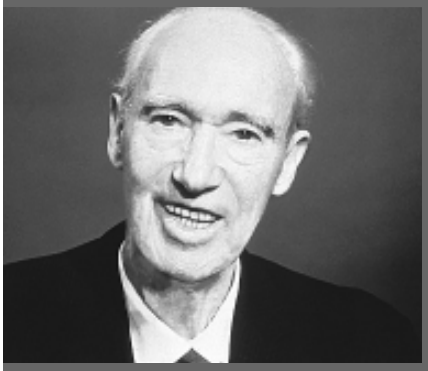
National Asthma Education and Prevention Program

ASTHMA in the ELDERLY



NAEPP Working Group Report:

Considerations for Diagnosing and Managing Asthma in the Elderly

NATIONAL INSTITUTES OF HEALTH
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

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FOREWORD

In a 1991 report, an expert panel of the National Asthma Education and Prevention Program (NAEPP) presented "Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma" (NHLBI, 1991) that are generally applicable to asthma in all age groups. These guidelines briefly noted that treatment of asthma in older patients should follow the recommendations for adults but with a number of special considerations. These considerations relate to polypharmacy, changes due to normal aging, and comorbid conditions that commonly occur in this patient population, interfere with usual treatments, and require special monitoring. Additional considerations concern the special educational efforts needed to encourage patient compliance and adherence. As part of its continuing effort to promote improved asthma management in all population groups, the National Heart, Lung, and Blood Institute invited a working group of experts to further assess the issue of asthma management in the elderly population and recommend what, if any, additional information and guidance should be provided to elderly patients with asthma, their families, and the health professionals responsible for their care.

The working group met four times between 1992 and 1994 and held several teleconferences. Working group members reviewed the relatively sparse published clinical and basic studies on asthma in the elderly found by Medline literature search as well as the clinical experience and opinions of practicing physicians and patient and family groups. They also wrestled with a number of important but difficult questions: When is a patient "elderly"? Is there an actual increase in the prevalence and incidence of asthma among the elderly and in mortality from asthma? Or are current data showing the apparent increase merely a reflection of the increasing recognition of the problem or the use of new classification systems? The working group chose to focus on the special problems that become increasingly frequent with advancing age rather than attempt to define the age when unique problems relevant to the elderly begin. Further, because of the scarcity of published data dealing with asthma in elderly patients, working group members felt it necessary to draw many of their recommendations from their own collective clinical and research experience and that of several consultants.

The conclusion was readily reached that no new guidelines for management of asthma in the elderly are necessary or possible. However, it was clear that published guidelines to managing asthma needed more detail on several important considerations relevant to the elderly population. These areas relate to diagnosis, pharmacologic therapy, and patient/family/caregiver education. This report focuses on these special considerations and is intended to serve as a companion to the 1991 "Guidelines for the Diagnosis and Manage-

ment of Asthma" (NHLBI, pub no 91-3042). Two later National Heart, Lung, and Blood Institute publications also complement this report: "International Consensus Report on Diagnosis and Management of Asthma" (NHLBI, 1992, pub no 92-3091) and "Global Initiative for Asthma: Global Strategy for Asthma Management and Prevention NHLBI/ WHO Workshop Report" (NHLBI, 1995, pub no 95-3659).

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Executive Summary

As part of its continuing effort to promote improved asthma management in all population groups, the National Heart, Lung, and Blood Institute convened a panel of experts to assess if specific guidelines are necessary for the management of asthma in older adults. The working group concluded, after review of the literature and group discussion, that the general approach to asthma management recommended in current guidelines is applicable to patients of all ages; however, diagnosing and managing asthma in elderly patients pose special challenges. Physiologic, psychologic, and psychosocial changes associated with normal aging and an increased frequency of concomitant medical problems may require some modification to asthma management approaches used for children and younger adults.

Diagnosis

At all ages, asthma is characterized by airflow obstruction that is reversible (but not completely so in some patients) either spontaneously or with treatment, airway inflammation, and increased airway responsiveness to a variety of stimuli. Asthma can present in the elderly either as a *de novo* occurrence or as a continuation of a disease entity that began in earlier years. In elderly patients, incomplete reversibility becomes increasingly common. Distinguishing between asthma with a component of fixed airflow obstruction and chronic obstructive pulmonary disease (COPD) is important, especially in current and ex-smokers. Asthma has a different natural history and a better prognosis with treatment, with asthma medication often able to relieve some symptoms and improve quality of life. A trial of systemic corticosteroid therapy is often useful to assess reversibility. Also, symptoms of acute episodes of wheezing, cough, shortness of breath, or chest tightness that mimic asthma may be due to other conditions common among the elderly, such as myocardial ischemia or pulmonary embolism.

Management

The Goals of Therapy

The overall goal of asthma treatment is to permit an optimal level of activity and maintain quality of life. More specific goals include: optimize pulmonary function, control cough and nocturnal symptoms, prevent exacerbations, promote prompt recognition and treatment of exacerbations, reduce (ideally eliminate) the need for emergency department visits or hospitalizations, avoid aggravating other medical conditions, and minimize adverse effects from medications. These goals may be more difficult to achieve for elderly patients. For example, normal lung function may be either unattainable or attainable only with high, potentially dangerous, pharmacologic doses. Conversely, elderly patients may have unnecessarily restricted their lifestyles to accommodate the disease. Education is needed to raise their expectations of treatment as high as feasible. In defining individual treatment goals for elderly patients with asthma, significant attention should be paid to quality-of-life issues—including the restoration, maintenance, and extension of an independent, active, and personally satisfying lifestyle.

The Four Components of Asthma Management

The considerations and modifications in treating and managing asthma in elderly patients for each of the four components recommended for asthma treatment and management (see "Guidelines for the Diagnosis and Management of Asthma" [NHLBI, pub no 91-3042]) include the following:

1. Educating Patients for a Partnership in Asthma Care. Working jointly with patients to set realistic, achievable goals and develop a specific treatment plan to reach those goals provides the basis for a partnership in care. Providing education on management to family and any in-home caregivers also promotes compliance with optimal therapy. Elderly patients may require additional education to understand the proper use of their medications. For example, metered-dose inhaler techniques can be increasingly difficult to master with advancing age due to decreased hand strength and arthritis; different inhalation devices and spacers may be helpful.

2. Monitoring. Successful management requires regular monitoring of clinical signs and symptoms, lung function, treatment effectiveness, and ability to follow the management plan. For all elderly patients with asthma, lung function monitoring (with FEV_1 or peak expiratory flow [PEF]) should be performed in the physician's office approximately every 3 to 6 months. Home PEF monitoring may be important, especially for those patients who do not perceive symptoms early or who mistakenly dismiss worsening signs and symptoms (for example, diminished tolerance to physical activity and interrupted sleep) as effects of aging rather than deteriorating asthma. However, for some patients, home PEF monitoring may be limited by age-related factors that compromise the effort required for accurate measurements. Symptom monitoring and using diaries may help elderly patients better assess their progress and become more sensitive to worsening asthma. Key indicators of worsening asthma include nocturnal or early morning wakenings with wheeze or cough, increased cough, increased use of or diminished response to $beta_2$-agonist, and decreased tolerance to exercise, including daily activities.

3. Environmental Control: Avoiding and Controlling Asthma Triggers. It appears that the same factors trigger acute exacerbations of asthma among the elderly as with other patients, although sensitivity to inhaled allergens is less prevalent. Among the most common asthma triggers for elderly patients are respiratory infections and medications for other diseases. Immunization is recommended against pneumococcal infections (every 5 to 7 years for individuals between 60 and 75; every 3 to 4 years for those over 75) and against influenza (annually). Smoking or exposure to tobacco smoke should be avoided. Other measures to avoid or control triggers should be specific to the patient's asthma and allergy history and should be feasible. Measures that are inappropriate or unrealistic may have an adverse effect on the older patient's quality of life without benefiting asthma management.

4. Pharmacologic Therapy. A stepwise approach to pharmacologic therapy is appropriate for asthma patients of all ages, with some special considerations for the older patient due to an increased likelihood of coexisting diseases and consequent disease and drug interactions. The suggested treatment for mild intermittent asthma is inhaled $beta_2$-agonists taken on an as-needed basis and avoidance of triggers. This treatment is increased (stepped up) if the need for $beta_2$-agonists increases. In patients with moderate asthma without COPD, daily chronic maintenance therapy with anti-inflammatory medication is recommended (inhaled corticosteroids may be preferred because nedocromil and cromolyn have been studied primarily in younger, allergic patients). A long-acting inhaled $beta_2$-agonist, ipratropium bromide, or sustained-release theophylline (used cautiously and monitored regularly) may be added, especially to control nocturnal symptoms. Compared to patients without COPD, patients who have both asthma and COPD may use bronchodilators at higher rates, may benefit from introduc-

tion of ipratropium earlier in the course of treatment, and may have less apparent benefit from anti-inflammatory therapy. Further, patients with COPD often have other coexisting diseases that may complicate or even limit the management of asthma. Once control of asthma is achieved, pharmacologic therapy is decreased (stepped down) in order to maintain control with the least amount of medication necessary.

Treatment of exacerbations also follows a stepwise approach to therapy, with frequent administration of inhaled beta$_2$-agonist, early administration of systemic corticosteroids, and oxygen supplementation that is carefully monitored. Ipratropium bromide may also be used; it may cause less tremor and arrhythmias than beta$_2$-agonists. Continuous electrocardiographic monitoring may be needed when administering high doses of beta$_2$-agonist therapy, particularly in those with coexisting cardiac conditions. It is essential that the older patient learn how to detect symptoms of worsening asthma and that a written plan be developed in advance for dealing with exacerbations. The plan should specify thresholds for medical supervision, particularly because heart disease and other coexisting conditions or their therapy can confound symptoms and treatment of asthma exacerbations.

The risk of adverse effects from asthma treatment increases with increasing age and often limits the choice, dosage, and frequency of medications. The potential for drug interactions because of coexisting conditions also increases, and all medications that the patient takes should be reviewed at every visit. In addition to considering the risk of adverse effects, such review must also consider the risk of uncontrolled asthma.

Possible adverse effects from asthma medications:

- *Inhaled corticosteroids* facilitate control of asthma for all ages and are the preferred anti-inflammatory medication for elderly patients. At high doses (e.g., more than 1,000 mcg per day), dermal thinning with increased potential for bruising has been observed. Possible adverse side effects, especially in older women with asthma, also include dose-dependent loss in bone mineral content and acceleration of osteoporosis. Calcium and vitamin D supplementation is recommended, and bone densitometry tests may be indicated to monitor patients who take high doses.
- *Systemic (oral and parenteral) corticosteroids* pose increased risks because they have a lower metabolic clearance rate in elderly patients. Possible adverse side effects, particularly with long-term use, include cardiovascular and metabolic disturbances (monitor routinely for electrolyte imbalance, hypokalemia, hypertension, hyperglycemia), musculoskeletal changes (monitor for osteoporosis), ophthalmologic disease (monitor routinely for worsened glaucoma due to increased intraocular pressure), gastrointestinal disturbances (monitor routinely for aggravation of existing peptic and gastric ulcers), and depression (monitor for effects of asthma therapy on depression and vice versa, that is, depression can reduce compliance with asthma therapy).
- *Theophylline* should be used cautiously because older patients have increased susceptibility to theophylline's adverse side effects. These include cardiac arrhythmias, nausea, insomnia, and liver disease. Further, some medications for coexisting conditions may affect theophylline elimination and hence serum theophylline level. The target serum concentration should be between 8 and 12 mcg/mL and should be monitored routinely for signs of toxicity—heart rate and rhythm, central nervous system status.
- *Inhaled beta$_2$-agonists.* In long-term asthma management, particularly in the elderly, possible adverse side effects of inhaled beta$_2$-agonists to consider and monitor include electrocardiogram changes, hypokalemia, tremor, and hypoxemia. These potential effects should be monitored routinely; in acute severe asthma, consider monitoring continuously in patients with comorbid cardiac conditions.

- *Oral long-acting beta$_2$-agonists* should be avoided in asthma management in the elderly because of possible tremors as well as increased heart rate and blood pressure.

Possible adverse effects from drugs taken for coexisting conditions (the following discussion lists selected drugs commonly used by older patients for coexisting conditions such as cardiovascular disease, glaucoma, and arthritis):

- *Beta-adrenergic blocking agents,* used for hypertension, coronary artery disease, cardiac arrhythmias, and glaucoma, place elderly patients with asthma at risk for acute bronchospasm. In general, beta blockers should not be taken by patients with asthma, and patients should ask specifically about the contents of eye drops. For patients who must take a beta-adrenergic blocker, a selective agent should be used. Asthma patients who take a beta blocker should be given ipratropium bromide as the preferred bronchodilator as long as long as the patient's responsiveness to ipratropium is established.
- *Nonsteroidal anti-inflammatory drugs (NSAID's),* including aspirin, are frequently taken by elderly patients with asthma for cardiovascular or musculoskeletal conditions associated with aging. A small but significant percentage develop sudden and severe bronchospasm when NSAID's are taken. For these patients, acetaminophen is recommended for pain therapy.
- *Diuretics* are more likely to be taken by elderly patients because of the increased incidence of hypertension and left ventricular failure. When diuretics that do not spare potassium (e.g., thiazides) are combined with beta$_2$-agonists, significant hypokalemia and hypomagnesemia may result, which increases the risk of cardiac arrhythmias, particularly if the elderly patient is receiving digitalis. For patients taking both medications, consider monitoring for electrolyte imbalance and treating appropriately with magnesium or potassium supplementation.
- *Antihistamines* are often taken by elderly patients with asthma who also have rhinitis and sinusitis. Nonsedating antihistamines (e.g., astimizole and terfenadine) may cause arrhythmias, particularly if the patient is also taking a diuretic or a beta$_2$-agonist.
- *Angiotensin-converting-enzyme (ACE) inhibitors,* which are frequently taken as antihypertensive medications by elderly patients with asthma, produce cough in some patients, which can confuse both the diagnosis and treatment of asthma. Discontinuing the ACE inhibitor will resolve the cough if it is due to the drug.

The Need for Research

The conclusions and recommendations in this report are based on an assessment of the current understanding of the epidemiology, etiology, pathophysiology, and treatment of asthma in the elderly population. However, the assessment revealed significant gaps in our understanding of asthma in the elderly. Some of these gaps relate to the epidemiology and natural history of asthma in the elderly; the roles of familial, genetic, and immune factors in the occurrence and progression of the disease in the elderly; and the cellular and molecular mechanisms that lead to reversible and irreversible airway obstruction in the elderly. Research is urgently needed to evaluate the effectiveness and safety of current asthma therapies—including inhaled corticosteroids, particularly at high doses, nedocromil, and long-acting inhaled beta$_2$-agonists. Future research should also include developing a methodology for comparing the functional capabilities and severity of illness of older and younger patients with asthma. It should also include developing methods and instruments for measuring and routinely monitoring functional status and health-related quality-of-life treatment outcomes relevant to older patients with asthma.

The following report elaborates upon these considerations for diagnosing and managing asthma in the elderly. It provides more detailed recommendations and documentation from the available scientific literature.

Chapter 1
Definition, Epidemiology and Natural History, and Pathogenesis of Asthma in the Elderly

Key Points

- Asthma, in all ages, is a lung disease characterized by (1) airflow obstruction that is reversible (but not completely so in some patients), either spontaneously or with some treatment; (2) airway inflammation; and (3) increased airway responsiveness to a variety of stimuli. However , incomplete reversibility becomes increasingly common among elderly patients, especially when asthma is longstanding or severe; the lack of reversibility probably results from smooth muscle hypertrophy and fibrosis.
- Available data and clinical observations suggest that asthma does occur frequently among the elderly.
- Normal changes in the lung that occur with aging may interact with asthma-related pathophysiologic events. Irreversible airflow obstruction is more likely to develop if asthma is severe and longstanding.
- Events that trigger acute exacerbations of asthma are the same for all ages, but sensitivity to inhaled allergens is less prevalent in elderly patients, especially if the asthma is of recent onset.

Definition

Asthma is a lung disease with the following characteristics: (1) airflow obstruction that is reversible (but not completely so in some patients), either spontaneously or with some treatment; (2) airway inflammation; and (3) increased airway responsiveness to a variety of stimuli (NHLBI, 1991).

This general definition applies to asthma in the elderly, but incomplete reversibility becomes increasingly common in these patients, especially when asthma has been severe or persistent, and some patients develop severe chronic airflow obstruction (Burrows, Barbee et al., 1991; Traver et al., 1993; Braman, Corrao et al., 1991). This coexistence of asthma and chronic obstructive pulmonary disease (COPD)—in which airflow obstruction is not reversible—creates diagnostic confusion, especially in individuals who have a history of smoking.

Epidemiology and Natural History

Little is known about the epidemiology and natural history of asthma in older subjects, although available data and clinical observations suggest that it is not rare and may appear *de novo* during the eighth and even ninth decades of life (Broder et al., 1962; Burr et al., 1979; Derrick,

1971; Dodge & Burrows, 1980; Lee & Stretton, 1972).

Mortality from asthma in older adults is reported to be increasing (Sly, 1984), but how much of this is a result of transferring the cause of death from COPD to asthma is uncertain (Barger et al., 1988). Further, inaccuracies in death certificates tend to increase with increasing age at death (Sears & Beaglehole, 1987).

Whether there is a gender difference in the distribution of asthma in the elderly is also not clear, and the relevant data are inconsistent. In a study in the United Kingdom, asthma was found to be much more common in elderly men (Burr et al., 1979), although a preponderance of elderly women with asthma was noted in three U.S. reports (Braman, Kaemmerlen et al., 1991; Burrows, Barbee et al., 1991; Yunginger et al., 1992).

Hospitalization for asthma in the elderly is also reported to be increasing slightly, but diagnostic difficulties make such data difficult to interpret. No increase was noted in the incidence of adult-onset asthma between 1964 and 1983 in one study, although an overall high incidence of the disease (about 1 per 1,000) was noted during this period (Yunginger et al., 1992). Data in the Medicare Statistical System (A.M. McBean, personal communication, 1993) revealed that overall hospitalization rates for asthma among Medicare beneficiaries, age 65 and older, changed little between 1986 and 1990. Interestingly, admission rates for both men and women were 40 to 70 percent greater in African-Americans than Caucasians, and the admission rates for women were approximately 20 to 40 percent higher than for men in both races.

The natural history of asthma appears to be extremely variable. Some patients have a history of childhood asthma that continues through later life, although a period of remission during adolescence is common. Many elderly patients deny having any symptoms until quite late in life, but they may have forgotten experiencing asthma symptoms or having been diagnosed with asthma during childhood. Many elderly patients with mild asthma symptoms and slight chronic airflow obstruction remain undiagnosed unless their asthma exacerbates. Furthermore, there may also be considerable misclassification of asthma as chronic bronchitis in these patients, leading to inappropriate therapy (Banerjee et al., 1987).

The presenting symptoms of asthma in the elderly person are similar to those in the younger adult. Wheezing, otherwise unexplained productive cough, or mild airflow obstruction (especially in subjects with allergic rhinitis, eosinophilia, positive allergy skin tests, or a serum IgE that is high for the person's age) are likely to be associated with a subsequent diagnosis of asthma (Burrows, Lebowitz et al., 1991).

The association of asthma with allergic markers is not clear in the elderly. Elderly patients with asthma may not demonstrate allergic skin sensitivity to aeroallergens (Derrick, 1971; Ford, 1969), nor may they demonstrate exacerbations triggered by exposure to aeroallergens, both common features of asthma in the young (Braman, Kaemmerlen et al., 1991; Burrows, Barbee et al., 1991). The skin test findings are confounded by the fact that skin reactivity generally decreases with age, so that even though the frequency of positive skin tests is less in the elderly than in young patients with asthma, positive skin tests among the elderly are still more frequent in those with asthma than those without the disease (Burrows & Martinez, 1989). Serum IgE and eosinophilia are more predictive of asthma in older adults than skin tests (Burrows et al., 1989; Burrows, Lebowitz et al., 1991; Tollerud et al., 1991), with the relationship of asthma prevalence to the age-sex standardized serum IgE level being similar at all ages (Burrows, Lebowitz et al., 1991).

Some studies indicate that asthma may be more severe in patients with an early onset and long duration (Braman, Kaemmerlen et al., 1991; Finucane et al., 1985), but this has not been noted by others (Burrows, Barbee et al., 1991). Asthma tends to become more persistent and show increasing chronic airflow obstruction as the patient ages; but the abnormality in FEV_1 appears to relate to the severity of symptoms in patients of all ages (Finucane et al., 1985; Traver et al., 1993).

Reports on the rate of decline of pulmonary function in elderly patients with asthma are contradictory. For example, airflow obstruction in diagnosed asthma patients showed little worsening over time in one study (Burrows, Barbee et al., 1991), but it worsened at an excessive rate with increasing age in another study (Peat et al., 1987). The reasons for these different observations are not clear.

Although a logical assumption is that smoking has a devastating effect on the course of asthma and is also the most important cause of COPD, the influence of past history of smoking on the severity and progression of asthma seems to be surprisingly slight (Burrows, Barbee et al., 1991; Finucane et al., 1985; Peat et al., 1987). This finding could be because patients with asthma tend to give up smoking. A history of smoking is not sufficient grounds for excluding a diagnosis of asthma, even if there is also a diagnosis of COPD, especially in individuals with less than 10 pack-years of cigarette consumption earlier in life. Correct diagnosis is important because severe chronic asthma responds better to therapy (Burrows et al., 1987) and has a better prognosis than smoking-related COPD, independent of smoking history (Burrows, 1991).

PATHOGENESIS

Age by itself has no particular bearing on the multifactorial pathogenesis of asthma—which has been discussed in depth in earlier NHLBI reports (see NHLBI, 1991, 1992). Since the publication of those reports, information from many studies has clarified the cellular and molecular aspects of the pathogenesis of both hyperresponsiveness and inflammation in asthma. However, because the new information is not specific to the elderly, it is not reviewed in this report.

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Chapter II
Differential Diagnosis of Asthma in the Elderly

Key Points

- The differential diagnosis of episodic chest symptoms in the elderly expands as cardiovascular disease and other forms of chronic lung disease become more prevalent.
- In addition, the coexistence of asthma with other chronic cardiovascular or lung diseases may complicate the diagnosis.
- It is important not to misdiagnose asthma as COPD because asthma has a different natural history and a better prognosis with treatment.
- Because elderly patients with asthma can also have chronic, persistent airflow obstruction with poor bronchodilator responsiveness, a trial of therapy with corticosteroids may be necessary to establish that there is reversible airflow obstruction.

Diagnosis

At any age, the diagnosis of asthma is based on a clinical history of typical symptoms with confirmatory objective information gained from physical examination and laboratory studies. Asthma diagnosis in the young is facilitated by a relative scarcity of other conditions that mimic asthma or complicate its clinical presentation. In the elderly, however, the differential diagnosis of episodic chest symptoms expands as cardiovascular disease and other forms of chronic lung disease become more prevalent. The diminishing role of allergic factors and the emergence of a fixed component of airflow obstruction in the elderly patient with asthma also add to the challenge of distinguishing between asthma and COPD, especially in current and former smokers. Yet it is important not to misdiagnose asthma as COPD because asthma has a different natural history, different treatment, and a better prognosis. The following elements of the clinical and laboratory evaluation are important to consider in the diagnosis of asthma in the elderly.

History and Physical Examination

A history of signs and symptoms and the patterns of their occurrence and exacerbation are important diagnostic components for the elderly.

Wheezing, Chest Tightness, Cough, and Dyspnea

Episodic wheezing, chest tightness, shortness of breath, and cough, which usually suggest a diagnosis of asthma in young individuals, can be manifestations of other disorders in an elderly patient. For example, periodic exacerbations of chronic bronchitis as well as episodes of angina or congestive heart failure, particularly those associated with nocturnal dyspnea and wheezing,

can be confused with acute episodes of asthma. Nevertheless, episodic wheezing is a useful sign of asthma even in the elderly, and when it occurs in a nonsmoker, the diagnosis of asthma should receive strong consideration. Wheezing with a history of smoking might suggest COPD, but smoking should not by itself rule out asthma.

Chest tightness has been reported to occur more often in association with asthma than with other pulmonary or cardiac conditions (Simon et al., 1990), but it is important to discriminate between chest tightness and angina.

Chronic cough with sputum production is not unusual in elderly patients with asthma, although it is usually associated with smoking, chronic bronchitis, and several other conditions. If the patient is a nonsmoker and has a normal chest x-ray, asthma, chronic rhinosinusitis, and gastroesophageal reflux should be considered as possible diagnoses. A trial of therapy with antiasthma medication (corticosteroids or bronchodilators), decongestants, or H_2 blockers may establish the cause of cough (Irwin et al., 1989).

Elderly patients with asthma may have chronic as well as episodic dyspnea similar to patients with COPD, but elderly patients may report dyspnea less often because they have a diminished ability to perceive increases in airway resistance and may be more sedentary (Altose et al., 1985; Burdon et al., 1982). Nocturnal dyspnea is not only a feature of asthma but also of left ventricular failure because acute increases in left atrial pressure and pulmonary vascular pressures can lead to pulmonary edema and narrowing of the airways with dyspnea and wheezing. However, the timing of nocturnal symptoms may be the clue: Symptoms associated with poorly controlled asthma typically occur in the early morning hours between 4:00 and 6:00 a.m., whereas those associated with heart failure typically occur 1 to 2 hours after retiring. In the elderly patient with an exacerbation, it is important to allow the patient to characterize his or her dyspnea. When a patient with confirmed asthma says "my shortness of breath is different," it provides a clue that the exacerbation may be due to some other cause than asthma. Peak expiratory flow measurements may help confirm asthma as the source of dyspnea (McNamara & Cionni, 1992).

Allergies and Associated History

A history of rhinitis, sinusitis, and nasal polyposis, as well as respiratory symptoms caused by drugs such as aspirin, nonsteroidal anti-inflammatory drugs, and beta blockers, may suggest that the symptoms are due to asthma rather than other conditions. A history of symptoms associated with exposure to environmental allergens may suggest asthma, but the absence of such history does not rule out asthma. Asking the patient about past or current exposure to occupational sensitizers can also be helpful. Other nonallergic environmental factors (weather extremes, episodes of air pollution) may also precipitate symptoms.

LABORATORY STUDIES

The most important tests and laboratory studies in the differential diagnosis of new-onset asthma include pulmonary function tests, chest radiography, electrocardiography, and complete blood count with differential.

Pulmonary Function Tests

Spirometry. Spirometry is used to measure the volume of air expired in 1 second from maximum inspiration (forced expiratory volume in 1 second or FEV_1) and the total volume of air expired as rapidly as possible (forced vital capacity or FVC). The diagnosis of asthma is usually confirmed by:

- Demonstration of airflow obstruction by FEV_1 less than 80 percent of predicted and a FEV_1/FVC ratio less than 70 percent. (The lower limit for a "normal" ratio is lower than that for younger patients.)

- Evidence that the airflow obstruction is reversible (more than 12 percent and 200 mL FEV_1) (American Thoracic Society, 1995) either after bronchodilator administration, with repeated measures over time, or after a course of corticosteroids.

Standards for spirometry are available (American Thoracic Society, 1979, 1987, 1995), but in the older patient these demanding standards can be difficult to meet (Enright et al., 1993). Poor techniques as well as weakness, dizziness, severe airflow obstruction with air trapping, and bronchoconstriction induced by the forced expiratory effort itself can interfere with patient performance. Training technicians to recognize these problems is important (Gardner et al., 1986). A consistent pattern of decreasing FEV_1 in tests repeated during the session is suggestive of asthma.

Published data and clinical experience indicate that many elderly patients with asthma have a persistent degree of airflow obstruction even when optimally treated (Braman et al., 1991; Burr et al., 1979; Burrows, Barbee et al., 1991; Lee & Stretton, 1972; Peat et al., 1987). Reversibility of the obstruction following a bronchodilator is strongly indicative of asthma, but lack of complete reversibility does not rule out asthma. Longer term therapy, often with corticosteroids, may be necessary to achieve appreciable improvement in the elderly patient with asthma.

Elderly patients with asthma often fail to demonstrate more than 12 percent improvement in FEV_1 after receiving an inhaled bronchodilator such as albuterol. To distinguish these patients from patients with COPD, it may be necessary to check for reversibility with a trial of corticosteroid therapy. Eosinophilia may be a useful predictor of this response—see Sputum Examination. The following protocol for a trial of corticosteroid therapy is recommended for differential diagnosis:

- Obtain baseline spirometric measurements.
- Administer the equivalent of 0.3 to 0.5 mg/kg prednisone daily for a period of 2 weeks.
- At the end of 2 weeks, repeat spirometry.
  - — If the FEV_1 has improved less than 200 mL, discontinue corticosteroids.
  - — If the FEV_1 before or after bronchodilator administration has improved more than 500 mL, the patient can be considered to have reversible obstruction.
  - — If the improvement is between 200 and 500 mL, the response is indeterminate; a longer trial may be indicated if there are other indicators that a diagnosis of asthma is likely.
- Note that continuation of oral corticosteroids beyond 2 weeks may pose considerable risk to the patient.

Peak Expiratory Flow (PEF) Measurements. PEF—the maximum flow (expressed in liters per second) that can be generated during a forced expiratory maneuver with fully inflated lungs—is measured using a peak flow meter. PEF measurement before and after bronchodilator administration may be useful in asthma diagnosis (Banerjee et al., 1987). PEF requires maximum effort for accuracy. A pattern of greater than 20 percent variation in PEF from p.m. (late afternoon) to a.m. (upon arising) confirms the presence of variable airflow obstruction, which is indicative of asthma. Variability is defined (Lebowitz, 1991; Quackenboss et al., 1991) by:

$$\frac{\text{PEF p.m.} - \text{PEF a.m.}}{1/2\ (\text{PEF p.m.} + \text{PEF a.m.})} \times 100$$

PEF measurements may pose several problems, however. The sensitivity and specificity of PEF in the elderly have not been sufficiently explored. Furthermore, age-related factors may affect the principal determinants of PEF. For example, increasing rigidity of the chest wall and muscle

weakness tend to enhance the influence of elastic forces and diminish the relative importance of airway diameter as a determinant of PEF. Thus, elderly patients with asthma may have a decrease in diurnal variability. Further, poor coordination and muscle weakness may compromise the effort required for an accurate measure. In addition, elderly patients with asthma may have a greater degree of small airway pathology (Antic & Macklem, 1976) that is not measured by PEF. Because of these problems, a lack of significant change in PEF does not exclude the diagnosis of asthma or the presence of an exacerbation.

Other Pulmonary Function Tests. Other function tests, together with spirometry, may help to detect the presence of interstitial lung disease as well as to quantify the extent of derangement. Measurement of lung volumes (residual volume, functional residual capacity, and total lung capacity), which assess the mechanical properties of the lungs, and measurement of diffusing capacity of the lung for carbon monoxide should be considered when:

- The chest x-ray shows interstitial abnormalities or small lung volumes.
- The spirogram reveals a low FVC and FEV_1 but a normal FEV_1/FVC ratio (i.e., restrictive pattern).
- Digital clubbing is found on examination.
- The patient is or was a chronic cigarette or cigar smoker.

Arterial blood gas measurements, although typically not part of the routine diagnostic evaluation of asthma, are indicated when elderly patients have acute exacerbations in which pulmonary function is severely impaired.

Chest X-Ray

The chest radiograph is generally unremarkable in patients with uncomplicated asthma, regardless of age, but useful for excluding other causes of respiratory symptoms such as Churg Strauss syndrome, allergic bronchopulmonary aspergillosis, and pneumothorax or mediastinal emphysema (Hodson et al., 1974; Lee & Stretton, 1972; Simon et al., 1973; Zieverink et al., 1982). Hyperinflation may be seen during acute exacerbations (Rebuck, 1970; Simon et al., 1973) and in patients with chronic symptomatology. Bronchovascular markings giving the appearance of a "dirty lung" may be seen in elderly patients with significant smoking histories in whom asthma may coexist with chronic bronchitis (Miller et al., 1965). In patients with emphysema, decreased markings reflect diminution in the caliber of pulmonary vessels; hyperinflation with flattened diaphragms and bullous changes may also be prominent. Cardiomegaly and evidence of pulmonary vascular congestion indicate heart disease. Focal infiltrates and mass lesions are indicative of acute infection or cancer.

Electrocardiogram (ECG)

An ECG may help identify the presence of cardiac disease. An ECG can also assess the risk-benefit aspects of $beta_2$-agonist and theophylline administration in patients with both asthma and cardiac disease. ECG abnormalities are usually not associated with asthma during remission but can occur during an acute exacerbation and can include sinus tachycardia, P-pulmonale, right axis deviation, right bundle branch block, right ventricular strain, repolarization abnormalities, and arrhythmias (Gelb et al., 1979; Grossman, 1976).

Complete Blood Count (CBC) With Differential

Elderly patients with asthma, like younger patients, can have significant blood eosinophilia (Burrows, Lebowitz et al., 1991; Lee & Stretton, 1972), but eosinophilia may not be demonstrable in patients taking corticosteroids. Blood eosinophilia greater than 4 percent or 300 to 400 per mm^3 may be used as a predictor of asthma, but its absence does not rule out asthma.

Additional Laboratory Studies

Sputum Examination. The usefulness of sputum examination as a clinical marker for asthma has not been clearly established. However, appearance of eosinophils in the sputum is characteristic of asthma (Burr et al., 1979; Lee & Stretton, 1972). In contrast, chronic bronchitis is characterized by the presence of neutrophils, especially during acute exacerbations (Chodash, 1991).

Imaging Studies. Standard x-rays and computed tomographic studies of the sinuses may be helpful in establishing the presence of acute and chronic sinusitis. Although the link between asthma and sinusitis is not clear, it appears that failure to treat sinusitis may impede adequate management of asthma (Slavin et al., 1983).

Allergy Tests. Allergy skin tests or studies of specific IgE need not be routinely performed because allergens seem to play a less important role for elderly patients than younger patients and a less important role in those who develop asthma after age 65 than in those who have had asthma for a number of years (Braman et al., 1991). If there is a history of allergic rhinitis, or of asthma-like response to aeroallergens, and the response seems to disappear with allergen avoidance, confirming documentation with skin tests and specific IgE studies may be appropriate. Indoor allergens (dust mite, animal danders, and molds) may be more important to evaluate than outdoor allergens; the specific tests will vary by geographic region.

Bronchoprovocation Studies. The sensitivity, specificity, and safety of bronchoprovocation with methacholine, histamine, or exercise challenge in the elderly have not been studied systematically. Because of limitations on their usefulness and uncertainty regarding safety, bronchial challenges in the elderly should be considered as specialized procedures to be performed only by experienced personnel (Hopp et al., 1985; Ramsdale et al., 1984).

DIFFERENTIATING ASTHMA FROM OTHER CONDITIONS

Chronic Obstructive Pulmonary Disease

Several signs and symptoms help distinguish asthma from chronic bronchitis and emphysema, the two components of COPD (see figures 2-1 and 2-2). Chronic cough and sputum production are typical for chronic bronchitis but also occur in some patients with asthma. Cyanosis, ankle edema, and distended neck veins indicate chronic bronchitis with cor pulmonale. Marked weight loss, spontaneous pursed-lip breathing, hyperinflation and bullous changes, palpable liver edge without hepatomegaly, and a quiet chest on auscultation with diminished breath and heart sounds characterize emphysema. Dyspnea is typically exertional in COPD and may be nocturnal in asthma, and the diurnal (a.m. versus p.m.) differences in PEF are greater in asthma.

Interstitial Lung Disease

Patients with interstitial lung disease may have severe dyspnea but are less likely to complain of wheezing, as in asthma. Differentiating characteristics of interstitial lung disease are a restrictive pattern on spirometry (proportionate reduction in FEV_1 and FVC with the FEV_1/FVC ratio normal or high), reduced lung volumes, and reduced pulmonary diffusing capacity. Clubbing, predominant inspiratory crackles, and absence of expiratory slowing are other clinical findings that distinguish interstitial lung disease from asthma.

Bronchiectasis

Acute exacerbations of bronchiectasis are frequently associated with dyspnea, cough, wheeze, and an obstructive defect in spirometry. Signs and symptoms that may help to distinguish bronchiectasis from asthma include the presence of clubbing, chronic production of mucopurulent sputum, increased markings on the chest x-ray, and hemoptysis during acute exacerbations.

Figure 2-1

DIFFERENTIATING ASTHMA AND COPD BY PULMONARY FUNCTION*

Test	Asthma	COPD
FEV_1	↓	↓
FVC	↓	↓
FEV_1/FVC	↓	↓
≥12% and ≥200 mL ↑ FEV_1**	+ +	±
Total lung capacity (TLC)	Normal (or ↑ during acute episode)	Normal or ↑
Residual volume (RV)	↑	↑
RV/TLC	↑	↑
Diffusing capacity of the lung for carbon monoxide	Usually normal	Usually ↓

*For discussion, see Evans & Ogilvie, 1970; Knudson et al., 1990; Stewart, 1988.
**Increase after inhaled bronchodilator.

Cardiac Disease (Angina, Congestive Heart Failure)
Abnormal spirometry, chest tightness ("a weight on my chest"), and nocturnal dyspnea may be present in both congestive heart failure and asthma. However, there is a mixed obstructive/restrictive pattern in congestive heart failure with a predominant restrictive component, and the degree of breathlessness may be out of proportion to the ventilatory defect (Pepine & Wiener, 1972; Sharp et al., 1958). Other signs and symptoms that are more likely to indicate cardiac disease include lower extremity edema, neck vein distention, precordial pulsations, gallop rhythm, inspiratory crackles, cardiomegaly, vascular congestion on chest x-ray (Harrison et al., 1971; Milne & Bass, 1969), and daytime dyspnea that is primarily associated with exertion and not relieved by $beta_2$-agonist.

Upper Airflow Obstruction
Encroaching tumors, vocal cord paralysis, and thyroid enlargement also produce airflow obstruction and wheezing, as in asthma. Due to their extrathoracic location, inspiratory obstruction is predominant. The inspiratory and expiratory wheezing may be grossly audible, but it is best heard by auscultation over the upper airway. The inspiratory sounds are predominant and in many situations produce classic stridor. If the obstruction is fixed, spirometry often demonstrates slowing of forced expiration. An inspiratory/expiratory flow volume loop can be used to assist in identification of extrathoracic airflow obstruction as opposed to the lower airflow obstruction that is more characteristic of asthma.

Pulmonary Embolism
Pulmonary embolism, which is more prevalent in the elderly (Braman & Davis, 1986), may be associated with chest pain, dyspnea, wheeze, and hypoxemia, also seen in asthma exacerbations. A goal of differential diagnosis should be to identify risk factors and, preferably, the source of the thromboembolism.

Bronchogenic Carcinoma
As in asthma, patients with bronchogenic carcinoma may also present with cough, dyspnea, and

Figure 2-2

DISTINGUISHING ASTHMA FROM COPD

Characteristic	Asthma	COPD
History		
Episodic wheeze	Common	Less common; may occur with exacerbations
Nocturnal dyspnea or cough	Common	Not common
Cough with phlegm	Present more than 40 percent of cases; common in those who smoke	Characteristic of chronic bronchitis
Other allergic symptoms (rhinitis, conjunctivitis)	Frequent	Infrequent
Smoking history	Less common	Almost always associated
Past history of asthma	Common	Uncommon
Family history of allergy	Frequent	Less frequent
Physical Examination		
Wheeze	Common	Common after forced expiration or cough
Laboratory Findings		
Pulmonary function	Similar to COPD	Similar to asthma
Chest x-ray	Often normal; may show hyperinflation	↓ vessels, focal hyperaeration (emphysema) ↑ markings (chronic bronchitis)
Eosinophilia	More common	Less common
Positive skin tests	More common	Less common
Total serum IgE	Usually elevated	Elevation less common
Response to Therapy		
FEV_1 response to $beta_2$-agonist	↑ FEV_1 with symptom relief	Little/no change in FEV_1 with poor symptom relief

wheeze. But the wheeze in bronchogenic carcinoma is often unilateral or localized to one area (Braman & Davis, 1986). Because of the likelihood of carcinoma in elderly patients with significant smoking histories, a chest x-ray is especially indicated.

Aspiration

In the elderly person, aspiration can cause or exacerbate cough and wheeze, symptoms of asthma. Factors contributing to aspiration in the elderly are waning gag reflex and diminished mental status caused by sedatives, alcohol, and neuropsychiatric disorders.

Gastroesophageal Reflux

Gastroesophageal reflux can increase symptoms of asthma (Barish et al., 1985; Gurevitch & Valenzuela, 1988; Nelson, 1990; Wald & Fernandez, 1987). This association of gastroesophageal reflux and asthma increases with age. In the elderly person with asthma who is unusually resistant to routine therapy and who has heartburn, cough, and nocturnal symptoms that occur early in the night, gastroesophageal reflux should be considered (Irwin et al., 1976).

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Chapter III
Interactions Among Effects of Aging, Asthma, and Coexisting Diseases

Key Points

- Differentiating the normal physiologic, psychologic, and psychosocial changes that accompany aging processes from abnormal changes that accompany age-associated diseases or asthma is difficult.
- Normal aging-associated changes in lung structure are likely to exaggerate asthma symptoms. These changes sometimes make it difficult to distinguish clearly between asthma and COPD, especially in patients who have smoked.
- Patients with COPD often have a reversible component to their condition, and asthma medications may relieve some symptoms and improve the patient's quality of life.
- Elderly patients may have a decreased response to influenza immunization as well as to pneumococcal vaccine and tetanus toxoid.
- Patient education and asthma management plans for elderly patients should take into consideration possible decreased ability to handle multiple complex stimuli, memory problems, loss of coordination and muscle strength that make it difficult to use metered-dose inhalers, hearing and visual difficulties, sleep disturbances that may impair cognitive function, and depression.
- Adverse asthma reactions from medications related to polypharmacy are greater in the elderly. It is important to ask what other medications the elderly patient with asthma is taking. Particularly hazardous are beta-adrenergic blocking agents (even ophthalmologic preparations) and, in some patients, nonsteroidal anti-inflammatory drugs and antidepressants.

The process of aging may bring normal physiologic, psychologic, and psychosocial changes as well as abnormal pathologic changes associated with those diseases that increasingly afflict the elderly. Differentiating the normal changes that accompany aging from abnormal changes related to disease can be difficult. Both the physiologic and pathologic changes associated with aging may qualitatively and quantitatively alter the expression of asthma symptoms as well as the response to pharmacologic and other medical interventions. Furthermore, the interventions themselves may have unpredictable or unwanted effects on coexisting diseases and vice versa.

Clinicians designing management strategies for elderly patients with asthma need to be aware of

the potential for interactions among the effects of aging, asthma, coexisting diseases, and the various medications elderly patients may be prescribed.

NORMAL AGING CHANGES

Changes in Lung Structure and Function

Significant changes occur in lung structure and function with normal aging, but it is often difficult to separate them from the changes induced by prolonged exposure to potentially harmful inhalants and repeated infections. Lung changes usually associated with the normal aging process relate to connective tissue structural changes involving elastin and collagen networks and include altered alveolar shape resulting in increased alveolar diameter, decreased alveolar surface area available for gas exchange, and increased chest wall stiffness (Knudson, 1989, 1991).

These changes bring about decreased elastic recoil of the lung that, in turn, produces increased residual volume, decreased vital capacity, and premature airway closure in dependent portions of the lungs. With early airway closure, the mismatch of ventilation and perfusion increases, and arterial oxygen tension decreases (Sorbini et al., 1968). Another factor that can contribute to a decrease in arterial oxygen tension is a decrease in pulmonary diffusing capacity, apparently as a result of the decreased area available for gas exchange. However, the precise mechanisms for the decrease in diffusing capacity with age are still unclear.

These normal aging-associated changes in lung structure are likely to exaggerate the gas exchange and mechanical problems that arise from the abnormal narrowing of the airway lumen that occurs in asthma. The normal aging-associated changes also make it difficult to distinguish clearly between asthma and COPD in patients with a history of smoking. Such patients should be considered to have chronic obstruction with variable degrees of reversibility. Asthma medications may relieve some of the symptoms and improve quality of life for these patients.

Changes in Cardiovascular Function

Major changes in cardiovascular function accompany the aging process. These changes complicate diagnosis as well as management of asthma in elderly patients. The changes, resulting from the combined effects of normal aging, sedentary lifestyles, and progressive disease, include increased stiffness of the heart and blood vessels (Lie & Hammond, 1988; Olivetti et al., 1991), diastolic dysfunction due to impaired diastolic filling (Geokas et al., 1990; Manning et al., 1991; Wei et al., 1984), systolic dysfunction due to increased left ventricular afterload (Geokas et al., 1990; Nichols et al., 1985; Pan et al., 1986; van Brummelen et al., 1981), and decreased cardiac output at rest and with exercise (Geokas et al., 1990; Julius et al., 1967; Ogawa et al., 1992; Wid, 1992). Heart failure is frequent among the elderly, occurring six times as often in the seventh than in the fifth decade of life (Kannel, 1989; McKee et al., 1971). In three out of four patients with heart failure, hypertension or coronary artery disease seems to be the underlying cause (McKee et al., 1971). It appears that disease rather than normal aging is the major determinant of clinically significant cardiovascular dysfunction in the elderly. For elderly patients with asthma, this means an increased likelihood of a comorbid condition that could aggravate asthma and vice versa.

Changes in Immune Function

A variety of alterations in immune response accompany the normal aging process (Adler & Nagel, 1990; Ben-Yehuda & Weksler, 1992; Powers et al., 1990; Thoman & Weigle, 1989). Among these is a major change relating to the nature and quantity of antibodies produced. In the elderly there is a decreased response to

immunization with influenza (Ben-Yehuda & Weksler, 1992; Ershler et al., 1985; Feery et al., 1979; Levin et al., 1992), although the number of peripheral B cells is normal (Utsuyama et al., 1992). Response of the elderly population to pneumococcal polysaccharide and tetanus toxoid is also reduced and of shorter duration. Some physicians recommend revaccination every 6 years in patients over age 60 (Ben-Yehuda & Weksler, 1992; Kishimoto et al., 1980, 1982; LaForce & Eickhoff, 1988; Landesman & Schiffman, 1981; Mufson et al., 1991; Centers for Disease Control, 1987; Shapiro et al., 1991; Yoshikawa, 1983). The most recent recommendations for pneumococcal vaccine are every 5 to 7 years for adults between ages 60 and 75, and every 3 to 4 years for those over age 75 (Musher, 1995). Others feel revaccination every 10 years is sufficient even for this age group (Balestra & Littenberg, 1993, 1994).

T-lymphocyte function, which is believed to relate to the production of IgE, is decreased in the elderly. Although total serum IgE as well as specific IgE antibodies to aeroallergens are reduced in the elderly, total IgE levels are greater in elderly asthma patients, compared with age-matched patients without asthma (Horst et al., 1990; Van Bever & Stevens, 1989). Lymphokine production by T lymphocytes is reported to decrease in the elderly (Al-Rayes et al., 1992), but it is unclear whether this explains the reduction in IgE production. Reduced T-lymphocyte function with age is apparently associated with an increase in memory phenotype T lymphocytes, which are less responsive to antigens. Although allergy is generally reduced in the elderly, certain allergens may well remain a factor in some elderly patients with asthma (Barbee, Halonen et al., 1987; Barbee, Kaltenborn et al., 1987; Duff & Platts-Mills, 1992; Freidhoff et al., 1984; Gergen et al., 1987; LaForce & Eickhoff, 1988; Ohman et al., 1993; Pollart et al., 1989; Rawle et al., 1983; Stoy et al., 1981; Vergnenegre et al., 1992), particularly in those with longstanding disease. Allergen avoidance as a management strategy for asthma may be less important or practical in the elderly.

A further effect of decreased T-lymphocyte production is decreased cell-mediated immune function. This decrease is reflected in reduced delayed-type skin test reactivity and increased incidence of tuberculosis and varicella-zoster. For elderly patients with asthma, the overall consequences of changes in immune function are increased susceptibility to tuberculosis and pneumococcal and influenza pneumonia, and decreased IgE response to allergens. Annual influenza vaccination is strongly encouraged for elderly patients.

Changes in Neurologic, Neuromuscular, and Sensory Functions

Aging is accompanied by a loss of neurons in certain areas of the brain that increases reaction time, decreases the ability to respond to multiple complex stimuli, and may impair an individual's ability to adapt to the environment (Mann & Yates, 1979; McGeer et al., 1977).

Memory changes are common in the elderly. Visual information seems to be retained better than auditory information, even though formal testing shows no substantial change in sensory memory with age (Ciocon & Potter, 1988). Long-term memory seems to show no substantial diminution with age, although short-term memory—the ability to acquire and retrieve new information—is affected. In addition, stroke, dementia, anemia, electrolyte imbalance, thyroid dysfunction, and poor cardiac function, pathologic conditions that are more frequent in the elderly, may lead to confusion and affect the ability to learn and use new information. Such memory problems may require special measures to help elderly patients with asthma comply with routine maintenance regimens.

Neuromuscular changes that occur with aging include loss of muscle tone, decreased motor

speed, decreased nerve condition, and decreased muscle fiber diameter and bulk, especially in the small muscles of the hand (Calne, 1985; Carter, 1986). These neuromuscular changes may interfere with coordination and muscle strength and make it difficult to use metered-dose inhalers (MDI's).

Other aging-associated sensory changes include hearing and visual difficulties such as decreased visual acuity and color discrimination. Sleep disturbances occur more frequently in the elderly and lead to fatigue and impaired cognitive function. Patient education and asthma management plans for the elderly should take these problems into consideration.

Psychologic and Behavioral Changes

Only about 10 percent of the elderly are mentally debilitated; however, when present, mental problems can have a major effect on asthma management. The most common psychologic problems are the affective disorders and organic mental disorders, particularly dementia (Billig, 1989).

It is not clear whether depression is associated with advanced age (Blazer et al., 1991). Classic symptoms of depression—for example, diminished interest in activities, weight and appetite disturbance, insomnia, hypersomnia, psychomotor change, fatigue, guilt, low self-esteem, concentration problems, indecision, anxiety, and thoughts of death or suicide—may be present in the elderly. Depression is strongly associated with chronic illness and disabling conditions (Cassem, 1990; Frank et al., 1992; Turner & Beiser, 1990; Williamson & Schultz, 1992) and has been implicated in asthma mortality (Picado et al., 1989; Sly, 1989). Depression may also be caused by medications (e.g., corticosteroids, antihypertensives, anti-Parkinsonians). Estimates of the prevalence of depressive disorders in the elderly range from 10 to 15 percent (Palinkas et al., 1990) or higher (Alexopoulos et al., 1988; Hendrie & Crosset, 1990). Depression may reduce not only compliance with treatment plans but also patient motivation to engage in normal activities, thus inappropriately lowering the goals of asthma therapy in elderly patients. Depression is one of the most treatable problems in the elderly (Billig, 1989), and asthma management in elderly patients should be tailored to the degree and nature of this and other behavioral problems.

EFFECTS OF COEXISTING DISEASES AND THEIR THERAPIES

Elderly patients with asthma frequently have coexisting diseases and related treatments that should be considered in the diagnosis and management of asthma. Specifically, the physician should recognize common comorbid conditions and potential disease-drug interactions that may complicate the safe and effective control of asthma and require modification of treatment.

- Asthma symptoms may be initially masked by or misdiagnosed as other disorders such as congestive heart failure (see previous chapter on differential diagnosis).
- Coexisting conditions (e.g., respiratory infections, gastroesophageal reflux) may exacerbate asthma, hinder effective therapy, and reduce asthma control.
- Therapy for coexisting diseases may worsen asthma control by inducing bronchospasm (e.g., beta-adrenergic blocking agents for cardiovascular disorders or glaucoma or nonsteroidal anti-inflammatory agents for arthritis).
- Some asthma medications (e.g., theophylline, beta-adrenergic bronchodilators) can elicit adverse responses (e.g., cardiac ischemia or arrhythmia, drug toxicity, gastroesophageal reflux) in susceptible patients with coexisting disorders (e.g.,

ischemic heart disease, congestive heart failure, acute myocardial infarction, gastroesophageal reflux).

Specific Potentially Adverse Medication Interactions

All medications should be carefully reviewed to prevent adverse effects related to polypharmacy (Kellaway & McCrae, 1973). Approximately 10 percent of admissions to acute geriatric units in the United Kingdom are solely or partly for adverse reactions to drugs (Williamson & Chopin, 1980), mostly due to altered pharmacodynamics and pharmacokinetics, polypharmacy, and other illness (Denham, 1990).

Adverse reactions appear to increase with age, although it is not clear whether they are more frequent or more severe in elderly patients (figure 3-1). Further, in a confused patient, identifying the specific drug interactions or distinguishing them from aging-related factors may be difficult, often because of incomplete drug histories.

Beta-Adrenergic Blocking Agents. Beta-adrenergic blocking agents are used frequently for the management of conditions that are more common in elderly patients (e.g., hypertension, coronary artery disease, cardiac arrhythmias) (Dannenberg et al., 1988; NHLBI, 1991) and glaucoma. Nonselective beta-adrenergic blocking agents, such as propanolol, can induce acute bronchospasm, even when administered as ophthalmic solutions (e.g., timolol). The bronchospasm results from the blocking of $beta_2$-adrenergic receptors on airway smooth muscle (Odeh et al., 1991). In patients with cardiac diagnosis, hypoxemia resulting from bronchospasm may further compromise cardiac function and lead to more serious consequences than in younger patients.

Despite these problems, substantial numbers of elderly patients with asthma are prescribed beta-adrenergic blocking agents (Graft et al., 1992). One reason may be lack of communication among physicians responsible for the management of different illnesses in the same patient. A retrospective analysis of patients with asthma who also received beta blockers revealed that 61 percent of them had one clinician treating their asthma and another prescribing the beta-adrenergic blocking agent (Graft et al., 1992). This situation is made worse if patients have to change clinicians frequently due to insurance and cost control problems. Because some elderly patients may be unable or unwilling to volunteer information on all the medications they are receiving, the health care provider should specifically ask the patient whether he or she is taking a beta-blocking agent. In general, nonselective beta-adrenergic blocking agents, even ophthalmic solutions, should not be prescribed for patients with asthma, because they can produce severe bronchospasm and perhaps anaphylaxis. Further, patients who are taking beta-adrenergic blocking agents and develop anaphylaxis may not respond to usual treatment. Elderly patients with asthma and cardiovascular disease appear to be at particular risk (Toogood, 1988).

Nonsteroidal Anti-Inflammatory Drugs (NSAID's). Elderly patients with asthma frequently take aspirin or other NSAID's for cardiovascular and/or musculoskeletal conditions associated with aging. A small but significant percentage of patients with asthma, especially those who have roentgenographically confirmed sinus disease, nonallergic eosinophilic rhinitis, and/or nasal polyps (Stevenson, 1984), develop sudden, severe, potentially life-threatening bronchospasm after ingestion of aspirin or other NSAID's. NSAID-sensitive patients should generally avoid using NSAID's. Both clinicians and patients should be aware of this reaction to a highly common medication. Even patients who are aware of the potential reaction may not realize that aspirin is a common component of many over-the-counter preparations.

Figure 3-1

NONASTHMA MEDICATIONS WITH INCREASED POTENTIAL FOR ADVERSE EFFECTS IN THE ELDERLY PATIENT WITH ASTHMA

Medication	Comorbid Condition(s) For Which Drug Is Prescribed	Adverse Effect	Comment
Beta-adrenergic blocking agent	Hypertension Heart disease Tremor Glaucoma	Worsening asthma • bronchospasm • decreased response to bronchodilator Decreased response to epinephrine in anaphylaxis	Avoid where possible; when must be used, use a highly beta-selective drug
Nonsteroidal anti-inflammatory drugs	Arthritis Musculoskeletal diseases	Worsening asthma • bronchospasm	Not all elderly with asthma have nontolerance of NSAIDs, but are best avoided if possible
Non-potassium-sparing diuretics	Hypertension Congestive heart failure	Worsening cardiac function/ dysrhythmias due to hypokalemia	Additive effect with antiasthma medications that also produce potassium loss (steroids, beta-agonist); elderly also more likely to be receiving drugs (e.g., digitalis) where hypokalemia is of increased concern
Certain nonsedating antihistamines (terfenadine and astemizole)	Allergic rhinitis	Worsening cardiac function/ ventricular arrythmias due to prolonged QT_C interval	
Cholinergic agents	Urinary retention Glaucoma	Bronchospasm Bronchorrhea	Also note that some over-the-counter asthma medications contain ephedrine, which could aggravate urinary retention, glaucoma
ACE inhibitors	Heart failure Hypertension	Increased incidence of cough	

Diuretics. Because of the increased incidence of hypertension and left ventricular failure, elderly patients are more likely to be taking diuretics. However, the combination of diuretics that do not spare potassium (e.g., thiazides) and $beta_2$-agonists has the interactive potential to produce clinically significant hypokalemia and hypomagnesemia, which increases the risk of cardiac arrhythmias (Holland et al., 1981; Hollifield, 1989a; Kaplan, 1984), particularly in elderly patients with asthma receiving digitalis. Older patients with asthma who have heart disease and who may develop periodic hypoxia may be at great risk of developing cardiac arrhythmias

secondary to hypokalemia. One study recommends that elderly patients receiving thiazide diuretics and beta$_2$-agonists have routine monitoring of serum potassium and magnesium for early detection of electrolyte imbalance and appropriate initiation of treatment with magnesium or potassium supplementation (Hollifield, 1989b). System corticosteroids may also contribute to hypokalemia and amplify the interaction between diuretics and beta$_2$-agonists.

Antihistamines. Many elderly patients with asthma have concurrent rhinitis or sinusitis for which they take antihistamines. It should be recognized that, under certain conditions, terfenadine and astemizole have the potential to produce prolongation of the QT_c interval, which could lead to ventricular arrhythmias such as Torsade de Pointes (Kemp, 1992). The risk of this event may be increased in elderly patients if they are also taking beta$_2$-agonists and/or diuretics, which can produce hypokalemia and hypomagnesemia—conditions associated with prolongation of the QT_c interval (Windom et al., 1990) and ventricular arrhythmias. The sedative effects of some antihistamines may also be of concern in elderly patients receiving medications for insomnia or depression.

Angiotensin-Converting-Enzyme (ACE) Inhibitors. Elderly patients are likely to be on antihypertensive medications, including ACE inhibitors. It has been well documented that ACE inhibitors can produce cough in some patients. It is also well recognized that patients with asthma can present with cough alone. This distinction is important because discontinuing the drug will be enough to resolve the cough, if it is due to the ACE inhibitors.

Antidepressants. Depression is common in the elderly, particularly in those who are chronically ill. It is important to be aware that some drugs—such as systemic corticosteroids, antihypertensives, anti-Parkinsonians, narcotic analgesics, and sedative hypnotics (McCullough, 1991)—may cause depressive syndromes and that significant interactions can occur between medications used to treat depression and other medications.

Another interactive effect to be aware of is that tricyclic antidepressants—such as drugs used to block potassium channels, which are frequently prescribed for elderly patients—can produce prolongation of the QT_c interval.

In addition, concomitant use of beta$_2$-agonist bronchodilators and monoamine oxidase (MAO) inhibitors, although infrequent, is not generally recommended because of the danger that the vascular effects of sympathomimetic amines may be potentiated following the use of MAO inhibitor medications (Goodman & Gilman, 1990).

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Chapter IV
Management of Asthma in the Elderly: Adapting the Four Components

Key Points

- Quality of life and the ability to live independently are important considerations in asthma management plans for the elderly. Each patient's personal objectives should be explored and incorporated in treatment goals.
- Desired therapeutic and clinical outcomes may be more difficult to achieve in elderly patients with asthma. Normal lung function may either be unattainable or be attainable only with potentially dangerous, high pharmacologic doses. Treatment goals may need to be modified to maintain a desirable quality of life. Conversely, some elderly patients do not appreciate the possibilities treatment offers, and they may have unnecessarily accommodated their lifestyles to their perceived limitations. It is important, therefore, to set realistic goals for therapy.
- Medication for asthma management is similar for all ages, but ipratropium bromide may be useful, especially for those elderly patients who have chronic obstructive pulmonary disease or who experience tremor, angina, or arrhythmia from beta$_2$-agonists.
- Because compliance with multiple therapies—for both asthma and coexisting diseases and conditions—may be difficult, elderly patients often need special education and training in using asthma medications and devices.
- The potential for drug interactions is greater in elderly patients with asthma because these patients are likely to be on multiple medications for other conditions, particularly heart disease.
  - — Beta$_2$-agonist and theophylline use should be monitored carefully because they can cause tachyarrhythmias and aggravate ischemic heart disease.
  - — If theophylline is used, it should be used with caution, especially in patients with congestive heart failure.
  - — Systemic corticosteroids may aggravate congestive heart failure and lower serum potassium with potentially adverse cardiac effects (see figure 4-3).
  - — Corticosteroids in high doses may reduce bone mineral content and may accelerate development of osteoporosis.

KEY POINTS (CONTINUED)

- The effectiveness of home peak flow monitoring among the elderly has not been clearly established. Because some elderly patients may have a poor perception of symptoms or symptom severity, PEF monitoring may contribute significantly to management. It may also help distinguish asthma symptoms from symptoms of coexisting heart and lung diseases. However, the usefulness of PEF monitoring may be limited by age-related factors that compromise the effort and perceptual and motor skills required for accurate measurements. Assistance from a caretaker may be useful.
- Avoidance of environmental triggers, including tobacco smoke and aeroallergens to which the patient is sensitive, is useful for many elderly patients with asthma.

The components of asthma management in the elderly are generally similar to those recommended for all adults (NHLBI, 1991)—educating patients for a partnership in asthma care; monitoring with objective parameters as well as symptoms; environmental control; and pharmacologic therapy—although modifications to accommodate the effects of aging and coexisting diseases and conditions are required.

COMPONENT 1—EDUCATING PATIENTS FOR A PARTNERSHIP IN ASTHMA CARE

Much of the day-to-day responsibility for asthma management falls on the patient and the patient's family or caregiver. The establishment of a partnership among the patient, family (or at-home caregiver), and health professional is essential in planning, implementing, evaluating, and maintaining a successful treatment program. The basis for this partnership begins during the process of differential diagnosis, when the clinician becomes the patient's guide and counselor for the patient's daily asthma self-management.

Encourage Open Communications

A partnership involves encouraging patient and family questions and communications and developing together a management plan to prevent and treat symptoms. However, because many elderly patients (and others) do not volunteer information or spontaneously try to resolve their concerns, the clinician must often not only listen but also encourage patients to ask questions and discuss their fears or concerns about asthma or asthma treatment. A concerted effort may be necessary to establish a partnership that encourages exchange of information and gives elderly patients a sense of independence as well as involvement in the control of their treatment program and management of symptoms.

Set Achievable Goals

Defining the goals of therapy for the specific individual is one of the first tasks of a partnership. General goals of asthma therapy for elderly patients are to:

- Permit the desired level of activity and maintain quality of life
- Optimize pulmonary function
- Control cough and nocturnal symptoms
- Prevent exacerbations

- Promote prompt recognition and treatment of exacerbations to avoid hospitalizations or emergency department visits
- Avoid aggravating other medical conditions
- Minimize adverse effects from medications.

Desired therapeutic and clinical outcomes are often more difficult to achieve in elderly patients with asthma because of irreversible airway obstruction and/or coexisting COPD. Normal lung function may be unattainable or attainable only with high-dose medication and thus more modest treatment goals based on maintaining a desirable quality of life may be preferred.

The clinician and patient should work in partnership to tailor goals for therapy to meet the patient's unique needs. Factors that influence goals set for elderly patients include comorbid conditions, patient health care values, cognitive status, sensory limitations, financial status, and family health and support. Factors critical to the patient's quality of life must also be considered in setting goals. These goals, which may include living independently and participating in leisure activities such as traveling with grandchildren, are much stronger motivations for compliance with asthma therapy than is improving performance on successive tests of lung function.

Setting realistic personal goals is important. It is quite common for patients with poorly controlled asthma to misunderstand the diagnosis and the possibilities treatment offers. They may accommodate their lifestyle to their perceived limitations, letting their expectations slide. Others may not have accepted the diagnosis, or they may be angry about their limitations and may aim too high. Unrealistic goals—too low or too high—are often a clue that the patient requires further education or counseling. Negotiation between clinician and patient may be necessary to set goals that are both medically acceptable and practical for the patient.

Educate Patients About Asthma Management

Patient education is critical to help patients and their families establish a partnership in their asthma care. Patient education involves:

- Helping patients learn and practice the skills necessary to manage asthma (e.g., take medication correctly; follow a management plan; avoid asthma triggers; monitor personal status using symptoms and, if possible, PEF indicators; recognize signs and symptoms of worsening asthma; seek medical help appropriately),
- Developing patient confidence that the patient can control asthma, and
- Supporting patients for appropriate asthma management behaviors and adherence to the treatment plan.

Selected patient education strategies for elderly patients are included in this chapter for each component of asthma care.

Patient Education Strategies

To promote open communication, adherence to the management plan, and the development of self-management skills, the clinician should:

- Make sure the patient and family understand the meaning and significance of commonly used terminology in the early stages of a partnership. For example, review the meaning of "asthma" versus "chronic obstructive pulmonary disease," and ensure that the patient understands the difference between medication used to *prevent* symptoms or exacerbations and medication used to *treat* symptoms.
- Use open-ended questions to elicit patients' understanding and concerns about asthma and asthma treatment.

- Use a variety of teaching methods and materials suitable for elderly patients to demonstrate asthma management skills. For example, personal demonstrations can be supplemented with video materials and written materials that use large type. Group activities among asthma patients may provide important reinforcement and social support.
- Provide a written asthma management plan that includes:
  - Agreed upon goals for therapy
  - Avoidance strategies
  - Management steps for daily medication
  - Action steps for handling exacerbations

  (see Monitoring by Objective Assessment)

COMPONENT 2—MONITORING BY OBJECTIVE ASSESSMENT

Successful management of asthma includes frequent monitoring of clinical signs, symptoms, and objective measures of lung function in order to identify deterioration and assess the effectiveness of treatment strategies.

How frequently the patient should be seen for followup evaluation by the clinician depends on the severity of the condition and how skillful the patient is in monitoring asthma at home and communicating with the clinician concerning changes. All patients, even those with mild asthma, should be seen at least every 3 to 6 months because deterioration in lung function can occur insidiously. Furthermore, elderly patients often mistakenly dismiss worsening signs and symptoms, such as diminished tolerance to physical activity or interrupted sleep, as effects of aging rather than of deteriorating asthma. Figure 4-1 provides a questionnaire for a routine followup office visit, and figure 4-2 illustrates how measures of lung function and symptom evaluations can be used together for patient monitoring. Written asthma management plans are an important part of patient monitoring for clinicians and patients (see Patient Education Strategies).

Monitoring Lung Function

Spirometry or PEF should be obtained at every office visit. Objective measures of lung function are particularly important for:

- Evaluating changes in symptoms
- Quantitating the severity of an exacerbation and evaluating immediate treatment response (Banner et al., 1976; Nowak et al., 1982; Stein & Cole, 1990)
- Monitoring progress following emergency department or hospital care for an exacerbation
- Evaluating patient response to new therapy (Beasley et al., 1989; Woolcock et al., 1988).

Home peak flow monitoring can be useful for asthma management (Beasley et al., 1989; Woolcock et al., 1988) for all age groups over age 5 years by permitting early detection of airflow obstruction and timely interventions. This benefit may be particularly important for the elderly, many of whom may be poor perceivers of symptoms or symptom severity. Elderly patients most likely to benefit from home PEF monitoring include those who experience episodic worsening of symptoms, require emergency department care for exacerbations, and have coexisting heart and lung diseases that PEF may help distinguish. However, the usefulness of home monitoring by elderly patients with asthma may be limited by the effects of the aging process, such as changes in lung and chest wall mechanical properties, decreasing variability in lung function, and greater degrees of irreversible obstruction and small airway pathology. Some patients with physical or cognitive disabilities may not be able

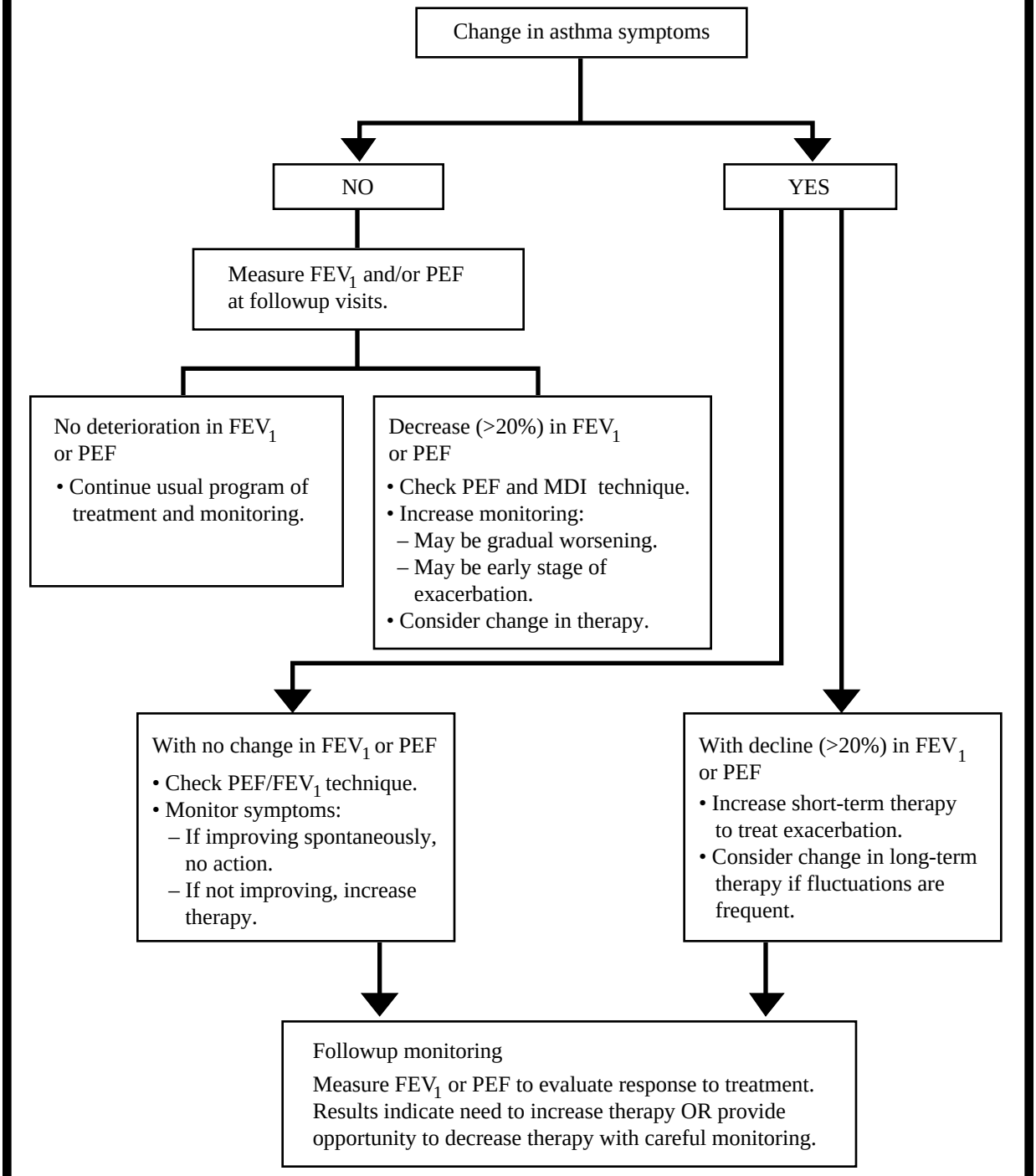
Figure 4-1

BASIC ELEMENTS OF A FOLLOWUP OFFICE VISIT FOR ASTHMA

- The clinician should ask the patient if he or she has experienced a change in symptoms:
  - Nocturnal or early morning awakening with wheezing and cough
  - Shortness of breath
  - Cough or phlegm
  - Acute episodes of shortness of breath or wheezing
- The clinician should ask the patient if he or she has experienced a change in exercise tolerance or inability to perform at the usual level of exertion.
- The clinician should ask the patient about medications taken, including:
  - All prescribed and over-the-counter medications and "health food" preparations
  - Asthma medications and those for other problems
  - Dosage and frequency
  - Any increase or change in drug use, especially beta$_2$-agonists.
- The clinician should note physical findings, especially:
  - Change in ventilatory pattern at rest (accessory muscle use, forced expiration)
  - Change in ventilatory pattern with activity
  - Ability to speak in full sentences
  - Signs of airflow obstruction (expiratory slowing, wheeze, poor aeration)
  - Signs and symptoms of poor oxygenation (tachycardia, cyanosis)
  - Signs of heart failure (edema, gallop rhythm, neck vein distension).
- Perform spirometry or PEF. The clinician should review PEF home monitoring records, if the patient uses PEF at home, and provide feedback about the observations.
- The clinician should observe the patient's metered-dose inhaler technique and provide appropriate feedback.
- The clinician should review the patient's asthma management plan.

Figure 4-2

USING PULMONARY FUNCTION MEASURES AND SYMPTOM EVALUATION TO MONITOR THE PATIENT



to use a peak flow meter appropriately. Thus, the decision to use home peak flow monitoring will depend on individual patient circumstances.

PEF measurements are used to adjust therapy on the basis of changes in PEF from baseline measures—either predicted or personal best (best value recorded for the patient), although, especially in the elderly, personal best measures are recommended.

- Predicted values as a baseline measure use normal standards that are available for individuals over 65 years of age (Koenigsberg & Holden, 1989; Nunn & Gregg, 1989). A 20 percent change from these predicted values is usually considered significant, although the clinical importance of the change will also depend on the actual PEF value.
- Personal best as a baseline measure is recommended because there is considerable heterogeneity in optimal levels of lung function for elderly patients with asthma who have a component of fixed airflow obstruction or coexisting COPD (Braman et al., 1991; Burr et al., 1979; Burrows et al., 1991; Lee & Stretton, 1972). Personal best measurements are obtained when the patient is under optimal treatment and is experiencing minimal symptoms. Personal best measurements are more likely to be obtained in the late afternoon than in the early morning. It is important to note that obtaining a personal best measurement may require a trial burst of oral corticosteroids and often involves an observation period during which morning and mid to late afternoon postbronchodilator (if the patient is using a bronchodilator) PEF's are measured.

Correct technique is critical for PEF measurements, and frequent review of patients' technique is essential. Maximal expiratory effort should be emphasized with each measurement; a strong, short "huff" is more effective than a prolonged expiration.

Symptom Monitoring

Monitoring patient symptoms, such as chest tightness, cough, wheeze, or dyspnea, can provide a reliable measure of a patient's need for and response to therapy. Differences among patients are considerable in regard to which symptoms are most prominent, how symptoms are interpreted and tolerated, and how they relate to physiologic alterations including lung function. Thus careful discussion with the patient is needed to establish a meaningful way of interpreting the symptoms. Questions in the patient history can help identify a predictive pattern of symptoms. For example: Have prior exacerbations been characterized by rapid deterioration or slow deterioration? What symptoms were prominent during early stages of prior exacerbations? Does the severity of an exacerbation seem related to a specific trigger?

Teaching patients that changes in their symptoms may be a significant sign of deterioration and may warrant a change in therapy is important. Clinical experience and some studies correlating increased symptoms with declining lung function (Juniper et al., 1990) show that the following signs and symptoms often indicate poor control of asthma:

- Nocturnal or early morning awakenings with wheeze or cough
- Increased cough and/or sputum
- Increase in use of or diminished response to inhaled $beta_2$-agonist
- Decrease in tolerance of exercise, including normal daily activities
- Change in the intensity of dyspnea.

Symptom scoring systems (Gibson et al., 1992; Marks et al., 1993) and patient diaries (see NAEPP "Guidelines for the Diagnosis and Management of Asthma" [NHLBI, 1991] for examples) may help patients observe and report their symptoms.

Patient Education Strategies

To promote accurate measurements of lung function and effective symptom monitoring, the clinician should:

- Develop for each patient a *written* management plan that includes an asthma management zone system that classifies levels of asthma control as different zones based on the frequency and severity of symptoms and the PEF measured. The system then indicates the appropriate therapy for each zone. (See NAEPP "Guidelines for the Diagnosis and Management of Asthma" for examples of plans and zones.)
- Include in the written asthma management plan the specific dose of long-term preventive medication to control the patient's asthma and prevent symptoms; the specific asthma triggers to avoid; and specific guidelines for what to do if asthma worsens (such as how to recognize decreasing control, the name and dose of the bronchodilator to be taken immediately) and how and when to seek medical attention.
- Assist the patient in recognizing symptoms and correlating them with decreases in PEF. Review of peak flow and symptom diaries at each clinic visit is a useful way to accomplish this objective.
- Ask patients to bring their peak flow meters and their devices to each clinic or office visit and demonstrate use. Review and correct technique, and ask patients to repeat demonstrations, as needed.
- Make sure patients can fill out and interpret diaries, if diaries are used. (See NAEPP "Guidelines for the Diagnosis and Management of Asthma" for examples.) Ask patients to bring them to each visit, and review at each visit. In the review, focus particularly on episodes of increased symptoms and falls in peak flow.
- Use large type for all materials for elderly patients.

COMPONENT 3—ENVIRONMENTAL CONTROL: AVOIDING OR CONTROLLING TRIGGERS

Avoidance of exposure to allergens and tobacco smoke, both active and passive, is important. Patients who smoke benefit from participation in smoking cessation programs and positive reinforcement for their efforts.

Measures to avoid or reduce exposure to aeroallergens—dust mite, animal (especially cat), cockroach, Alternaria, grass and perhaps other pollens—can help reduce symptoms and medication requirements among patients sensitive to these aeroallergens. Avoidance includes reducing the dampness that favors growth of dust mites, removal of animals, and extermination of cockroaches.

Taking environmental control measures can be difficult for some elderly patients, however. For example, a cat may be the major source of companionship, and separation from the animal could have psychologic consequences. If sensitivity to a specific allergen is established, the clinician and the patient should work together to find feasible measures to control exposure to that allergen. In the absence of sensitivity to a specific allergen, strict environmental controls are not recommended.

Prophylactic pneumococcal and influenza immunization is recommended for elderly patients with asthma unless contraindicated by established egg allergy. The influenza vaccine should be administered yearly. The pneumococcal vaccine should be administered every 5 to 7 years in adults between ages 60 and 75, and every 3 to 4 years in adults over age 75 (Musher, 1995).

The effectiveness of allergen immunotherapy for managing asthma in the elderly is uncertain, and anaphylaxis is a complication of immunotherapy

that is particularly dangerous in elderly patients with significant cardiovascular disease.

Patient Education Strategies

To promote patient understanding and use of necessary environmental control measures, the clinician should:

- Include in each patient's asthma management plan information on the specific environmental control measures required.
- Tailor control measures to the special individual and the special situation. Measures should be feasible for and acceptable to the patient. Those that are inappropriate or unrealistic to the patient's situation could have an adverse effect on the patient's quality of life without benefiting asthma management.
- Refer patients (or family members) who smoke to smoking cessation programs, remind them of the importance of reducing exposure to tobacco smoke to improve asthma control, and provide positive reinforcement for their efforts.
- When necessary, conduct or ask for a home health visit to evaluate the home setting and institute appropriate measures.

COMPONENT 4—PHARMACOLOGIC THERAPY

The medications used to treat asthma in the elderly do not differ significantly from those for younger patients. However, the risk of adverse effects from asthma treatment is greater, as discussed in the following section on long-term management, and the potential for drug interactions is greater because of many coexisting conditions, as described in the chapter on interactions among the effects of aging, asthma, and coexisting diseases. Figure 4-3 lists potential adverse effects associated with medications used to treat asthma in the elderly. It is important to establish the appropriateness of asthma medications and doses by regularly evaluating the patient's response to therapy. Review of patient technique in taking medications is also important; not infrequently, a failure to respond adequately to therapy is a result of improper medication/inhaler technique.

Anti-Inflammatory Agents

Corticosteroid therapy is the most effective anti-inflammatory treatment for asthma (Adelroth et al., 1990; Djukanovic et al., 1992; Holgate et al., 1977; Marom et al., 1984). Underutilization of corticosteroids is believed to be a significant factor in fatal or near-fatal exacerbations of asthma in these patients (Ernst et al., 1992; Seaton, 1985).

Oral Corticosteroid Therapy. In severe asthma exacerbations, oral or parenteral corticosteroid therapy is beneficial in both young and elderly asthma patients. The metabolic clearance of prednisolone is slower in elderly populations (Stuck et al., 1988) and results in a higher concentration of total and free prednisolone, but there are no data to indicate that the elderly have an inherently increased risk of corticosteroid side effects. However, use of oral corticosteroid therapy may be complicated by increases in frequency and severity of side effects due to diseases and conditions more common in older age groups (e.g., diabetes and osteoporosis).

Adverse effects of oral corticosteroid therapy in long-term asthma management in the elderly include the following:

- Cardiovascular and metabolic side effects. The renal effects of oral corticosteroids result in positive Na^+ balance and expansion of fluid volume, hypokalemia, and alkalosis (Haynes, 1990), and these effects could aggravate the electrolyte and water balance in elderly patients with preexisting heart disease or renal disease. The use of thiazide diuretics accentuates the hypokalemic alkalosis. The hypokalemia is a particular concern because of therapy with potassium-sensitive drugs such as digitalis in the elderly (Nicklas, 1991) and the

Figure 4-3

ASTHMA MEDICATIONS AND POTENTIAL ADVERSE EFFECTS

Class of Therapeutic Agent	Drug	Potential Adverse Clinical Effects
Anti-inflammatory	Oral corticosteroids	↑ Blood pressure, edema, congestive heart failure due to Na^+ retention
		Hypokalemia, alkalosis, and resulting arrhythmias due to K^+ and H^+ excretion
		Worsening diabetes mellitus, cataracts, polyuria with dehydration due to elevated blood glucose
		Thinning of the skin, reduced muscle mass with myopathy, osteoporosis, ↑ blood urea nitrogen without change in renal blood flow due to protein catabolism
		Hypoadrenalism due to decreased ACTH
		Cataracts
		Altered cognitive function, depression
		Joint effusions and articular pain with corticosteroid withdrawal
		Osteoporosis due to decreased calcium absorption
		Glaucoma due to decreased absorption of aqueous humor
		Aggravation of existing peptic ulcer disease
	Inhaled corticosteroids	Cough, dysphonia, loss of taste, laryngomalacia, oral candidiasis
	(High doses, e.g., >1.6 mg/day)	? Effects on ACTH secretion with hypoadrenalism
		? Effects on calcium absorption with acceleration of osteoporosis
		? Development of cataracts
	Cromolyn sodium	No significant adverse effect known
	Nedocromil	No significant adverse effect known

Figure 4-3

ASTHMA MEDICATIONS AND POTENTIAL ADVERSE EFFECTS (CONTINUED)

Class of Therapeutic Agent	Drug	Potential Adverse Clinical Effects
Bronchodilator	Short-acting $beta_2$-agonists	Myocardial ischemia due to ↑ myocardial oxygen consumption and mild increase in hypoxemia
		Complex ventricular arrhythmia due to ↑ myocardial irritability
		Cardiac arrhythmias and muscle weakness related to hypokalemia
		Hypotension or hypertension
		Tremor
		With excessive use, ↓bronchodilator effect and ↑ airway hyperresponsiveness related to downregulation of beta receptors
	Long-acting $beta_2$-agonists	Same as for short-acting $beta_2$-agonists
	Theophylline	Cardiac arrhythmias; effect is related to ↑ catecholamine release and is additive with $beta_2$-agonists
		Nausea and vomiting from gastric irritation, gastroesophageal reflux
		Insomnia, seizures related to central nervous system stimulant
		Cardiac arrhythmia due to inotropic and chronotropic effects
		Serum levels increased by heart failure, liver disease, beta-blocker therapy, selected H_2 blocker therapy, quinolone therapy, macrolide therapy, ketoconazole therapy
	Ipratropium bromide	Mucosal dryness

concomitant use of diuretics and beta$_2$-agonist therapy, which may decrease serum potassium.

Hypertension, sometimes a result of oral corticosteroid therapy, is a potential problem because of the higher prevalence of preexisting hypertension in the elderly.

Blood sugar and blood urea nitrogen are increased by oral corticosteroids. Because diabetes and glucose intolerance are more prevalent in the elderly, the increase in blood sugar increases the susceptibility of this age group to clinically significant hyperglycemia secondary to oral corticosteroid therapy. The increase of blood urea nitrogen could be misinterpreted as worsening of chronic renal disease in the elderly, who have an increased prevalence of underlying renal insufficiency.

- Cognitive function side effects. The adverse effects of oral corticosteroids on cognitive function are likely to have a greater impact if the elderly patient has preexisting impairment (Seaton, 1985).
- Musculoskeletal side effects. A significant reduction in bone mineral content has been associated with corticosteroid use regardless of route of administration (Crompton, 1987). Corticosteroid acceleration of osteoporosis, which is more prevalent in the elderly, is a concern. Further, normal changes in estrogen levels in females affect calcium utilization, and many elderly persons are less active and less likely to participate in the weight-bearing activities that help prevent or reduce the effects of osteoporosis.

  Another possible effect is that myopathy during treatment with oral corticosteroids and articular pain with withdrawal potentially limit the mobility of elderly patients because of their decreasing muscular strength and increasing prevalence of arthritis.
- Ophthalmologic side effects. An increase in intraocular pressure is a side effect of oral corticosteroid therapy, and this is a significant concern because glaucoma is a relatively common condition in the elderly. The cataracts of the elderly differ from the posterior subcapsular cataracts resulting from oral corticosteroid therapy (Urban & Cottleir, 1986). However, the increase in lens opacity from corticosteroids could have a greater impact on sight when superimposed on preexisting cataracts or retinal disease in the elderly.
- Gastrointestinal side effects. Oral corticosteroids may aggravate existing peptic and gastric ulcer disease, both of which are not infrequent in the elderly, who are often treated with nonsteroidal, anti-inflammatory drugs (Messer et al., 1983).

Inhaled Corticosteroid Therapy. Inhaled corticosteroids are particularly important in the elderly to facilitate control of asthma and avoid the adverse effects of systemic corticosteroids (Toogood, Jennings et al., 1993). The chronically impaired lung function of many elderly asthma patients does not decrease the therapeutic potential of inhaled corticosteroids (Woolcock et al., 1988).

Although safer than systemic therapy, long-term inhaled corticosteroid therapy used in relatively high doses (greater than 1.6 mg/day) can cause dose-dependent adverse effects. The benefits of inhaled corticosteroids must be weighed against the risk of inadequately treated asthma and the risks of other treatment forms. These include the following adverse effects:

- Posterior subcapsular cataracts, although rare, have been reported in subjects who received inhaled corticosteroid therapy. Further study indicates this effect is instead related to the dose and duration of patients' past or current treatment with systemic corticosteroids; the general risk of cataracts for patients taking inhaled corticosteroids is

negligible, although there is a potential risk for individuals with a high inherent susceptibility to cataracts (Toogood, Markov et al., 1993).

- A dose-dependent, yet significant reduction in bone mineral content of subjects with asthma has been associated with inhaled corticosteroid use (Jutta, 1994; Packe et al., 1992; Puolijoki et al., 1992; Reid et al., 1986; Toogood et al., 1988). Elderly patients may be more at risk due to preexisting osteoporosis and previous use of oral corticosteroid, the normal changes of estrogen in aging that affect calcium utilization, and a sedentary lifestyle.
- Dermal thinning and increased ease of skin bruising have been observed in elderly subjects treated with inhaled corticosteroids. Select members of the population have increased susceptibility to this adverse event. The effect is dose dependent, but the threshold dose is variable. At the least, this development indicates that systemic effects occur with inhaled corticosteroids. Dermal thinning tends to be primarily cosmetic but could lead to reduced compliance.

Cromolyn Sodium. Therapy with cromolyn sodium does not seem as effective in the elderly as it is in children, but the apparent ineffectiveness may be related to the fixed obstructive lung disease or chronic bronchitis components of asthma in the elderly (Murphy, 1992).

Nedocromil Sodium. The role of nedocromil sodium is as yet undefined for elderly patients, although its profile of minimal adverse effects makes a therapeutic trial a consideration for some subjects.

Leukotriene Antagonists. Pharmacologic agents that interfere with the synthesis or action of leukotrienes may soon become available. Leukotriene antagonists reduce bronchospasm following exercise, aspirin challenge in aspirin-sensitive subjects, and allergen challenge in allergic subjects. Studies suggest leukotriene antagonists may permit modest reductions in inhaled corticosteroids, reduce use of beta-agonists, and reduce the frequency of asthma exacerbations (Drazen & Israel, 1995). However, the role of these agents in the management of asthma is yet to be determined.

Bronchodilators

Inhaled Beta$_2$-Agonists. Inhaled short-acting beta$_2$-agonists are the most effective bronchodilator for patients with asthma regardless of age. Some elderly patients with asthma may prefer nebulizer rather than metered-dose inhaler delivery because of the moisturizing effect and because hand-diaphragm coordination is not required. Other patients may feel that reliance on a machine negatively affects their quality of life.

Long-acting inhaled beta$_2$-agonists are now available (Lofdahl & Chung, 1991). This class of bronchodilators have a duration of action exceeding 12 hours, are more potent bronchodilators in puff-to-puff comparisons with short-acting beta$_2$-agonists, and inhibit allergen-induced early and late asthmatic responses. The inhibition of the late response is apparently by functional antagonism of bronchoconstriction rather than intrinsic anti-inflammatory effects (Weersink et al., 1994; Gardiner et al., 1994). Long-acting inhaled beta$_2$-agonists reduce asthma symptoms and may reduce, or at least do not increase, the frequency of exacerbations (Greening et al., 1994; Lotvall & Svedmyr, 1993). Their specific role in the management of asthma in the elderly is uncertain. In general, long-acting inhaled beta$_2$-agonists may be helpful as an adjunct to anti-inflammatory therapy in controlling chronic symptoms, especially nocturnal symptoms. It must be emphasized to the patient that long-acting inhaled beta$_2$-agonists are *not* to be used to treat acute symptoms or exacerbations.

Oral beta$_2$-agonists are usually avoided in the elderly because of side effects such as tremors.

Controversy concerning $beta_2$-agonist therapy (Wanner & Sears, 1995) and concerns about its contribution to increased morbidity and mortality from asthma continue (Fanta, 1989; Spitzer et al., 1992). Discussions so far have not focused on the elderly, but it may be assumed the problems are similar.

Adverse effects of $beta_2$-agonist therapy that should be considered in long-term asthma management in the elderly include the following:

- Myocardial oxygen consumption is increased, even by those $beta_2$-agonists relatively selective for the $beta_2$-receptor (Nicklas, 1991).
- Electrocardiogram changes, such as ST-T wave changes, and an increase in complex ventricular arrhythmias have been reported (Kinney et al., 1978).
- Hypokalemia, which is likely to be a more serious problem in the elderly, may result from the regular use of $beta_2$-agonists (Haalboom et al., 1985).
- Blood pressure may be increased, and the elderly are less able to adapt to these changes (Nicklas, 1991).
- Tremor, the result of stimulation of $beta_2$-receptors in skeletal muscle, is more likely to be a significant problem in the elderly (Fanta, 1989).
- Hypoxemia is little improved and sometimes aggravated. For the elderly with an increased prevalence of vascular and cardiac disease, hypoxemia is a potential risk (Collins et al., 1967; Harris, 1972).

Methylxanthines. Theophylline has been used for the treatment of chronic asthma and may be helpful in selected cases of acute severe asthma. Theophylline is generally considered a bronchodilator but may have other beneficial effects in the treatment of airway obstruction, for example, improvement of respiratory muscle function and stimulation of respiratory drive (Barnes & Pauwels, 1994; Djukanovic et al., 1995; Sullivan et al., 1994). However, theophylline has a narrow therapeutic range, and elderly patients have increased susceptibility to theophylline's adverse side effects, which include the following:

- Theophylline may produce cardiovascular side effects, particularly supraventricular tachycardias, and intensify the adverse effect of $beta_2$-agonists (Higbee et al., 1982; Levine et al., 1985). The cardiovascular effects are probably the result of cardiac adenosine receptor antagonism.
- Theophylline reduces exercise-induced angina and ST-segment depression but is arrhythmogenic. Although the relative cardiac toxicities of theophylline compared with the $beta_2$-agonists have not been defined, their combination is additive.

In addition, many elderly patients are more susceptible to changes in metabolism and the toxicities of theophylline. If the drug is used, elderly patients should be monitored for signs of toxicity (heart rate and rhythm, and central nervous system status), and target serum concentrations of 8 to 12 mcg/mL are recommended. Elderly subjects are at greater risk of theophylline toxicity than younger individuals, and serum levels should be monitored more carefully if serum concentration levels exceed 12 mcg/mL. Further, some medications may affect theophylline elimination and hence the serum theophylline level. For example, phenobarbital, phenytoin, isoproterenol, rifampin, and carbamazepine decrease serum theophylline levels, whereas cimetidine, troleandomycin, erythromycin, high-dose allopurinol, propranolol, clarithromycin, estrogen, mexiletine, pentoxifylline, tacrine, ticlopidine, ciprofloxacin, and verapamil increase serum theophylline levels.

Anticholinergics. Although ipratropium bromide, a synthetic atropine-like compound, is not considered primary asthma therapy, it may offer significant benefit for elderly patients. The drug may be more effective in older patients with a bronchitic component or those with longstanding asthma (Easton et al., 1986), perhaps because of the chronic, fixed obstruction that develops or because ipratropium has a lower incidence of tremor and arrhythmia (Atsmon, 1989) and is tolerated better than beta$_2$-agonists. Ipratropium is the bronchodilator of choice for patients taking beta-adrenergic blocking agents.

A side effect that is relatively common, but usually mild, is dry mouth and pharyngeal irritation (which may be a particular problem with elderly patients with idiopathic mucosal dryness or Sjögren's syndrome).

Patient Education Strategies

Inhalation Therapy. Appropriate inhalation therapy can be difficult for patients of all ages. Consensus on technique (open versus closed mouth; inhalation from functional residual capacity versus residual volume; head tilted back versus head held straight) is lacking. Improper technique even in patients previously instructed is common. Some usage problems are more likely to be seen in elderly patients than in younger patients.

- MDI technique should be observed at every patient visit, and the individual patient should be reinstructed as needed. Placebo inhalers are available from the pharmaceutical companies for use in teaching.
- Many elderly patients are physically unable to activate metered-dose inhalers because of decreased hand strength and arthritis. Their metered-dose inhaler technique should be observed and consideration given to use of spacers or breath-actuated inhalers.
- The closed-mouth technique is thought by the working group to be more successful because of the problem of coordination in the elderly. The closed-mouth technique is especially recommended in patients who use ipratropium (to avoid unintentionally spraying the eyes).
- The use of breath-actuated inhalers and dry aerosols may improve drug delivery to elderly patients.
- The use of spacers or reservoir units to improve the efficacy of drug delivery via MDI's is encouraged by the working group. Valved holding chambers may be more effective than tube spacers. A spacer or reservoir is required for inhaled corticosteroids to reduce deposition of the drug in the mouth. Clinicians should be familiar with several of these devices. Some patients, for example, do well with a tube-type spacer; others do better with a reservoir that can be observed to deflate with inspiration.
- Providing written instructions—in large type—and including illustrations on how to use a metered-dose inhaler and instructing a caregiver who is in the home are helpful for elderly patients with short-term memory problems.
- In teaching the use of inhalers and spacers, specific points to consider include the following:
  - Prior to each actuation the MDI should be shaken.
  - The inspiratory maneuver should be a slow, deep breath followed by an inspiratory hold.
  - When using a reservoir or holding device, the patient should activate the inhaler and then take a slow deep breath.
- Small-volume nebulizers are often recommended for patients who are unable to use MDI's appropriately. However, these patients

may have problems correctly preparing nebulized medications and problems in cleaning and disinfecting the equipment because of visual or hand-coordination difficulties. Thus unit dose preparations are necessary for many elderly patients because they may be unable to prepare the correct drug dosage using a dropper.

Medication Schedules. It is important to assist the patient in developing an achievable medication schedule (Opdycke et al., 1992). Many elderly patients have relatively unusual wake/sleep patterns, and many are taking multiple drugs. Their medication schedules need to be adjusted and simplified accordingly. Make clear which medications can be taken at the same time. It is also important to simplify the total regimen as much as possible. Possibilities include limiting the number of medications to be taken each day and prescribing twice a day dosing schedules. Although more frequent dosing may be necessary if symptoms are difficult to control, patient adherence to a treatment plan decreases with increasing complexity of the regimen (Becker, 1990). Elderly patients may find that reminder techniques are helpful, such as commercial medicine holders (or homemade holders using egg cartons) or large signs on the refrigerator. For drugs with doses that vary from day to day (for example, an oral corticosteroid prescribed every other day or during a period when medication is being tapered), a calendar on which the patient can mark off each daily dose promotes compliance with the treatment program.

Polypharmacy. Every visit by an elderly patient should include a review of what medicines the patient is taking and how the medicines are taken. Elderly patients who by history and past experience are known to confuse different medications should be encouraged to bring their medications to every visit. Others should do so occasionally. As already noted, drug interactions can cause severe problems. Factors that contribute to such problems, as well as to noncompliance with treatment plans, include lack of understanding of the importance of the medications or of how they are to be taken, use of nonprescription drugs, lack of social supervision, being too ill or tired to take the medications, and sensory losses.

LONG-TERM MANAGEMENT: A STEPWISE APPROACH TO THERAPY

The therapeutic approach to asthma in the elderly does not differ significantly from that recommended for younger adults with asthma (see NHLBI, 1991, 1992, 1995). There is no evidence to suggest that the overall therapeutic approach in the adult should be modified on the basis of the patient's age.

Asthma is classified by severity, and treatment is stepped up or stepped down as needed. Because asthma in elderly patients tends to be less episodic and variable, with more irreversible obstruction than in younger patients, the severity may be more difficult to classify (Barbee, 1995). Long-term management strategies for the elderly must take into consideration the greater likelihood of coexisting conditions and diseases. For example:

- The risk for adverse effects of asthma treatment is higher and the consequences may be more severe in elderly patients because their hepatic and renal functions—which represent the primary routes of drug metabolism and excretion—may be reduced. Alterations in protein binding and in percentage of total body water and fat may further affect the distribution of drugs in the body.
- Whenever therapy is increased (stepped up), the potential for drug and disease

interactions is greater in elderly patients with asthma because they tend to receive more medications for other conditions, such as heart disease, than do younger patients. As figure 4-3 indicates, toxic effects of beta$_2$-agonists and theophylline include tachyarrhythmias and possible aggravation of ischemic heart disease; and systemic corticosteroids may aggravate congestive heart failure and lower serum potassium with potentially adverse cardiac effects. Oral steroids and high-dose inhaled corticosteroids (e.g., more than 1,000 mcg/day) have the potential of accelerating osteoporosis. Although no clinical studies have proven that inhaled corticosteroids accelerate osteoporosis, some studies suggest there are some systemic effects of inhaled corticosteroids at doses greater than 1,000 mcg/day (Hollister, 1992; Packe, 1992; Ward, 1993). Nonetheless, the possible effect of not using inhaled corticosteroid is poorly controlled asthma, which in turn may reduce physical activity and/or require systemic corticosteroid therapy, both of which are factors proven to accelerate osteoporosis.

- Adherence to recommended asthma therapies may be difficult for elderly patients because of concurrent medical and other problems. Extensive patient education and special techniques (as discussed for each management component) are often needed to ensure optimum use of medications and procedures.
- The usefulness of environmental control measures is less certain among elderly patients with asthma. However, reducing exposure to known irritants and allergens may reduce symptoms and medication requirements.
- Measuring therapeutic outcome may be more difficult because of the increased prevalence of irreversible obstructive lung disease in the elderly. Achieving normal lung function may either be unattainable or require dangerously high pharmacologic doses. Close interaction between the clinician and the elderly asthma patient with significant attention to quality-of-life issues—including the restoration, maintenance, and extension of an independent, active, and personally satisfying lifestyle—should be an essential element in defining treatment goals.

The stepwise approach presented here represents general guidelines for making clinical decisions for treating asthma. Specific strategies for the long-term management of asthma must be tailored to the individual needs and circumstances of the individual patient.

Mild Asthma

A patient has mild, intermittent asthma if: the patient experiences symptoms or exacerbations less than two times a week, nocturnal symptoms less than two times a month, and is asymptomatic between exacerbations. Mild, intermittent asthma is treated as needed with the following:

- Inhaled bronchodilators (short-acting inhaled beta$_2$-agonists);
- Avoidance of known triggers;
- Annual influenza vaccination;
- Pneumococcal vaccination every 6 to 10 years, and;
- In some cases, an inhaled beta$_2$-agonist, cromolyn, or nedocromil prior to exposure to identified triggers.

If the patient has an increasing need for short-acting beta$_2$-agonist (e.g., uses short-acting beta$_2$-agonist more than three to four times in 1 day for an acute exacerbation or uses more than one canister a month for symptoms), the patient may require a stepup in therapy. But first, the patient's technique for using inhalers should be evaluated.

Moderate and Severe Asthma

A patient has moderate asthma if: the patient experiences exacerbations more than two times a week and the exacerbations affect sleep and activity; the patient has nighttime awakenings due to asthma more than two times a month; the patient has chronic asthma symptoms that require short-acting inhaled $beta_2$-agonist daily or every other day; and the patient's pretreatment baseline PEF or FEV_1 is 60 to 80 percent predicted and PEF variability is 20 to 30 percent.

A patient has severe asthma if: the patient has almost continuous symptoms, frequent exacerbations, frequent nighttime awakenings due to asthma, limited activities, PEF or FEV_1 baseline less than 60 percent predicted, and PEF variability of 20 to 30 percent.

Therapeutic considerations for the management of moderate asthma or severe asthma in the elderly are influenced by the presence or absence of a significant irreversible component of obstruction. The clinician may find it useful to administer a short course of oral corticosteroids (e.g., prednisone 0.3 to 1 mg/kg daily for 1 to 2 weeks) as a trial to assess improvement in pulmonary function.

Elderly Patients With Significant Reversibility of Obstruction (Without COPD).

- Anti-inflammatory therapy (inhaled corticosteroids, nedocromil, or cromolyn) should be initiated for patients with moderate-to-severe asthma. Inhaled corticosteroids may be the preferred anti-inflammatory therapy over nedocromil and cromolyn, which have been studied primarily in younger, allergic patients.
- Most importantly, a decision to initiate anti-inflammatory therapy should be patient-specific. The presence of concurrent medical conditions that limit the quality of life or increase the potential of drug toxicity, the need for other chronic medical treatment, which might reduce compliance or ability to afford chronic asthma therapy, and the consideration of the potential risks and benefits of asthma therapy may influence the decision concerning the use of anti-inflammatory agents.
- Long-acting inhaled $beta_2$-agonists, ipratropium, or sustained-release theophylline products may also be considered, especially to control nocturnal symptoms. If theophylline is used, it should be used cautiously in the elderly, especially due to potential cardiac toxicity; serum theophylline concentrations should be monitored routinely with target serum concentration between 8 and 12 mcg/mL.
- Short-acting $beta_2$-agonist therapy should be administered on an as-needed basis for acute symptoms. Monitoring the rate of use will provide an indication of need for additional therapies.
- Step up the regimen when asthma worsens or does not respond in a patient who is adherent with appropriate therapy of anti-inflammatory medication and long-acting bronchodilators and is using inhalers correctly. The regimen can be stepped up by increasing the dose of inhaled corticosteroid (e.g., to the equivalent of 1 to 2 mg of beclomethasone). Full response to therapy may require 4 to 8 weeks with continuing improvement seen up to 6 months. To improve compliance, patients should be reminded about the inflammatory nature of asthma and the rationale for chronic anti-inflammatory therapy. They should also be reassured about the safety of inhaled corticosteroids and advantages over systemic corticosteroid therapy. Oral side effects of inhaled corticosteroids (oral candidiasis, cough, and dysphonia) can be reduced by rinsing the mouth well after use and using a spacer/reservoir device.

- In some cases of worsening symptoms, a short course (7 to 14 days) of systemic corticosteroids may be needed. If prolonged systemic corticosteroid therapy is required, a regimen of alternate day, morning doses should be attempted to reduce the potential for adverse effects.
- Calcium (1,000 to 1,500 mg per day) and vitamin D (400 units per day) supplementation may be helpful for elderly female patients with asthma who are taking inhaled corticosteroids (Kanis & Pitt, 1992; Worth et al., 1994). Patients who require high doses of inhaled corticosteroids (e.g., more than 1,000 mcg per day) or systemic corticosteroids may require additional therapy such as estrogen replacement therapy, calcitonin, or bisphosphonates. At the present time, the optimal approach for identifying patients at greatest risk for accelerated bone loss due to corticosteroid therapy is to conduct bone densitometry prior to initiation of the high-dose corticosteroid therapy and repeat the bone densitometry 6 months later.

Elderly Patients Without Significant Reversibility of Airflow Obstruction (Presence of COPD). The coexistence of asthma and COPD often influences the selection of pharmacotherapy and the overall goals of treatment. For example:

- Goals of treatment vary because the response to bronchodilator medications may be less.
- Bronchodilator therapy is the primary therapy for the COPD patient, and thus higher rates of use will be expected (e.g., three to four times a day) than in patients with asthma alone. An increasing use of inhaled $beta_2$-agonist therapy remains an important indication of worsening asthma and a consequent need for increased anti-inflammatory therapy.
- The benefits of anti-inflammatory therapy (inhaled corticosteroids) for chronic management may be less apparent in patients with asthma who also have fixed obstruction. Nonetheless, these patients may benefit significantly from a therapeutic trial of inhaled corticosteroids.
- Ipratropium bromide therapy is considered earlier in the course of treatment for patients with chronic bronchitis or chronic fixed obstruction. Ipratropium bromide usually causes less tremor or arrhythmias than inhaled $beta_2$-agonists.
- Spirometry and peak flow measurements may be less reliable in assessing therapeutic endpoints in the elderly. Subjective parameters such as the number of symptomatic days, nighttime awakenings, and exercise tolerance may be more useful indices for monitoring the asthma and the patient's response to therapy.
- Elderly patients with asthma who have a significant component of COPD tend to be more chronically ill and have more coexisting diseases. These clinical factors may complicate, or even limit, the management of asthma.

MANAGEMENT OF EXACERBATIONS

Exacerbations are acute or subacute episodes of progressively worsening shortness of breath, cough, wheezing, or chest tightness, a loss of bronchodilator response, or some combination of these symptoms and signs. Management strategies for both home- and urgent care/hospital-based management of exacerbations for the elderly are, in general, the same as those recommended in the NAEPP guidelines (NHLBI, 1991). However, some changes due to the normal processes of aging, concerns about comorbid conditions and their treatment, and the presence of irreversible obstruction are warranted.

Home Management

Health care professionals need to make sure elderly patients understand how to monitor symptoms and identify signs (such as awakening at night due to asthma, an increased need for inhaled $beta_2$-agonist to relieve symptoms, or diminished response to inhaled $beta_2$-agonist) or changes in PEF (if PEF monitoring is used) that indicate their asthma is worsening. Each patient needs a written management plan that includes clear information on what to do.

Initiation of appropriate therapy at the earliest possible signs of worsening asthma is important. When patients are able to begin treatment at home, they not only avoid delays in treatment but also add to their sense of control over their asthma. The degree of care provided at home depends on the health care professional's and the patient's experience as well as the availability of medications and emergency care. For elderly patients, it also depends on their coexisting conditions, including their functional abilities, living situations, and social support.

Because action plans for managing exacerbations in elderly patients often need to accommodate comorbid diseases, the plans may need to specify earlier thresholds for medical supervision. For example, some patients may have heart disease and hypoxemia associated with the exacerbation, and hypokalemia from concomitant medications—particularly $beta_2$-agonists—may increase the risk of cardiac arrhythmias.

Written management plans should also include instructions on what to do when urgent medical attention is required—for example, if the response to inhaled $beta_2$-agonist is not prompt and sustained, if the attack is severe, or if the patient has difficulty talking in complete sentences, has difficulty walking, or has fingernails or lips that have turned blue. Further, steps on how to reach medical care should be clearly specified and easy to understand and follow.

Urgent Care and Hospital Management

Severe exacerbations of asthma are potentially life threatening. Care must be expeditious and in an urgent care or hospital-based setting.

Assessment. A brief history and physical examination prior to treatment will help determine that the episode is truly asthma and not acute pulmonary edema, myocardial ischemia, or some other event. The history should document possible coexisting cardiac disease, the presence and character of chest pain, all medications the patient is presently taking (including those not related to asthma management), and the history of any prior episodes of respiratory failure during an exacerbation in addition to symptom severity, possible causes of the present episode, and treatment that the patient may have initiated at home.

The physical examination should focus on excluding cardiac decompensation, determining the severity of the exacerbation, and identifying potential complications. Attention should be paid to signs of heart failure, including crackles, neck vein distension, gallop rhythm, and evidence of fluid overload. Wheezing may be a manifestation of pulmonary edema and is not a precise gauge of airflow obstruction. Extremely severe obstruction can be associated with a silent chest (Shim & Williams, 1980). Use of accessory muscles of respiration and the presence of pulsus paradoxus may be useful in predicting the severity of the airflow obstruction (Viola et al., 1990), but objective measures are still needed.

Physiologic assessments include spirometry or peak expiratory flow measures. In many elderly patients spirometry is preferred (see chapter II).

Arterial blood gas measurements should be obtained in all patients who demonstrate an FEV_1 of 25 percent or less of predicted or a PEF of 150 L/min or less, patients with a history of coexisting chronic obstructive pulmonary disease, patients who demonstrate altered mental status,

and patients who have a prior history of respiratory failure. The occurrence of severely altered gas exchange is more likely in the elderly because of aging effects on gas exchange (see chapter III) and the increased likelihood of coexisting heart and lung disease. For patients with significant irreversible obstruction, the usual hyperventilation during an acute exacerbation may not be mechanically possible, resulting in a normal $PaCO_2$ or, in those with severe disease, hypercapnia.

In elderly patients, the possibility of ventilatory failure is always a risk during an acute exacerbation of asthma, although clinicians who have thorough documentation of patients' baseline obstructive ventilatory defects are better able to predict which patients may be at risk of ventilatory failure (acute CO_2 retention) with an exacerbation. Pulse oximetry is not sufficient to rule out ventilatory failure.

Other assessments important in the elderly include chest x-rays and electrocardiograms. In order to differentiate asthma from acute cardiac disease, these measures often have high priority for older patients.

If the patient is on theophylline, measurements of serum theophylline are necessary because of the relationship in the elderly between elevated serum levels and cardiac symptoms.

Treatment. Most elderly patients do not require intubation (Mountain et al., 1990), but in the small minority who present *in extremis*, the first management question is whether to intubate. Arterial blood gas measurements provide information on the severity of the ventilatory failure (hypercapnia and acidemia), but deciding whether more conservative therapy is appropriate depends on the specific clinical situation and the clinician's judgment. If the patient is alert and responsive, bronchodilator therapy may reverse the situation to the point where intubation is not required. In the elderly, comorbid conditions, patient and family wishes, and living wills are also more likely to influence the decision. An elderly patient who requires mechanical ventilation should be managed by a physician skilled in this area (Brochard et al., 1995; Tobin, 1994).

As in younger patients, the primary medications to treat an exacerbation in an elderly patient are inhaled $beta_2$-agonists and systemic corticosteroids. Ipratropium bromide may also be used. Special considerations in the use of these—and other medications—in the care of the elderly are related to the side effects of the medications rather than differences in therapeutic effect. Possible side effects are discussed in Component 4—Pharmacologic Therapy, and potentially adverse interactions with nonasthma medications are examined in chapter III (see figures 3-1 and 4-3).

Repeated doses of aerosolized $beta_2$-agonists every 20 to 30 minutes during the first hour are safe in most elderly persons with asthma. However, attention should be given to changes in cardiac rhythm: continuous electrocardiographic monitoring may be needed during the initial stages of intense $beta_2$-agonist therapy, particularly in those with comorbid cardiac conditions and in those who have demonstrated arrhythmias. The working group members recommend the use of nebulizer-generated aerosols to ensure optimal delivery of $beta_2$-agonists in the elderly, even though specific data on the effectiveness of nebulizers versus metered-dose inhalers in urgent care are not yet available.

Patients who demonstrate hypoxemia (PaO_2 of less than 60 torr) should receive supplemental oxygen. The saturation in the initial blood gas measurements should be checked against those obtained with pulse oximetry, and the response to therapy in most circumstances can then be followed by pulse oximetry. (The changes in the oxyhemoglobin dissociation curve in response to changes in $PaCO_2$ and pH must be considered.) Administration of 1 to 2 L/min of oxygen by

nasal cannula is usually sufficient to bring the PaO_2 into an acceptable range. Note that giving oxygen in patients with asthma does not increase $PaCO_2$ as is frequently seen in COPD with CO_2 retention.

In addition, because arterial oxygen saturation may intermittently decline in response to $beta_2$-agonist therapy, elderly patients—especially those with known coronary artery disease—should receive supplemental oxygen to maintain arterial oxygen saturation greater than 92 percent.

The patient's response to initial therapy should be assessed by clinical symptomatology, objective measures of airflow obstruction, and measures of gas exchange. Failure of the FEV_1 to improve to a level of at least 50 percent of the patient's personal best indicates an unsatisfactory response. Note that the patient's spirometric or peak flow measures should use the patient's personal best as the reference value rather than predicted values. Many elderly patients have persistent airflow obstruction and may never have an FEV_1 of greater than 50 percent of predicted. However, if the personal best is not known, and the patient continues to demonstrate severe obstruction (FEV_1 less than 50 percent predicted), a conservative approach with prolonged observation of the patient is indicated. If the patient has required oxygen supplementation, arterial blood gas measurements or pulse oximetry should be monitored to evaluate response to oxygen and appropriate withdrawing of oxygen. In some patients, especially those with a nonreversible component of airflow obstruction, the gas exchange abnormality may not resolve as quickly as the airflow obstruction improves (Timms et al., 1981). Careful attention should be paid to the adequacy of gas exchange because elderly patients with a significant irreversible component to their airflow obstruction may be more likely to experience respiratory failure. An adequate oxygen saturation on room air should be documented before discontinuing oxygen.

Immediate administration of systemic corticosteroids (intravenous or by mouth) should be considered in patients with severe exacerbations who fail to improve after the initial dose of $beta_2$-agonist, in patients who develop an exacerbation while already taking oral corticosteroids, and in patients who have a history of frequent refractory episodes that require corticosteroids for resolution. Although the beneficial effects of the corticosteroids are delayed by 6 hours or more (Ellul-Micallef, 1982; Ellul-Micallef & Renech, 1975; Fanta et al., 1983), systemic corticosteroids given early in the course of treatment enhance the exacerbation's resolution.

In younger adults, subcutaneous administration of a $beta_2$-agonist is considered when the response to initial therapy is inadequate; but because of the danger of cardiac stimulation, subcutaneous bronchodilators are administered to the elderly only in life-threatening situations, and these patients should have electrocardiographic monitoring.

Ipratropium bromide is a therapy to consider in those patients with coexistent chronic obstructive pulmonary disease and to continue for those who have been taking the drug on a regular basis. Ipratropium bromide can be administered in solution form via a small-volume nebulizer, either by itself or together with a $beta_2$-agonist, for patients who are unable to use metered-dose inhalers effectively. In addition, administering ipratropium and $beta_2$-agonist together via a small-volume nebulizer often enhances the bronchodilator response.

Theophylline should be avoided in the initial (e.g., first 4 hours) emergency treatment of severe exacerbations in the elderly because of the uncertain benefits and the increased risk of toxicity and cardiac arrhythmias (Josephson et al., 1979; Rossing et al., 1980; Siegel et al., 1985). However, theophylline should be considered in treating a severe exacerbation that is unrespon-

sive to inhaled beta-agonist and corticosteroids, especially in a patient who is hospitalized or who is in respiratory failure.

Antibiotics are not recommended as routine therapy for asthma exacerbations. However, some elderly patients with asthma and coexisting COPD may benefit from a course of antibiotic therapy, especially if the exacerbation is characterized by an increase in sputum volume and viscosity. Greenish-yellow discoloration of sputum does not always signify infection. Eosinophils, which are commonly found in respiratory secretions in acute asthma, can cause sputum to have a mucopurulent appearance. Microscopic examination of the sputum to detect eosinophilia or neutrophilia may be helpful in making this decision. If the patient has increased sputum production, Gram stains are recommended to ensure that no unusual pathogen is present.

Attention should be paid to fluids and electrolytes (e.g., potassium levels). When elderly patients with asthma exacerbations are admitted to the hospital, they may be dehydrated due to the effect of dyspnea on fluid intake and increased insensible fluid loss. Hydration to reestablish normal balance should be instituted with care in order to restore cardiac filling pressures but avoid overhydration, which might lead to pulmonary vascular congestion and interstitial edema.

Discharge From Urgent Care or Emergency Department Setting. In discharging an elderly patient with asthma from urgent or emergency care, important considerations include the following:

- As a rule, continued treatment in the urgent care or emergency department setting should not be extended beyond 4 hours. If the elderly patient has not achieved sufficient improvement by that time, admission to the hospital is warranted. Alternatively, extended treatment in a holding area, clinical decision unit, or overnight unit with sufficient monitoring and nursing care may be appropriate.
- Aggressive therapy should continue for 3 to 5 days after discharge and should include a short course of oral corticosteroids.
- Close followup is recommended. Patients should be provided with clear instructions for contacting their asthma care provider for a followup office visit—or at least telephone contact—within 3 days of discharge from an urgent care or emergency department setting. The health care professional should consider contacting the patient after discharge to encourage followup.
- Medications should be carefully reviewed with the patient, with special attention to the schedule for corticosteroids. A written calendar is helpful. The patient's total medication program should also be reviewed to ensure, for example, that the patient does not discontinue nonasthma medication. Use of an inhaler and spacer, if prescribed, should be reviewed. Further, all medications should be reviewed with any person serving as a caregiver to the patient.
- Patients who are provided peak flow meters to use as part of their management program require instruction in how to use the meter and how to record the results. (See NAEPP "Guidelines for the Diagnosis and Management of Asthma" for examples [NHLBI, 1991].)
- Patients need written instructions on when and how to communicate with their health care provider. The asthma management plans for these patients may require revision and updating to ensure better asthma control.

Discharge From Hospital. The decision to discharge an elderly patient with asthma for home care is based on both subjective and objective criteria. Ideally the patient should be

symptom free. However, because more elderly persons with asthma have chronic persistent airflow obstruction even when optimally treated, such a goal may be unrealistic. At least 24 hours prior to discharge, the patient should be receiving all medications by the same routes by which they will be delivered at home (for example, using a metered-dose inhaler versus a small-volume nebulizer, and preparing his or her own nebulizer treatments if a nebulizer is to be used at home). Such planning also allows time to ensure the adequacy of the home program, provide patient education, and evaluate the person's ability to self-administer the therapy.

Some patients, who were previously not hypoxemic, may require oxygen at the time of discharge. In order to provide home oxygen, objective criteria documenting the need for oxygen must be met. Medicare and many third-party payers require that the resting PaO_2 while breathing room air be 55 torr or less, or that the arterial saturation (pulse oximetry is acceptable) be 88 percent or less. Other concurrent medical conditions or special considerations of changes in oxygenation during exercise or sleep affect the criteria. The clinician should contact the persons responsible for helping to arrange home oxygen therapy for specific criteria. (Note that most insurance plans, including Medicare, do not cover as-needed oxygen.) Oxygen is an expensive therapy that can have a dramatic effect on the person's lifestyle. It should be used to treat documented chronic hypoxemia and not prescribed for episodic dyspnea. If the patient did not previously require home oxygen therapy but does at the time of discharge after the exacerbation, the patient's oxygenation should be reassessed in several weeks; in many instances it requires a month for the person to return to his or her previous level of gas exchange (especially if the patient also has chronic obstructive pulmonary disease) (Levi-Valensi et al., 1986; Timms et al., 1981).

At discharge from the hospital, as from the urgent care or emergency setting, the patient must be instructed in the total medication program. Because the hospitalization may have resulted in changes in asthma and nonasthma medications, reviewing the entire program—and asking about other medicines taken at home that may not be listed in the present program—is important. Instructing the patient in home monitoring of asthma symptoms is also helpful.

The general physical condition of the elderly person must be considered prior to discharge. The elderly can rapidly become deconditioned when incapacitated, even for brief periods of time. Although prolonged hospitalization may further contribute to deconditioning, discharging a patient who cannot maintain activities of daily living in the home setting is unacceptable. Assessment of the home situation, including the physical capabilities of others in the home setting, may influence discharge plans. In some instances skilled nursing may be required in the home setting, and an interim supervised setting may be required before discharge to home.

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Chapter V
Research Recommendations

To increase our understanding of asthma in the elderly, the working group recommends further research that will:

- Increase knowledge of the epidemiology and natural history of asthma in the elderly by answering such questions as—
  - — Is there a real increase in asthma morbidity and mortality in the elderly?
  - — Are the epidemiology, natural history, pathophysiology, and pathology of late-onset asthma different from those of early-onset asthma? What are the etiologic and risk factors? Do race and gender play any part? Does long-term asthma lead to emphysema? What role does occupational exposure have in late-onset asthma?
- Clarify the role of familial and genetic factors in asthma that begins late in life.
- Evaluate the role of immune factors (particularly various cytokines and their cells of origin), neural factors, and viral and other infections in asthma in the elderly.
- Determine the relationship between pathologic changes and indices of lung function in elderly patients with asthma, particularly in relation to variations in the degree of irreversible obstruction.
- Determine the cellular and molecular mechanisms of the long-term effects of airway inflammation in relation to the development of irreversible obstruction.
- Evaluate possible quantitative differences between older and younger patients with asthma in terms of functional capabilities, severity of illness, comorbidity, emotional and cognitive status, and expectations from medical care.
- Determine the sensitivity, specificity, and role of PEF in elderly patients by—
  - — Comparing PEF with other tests of pulmonary function in detection of airflow obstruction in older populations.
  - — Determining relative usefulness of spirometry and PEF in the elderly for the assessment of exacerbations.
- Determine the sensitivity, specificity, and safety of bronchoprovocation with methacholine, histamine, and exercise challenge in the elderly.
- Evaluate differences in the relative efficacy of nebulizer-generated aerosols versus metered-dose inhalers in elderly patients with asthma in the emergency department setting.
- Evaluate the long-term safety of inhaled corticosteroids in elderly patients with asthma.
- Determine the effectiveness of nedocromil sodium in elderly patients with asthma.
- Reevaluate criteria for the exclusion of elderly patients from clinical pharmacology trials based on their comorbid conditions. Unnecessarily restrictive study entry criteria

limit the general application of research results. Further, the study of elderly subjects requires improved statistical methods to control for confounding variables encountered in clinical trials

- Determine methods and instruments for measuring functional status and health-related quality-of-life treatment outcomes that are of particular importance to elderly patients with asthma.

Discrimination Prohibited: Under provisions of applicable public laws enacted by Congress since 1964, no person in the United States shall, on the grounds of race, color, national origin, handicap, or age, be excluded from participation in, be denied the benefits of, or be subjected to discrimination under any program or activity (or, on the basis of sex, with respect to any education program or activity) receiving Federal financial assistance. In addition, Executive Order 11141 prohibits discrimination on the basis of age by contractors and subcontractors in the performance of Federal contracts, and Executive Order 11246 states that no federally funded contractor may discriminate against any employee or applicant for employment because of race, color, religion, sex, or national origin. Therefore, the National Heart, Lung, and Blood Institute must be operated in compliance with these laws and Executive Orders.

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