD are two major chronic obstructive airway diseases, but many patients present symptoms and features of both asthma and COPD. A graphic representation of this relationship was first presented as the non-proportional Venn diagram, reported in the 1995 American Thoracic Society (ATS) COPD guidelines. In 2007 and subsequently in 2012, the Canadian and Spanish guidelines for COPD recognized that patients with COPD and an asthma component may require a different treatment and the early introduction of inhaled corticosteroids (ICS) represents the best therapeutic option. In 2014, a GINA-GOLD committee developed a consensus based document in order to distinguishing between asthma, COPD and the overlap of asthma and COPD, so called Asthma COPD Overlap Syndrome (ACOS). In this manuscript, ACOS was described as a complex syndrome that usually involves adults (≥ 40 years), characterized by respiratory symptoms, persistent airflow obstruction with wide variations, history of doctor-diagnosed asthma, allergies and history of noxious exposures.

Louie et al. defined ACOS as one of the two clinical phenotypes: asthma with partially reversible airflow obstruction, with or without emphysema or reduced carbon monoxide diffusing capacity (DLCO) to less than 80% predicted; and COPD with emphysema accompanied by reversible or partially reversible airflow obstruction, with or without environmental allergies or reduced DLCO. Several studies reported that ACOS becomes more prevalent in older patients. Louie et al. defined ACOS as one of the two clinical phenotypes: asthma with partially reversible airflow obstruction, with or without emphysema or reduced carbon monoxide diffusing capacity (DLCO) to less than 80% predicted; and COPD with emphysema accompanied by reversible or partially reversible airflow obstruction, with or without environmental allergies or reduced DLCO. Several studies reported that ACOS becomes more prevalent in older patients. lounge et al. defined ACOS as one of the two clinical phenotypes: asthma with partially reversible airflow obstruction, with or without emphysema or reduced carbon monoxide diffusing capacity (DLCO) to less than 80% predicted; and COPD with emphysema accompanied by reversible or partially reversible airflow obstruction, with or without environmental allergies or reduced DLCO. Several studies reported that ACOS becomes more prevalent in older patients. The combination of pulmonary function tests and chest HRCT showed that asthmatic elderly patients could be classified into three different phenotypes: asthma-predominant (absence of airflow obstruction), asthma-obstructive Airways disease overlap (irreversible airflow obstruction without emphysema) and asthma-emphysema overlap (combination of obstructive ventilatory defect and emphysema).

**Bronchial Hyper-responsiveness**

Bronchial hyper-responsiveness (BHR) is often regarded as a ‘hallmark’ of asthma, also in the elderly. Bronchial hyper-responsiveness indicates a temporary airflow limitation when exposed to a broncho-constriction stimulus and broncho-provocation testing is frequently performed to support a diagnosis of asthma. The most
widely used is the methacholine challenge test, but histamine, exercise, eucapnic voluntary hyperventilation or inhaled mannitol tests may also be used. These tests are moderately sensitive for the diagnosis of asthma but are commonly poor specific. For example, BHR to methacoline can be found in COPD, allergic rhinitis, gastro-esophageal reflux and after viral or Mycoplasma infection.

Methacholine BHR exhibits a bi-modal age distribution in the general population, increasing in the elderly, and may contribute to accelerated lung function decline and the development of asthma in later stages of life. For this reason we believe it would be helpful in elderly patients who has a mild obstruction, not reversible (FEV1 > 70%, even with history favoring the diagnosis of COPD (smoker, onset of respiratory symptoms in adulthood, radiological signs of emphysema) a methacholine challenge; the positivity to this test may involve a detachment from what is recommended by current COPD guidelines, since the presence of BHR will require treatment with inhaled steroids, in addition to a bronchodilatator (LABA o LAMA). A usefull test in diagnostic of obstructive diseases could be represented by airway hyperresponsiveness (AHR) to adenosine 50-monophosphate. Spicuzza et al. showed that a single dose of inhaled fluticasone propionate (1000 mg) on AHR to inhaled AMP is able to distinguish in subjects with asthma and COPD; infact, FP caused a substantial reduction in the bronchoconstricter response to AMP in subjects with asthma but not COPD.

**IMPACT OF COMORBIDITIES IN ASTHMA ELDERLY PATIENTS**

**RHINITIS AND RHINOSINUSITIS**

Asthma and rhinitis are considered as two different features of the same airway disease and are commonly associated to atopy. A growing body of clinical-epidemiological investigations indicate a close relationship between asthma and allergic rhinitis. According to cross-sectional studies asthma and rhinitis often coexist and share common risk factors, including atopy. Several mechanisms might be responsible for the interaction between the upper and lower airways in asthmatic individuals; both respiratory and systemic pathways are implicated in the naso-bronchial cross-talk. Loss of protective functions of the nose, aspiration of nasal secretions in lower airways (post-nasal drip), alteration of nasal nitric oxide (NO) production have been associated to lower airway dysfunctions. Despite the small number of studies, a relationship between asthma and chronic rhino-sinusitis (CRS) has been reported in elderly patients. Song et al. observed that CRS is an independent risk factor for frequent asthma exacerbation and disease severity in elderly patients. In addition, Jarvis et al. showed that non-atopic CRS was positively associated with adult-onset asthma.

In patients with late-onset asthma, nasal polyposis and sinusitis have been strongly associated to severe asthma outcome. In the Severe Asthma Research Program (SARP), 54% of patients with severe asthma had a history of sinusitis vs 33% of those with mild asthma, and 37% of those with moderate asthma (P < 0.001). Also, a meta-analysis focusing the role of sinus surgery among patients with asthma has revealed that surgery had positive effects on the clinical course of asthma with comorbid chronic rhino-sinusitis.

These evidences indicates that disease of upper airway may influence the onset and severity of asthma and in particular appears to be associated to poor outcomes in adult-onset asthma.

**GASTROESOPHAGEAL REFUX DISEASE**

Gastroesophageal reflux disease (GERD) is a major upper gastrointestinal disorder seen in the elderly. In older subjects, there is a considerable decrease in the amplitude of peristaltic contraction and an increase in the frequency of non-propulsive and repetitive contractions compared to younger individuals, often referred to as presbyesophagus. Salivary production slightly decreases with age and is associated with a lower salivary bicarbonate response to acid perfusion of the esophagus. Finally, many drugs and diseases may adversely affect esophageal motility. In particular LES, Parkinson’s disease, diabetes mellitus, cerebro-vascular, cardiovascular and pulmonary diseases are associated to esophageal dismotility. Asthma is associated with GERD in 12 to 85% of patients; the wide variation is dependent on the method used to define GERD. Although an association between gastro-esophageal reflux disease (GERD) and asthma has also been reported, the underlying mechanism of this relationship remain unclear. The development of pulmonary complications in GERD is due not only to the pulmonary aspiration of refluxed material but also involves a neurally mediated reflex bronchoconstriction due to esophageal irritation by acid. However, inconsistent results have been obtained in several studies on the effects of treatment of GERD on asthma outcomes. In 2003, Gibson et al. showed that anti-reflux therapy did not consistently improve lung function, asthma symptoms, nocturnal asthma or the use of asthma medications. By contrast, some studies reported that PPI therapy...
improves nocturnal asthma symptoms, daytime asthma symptoms, pulmonary function and decreases requirement of asthma medications in patients with GERD. In elderly asthmatic patients although definitive remarks require further observations, GERD diagnosis should be considered in patients with poor symptoms control.

**Sleep Disturbances (SD) and OSAS**

Sleep disturbances (SD), and OSAS in particular, are a common finding in patients with late asthma onset impacting on quality of life (QoL) and clinical course of the disease. OSAS is characterized by repeated episodes of upper airways occlusion that results in brief periods of breathing cessation (apnea) or a marked reduction in flow (hypopnea) during sleep. This pattern is related to oxyhemoglobin desaturation, persistent inspiratory efforts against the occluded airway, and arousal from sleep. The prevalence of OSAS increases with age, independently from other risk factors.

The first case reporting a possible link between asthma and OSAS was published in 1979, by Hudgel and Shruh. Over the years more evidence were added to the knowledge about this topic. Many mechanisms may influence asthma control in patients with concomitant OSAS, including neuro-mechanical reflex bronchoconstriction, gastro-esophageal reflux, systemic inflammation.

In OSAS patients, the increased vagal tone observed occurring during apneas and could be a potential trigger for nocturnal asthma attacks in sleep apnea patients. An additional broncho-constrictive trigger is represented by hypoxia stimulation of the carotid body as results of obstructive apnea events.

OSAS patients have a higher incidence of gastroesophageal reflux. It is postulated that the increase in negative intra-thoracic pressure caused by upper airway obstruction can predispose to retrograde movement of gastric contents. GER occurring during sleep is a well-known trigger for nocturnal asthma and can provoke asthma symptoms through vagal reflexes induced by exposure of the esophagus to acid.

In individuals with OSAS, even in the absence of an inflammatory insult, chronic, low-grade systemic inflammation is characterized by increased serum concentrations of cytokines, and chemokines. The origin of this systemic inflammation appears to be, at least in part, the oxidative stress induced by oxygen desaturation during sleep apneas.

OSAS has been shown to lead to many cardiovascular consequences, which may complicate a co-existing airway obstruction in asthmatic patients. Another cause of the high incidence of OSAS in asthmatic patients may be the reduction of airway cross-sectional area and upper airway patency; the functional residual capacity of the asthmatics has been show to decline during sleep, which might partly contribute to the nocturnal increase in airway resistance.

A vicious cycle among GERD, obesity, cardiovascular diseases, systemic inflammation seems to contribute to worsens sleep apnea, which leads to increased severity of both asthma and OSAS.

**Risk Factors for Adult-Onset Asthma**

Late-onset asthma may have more complex pathogenic mechanisms other than the conventional Th2-mediated pattern which is largely mediated by atopy conditions. In adults a number of comorbid conditions are associated with different asthma outcomes (Tab. I).

**Depression**

Depression commonly coexists with asthma and is associated with more severe asthma and poorer asthma management. Coogan et al. reported that exists a positive association between CES-D (Center for Epidemiological Studies-Depression Scale) score and incidence of adult-onset asthma.

Some data suggest that depressed or sad moods elicited under laboratory conditions can produce pulmonary effects consistent with decreased airway function.

Stress is a recognized trigger of asthma exacerbation and may cause poor adherence to asthma treatment. Conversely, remission from depression is associated with improved asthma control.

The mechanism by which depression may “cause” asthma in unclear. Multiple pathways have been hypothesized: it seems that stress effects on the immune and autonomic nervous systems are relevant to the development of asthma, as well as co-existence of common comorbidities and inflammatory/ neuroendocrine mechanisms. Major depressive disorder leads to alteration in the hypothalamic-pituitary-adrenal axis that results in endogenous glucocorticoid resistance. This, in turn, could increase vulnerability to asthma onset by biasing the immune system toward a T helper type 2 response.

**Menopause**

Menopause is associated with relevant hormonal and metabolic changes: estrogen levels are low after menopause, and features of the metabolic syndrome become more prevalent paired with increasing risk of chronic conditions, such as diabetes and cardiovascular diseases. It has been suggested that late-onset asthma can be triggered by a change in systemic inflammation.

Sex hormone reduction has been found to be associated with a spontaneous synthesis, release, and action of...
several inflammatory cytokines. Foschino-Barbaro et al. described a new phenotype of menopausal asthma, which is mainly characterized by a neutrophilic airway inflammation, non-sensitivity to steroids, poor symptom control, and higher levels of LTE-4.

Airways inflammation in postmenopausal asthmatic patients seems to be different from that of patients with earlier-onset asthma, and is characterized by poorer response to anti-inflammatory treatment, as well as more frequent and severe exacerbations.

**CONCLUSIONS**

Asthma diagnosis in older subjects is not straightforward and under-diagnosis may occur as consequence of poor symptoms perception. A multidisciplinary approach is required as co-morbidities are frequently associated to asthma in elderly patients. A careful assessment and management of all potential concurrent disorders is essential to achieve a better asthma control and an adequate response to treatment.

Performing metacholine challenge test is central to clinical disease management, also in elderly asthmatic patients; metacholine BHR seems, indeed, to be very common in old patients, with relevant implications in terms of appropriate treatment.

In this regard, significant progress in the management of asthma in the elderly could be made by introducing a tests that discriminate between asthma and COPD bronchial hyper responsiveness trough using adenosine 50-monophosphate; a single dose of inhaled

---

**Table 1. Clinical and therapeutical issues of comorbidities in elderly asthmatic patient. Impact of comorbidities on asthma outcomes.**

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Asthma outcomes</th>
<th>Pathophysiology</th>
<th>Treatment recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related to ageing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>• Poor adherence to asthma treatment • Increase of asthma exacerbations</td>
<td>• Stress effects on the immune and autonomic nervous systems • Inflammatory/neuroendocrine mechanisms</td>
<td>Assess to avoid drug interaction or treatment failure</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>• Poor adherence to asthma treatment • Altered perception of symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menopause</td>
<td>• More frequent and severe exacerbations</td>
<td>• Low estrogen levels • Increase of systemic inflammation • Increasing risk of chronic conditions</td>
<td></td>
</tr>
<tr>
<td>Rhinitis and rhinosinusitis</td>
<td>• Increase of asthma exacerbations • Increased severity of both asthma</td>
<td>• Loss of protective functions of the nose • Aspiration of nasal secretions in lower airways (post-nasal drip) • Alteration of nasal nitric oxide (NO) production</td>
<td>Treat independently to improve asthma outcomes</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease (GERD)</td>
<td>• Increase of asthma symptoms • Nocturnal asthma • Pulmonary complications</td>
<td>• Pulmonary aspiration of refluxed material • Neuromechanically reflex bronchoconstriction due to esophageal irritation by acid</td>
<td></td>
</tr>
<tr>
<td>Sleep disturbances (SD) and OSAS</td>
<td>• Increase of nocturnal asthma attacks • Increased severity of both asthma</td>
<td>• Neuro-mechanical reflex bronchoconstriction (increased vagal tone) • Gastro-esophageal reflux • Systemic inflammation</td>
<td></td>
</tr>
<tr>
<td>COPD (Asthma copd overlap syndrome - ACOS)</td>
<td>• More respiratory symptoms (dyspnea and wheezing) • Reduced physical activity • More frequent exacerbations • Impaired health-related quality of life</td>
<td>• Persistent airflow obstruction with wide variations • History of doctor-diagnosed asthma and allergies • History of noxious exposures</td>
<td></td>
</tr>
<tr>
<td>Congestive Heart Failure and Cardiac Asthma</td>
<td>• Symptoms of acute and chronic cardiac and respiratory illnesses overlap • Wheezing, coughing and orthopnea</td>
<td>• Pulmonary edema • Pulmonary vascular congestion • Airway obstruction is probably amplified by circulating inflammatory factors and tissue growth factors</td>
<td></td>
</tr>
</tbody>
</table>
fluticasone propionate (1000 mg) on adenosine’s AHR has been shown to determine a remarkable reduction in the bronchoconstriction in asthmatic subjects but not in patients with COPD. Finally, the approach to asthmatic patients requires to consider the role of S. Aureus that seems to be largely implicated in older patients causing more severe symptoms, major airway hyperresponsiveness and worse control of the disease. For these reasons, a specific treatment against SA need to be considered to improve asthma management of in the elderly.

References
Bronchial asthma in the elderly patient

34 Zhuo L, Koozehchian MS, Chen LL. Characterization of reactive nitrogen species in allergic asthma. Ann Allergy Asthma Immunol 2014;112:18-22.
66 Li N, Nel AE.


Teramoto S, Yamamoto H, Ouchi Y. Increased C-reactive protein and increased plasma interleukin-6 may synergistically effect the progression of coronary atherosclerosis in obstructive sleep apnea syndrome. Circulation 2003;107:E40.


