Abstract
Atopic diseases such as rhinitis and asthma are relatively common in children and young adults. However, many patients aged >65 years are also affected by these disorders. Indeed, the literature suggests that between 3–12% and 4–13% of individuals in this age range have allergic rhinitis and asthma, respectively. However, these numbers are most likely underestimates because atopic diseases
are frequently not considered in older patients. The diagnosis of both allergic rhinitis and asthma in older patients is more difficult than in younger patients because of a wide differential diagnosis of other diseases that can produce similar symptoms and must be excluded. Furthermore, treatment of these disorders is complicated by the potential for drug interactions, concern about the adverse effects of medications, in particular corticosteroids, and the lack of drug trials specifically targeting treatment of older patients with allergic rhinitis and asthma.

1. Allergic Rhinitis

1.1 Pathophysiology and Prevalence in the Elderly

Antigen-specific allergic antibodies (IgE) play a critical role in the pathogenesis of allergic rhinitis. Following exposure to antigens in sensitized individuals, IgE molecules that coat the surface of the nasal mast cells are cross-linked, releasing several preformed mediators, in a process labelled the ‘early phase response’. These mediators include histamine, kinins, prostaglandins and platelet-activating factor. Activation of histamine receptors constricts the vascular endothelium, resulting in vascular leak and mucosal oedema, and stimulates irritant receptors, producing itching and sneezing. The release of these early mediators induces the ‘late phase response’, which occurs 4–8 hours later and is characterized by recruitment of other inflammatory cells to the mucosa, such as neutrophils, eosinophils, lymphocytes and macrophages. The increased nasal inflammation sustains the inflammatory response and causes a return of symptoms in as many as one-half of patients.[1]

Allergic rhinitis is a common problem in younger individuals, affecting between 15% and 45.2% of people worldwide.[2-4] Although studies have suggested that antigen-specific IgE declines with age,[5] older patients may become sensitized to allergens.[6] Allergic rhinitis has been estimated to affect 3–12% of patients aged >65 years.[7,8] The disorder is not insignificant as it impacts on general health and quality of life;[9,10] it may also exacerbate asthma, produce sinus infections and otitis media with effusions[11] and induce nasal polyp formation.
1.2 Diagnosis

1.2.1 History

Clinical suspicion is the first key step in making a diagnosis of allergic rhinitis. Allergic rhinitis typically presents with sneezing, pruritus, nasal congestion and/or rhinitis, and is frequently associated with conjunctivitis. In the past, allergic rhinitis was classified as seasonal (occurring only during times of pollination) or perennial (year-round symptoms). More recently, the Allergic Rhinitis and Its Impact on Asthma workshop recommended that patients with allergic rhinitis be reclassified as intermittent (symptoms <4 days per week or <4 weeks per year) or persistent (those with symptoms of longer duration). Patients are further classified into having mild or moderate/severe allergic rhinitis based upon the degree to which symptoms impair daily activities and sleep patterns.

When considering the diagnosis of allergic rhinitis in an older patient it is critical to exclude other diseases with similar presentations. Older patients are at risk for developing rhinitis from structural changes in the connective tissue and vasculature of the nose. Additionally, decreased blood flow in the nose induces nasal mucosal atrophy, producing congestion, nasal crusting and a foul odour. Several medications, in particular antihypertensives, may produce nasal congestion as an adverse effect. Examples include central adrenoceptor antagonists (clonidine), β-adrenoceptor antagonists, α-adrenoceptor antagonists (prazosin), vasodilators (hydralazine) and diuretics (hydrochlorothiazide). Use of conjugated estrogens may also generate nasal congestion. "Rhinitis medicamentosa" results when patients use α-adrenergic nasal decongestants for extended periods of time, producing a rebound nasal congestion. Vasomotor rhinitis (VMR) is a condition in which patients experience symptoms similar to allergic rhinitis after exposure to irritants such as perfume, cold air and spices, but on examination there is no evidence of allergen sensitization. The mechanism of VMR is not completely understood, although it is believed to be secondary to parasympathetic hypersensitivity of the upper airways and C-fibre desensitization or degeneration. Non-allergic rhinitis with eosinophilia syndrome also presents similarly to persistent allergic rhinitis. Nasal smears demonstrate an elevated number of eosinophils; however, evaluation for IgE sensitization is negative.

Other diseases that need to be considered in older patients with nasal complaints include hypothyroidism and granulomatous diseases such as Wegener’s granulomatosis or sarcoidosis. If patients have unilateral symptoms, especially obstruction, evaluation for a neoplasm should be undertaken. Finally, patients with a sweet-tasting clear nasal drainage that is exacerbated by coughing or changing head position should be evaluated for a cerebrospinal fluid leak.

1.2.2 Laboratory Evaluation

The first step in determining if rhinitis is secondary to allergen sensitization is to evaluate whether the patient has evidence of IgE to common aeroallergens. IgE sensitivity to an allergen can be determined by skin prick testing or serum evaluation. The advantage of the skin prick test is that results are available within approximately 15 minutes and the test may be more sensitive than serum testing. The principle of skin testing is that allergens will bind to the specific IgE antibodies coating skin mast cells. Similar to the cross-linking of IgE molecules in the nasal mucosa, intracellular mediators, such as histamine, are released immediately. A positive skin prick test results in a ‘wheal (swelling) and flare (erythema)’ response, which may resemble a mosquito bite. However, with aging, there are changes in the skin that may suppress skin prick test responses. These include a reduction in the number of blood vessels and mast cells, and photo damage. A decrease in skin test reactivity to histamine (a positive control) has been noted in people aged >50 years, but this subsequently plateaus after 60 years. Therefore, if results from prick skin testing are inconclusive, or if the histamine positive control is negative, in vitro testing for allergen specific IgE is warranted.

Nasal provocation testing, in which the nasal mucosa is exposed to the offending allergen, is frequently used in clinical studies to confirm the
Table I. Allergen avoidance measures

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Avoidance measures</th>
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<tr>
<td>Dust mites</td>
<td>Cover pillow and mattress in impermeable (‘anti-dust mite’) covers</td>
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<tr>
<td></td>
<td>Wash bedding frequently at 130°F (55°C)</td>
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<td></td>
<td>Remove or minimize carpeting</td>
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<td></td>
<td>Reduce humidity</td>
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<tr>
<td>Pets</td>
<td>Remove pets from home</td>
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<td></td>
<td>Reduce pet hair reservoirs (e.g. sofas, carpets)</td>
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<tr>
<td></td>
<td>Keep pets out of bedroom</td>
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<tr>
<td>Molds</td>
<td>Clean visible sources of mold</td>
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<tr>
<td></td>
<td>Reduce humidity</td>
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<tr>
<td></td>
<td>Avoid basements</td>
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<tr>
<td>Cockroaches</td>
<td>Frequently remove kitchen trash</td>
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<td></td>
<td>Use traps containing ‘bait’</td>
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<tr>
<td>Outdoor allergens</td>
<td>Keep windows and doors shut during pollination</td>
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<td>Air-conditioning</td>
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diagnosis of allergic rhinitis, although it is not widely accepted as standard practice. Furthermore, changes in nasal pressure and airflow during breathing, as measured by rhinomanometry (which could aid in the diagnosis of allergic rhinitis), is employed for research purposes only. Nasal endoscopy and computerized tomography are not routinely performed for the diagnosis of allergic rhinitis; however, these may be useful to exclude other aetiologies of nasal congestion such as structural defects or malignancies.

1.3 Management

1.3.1 Allergen Avoidance

The initial approach to treating allergic rhinitis is to avoid contact with the antigens to which the patient is sensitized, and to which exposure induces symptoms. Sensitization alone, without a good clinical history of allergic symptoms upon exposure to that specific allergen, does not necessarily signify that the antigen is the cause of the symptoms.

Although allergen avoidance is important, it is often difficult to remove all offending allergens from the indoor environment, and patients therefore frequently need medical therapy to control symptoms. Examples of allergen avoidance techniques are listed in table I. Many of these measures, such as removing a pet, which is a companion, or wall to wall carpeting, if the patient is in an assisted living facility, may be particularly difficult for older people. It is important to advise patients with limited incomes about products that claim to remove allergens and irritants from the environment. Some of these products, such as anti-dust mite covers for bedding, have been scientifically proven to reduce allergen exposure, whereas chemical agents that kill dust mites do not produce long-lasting effects and are not recommended as routine care.

1.3.2 Intranasal Corticosteroids

Intranasal corticosteroids (INS) are the first-line therapy for moderate/severe persistent allergic rhinitis. They reduce rhinitis, nasal congestion and nasal itching, and, to a lesser degree, improve ocular symptoms. INS have the benefit of delivering a high concentration of corticosteroids to the target organ (the nose), thereby avoiding systemic effects. However, when patients have complete nasal blockage, delivery of INS is less effective, and patients may need pre-treatment with a systemic corticosteroid for 4–7 days to open the nasal passageways in order to enable better deposition of the INS. In such circumstances, a short dose of an oral corticosteroid does not need tapering, but patients should be warned of short-term adverse effects, including mood, sleep and appetite changes. It is important to remind patients that INS need to be administered on a daily basis, and that it may take up to 2 weeks before improvement of symptoms is noticed. Currently available INS reduce allergic rhinitis symptoms with equal efficacy.
There are several formulations of INS, all of which are delivered in an aqueous solution.[27] The adverse effects of INS are mostly local and include nasal burning, dryness and epistaxis, which can occur in about 5–10% of patients.[26] Two separate studies using different preparations of INS (fluticasone propionate, mometasone) demonstrated that nasal mucosal atrophy does not occur with long-term use.[28,29] There have been a few case reports of adrenal suppression in adults taking INS within the licensed dose range;[30] however, most reports show little to no hypothalamic-pituitary-adrenal axis suppression.[27,31] There is a theoretical risk that high doses of INS will produce osteoporosis, although studies have failed to demonstrate an increased risk of fractures or bone turnover in adults.[30,32,33] One study in older patients (mean age 81 years) demonstrated no increased risk of fractures with use of INS.[33] Presently, there are insufficient data to draw a conclusion as to whether INS increase intraocular pressure. There have been case reports (one in a 71-year-old male,[34] and another in a group of 12 patients[35] [mean age 66 years]) describing increased intraocular pressure after commencement of INS and subsequent abatement after treatment was discontinued. However, a position statement on the use of INS concluded that although there are inadequate data to draw a conclusion, physicians should monitor for glaucoma in patients using INS, especially those who are also taking corticosteroids for other diseases such as asthma.[36] The role of INS in cataract formation, especially in older patients, is even more unclear. A large study that examined the correlation between the use of INS and cataract formation in individuals <70 years of age found no association.[37]

### 1.3.3 Antihistamines

Histamine is a key mediator released during the 'early phase response'. It produces several classic symptoms of allergic rhinitis, including itching, nasal congestion, mucus production and rhinitis after binding to the histamine H1 receptor. H2 receptor binding accounts for symptoms associated with oesophagitis and gastro-oesophageal reflux, but can also be responsible for some symptoms of allergic rhinitis.

Antihistamines are classified into different generations based upon when they were initially developed and their pharmacological properties (table II). First-generation H1 receptor antagonists are lipophilic, readily cross the blood-brain barrier, bind to central H1 receptors, and produce sedation, dizziness, reduced mental alertness and confusion, which are especially troublesome adverse effects in older patients. First-generation H1 receptor antagonists lack specificity for the H1 receptor, having dopaminergic, serotonergic, muscarinic and cholinergic adverse effects.[38] This nonspecific binding can create other adverse effects, including urinary retention, constipation, arrhythmias and postural hypotension, which can be significant in older patients. Because many of these first-generation antihistamines are available over the counter, taking a careful medication history is important.

Second-generation H1 receptor antagonists (e.g. fexofenadine, cetirizine, loratadine and desloratadine) have a reduced ability to cross the blood-brain barrier, and a greater specificity for the H1 receptor. Of the second-generation antihistamines, cetirizine is labelled as producing an increased incidence of sedation at its recommended doses. Some of the second-generation H1 receptor antagonists have

<table>
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<th>Table II. Classification of antihistamines</th>
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<tr>
<td><strong>First-generation</strong></td>
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<tr>
<td>Chlorphenamine</td>
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<td>Diphenhydramine</td>
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<tr>
<td>Hydroxyzine</td>
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<tr>
<td>Cyproheptadine</td>
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<tr>
<td><strong>Second-generation</strong></td>
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<tr>
<td>Cetirizine</td>
</tr>
<tr>
<td>Levocetirizine</td>
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<tr>
<td>Loratadine</td>
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<tr>
<td>Desloratadine</td>
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<tr>
<td>Acrivastine</td>
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<tr>
<td>Ebastine</td>
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<tr>
<td>Fexofenadine</td>
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<tr>
<td>Mizolastine</td>
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<tr>
<td>Azelastine</td>
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<tr>
<td>Levocabastine</td>
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<tr>
<td>Ketotifen</td>
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1.3.5 Allergen Immunotherapy

In younger patients who have persistent symptoms despite medical treatment, allergen immunotherapy (‘allergy shots’) may be considered. Allergen immunotherapy involves the subcutaneous, and more recently, sublingual administration, of antigens to which the patient is sensitized. Studies have demonstrated that 3–4 years of treatment with specific subcutaneous immunotherapy reduces symptoms of allergic rhinitis, and that the effect persists for up to 3 years after discontinuation of treatment. Most studies of immunotherapy for treatment of allergic rhinitis have excluded older patients either because of safety concerns (e.g. risks of developing anaphylaxis, particularly in patients taking a β-adrenoceptor antagonist, who may not respond to rescue epinephrine [adrenaline]) or the belief that long-standing disease may not respond to this treatment. Two studies have nonetheless shown that immunotherapy in healthy patients aged >60 years is safe and effective.

Immunotherapy requires frequent office visits for injections and is not effective in all patients. Furthermore, it has other limitations that must be addressed when considering commencing patients on this form of treatment. Firstly, allergen immunotherapy is more likely to be successful when given as a single allergen, as opposed to multiple allergens. Secondly, patients are at risk of developing a systemic reaction requiring rescue treatment with antihistamines, corticosteroids and epinephrine. The systemic reaction rate has been estimated to be between 2.1% and 7% of patients receiving immunotherapy over a 1-year period, accounting for approximately 3.4 deaths per year in the US. Furthermore, not all patients will have improvement of their allergic symptoms from allergen immunotherapy, and it is difficult to determine which patients will derive a benefit. Finally, allergen immunotherapy requires a time commitment from patients. Patients usually receive 1–2 injections per week, until they reach a maintenance dose, which may take up to 6 months.

Antihistamine medications are used as monotherapy for patients with intermittent or mild persistent allergic rhinitis. They may also be added to INS in patients for whom these medications do not control all symptoms, or administered to patients unwilling or unable to administer a nasal medication. Antihistamines are available as nasal sprays, such as azelastine or levocabastine (not available in the US), which may be used in conjunction with INS or oral antihistamines. Intrasinal antihistamines generally have a faster onset of action than INS.

1.3.4 Decongestants

In some patients with allergic rhinitis, nasal congestion may be particularly bothersome. Oral antihistamines have been shown to alleviate nasal congestion but INS are more effective. If patients have persistent symptoms despite the use of these medications, the practitioner may consider adding an oral decongestant. Pseudoephedrine, an α-adrenoceptor agonist, is the most commonly used oral decongestant, and several oral antihistamine preparations contain this agent. Oral decongestants should be used cautiously in older patients as they may increase heart rate and cause dry mouth, anxiety, insomnia and irritability. They should be avoided in patients with poorly controlled hypertension, coronary heart disease and prostatism. Using nasal decongestants averts many of the systemic affects of oral decongestants, although they should be used only for short periods of time (<5–7 days) because rhinitis medicamentosa can develop with prolonged use.

some anti-inflammatory properties, although their relevance is not clear. Although these second-generation H1 receptor antagonists are more specific for the H1 receptor, and generally safe in older patients, they still need to be prescribed with care. Administration of ketoconazole with either fexofenadine or desloratadine can increase the plasma concentrations of these antihistamines by 135% and 40%, respectively. For patients with renal failure, fexofenadine doses need to be adjusted, and desloratadine must be avoided.

Antihistamine medications are used as monotherapy for patients with intermittent or mild persistent allergic rhinitis. They may also be added to INS in patients for whom these medications do not control all symptoms, or administered to patients unwilling or unable to administer a nasal medication. Antihistamines are available as nasal sprays, such as azelastine or levocabastine (not available in the US), which may be used in conjunction with INS or oral antihistamines. Intranasal antihistamines generally have a faster onset of action than INS.
1.3.6 Other Treatments

Leukotrienes are released after exposure to an antigen in a sensitized individual and increase vascular permeability, mucus production and vascular constriction, all of which result in nasal obstruction. Although medications targeting leukotrienes were initially developed for the treatment of asthma, montelukast reduced allergic rhinitis symptoms in several studies that included patients up to 75\(^{[56]}\) and 82\(^{[57]}\) years of age. Montelukast antagonizes one of the leukotriene receptors. It works best when used with an oral antihistamine and/or ICS, and not as mono-therapy.\(^{[58]}\)

Inhibition of binding of IgE to mast cells and basophils by omalizumab, a monoclonal anti-IgE molecule, has been shown in several clinical trials to reduce nasal symptoms and use of nasal antihistamines in patients with allergic rhinitis.\(^{[59-61]}\) Although these trials were not specifically designed to study older patients, several included patients up to 75 years of age. Currently, anti-IgE therapy is approved for use only in asthma.

Ipratropium bromide is an intranasal antimuscarinic agent that decreases secretions from serous and seromucous glands.\(^{[62]}\) It may reduce rhinorrhea and is safe when taken at prescribed doses.\(^{[62]}\) Cromolyns inhibit degranulation of mast cells but require frequent daily administration, take at least 1 week for symptom relief to be detected and provide only modest symptom relief. Consequently, they are rarely used in the treatment of allergic rhinitis, despite their excellent safety profile.

2. Asthma

2.1 Pathogenesis

The National Heart Blood and Lung Institute (NHLBI) defines asthma as a chronic inflammatory disorder of the airways that produces airflow obstruction and bronchial hyper-responsiveness which is reversible in most patients.\(^{[24]}\) The specific inflammatory events in asthma are reviewed in more detail elsewhere;\(^{[63]}\) however, in general, they are characterized by an increase in CD4+ T-lymphocytes (particularly of the T helper-2 subset), eosinophils, mast cells and basophils. When a particular insult (e.g., an allergen in a sensitized individual, irritant or an upper respiratory viral infection) is inhaled or acquired, the inflammatory cells of the airway are activated. These cells release mediators, including cytokines, histamine and leukotrienes, which acutely increase cellular activation and recruitment to the airways, induce bronchoconstriction and increase mucus secretion. This produces the typical symptoms of asthma, including cough, shortness of breath and wheezing.

The prevalence of asthma in older individuals has been estimated at between 4% and 13%;\(^{[64-69]}\) however, this number is likely to be an underestimate because asthma in the elderly may be underdiagnosed.\(^{[66,70,71]}\) There is increased mortality and morbidity associated with asthma in the elderly. One study noted a 3-fold greater increase in the death rate among the oldest patients with asthma.\(^{[72]}\) Between 2001 and 2003, over half of the 4210 asthma deaths in the US involved patients aged >65 years.\(^{[73]}\) Older patients with asthma are hospitalized more frequently than younger patients.\(^{[74,75]}\) The reasons for these trends are most likely multi-factorial. One explanation is that older age groups have an increased risk of other co-morbid conditions. Coronary artery disease, cancer, diabetes mellitus and hypertension are risk factors for emergency visits and hospitalizations for asthma.\(^{[76,77]}\) Additionally, many elderly patients with asthma may have co-existing lung disease, which can worsen their asthma. In a Norwegian study of patients aged >70 years with asthma, 36% reported also having chronic bronchitis, 23% emphysema and 33% both bronchitis and emphysema.\(^{[78]}\) Another cause for the increased morbidity in older patients with asthma is that they are more likely to be undertreated with controller medications than younger patients.\(^{[66,70]}\)

Despite increased morbidity and mortality in older patients with asthma, the pathogenesis in this age group is not well characterized. Asthma in the elderly may result from persistence of childhood asthma, return in later life of childhood asthma that was quiescent in adulthood, or asthma that developed later in life (‘late-onset asthma’). While allergen
sensitization, environmental influences and genetic factors are critical to the development of childhood asthma, their role in late-onset asthma and persistence of asthma into older age is less certain. In children and young adults with asthma, between 60% and 80% have evidence of allergen sensitization. For many years, the belief was that asthma in the elderly did not have an atopic component. However, several groups have subsequently demonstrated that elevated IgE and antigen-specific IgE can develop later in life, and in one report, was present in up to 72% of older patients with newly diagnosed asthma. Sensitization to cockroach allergen is associated with more severe asthma in older patients living in the inner city. Also, in a population of Japanese individuals, an association between polymorphism of the high-affinity IgE receptor and a promoter for the RANTES (Regulated on Activation, Normal T Cell Expressed and Secreted) gene (a chemoattractant for T cells, eosinophils, basophils and mast cells) was found to be a risk factor for the development of asthma after the age of 40 years. However, polymorphisms in the IgE receptor were not found to be associated with late-onset asthma by a group in the UK.

Although a family history of asthma is an important risk factor for onset of childhood asthma, its role in later life is not certain. Some studies have suggested that a family history of asthma is a risk factor for the development of late-onset asthma whereas other studies have questioned its role. In individuals between 50 and 59 years of age who had a family history of asthma, bronchial hyper-responsiveness was greater and bronchoalveolar lavage fluid lymphocytes were higher than in same-aged individuals who developed asthma without a family history. Furthermore, upper and lower viral respiratory infections (in particular, respiratory syncytial virus and rhinovirus) may predispose younger patients to developing asthma. Studies have also suggested that respiratory infections produced by viruses or by Chlamydia pneumoniae may play a more important role than atopy in the development of ‘late-onset asthma’. Finally, although smoking may lead to development of chronic obstructive pulmonary disease (COPD), it may also be a factor in the development of late-onset asthma in older patients.

2.2 Airway Changes with Aging

Aging is associated with several changes in lung structure and function that may affect morbidity and mortality in older individuals with asthma. With age, the lung matrix becomes altered, leading to a decline in elastic recoil. This may allow the smaller airways to trap air, decrease the expiratory flow rate and increase bronchoconstriction during acute asthma exacerbations. Respiratory muscle strength also declines with aging; it has been suggested that diaphragm strength decreases by approximately 25% with age.

2.3 Diagnosis in the Elderly

2.3.1 History

The typical symptoms of asthma, such as shortness of breath, chest tightness, cough and wheezing, are similar in both elderly and young patients. However, when considering the diagnosis of asthma in an older patient, there are a greater number of diseases that must be included in the differential diagnosis. Congestive heart failure, chronic bronchitis and emphysema, angina, gastro-oesophageal reflux, pulmonary embolus, recurrent aspiration, respiratory tract tumours and laryngeal dysfunction produce symptoms that mimic asthma (table III).

Obtaining a patient’s recount of asthma symptoms may be more difficult in older patients than in younger ones. Older individuals may have poorer perception of airway obstructive symptoms and, therefore, be less likely to report them. Also, older patients may attribute asthma symptoms to ‘getting older’ rather than arising from a medical condition such as asthma. It is critical for the physician to ask the patient if he or she has modified any activities secondary to physical constraints of cough, shortness of breath or other symptoms consistent with asthma.

A careful medication history is required to identify any therapeutic agents, such as ACE inhibitors,
Table III. Differential diagnosis of asthma in older patients

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clinical/laboratory markers or helpful diagnostic tests</th>
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<tbody>
<tr>
<td>Anaemia</td>
<td>Complete blood cell count</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>CXR, ECG, Elevated BNP level (serum), Ankle oedema, Orthopnoea</td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>D-dimers, Arterial blood gases, ECG, Quick onset of symptoms</td>
</tr>
<tr>
<td>Cardiac arrhythmias</td>
<td>ECG</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>CXR (increased interstitial markings), Increased DLco</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>CXR, Fever</td>
</tr>
<tr>
<td>Bronchial neoplasm</td>
<td>CXR, Weight loss</td>
</tr>
<tr>
<td>Gastro-oesophageal reflux disease</td>
<td>Improvement with anti-reflux therapy</td>
</tr>
<tr>
<td>Vocal cord dysfunction</td>
<td>Abnormal inspiratory loop on spirometry</td>
</tr>
<tr>
<td>Tracheal stenosis</td>
<td>Endoscopy</td>
</tr>
<tr>
<td>Post-nasal drip</td>
<td>Clinical history, endoscopy</td>
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</tbody>
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BNP = brain natriuretic peptide; CXR = chest x-ray; DLco = carbon monoxide diffusing capacity.

which may produce a cough that mimics asthma. The medical history should include both a family and patient history of previous allergic diseases, including eczema, allergic rhinitis, drug and food allergies, because these diseases may be more prevalent with allergic asthma in the elderly.

### 2.3.2 Objective Measurements

Clinical symptoms suggestive of asthma should be evaluated by office spirometry, which determines the forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC). A ratio of FEV₁/FVC <0.7 or FEV₁ <80% predicted suggests obstructive lung disease but does not distinguish between asthma and COPD. Because office spirometry may not be performed in primary care settings, patients under evaluation for asthma should be referred to an asthma specialist (allergist or pulmonologist) for testing. If spirometry results are consistent with airway obstruction, it is essential to perform spirometry after a dose of an inhaled bronchodilator drug to determine if the obstruction is reversible. Bronchodilating medications include salbutamol (albuterol), which has a peak effect 5–10 minutes after administration, or a combination of salbutamol and ipratropium bromide, which has a peak effect after 30 minutes. If administration of these medications increases FEV₁ by 12% or 200 mL, this is suggestive of reversible obstructive airway disease, which can be medically improved.[99] However, in the elderly, some sympathetic and parasympathetic nervous system functions may diminish with age, thereby decreasing reversibility.[100,101] Additionally, the airways of older asthmatics may develop permanent changes such as fibrosis, tracheal instability or bronchiectasis, all of which decrease reversibility.[102]

There is a misperception that reliable spirometry measurements cannot be obtained from elderly individuals. However, several studies have demonstrated that between 82% and 93% of elderly patients are able to perform good spirometry.[103-107] Inability to perform reliable airway testing has been suggested by some groups to be a result of cognitive dysfunction and functional impairment.[105,106] but another study has not confirmed these findings.[107] In patients who are unable to perform spirometry,
clinicians may ask the patient to undergo body plethysmography; this allows the patients to breathe more ‘normally’ compared with spirometry, which requires patients to exhale forcibly. Forced oscillation is another method of measuring airway obstruction. However, this method has not been standardized for the diagnosis of asthma and is available only at research sites.\(^{[108]}\)

If there is a strong clinical history of asthma in a patient with normal spirometry, a bronchoprovocation airway challenge test should be performed. Bronchoprovocation testing involves aerosol administration of progressively increasing concentrations of a direct stimulus such as histamine or the cholinergic agent methacholine, or an indirect stimulus such as adenosine 5'-monophosphate or osmotic agents, with repeat spirometry to determine the dose producing bronchoconstriction. Although the airways of most individuals will constrict after high-dose stimuli, patients with asthma or COPD will respond at lower doses; therefore, a normal test will exclude asthma. The most commonly used agent is methacholine. Although many physicians may be reluctant to perform methacholine challenges in older patients, several studies have demonstrated that testing can be safely performed in this age group.\(^{[95,109]}\) However, as with any patient undergoing bronchoprovocation testing, the procedure must be performed by experienced personnel and special awareness is needed for patients with an FEV\(_1\) <70%. Patients with uncontrolled hypertension or a recent heart attack or stroke should not undergo methacholine challenge testing. In younger patients, the definition of bronchial hyper-responsiveness is a 20% drop in FEV\(_1\) at a dose of inhaled methacholine between 8 and 16 mg/mL, along with a strong pre-test probability of asthma. However, in older individuals, it may be more appropriate to set the threshold at 4 mg/mL because some studies have reported that bronchial hyper-responsiveness to methacholine is higher in elderly patients compared with middle-aged patients, even after correction for the baseline degree of airway obstruction, smoking status and atopy.\(^{[95,98,110]}\)

Office spirometry does not distinguish between asthma and COPD. To distinguish between these two obstructive lung diseases, formal spirometry, lung volumes and diffusion capacity should be performed. In patients with COPD, diffusion capacity is reduced, whereas in asthma it remains normal or is elevated.

### 2.3.3 Other Investigations

A chest radiograph should be obtained when first making the diagnosis of asthma in order to exclude other diseases. Cardiomegaly and pulmonary vascular congestion suggest congestive heart failure. Increased interstitial abnormalities suggest an interstitial lung disease that potentially requires further evaluation by CT. The chest x-ray is typically normal in controlled asthma, although it may reveal hyperinflation during exacerbations. An ECG helps exclude cardiac disease mimicking asthma and identifies patients potentially at risk from excess β-adrenoceptor agonist therapy. Well controlled asthma typically does not produce ECG changes; however, during acute bronchospasm, some patients may demonstrate sinus tachycardia, right ventricular strain or a right axis deviation. A complete blood cell count is useful for determining if a patient’s shortness of breath is secondary to anaemia. Patients with asthma may have elevated eosinophil levels. A significantly elevated eosinophil count and difficult to control disease warrants consideration of Churg-Strauss syndrome or corticosteroid-insensitive asthma. Finally, exhaled nitric oxide has been used as a research tool in the diagnosis and treatment of asthma, although its use has not yet been accepted in clinical practice. Elevated levels of exhaled nitric oxide have been demonstrated to correlate with increased bronchial hyper-responsiveness, airway eosinophilia and level of allergen sensitization in patients with asthma, and are suggestive of patients at risk of having an asthma exacerbation.\(^{[111]}\)

### 2.4 Management

Beginning in the early 1990s, two groups, the NHLBI\(^{[24]}\) and the Global Initiative for Asthma (GINA),\(^{[112]}\) established guidelines for the diagnosis and treatment of asthma which have been periodi-
ally updated. As both sets of guidelines are targeted at asthma in younger populations, a working group of experts in the treatment of asthma in the elderly published in 1996 an addendum to the first NHLBI asthma guidelines addressing special issues in the elderly asthmatic [113]. This report concluded that the guidelines for asthma in younger populations could be applied to older patients, with special considerations for education and medication use. The reports on treatment of asthma in children and adults, but not those for asthma in the elderly, have been recently updated by both groups. The sections that follow summarize the conclusions on asthma treatment from the most recent NHLBI 2007 guidelines, [24] the 1996 NHLBI addendum for asthma in older individuals, [113] and a review of published studies of asthma in the elderly.

2.4.1 Assessment and Monitoring

The goal of asthma therapy is to reduce symptoms and impairments in function and quality of life imposed by the disease. At the initial physician visit, the patient’s asthma severity should be assessed. Asthma severity is easiest to determine when the patient has not been started on therapy and is based upon the frequency of symptoms and objective measurements of lung function. Asthma severity is classified into either intermittent (no interference with daily activity, and symptoms occur less than twice per week during the daytime and on <2 nights per week) or persistent (limitation of normal activity and more frequent symptoms and need for rescue medications). Persistent asthmatics are further classified into mild, moderate or severe, based upon degree of impairment. [24] If patients have been previously started on medical therapy, the severity of asthma is determined by the therapy required to adequately control symptoms.

All patients with asthma should be seen by a practitioner every 1–6 months to assess the medical control of their disease. If a change in medication has been made, patients should be seen sooner, i.e. within 2–6 weeks. Table IV provides suggestions for follow-up visits. Control can be assessed by administration of standardized questionnaires such as the four question Asthma Control Test [114] or by asking questions about functional impairments in

Table IV. Components of follow-up visits for asthma [113]

<table>
<thead>
<tr>
<th>Symptom changes</th>
<th>Ask about any nocturnal or early morning awakenings with wheezing and cough</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication history</td>
<td>Ask about changes in shortness of breath (with rest or exertion)</td>
</tr>
<tr>
<td></td>
<td>Ask about increase in cough or phlegm</td>
</tr>
<tr>
<td></td>
<td>Ask about changes in exercise tolerance</td>
</tr>
<tr>
<td></td>
<td>Ask about changes in performing ADLs</td>
</tr>
<tr>
<td>Physical examination</td>
<td>Ask patient to bring all prescribed and over-the-counter medications to the visit</td>
</tr>
<tr>
<td></td>
<td>Ask about frequency of rescue β2-adrenoceptor agonists use</td>
</tr>
<tr>
<td></td>
<td>Review frequency and dosage of asthma medications</td>
</tr>
<tr>
<td></td>
<td>Note frequency of asthma medication refills</td>
</tr>
<tr>
<td></td>
<td>Check patient’s understanding of purposes of asthma medications</td>
</tr>
<tr>
<td>Objective data</td>
<td>Note ability to speak in full sentences</td>
</tr>
<tr>
<td></td>
<td>Check use of accessory muscles</td>
</tr>
<tr>
<td></td>
<td>Assess for cognitive and functional impairments limiting medication use</td>
</tr>
<tr>
<td></td>
<td>Check for signs of airflow obstruction (expiratory slowing, wheezing)</td>
</tr>
<tr>
<td>Review medication techniques</td>
<td>Conduct/order spirometry and compare results with symptom changes</td>
</tr>
<tr>
<td>Review asthma management plan</td>
<td>Review home PEF measurements</td>
</tr>
<tr>
<td></td>
<td>Observe patient’s ability to use MDI</td>
</tr>
<tr>
<td></td>
<td>Consider writing in larger print</td>
</tr>
</tbody>
</table>

ADL = activities of daily living; MDI = metered dose inhaler; PEF = peak expiratory flow.
lifestyle (e.g. sleep patterns, difficulty walking) secondary to asthma and asthma symptoms. Although it is difficult for some younger patients with asthma to recognize the severity of and changes in asthma symptoms, it is probably even more difficult for elderly patients. Spirometry and peak expiratory flow (PEF) provide objective data. When using PEF meters, a ‘personal best’ measure must first be established; this should be obtained in the middle to late part of the day, when patients are under optimal treatment, and using correct PEF meter technique. Home PEF monitoring may also be important for asthma management, especially for those patients who have episodic worsening of symptoms, require emergency room visits or frequent oral corticosteroid bursts, or have co-existing cardiac or lung disease that may mask asthma exacerbations. However, the benefit of home PEF monitoring is limited by changes in the mechanics of the lung due to aging, changes in airway structure caused by inflammation, and physical or cognitive declines that affect the patient’s ability to perform the PEF manoeuvre.

2.4.2 Education

Educating patients with asthma about their disease and how to assess and manage exacerbations reduces urgent care visits, decreases asthma-related healthcare costs and improves health status and quality of life and adherence to medication regimens. Asthma education in elderly patients centres on several key issues. At the initial visit, the medical staff should evaluate whether the older patient will need, or already has, assistance with medication administration from either family members or a care-giver. Many of the medications for asthma are taken via inhalation and older patients frequently have poor inhaler technique as a result of decreased cognitive function (as determined by Mini-Mental State Examination or a physical impairment. Although breath-activated medication devices may be easier for elderly patients to self-administer, some elderly patients may have difficulties in loading the spring of the device, or after inhalation do not ‘feel or taste’ the medication, making them unaware that they have received it. This is problematic if the canister is empty and the patient misses doses, or if the patient takes additional doses. To determine if patients can take their medications, it is beneficial to watch them administer them in the office. Trainer inhalers that do not contain active medication can be used to teach and observe the patient’s inhaler technique. Based upon the patient’s ability to use an inhaler, the clinician may decide to prescribe a pill or a nebulized form of the medication.

Patients and their care-givers should be taught what asthma is, how to recognize when the disease is worsening, and what steps to take during an exacerbation. Patient education needs to be reviewed at follow-up visits and occur at multiple points of care (nursing staff, pharmacists, family members and care-givers). Support groups may also offer important reinforcement and social support. Several mechanisms described in section 2.4.1 enable the clinician to determine if the patient’s asthma is not well controlled. Symptoms that suggest worsening of asthma include cough (especially during the night), audible wheezing, difficulty walking or climbing stairs because of shortness of breath or a decrease in normal daily activities. Patients and their care-givers should be given a written asthma management plan that includes daily medications, how to handle an exacerbation and strategies for avoiding triggers (see section 2.4.3). It may be helpful to distribute this information in a larger print handout. At each visit, the action plan and the patient’s list of asthma medications should be reviewed. Any compliance issues (e.g. not understanding the importance of taking the medication, inability to afford it, taking care of an ill spouse) or lack of understanding of the asthma action plan should be addressed.

Next, the patients, along with their care-givers or family members, should discuss the goals of asthma therapy with the physician. Discussion of treatment goals encourages a stronger partnership between the medical staff caring for the elderly asthmatic, and allows patients to take a more active role in their disease management, thereby improving asthma management. Examples of goals include free-
dom from symptoms, fewer emergency visits for asthma, longer walks or enjoying hobbies.

### 2.4.3 Control of Triggers and Co-Morbid Conditions Affecting Asthma

When performing the initial assessment it is critical to ask patients what triggers their asthma, as these exposures may be modified. Common triggers include aeroallergens, infections (commonly viruses and sometimes bacteria) and irritants, such as exposure to cigarette smoke, perfumes, cold air and pollution. Psychosocial factors, including depression and social isolation, have also been linked to the morbidity and mortality of asthma, and it is critical to determine if these factors play a role in the older patient’s asthma.[124]

All patients with persistent asthma should undergo an allergen sensitization evaluation performed as described in section 1.2.2.[24] Sensitization to indoor allergens may be particularly important for older patients who spend more time indoors, and has been linked to asthma severity in the elderly.[84] Measures to reduce the exposure to the offending allergen (only if the patient demonstrates IgE-mediated hypersensitivity) should be taken, as described in section 1.3.1. The NHLBI recommends that all patients with asthma and evidence of allergen sensitization be counselled in relation to allergen avoidance measures,[24] although a recent Cochrane Database review suggested that measures to control house dust mites may not affect asthma outcomes.[125] However, one study demonstrated that older adults with asthma are more likely to be hospitalized for disease exacerbation if they have not received allergen avoidance education.[126]

All elderly patients with asthma should receive a pneumococcal vaccination and yearly influenza vaccinations. It may be beneficial to administer the pneumococcal vaccination more frequently than every 5–10 years because, with aging, IgG opsonophagocytic activity and response to polysaccharide vaccination diminish.[127]

Several medications used to treat congestive heart failure, joint pains and glaucoma can worsen asthma. Furthermore, the patient’s medication list should be reviewed during each visit, as medications in the elderly may change frequently. Patients with asthma may be at higher risk of exacerbation if taking non-selective β-adrenoceptor antagonists such as propranolol, nadolol and esmolol for hypertension or coronary artery disease.[128] These agents also block the β2-adrenoceptors in airway smooth muscle. For those patients who need β-adrenoceptor antagonist therapy, it is best to use a selective β1-adrenoceptor antagonist (i.e. metoprolol or atenolol) at the lowest possible dose, and to administer the first dose in a physician’s office, monitoring lung function and symptoms before and approximately 2–3 hours afterwards.[129] Despite the risks, many elderly patients with asthma are still prescribed β-adrenoceptor antagonists,[130] which may be secondary to having more than one physician treating their illnesses and the patients not being able to recall and tell the other treating physician that they are taking medications for asthma. One study revealed that 61% of elderly asthmatics given β-adrenoceptor antagonists had one physician treating their asthma and another who had prescribed the cardiac medication.[130] Ophthalmologic solutions containing non-selective β-adrenoceptor antagonists (i.e. timolol) may produce a fatal asthma attack.[131] Some patients with asthma may be sensitive to aspirin (acetylsalicylic acid) and NSAIDs and experience a worsening of their disease. For these patients, using alternative pain controllers such as paracetamol (acetaminophen) is advisable.

Several other diseases that can worsen asthma should also be addressed. Gastro-oesophageal reflux disease (GERD) may exacerbate asthma, even in clinically ‘silent’ disease. It has been reported that as many as 80% of patients with asthma also have GERD, and that in 50% of these patients, their GERD is asymptomatic.[132] Obesity is also associated with increased prevalence and severity of asthma,[133] and weight reduction has been shown to improve asthma symptoms.[134] Finally, smoking cessation may decrease the severity of asthma.

### 2.5 Pharmacological Therapy

The medications used to treat older patients with asthma are not significantly different from those
used in younger patients. However, there are several important considerations when prescribing these medications in older patients, including dosage adjustments for metabolic rates, drug interactions, adverse effects, costs and delivery.

### 2.5.1 Anti-Inflammatory Medications

**Corticosteroids**

Asthma is a chronic inflammatory disease and all patients classified as having persistent asthma should therefore receive a daily anti-inflammatory medication to suppress airway inflammation. Corticosteroid therapy is the most effective form of anti-inflammatory medication for asthma.\(^{[24,135]}\) Airway inflammation may have detrimental effects that produce structural changes and, eventually, fixed obstruction. Corticosteroids may inhibit the development of chronic airway changes; however, this finding is controversial. Lack of bronchodilator reversibility on pulmonary function testing suggests permanent airway changes. For these patients, the benefit of ICS use may be lessened.\(^{[137]}\) To determine if ICS will have a clinical benefit, patients may be given a 2-week trial of oral corticosteroids at a dose of 0.3–0.5 mg/kg (a dose lower than used in younger patients), after which the lung function test can be repeated to determine if airways hyper-responsiveness is reversible.\(^{[24,113]}\)

Corticosteroids are administered by an inhaler (ICS), nebulizer (budesonide only), orally or intravenously. The latter two forms are typically used for an acute exacerbation; however, some patients with severe asthma need daily oral corticosteroids. Elderly patients with asthma are under-prescribed ICS for management of their disease.\(^{[70]}\) Sin and Tu\(^{[138]}\) found that 40% of patients aged <65 years discharged from hospital after an acute asthma exacerbation were not given a prescription for an ICS.\(^{[139]}\) Furthermore, the Cardiovascular Health Study Research Group found that fewer than one-third of elderly patients with moderate to severe asthma used ICS, and 39% were not taking any medications for their asthma.\(^{[66]}\) The reasons for these trends are not certain, although there are several hypotheses. Most of the studies undertaken to investigate the efficacy of ICS treatment in asthma involved younger patients, which makes medical professionals less willing to prescribe this medication to older patients. Additionally, elderly patients with greater numbers of co-morbidities are less likely to receive ICS prescriptions.\(^{[138,140]}\) Finally, patients treated by a primary care provider, as opposed to an asthma specialist, are less likely to receive ICS.\(^{[138,141,142]}\)

Patients may also not fill their ICS prescriptions. A survey of >500 elderly patients hospitalized for asthma indicated that only 25% had filled their prescriptions for an ICS during the previous year.\(^{[143]}\) Reasons for not filling an ICS prescription are several, and include inaffordability and lack of education on the importance of this medication.

ICS are available for delivery via a metered dose inhaler (MDI) or a dry-powder inhaler. The technique of using a MDI is challenging for many older patients.\(^{[104,118,121]}\) Attaching a spacer to the MDI may make medication administration somewhat easier and allows for a greater delivery of medication to the patient’s airway. Some of the newer ICS are in the form of breath-activated dry-powder devices, which may be easier for the elderly to use.\(^{[120]}\) If patients are unable to administer ICS, it may be prudent to switch to a nebulized corticosteroid. Bisgaard et al.\(^{[144]}\) demonstrated that treatment with nebulized budesonide was as effective as budesonide via MDI in reducing asthma symptoms, improving PEF measurements and decreasing β2-adrenoceptor agonist use. Furthermore, in a study of 2178 patients aged 50–99 years of age with either asthma or COPD, nebulized budesonide resulted in fewer emergency room visits and decreased the use of systemic corticosteroids.\(^{[145]}\)

ICS may produce local adverse effects, including hoarseness or oral candidiasis, which can be prevented by using a spacer or rinsing the mouth after use. When taken in large doses, generally over 1000 µg/day, ICS have the potential for systemic absorption, leading to similar effects as oral corticosteroids.\(^{[146,147]}\) The significant systemic adverse effects of corticosteroids include osteoporosis (with increased fracture risk), muscle weakness, cataracts, glaucoma, glucose intolerance, depression, elevated blood pressure, easy bruising and loss of teeth. Ele-
vated doses of ICS can suppress the hypothalamic-pituitary adrenal (HPA) axis and increase the risk for infections. A newer preparation of ICS, ciclesonide (not currently approved in the US), does not suppress the HPA axis.

A concern when prescribing ICS to older patients is increasing the risk of bone fractures. Several studies in premenopausal women suggest that ICS use decreases bone mineral density (BMD) in a dose-dependent manner. A study of patients aged 56–91 years demonstrated that women who took ICS had a modest decrease in BMD compared with women who did not take corticosteroids. There was no effect on BMD in men taking ICS. However, it is not clear whether a decrease in BMD in patients taking ICS results in an increased risk of fractures. In patients with a mean age of 62.3 years, taking >1600 µg of inhaled beclometasone equivalents per day increased the fracture risk. A database review of 800,000 women aged >66 years found that systemic, but not inhaled, corticosteroids were associated with an increased risk of hip fractures. Finally, Süssa et al. reported that ICS increased the risk of fractures in patients aged >65 years only at doses >2000 µg/day.

Certain measures should be taken to reduce a possible increase in fractures in older patients taking ICS. Firstly, patients should be prescribed an ICS with the lowest oral bioavailability. Budesonide, fluticasone propionate and mometasone have <1% oral bioavailability, whereas the oral bioavailability of beclometasone, triamcinolone and flunisolide is >10%. Secondly, patients should be given the lowest dose of ICS to control their disease, preferably <1600 µg/day. Thirdly, to lessen the effects of corticosteroids on bone resorption, patients should be encouraged to exercise, avoid excess alcohol intake and take daily supplemental calcium with vitamin D. The role of bisphosphonates in preventing fractures in patients taking ICS is controversial and studies have reported mixed results. Any patient administered high-dose ICS or oral corticosteroids should be followed closely for osteoporosis by measuring BMD when treatment begins, and again 6 months later. Finally, patients taking high-dose ICS or oral corticosteroids should undergo an eye examination every 6 months at which their vision should be checked in order to minimize the risk of falling and sustaining fractures.

The association between cataracts and the use of ICS appears to be related to the age of the patient, but no randomized controlled trials have been performed to establish this. In younger patients with asthma, the risk of cataract formation with ICS is not significant. However, observational studies in the elderly have suggested that use of ICS is associated with a small but significant risk of subcapsular and nuclear cataracts. Therefore, it is prudent to monitor elderly patients taking ICS by slit lamp examination every year for the development of cataracts. Observational studies have also suggested that elderly patients treated with ICS may have a small risk of developing glaucoma; however, further studies are needed.

Depression resulting from the use of oral corticosteroids has been reported and can be monitored by asking several quality of life questions concerning changes in participation in favourite activities, sleeping and eating patterns, and feelings of hopelessness. The role of high-dose ICS in depression is less well established. Mood changes have been linked with poor asthma medication compliance, poor treatment outcomes and even death.

Leukotriene Modifiers

In some patients with severe asthma, frequent use of oral corticosteroids cannot be avoided. In these patients, effort should be made to: (a) maximize treatment with ICS; (b) keep oral corticosteroids at a low dose by using an alternating day treatment regimen; or (c) add corticosteroid-sparing agents. Leukotriene modifiers are a class of anti-inflammatory agents that inhibit the effects of leukotrienes, which are potent bronchoconstrictors that recruit inflammatory cells to the airways and induce mucus hypersecretion. Leukotriene modifiers either: (a) inhibit the formation of leukotrienes from their precursor, arachidonic acid, by inhibiting 5-lipoxygenase (zileuton); or (b) prevent the actions of leukotrienes C4 and D4 by antagonizing the cysteinyl leukotriene receptor I (zafirlukast and montelukast). Although
these medications are available in pill form and may be easier for older patients to take, both zafirlukast and zileuton are heptatically metabolized and may interfere with the metabolism of other drugs commonly used in the elderly, such as warfarin, and produce liver function abnormalities. When compared with ICS, leukotriene receptor antagonists generally do not improve FEV1, symptom scores and other outcome measures to the same extent. Therefore, these agents are recommended as alternative therapies for patients who cannot tolerate ICS. Only two studies have investigated the role of leukotriene modifiers in patients with asthma of different ages, and these studies concluded that their effectiveness may be limited in elderly patients compared with younger patients.

2.5.2 Bronchodilating Medications

β2-Adrenoceptor agonists are divided into short-acting emergency ‘rescue medications’ (SABAs) or long-acting β2-adrenoceptor agonists (LABAs) used with ICS as part of ‘controller’ therapy. β2-Adrenoceptors may decrease in density with age, suggesting that their use may be less effective in elderly patients with asthma; however, these findings are not conclusive. SABAs are relatively safe in the elderly if used on an as-needed basis to treat exacerbations, although mild systemic absorption can produce tachycardia and tremor. Both SABAs and LABAs must be used cautiously in patients with heart disease and hypertension because overdose may cause life-threatening arrhythmias and hypokalaemia. Combining non-potassium-sparing diuretics (e.g. thiazides) and β2-adrenoceptor agonists may produce significant hypokalaemia and hypomagnesaemia, increasing the risk of cardiac arrhythmias. LABAs should only be used as add-on therapy in patients who have used ICS properly without relief; they are not effective as monotherapy for asthma.

Methylxanthines

Methylxanthines (e.g. theophylline) increase intracellular levels of cyclic adenosine monophosphate, which dilates the airways, and in lower doses have anti-inflammatory properties. Use of theophylline in asthma, especially in older patients, is limited by its relatively weak bronchodilator properties, many adverse effects and drug interactions. As a result, use of theophylline in the elderly has decreased significantly. If an elderly patient is placed on theophylline, it is critical to administer the drug at the lowest dose possible and monitor theophylline serum levels, aiming for a range of 8–12 µg/mL, which is lower than that for younger patients. With any given blood theophylline concentration, a patient aged ≥75 years has a 16-fold higher risk of theophylline toxicity than a patient aged <25 years. Elevated serum theophylline concentrations may produce nausea, vomiting, headache, arrhythmias, agitation and seizures. Metabolism of theophylline can be decreased by congestive heart failure, chronic liver disease or the use of other medications, including cimetidine, calcium channel antagonists, erythromycin, fluoroquinolones and allopurinol.

Other Agents

Other second-line anti-inflammatory agents include nonsteroidal agents such as sodium cromoglicate and nedocromil. However, the benefits of these medications appear to be greater in younger patients with asthma.

Other Agents

Other second-line anti-inflammatory agents include nonsteroidal agents such as sodium cromoglicate and nedocromil. However, the benefits of these medications appear to be greater in younger patients with asthma. Anticholinergic agents (available in nebulized form), although indicated for COPD, may offer some benefits to elderly patients with asthma, especially those with a bronchitic component. However, one report has suggested that use of ipratropium bromide in elderly asthmatics was associated with a slight increase in mortality, a finding that the investigators concluded was secondary to these patients having more severe asthma than those patients not receiving ipratropium bromide. However, anticholinergics, because of their atropine-like effects, may produce adverse effects in the elderly, including dry mouth, urinary hesitancy, constipation and exacerbation of glaucoma. In patients with glaucoma, it is prudent to administer anticholinergic therapy with either a spacer or, if given by a nebulizer, a mouthpiece and not a facemask, to limit deposition in the eye.
Anti-IgE (Omalizumab)

The anti-IgE molecule omalizumab has been approved by the US FDA recently for the treatment of chronic asthma. Although trials of this agent have not specifically targeted older patients, they have included patients up to the age of 75 years. Use of anti-IgE in asthma decreases asthma exacerbations and systemic corticosteroid use, as well as improving quality of life. Anti-IgE therapy for asthma is more expensive than other treatments for asthma and, therefore, has been recommended for patients requiring daily oral corticosteroids or high-dose ICS to control their asthma. Although in clinical trials omalizumab had a comparable profile to placebo, its use was also associated with an increased rate of malignancies (0.5% vs 0.2% with placebo), a higher rate of injection site reactions and a higher rate of anaphylactic reactions. Because of the small potential for a life-threatening allergic reaction, which has been reported to occur as late as 2–24 hours after injection of omalizumab, patients are encouraged to wait for 1–2 hours at the clinic after their injection and to carry self-injectable epinephrine. Furthermore, administration of anti-IgE is time consuming for patients, and requires an office visit every 2–4 weeks in which the patient will receive one to three injections. Anti-IgE is also limited to patients who weigh <150 kg and whose serum IgE is <700 IU/mL (many patients with an allergic component to their asthma have higher serum IgE levels).

3. Conclusion

Although allergic rhinitis and asthma are commonly thought of as paediatric diseases, they are not uncommon in older patients and are frequently underdiagnosed. The first step in making a diagnosis of either disease in older patients is to consider the diagnosis. Although diagnostic techniques are generally similar in younger and older patients, in the latter age groups, several other diseases must be considered in the differential diagnosis. Treatment of both allergic rhinitis and asthma in older patients is complicated by the potential for other co-morbid conditions and drug interactions. Furthermore, research on pathogenesis and guidelines for therapy of allergic diseases in older patients are limited, making treatment more difficult. These disorders can interfere with the patient’s quality of life and, in the case of asthma, can cause significant morbidity and mortality. Therefore, as our population ages, it is critical to understand how to diagnose and treat allergic rhinitis and asthma in older patients.

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