Medical Education Systems, Inc.

Course 606

ASTHMA TODAY: DEFINITION/DIAGNOSIS/CAUSES

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Asthma Today: Definition/Diagnosis/Causes

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Introduction

The information in this Continuing Education Unit is intended to aid health care professionals in diagnosing and managing patients with asthma. Much of the information is adopted from the National Asthma Education and Prevention Program Expert Panel Report II: Guidelines for the Diagnosis and Management of Asthma.

The recommendations for diagnosis and pharmacologic therapy are intended to be general guidelines for making therapeutic decisions. They are not intended to be prescriptions for individual treatment**.** Specific therapy should be tailored to the needs and circumstances of individual patients.

Learning Objectives

Upon successful completion of this continuing education module, you will be able to:

- Identify the definition, pathogenesis, and classification of asthma.
- Indicate the signs, symptoms, and diagnostic findings associated with asthma.
- Identify the available monitoring techniques and treatment measures for asthma
- Discuss the strategies for reducing exposure to asthma triggers.

Asthma Today

Recently, asthma has been getting quite a bit of attention in the popular news media. One example can be seen in a newspaper report:

CHICAGO -- Northwestern football player Rashidi Wheeler had the stimulant ephedrine in his system when he collapsed during a grueling Aug. 3, 2001 workout, but the banned substance did not cause his death, the Cook County medical examiner said Monday. "We do not think this contributed to his death," Dr. Edmund Donoghue said. "We think this is a classic case of exercise-induced bronchial asthma."

Wheeler, a chronic asthmatic, collapsed during a preseason conditioning drill involving a series of wind sprints and was pronounced dead a short time later at an Evanston hospital. Wheeler's mother, Linda Will, has said the university wasn't prepared to deal with such an emergency during what was supposed to be a voluntary preseason workout. She has enlisted the help of Rev. Jesse Jackson and attorney Johnnie Cochran Jr. The university is investigating the incident, including questions about whether Wheeler took a nutritional supplement containing a form of ephedrine, a substance banned by the NCAA that has been linked to strokes and heart attacks.

The amount of the stimulant in Wheeler's system was "well below toxic or lethal levels," Donoghue said. "The levels are consistent with what someone might have if you had taken that supplement the day he died," Donoghue said. A Northwestern spokesman reiterated Monday that university officials, coaches and players would not comment on the circumstances surrounding Wheeler's death until its review panel's report is released.
The spokesman said no date has been determined for the release of the report.

Attorneys for Wheeler's family have videotapes of his final practice. The tapes supplied by the university's athletic staff show Wheeler wobbling and dropping to his knees during wind sprints. During the sprints, unidentified persons are heard encouraging Wheeler to pick up the pace. The tape also shows paramedics trying unsuccessfully to save Wheeler's life -- while teammates continued a conditioning drill.

There were also stories about the Minnesota Vikings player Korie Stringer's death being somehow linked to an asthmatic condition. Those types of stories, and more focus on adult onset asthma have led to considerably more attention being paid to this potentially deadly disease condition.

The statistics surrounding asthma are also astounding:

Statistics

Statistics related to asthma and allergies:

According to the latest available from the National Institute of Allergy and Infectious Diseases (NIAID), consider the following statistics:

Asthma:

- More than 17 million people in the US have been diagnosed with asthma.
- Asthma is the sixth most common chronic condition in the US.
- Asthma affects more than 4.8 million US children, making it the most common serious and chronic disease among children.
- Asthma accounts for 10 million absences from school each year.
- Asthma is 26 percent more prevalent in African-American children than in Caucasian children.
- African-American children with asthma, most often from inner city populations, generally experience more severe disability from asthma and have more frequent hospitalizations than do Caucasian children.
- Asthma is the third most common cause of childhood hospitalizations under the age of 15.
- More than 200,000 children with asthma experience more severe symptoms due to exposure to secondhand smoke.
- About 10 million visits annually to office-based physicians result in a diagnosis of asthma.
- Asthma cases and asthma deaths have been on the rise. From 1979 to 1996, asthma deaths have risen 120 percent from 2,598 to 5,667.
- Hospitalizations for asthma have increased 256 percent from 1979 to 1996, to 474,100 people annually.
- Asthma treatment costs an estimated $11.3 billion, including direct and indirect expenditures each year.
- Asthma causes nearly 3 million lost workdays each year for people over age 18.

Allergy:

- Previous surveys estimate that allergies affect as many as 40 to 50 million people in the US.
- Pollen allergy (hay fever or allergic rhinitis) affects nearly 10 percent of the people in the US (26 million people), not including those with asthma.
- Allergic dermatitis (itchy rash) is the most common skin condition in children younger than 11 years of age.
- Urticaria (hives; raised areas of reddened skin that become itchy) and angioedema (swelling of throat tissues) together affect approximately 15 percent of the US population every year.
- Chronic sinusitis, most often caused by allergies, affects nearly 35 million people in the US.
- Allergic drug reactions, commonly caused by antibiotics such as penicillin and cephalosporins, occur in 2 to 3 percent of hospitalized patients.
- Eight percent of children younger than 6 years old experience food intolerances. Of this group, 2 to 4 percent appear to have reproducible allergic reactions to food. In adults, an estimated 1 to 2 percent are sensitive to foods or food additives.
- A severe allergic reaction known as anaphylaxis occurs in 3.3 percent of the US population as a result of insect stings. At least 40 deaths each year result from insect sting anaphylaxis.

These stories and statistics have lead us at Medical Education Systems to see the need for an overview/review course on the disease. We hope you benefit from the following information:

Pathogenesis and Definition

The clinician, physiologist, immunologist, and pathologist all may have different perspectives on asthma based on their individual viewpoints and experience. The merging of these different perspectives into an acceptable definition of asthma has begun to occur and is important for more specific and effective treatment of this disease and for investigation into its pathogenesis. Furthermore, even though this disorder affects virtually the entire spectrum of life, asthma has certain age-specific characteristics and differential diagnosis issues that need to be considered in both its treatment and its etiology.

Based on current knowledge, a working definition of asthma is: *Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, T lymphocytes, macrophages, neutrophils, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyperresponsiveness to a variety of stimuli* (NHLBI 1995). Moreover, recent evidence indicates that subbasement membrane fibrosis may occur in some patients with asthma and that these changes contribute to persistent abnormalities in lung function (Roche 1991).

This working definition and its expanded recognition of key features of asthma have been derived from studying how airway changes in asthma relate to various factors associated with the development of allergic inflammation (e.g., allergens, respiratory viruses, and some occupational exposures, as illustrated in figure 1). From this approach has come a more comprehensive understanding of asthma pathogenesis, the development of persistent airway inflammation, and the profound implications these issues have for the diagnosis, treatment, and potential prevention of asthma.

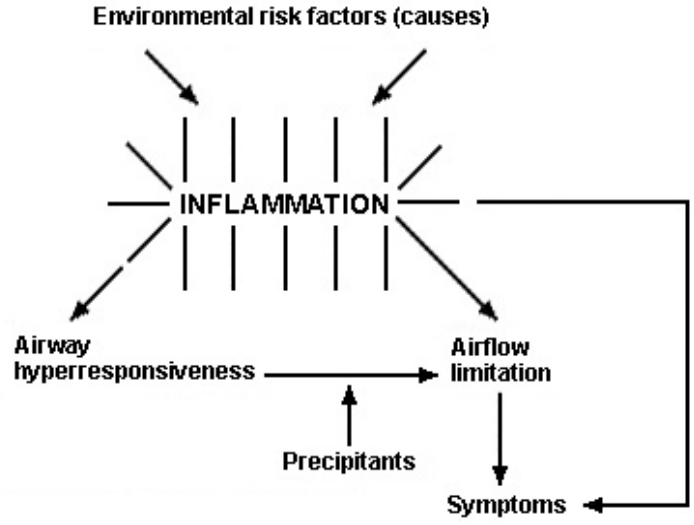

Figure 1: Mechanisms underlying the definition of asthma.

AIRWAY PATHOLOGY AND ASTHMA

Until recently, information on airway pathology in asthma has come largely from post-mortem examination (Dunnill 1960), which shows that both large and small airways often contain plugs composed of mucus, serum proteins, inflammatory cells, and cellular debris. Viewed microscopically, airways are infiltrated with eosinophils and mononuclear cells, and there is vasodilation and evidence of microvascular leakage and epithelial disruption. The airway smooth muscle is often hypertrophied, which is characterized by new vessel formation, increased numbers of epithelial goblet cells, and deposition of interstitial collagens beneath the epithelium. These features of airway wall remodeling further underscore the importance of chronic, recurrent inflammation in asthma and its effects on the airway. Moreover, these morphologic changes may not be completely reversible. Consequently, research is currently focused on determining whether these changes can be prevented or modified by early diagnosis, avoidance of factors that contribute to asthma severity, and pharmacologic therapy directed at suppressing airway inflammation.

Establishing the relationship between the pathologic changes and the clinical features of asthma has been difficult. Fiberoptic bronchoscopy with lavage and biopsy provide new insight into mechanisms of airway disease and features that link altered lung function to a specific type of mucosal inflammation (Laitinen et al. 1985; Beasley et al. 1989; Jeffery et al. 1989). From such studies, evidence has emerged that mast cells, eosinophils, epithelial cells, macrophages, and activated T cells are key features of the inflammatory process of asthma (Djukanovic et al. 1990), as illustrated in figure 2. These cells can influence airway function through secretion of preformed and newly synthesized mediators that act either directly on the airway or indirectly through neural mechanisms (Emanuel and Howarth 1995). Furthermore, with the use of cellular and molecular biological techniques, subpopulations of T lymphocytes (TH2) have been identified as important cells that may regulate allergic inflammation in the airway through the release of selective cytokines and also establish disease chronicity (Robinson et al. 1992). In addition, constituent cells of the airway, including fibroblasts, endothelial cells, and epithelial cells, also contribute to this process by releasing cytokines and chemokines.

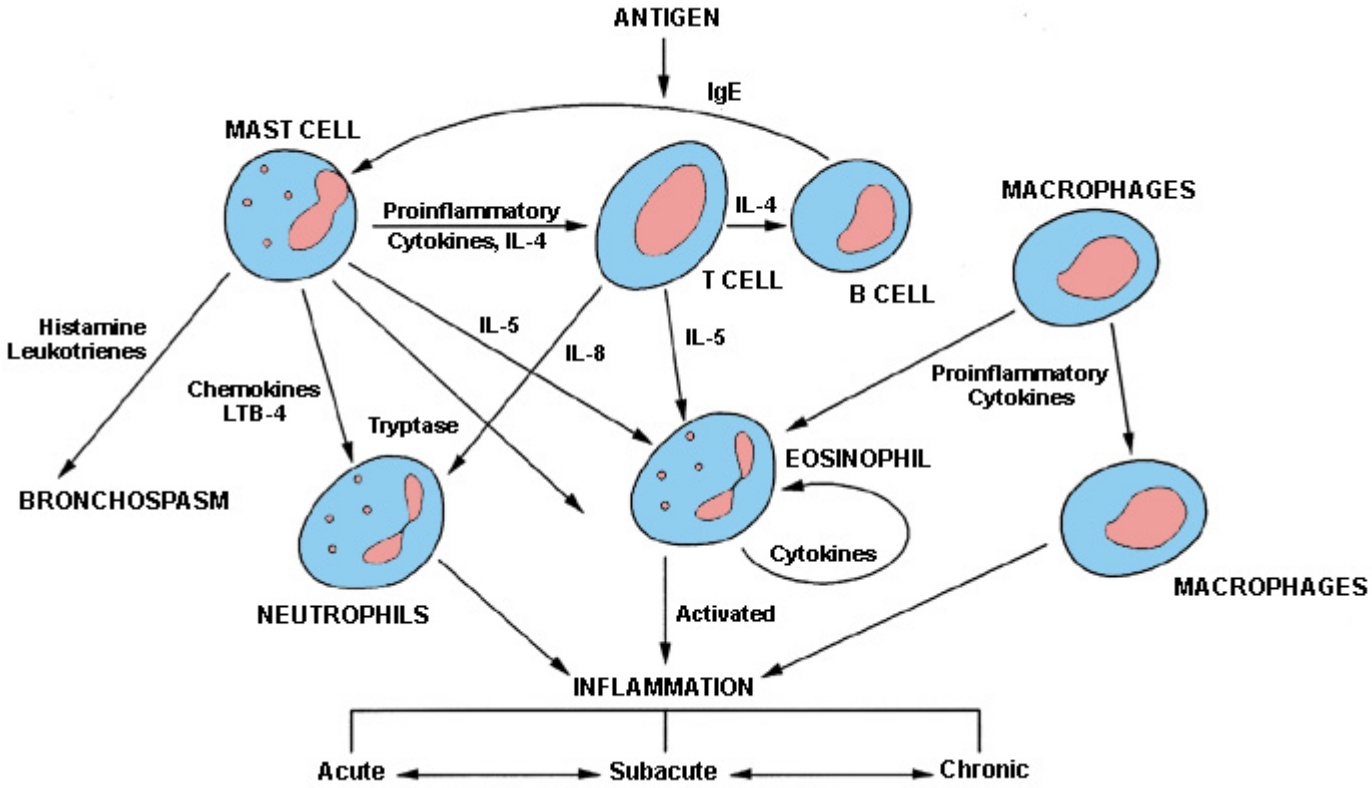

Figure 2: Cellular Mechanisms Involved in Airway Inflammation.

The above factors may be important in both initiating and maintaining the level of airway inflammation (Robinson et al. 1993). It is hypothesized that airway inflammation can be acute, subacute, and chronic. The acute inflammatory response is represented by the early recruitment of cells to the airway. In the subacute phase, recruited and resident cells are activated to cause a more persistent pattern of inflammation. Chronic inflammation is characterized by a persistent level of cell damage and an ongoing repair process, changes that may cause permanent abnormalities in the airway.

Finally, it is recognized that specific adhesion proteins, found in the vascular tissue, lung matrix, and bronchial epithelium, may be critical in directing and anchoring cells in the airway, thus causing the inflammatory changes noted (Albelda 1991). From these studies of the histological features associated with asthma has come evidence of an association between airway inflammation and markers of airway disease severity and an indication that this process is multicellular, redundant, and self-amplifying. Cell-derived mediators can influence airway smooth muscle tone, modulate vascular permeability, activate teneurons, stimulate mucus secretion, and produce characteristic structural changes in the airway (Horwitz and Busse 1995). These mediators can target ciliated airway epithelium to cause injury or disruption. As a consequence, epithelial cells and myofibroblasts—present beneath the epithelium—proliferate and begin to deposit interstitial collagens in the lamina reticularis of the basement membrane. This may explain apparent basement membrane thickening and the irreversible airway changes that may occur in some asthma patients (Roche 1991). Other changes, including hypertrophy and

hyperplasia of airway smooth muscle, increases in goblet cell number, enlargement of submucous glands, and remodeling of the airway connective tissue, are components of asthma that need to be recognized in both its pathogenesis and treatment. This inflammatory process is redundant in its ability to alter airway physiology and architecture.

Child-Onset Asthma

Asthma often begins in childhood, and when it does, it is frequently found in association with atopy, which is the genetic susceptibility to produce IgE directed toward common environmental allergens, including house-dust mites, animal proteins, and fungi (Larsen 1992). With the production of IgE antibodies, mast cells and possibly other airway cells (e.g., lymphocytes) are sensitized and become activated when they encounter specific antigens. Although atopy has been found in 30 to 50 percent of the general population, it is frequently found in the absence of asthma. Nevertheless, atopy is one of the strongest predisposing factors in the development of asthma (Sporik et al. 1990). Furthermore, among infants and young children who have wheezing with viral infections, allergy or family history of allergy is the factor that is most strongly associated with continuing asthma through childhood (Martinez et al. 1995).

Adult-Onset Asthma

Although asthma begins most frequently in childhood and adolescence, it can develop at anytime in life. Adult-onset asthma can occur in a variety of situations. In adult-onset asthma, allergens may continue to play an important role. However, in some adults who develop asthma, IgE antibodies to allergens or a family history of asthma are not detected. These individuals often have coexisting sinusitis, nasal polyps, and sensitivity to aspirin or related nonsteroidal anti-inflammatory drugs. The mechanisms of nonallergic, or intrinsic, asthma are less well established, although the inflammatory process is similar (but not identical) to that seen in atopic asthma (Walker et al. 1992). Occupational exposure to workplace materials (animal products; biological enzymes; plastic resin; wood dusts, particularly cedar; and metals) can cause airway inflammation, bronchial hyperresponsiveness, and clinical signs of asthma (Chan-Yeung and Malo 1994; Fabbri et al. 1994). Identification of the causative agent and its removal from the workplace can reduce symptoms; however, some individuals will have persistent asthma even though exposure to the causative agent is eliminated. The mechanisms of this form of asthma are not clearly established.

RELATIONSHIP OF AIRWAY INFLAMMATION AND LUNG FUNCTION

Airway Hyperresponsiveness

An important feature of asthma is an exaggerated bronchoconstrictor response to a wide variety of stimuli. The propensity for airways to narrow too easily and too much is a major, but not necessarily unique, feature of asthma. Airway hyperresponsiveness leads to clinical symptoms of wheezing and dyspnea after exposure to allergens, environmental irritants, viral infections, cold air, or exercise. Research indicates that airway hyperresponsiveness is important in the pathogenesis of asthma and that the level of airway responsiveness usually correlates with the clinical severity of asthma.

Airway hyperresponsiveness can be measured by inhalation challenge testing with methacholine or histamine, as well as after exposure to such nonpharmacologic stimuli as hyperventilation with cold dry air, inhalation of hypotonic or hypertonic aerosols, or after exercise (O'Connor et al. 1989). In addition, variability between morning and evening peak expiratory flow (PEF) appears to reflect airway hyperresponsiveness and may serve as a measure of airway hyperresponsiveness, asthma instability, or asthma severity. The factors contributing to airway inflammation in asthma are multiple and involve a variety of different inflammatory cells (as illustrated in figure 2) (Busse et al. 1993). It is also apparent that asthma is not caused by either a single cell or a single inflammatory mediator but rather results from complex interactions among inflammatory cells, mediators, and other cells and tissues resident in airways. An initial trigger in asthma may be the release of inflammatory mediators from bronchial mast cells, macrophages, T lymphocytes, and epithelial cells. These substances direct the migration and activation of other inflammatory cells, such as eosinophils and neutrophils, to the airway where they cause injury, such as alterations in epithelial integrity, abnormalities in autonomic neural control of airway tone, mucus hypersecretion, change in mucociliary function, and increased airway smooth muscle responsiveness.

The importance of the airway inflammatory response to airway hyperresponsiveness is substantiated by several observations. First, airway markers of inflammation correlate with bronchial hyperresponsiveness. Second, treatment of asthma and modification of airway inflammatory markers not only reduce symptoms but also diminish airway responsiveness. However, the relationship between airway inflammation and airway responsiveness is complex. Some investigations have shown that although anti-inflammatory therapy reduced airway hyperresponsiveness, it did not eradicate it. A small study found that control of airway inflammation did not control bronchial hyperresponsiveness (Lundgren et al. 1988). Thus, factors in addition to inflammation may contribute to airway hyperresponsiveness.

Airflow Obstruction

Airflow limitation in asthma is recurrent and caused by a variety of changes in the airway. These include:

- Acute bronchoconstriction. Allergen-induced acute bronchoconstriction results from an IgE-dependent release of mediators from the mast cell that include histamine, tryptase, leukotrienes, and prostaglandins (Marshall and Bienenstock 1994), which directly contract airway smooth muscle. Aspirin and other nonsteroidal anti-inflammatory drugs can also cause acute airflow obstruction in some patients, and evidence indicates that this non-IgE-dependent response also involves mediator release from airway cells (Fischer et al. 1994). In addition, other stimuli, including exercise, cold air, and irritants, can cause acute airflow obstruction. The mechanisms regulating the airway response to these factors are less well defined, but the intensity of the response appears related to underlying airway inflammation (Busse et al. 1993). There is emerging evidence that stress can play a role in precipitating asthma exacerbations. The mechanisms

involved have yet to be established and may include enhanced generation of pro-inflammatory cytokines (Friedman et al. 1994).

- Airway edema. Airway wall edema, even without smooth muscle contraction or bronchoconstriction, limits airflow in asthma. Increased microvascular permeability and leakage caused by released mediators also contribute to mucosal thickening and swelling of the airway. As a consequence, swelling of the airway wall causes the airway to become more rigid and interferes with airflow.
- Chronic mucus plug formation. In severe intractable asthma, airflow limitation is often persistent. In part, this change may arise as a consequence of mucus secretion and the formation of inspissated mucus plugs.
- Airway remodeling. In some patients with asthma, airflow limitation may be only partially reversible. The etiology of this component is not as well studied as other features of asthma but may relate to structural changes in the airway matrix that may accompany longstanding and severe airway inflammation. There is evidence that a histological feature of asthma in some patients is an alteration in the amount and composition of the extracellular matrix in the airway wall (Djukanovic et al. 1990; Laitinen and Laitinen 1994). As a consequence of these changes, airway obstruction may be persistent and not responsive to treatment. Regulation of this repair and remodeling process is not well established, but both the process of repair and its regulation are likely to be key events in explaining the persistent nature of the disease and limitations to a therapeutic response. Although yet to be fully explored, the importance of airway remodeling and the development of persistent airflow limitation suggest a rationale for early intervention with anti-inflammatory therapy.

RELEVANCE OF CHRONIC AIRWAY INFLAMMATION TO ASTHMA THERAPY

Although inflammation can be used to describe a variety of conditions in various diseases, the inflammatory response in asthma has special features that include eosinophil infiltration, mast cell degranulation, interstitial airway wall injury, and lymphocyte activation. Furthermore, there is evidence that a TH2 lymphocyte cytokine profile (i.e., IL-4 and IL-5) is instrumental in initiating and sustaining the inflammatory process (James and Kay 1995; Ricci et al. 1993) (see figure 2). These observations also have become important in directing treatment in asthma. It is hypothesized that inflammation is an early and persistent component of asthma. As a consequence, therapy to suppress the inflammation must be long term. Furthermore, preliminary evidence suggests that early intervention with anti-inflammatory therapy may modify the disease process (Agertoft and Pedersen 1994; Laitinen et al. 1992; Djukanovic et al. 1992). Observations into the basic mechanisms of asthma have had tremendous impact and influence on therapy. Studies have shown that improvements in asthma control achieved with high doses of inhaled corticosteroids are associated with improvement in markers of airway inflammation (Laitinen et al. 1992; Djukanovic et al. 1992). These observations indicate that a strong link may exist between features of airway inflammation, bronchial hyperresponsiveness, and asthma symptoms and severity. Furthermore, insight into the mechanisms of asthma with airway inflammation and

bronchial wall repair has become a driving factor in designing logical, and hopefully effective, treatment paradigms. Another area that needs clarification is the classification of compounds as anti-inflammatory in nature. Because many factors contribute to the inflammatory response in asthma, many drugs may fit this category. At present, corticosteroids are the anti-inflammatory compounds that have been demonstrated to modify histopathological features of asthma (Barnes 1995). It may be necessary to evaluate each new compound for the specificity of its “anti-inflammatory" action and determine from appropriate observations whether the compound is indeed anti-inflammatory and what consequences this has on the clinical features of the disease.

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Unit One: Measures of Assessment and Diagnosis of Asthma

Section A: Initial Assessment and Diagnosis of Asthma

Key Points:

To establish a diagnosis of asthma, the health care practitioner should determine that:

- **Episodic symptoms of airflow obstruction are present.**
- **Airflow obstruction is at least partially reversible.**
- **Alternative diagnoses are excluded.**

Recommended mechanisms to establish the diagnosis are:

- **Detailed medical history**
- **Physical exam focusing on the upper respiratory tract, chest, and skin**
- **Spirometry to demonstrate reversibility**

Additional studies may be considered to:

- **Evaluate alternative diagnoses**
- **Identify precipitating factors**
- **Assess severity**
- **Investigate potential complications**

Recommendations are presented for referral for consultation or care to a specialist in asthma care.

The guidelines to help establish a diagnosis of asthma presented in this Unit are based on the opinion of the Expert Panel. **The health care professional trying to establish a diagnosis of asthma should determine that:**

- **Episodic symptoms of airflow obstruction are present.**
- **Airflow obstruction is at least partially reversible.**
- **Alternative diagnoses are excluded.**

A careful medical history, physical examination, pulmonary function tests, and additional tests will provide the information needed to ensure a correct diagnosis of asthma (see Box 1). Each of these methods of assessment is described in this section. Clinical judgment is needed in conducting the assessment for asthma. Patients with asthma are heterogeneous and present signs and symptoms that vary widely from patient to patient as well as within each patient over time.

Box 1

Consider asthma and performing spirometry if *any* of these indicators are present.* These indicators are not diagnostic by themselves, but the presence of multiple key indicators increases the probability of a diagnosis of asthma. **Spirometry is needed to establish a diagnosis of asthma.**

- Wheezing—high-pitched whistling sounds when breathing out—especially in children. (Lack of wheezing and a normal chest examination do not exclude asthma.)
- History of any of the following:
  - Cough, worse particularly at night
  - Recurrent wheeze
  - Recurrent difficulty in breathing
  - Recurrent chest tightness
- Reversible airflow limitation and diurnal variation as measured by using a peak flow meter, for example:
  - Peak expiratory flow (PEF) varies 20 percent or more from PEF measurement on arising in the morning (before taking an inhaled short-acting $beta_2$ -agonist) to PEF measurement in the early afternoon (after taking an inhaled short-acting $beta_2$ -agonist).
- Symptoms occur or worsen in the presence of:
  - Exercise
  - Viral infection
  - Animals with fur or feathers
  - House-dust mites (in mattresses, pillows, upholstered furniture, carpets)
  - Mold
  - Smoke (tobacco, wood)
  - Pollen
  - Changes in weather
  - Strong emotional expression (laughing or crying hard)
  - Airborne chemicals or dusts
  - Menses
- Symptoms occur or worsen at night, awakening the patient.

*Eczema, hay fever, or a family history of asthma or atopic diseases are often associated with asthma, but they are not key indicators.

MEDICAL HISTORY

A detailed medical history of the new patient known or thought to have asthma should address the items listed in figure 1-1. The medical history can help:

- *Identify the symptoms likely to be due to asthma.* See figure 1-2 for sample questions.
- *Support the likelihood of asthma* (e.g., patterns of symptoms, family history of asthma or allergies).

- *Assess the severity of asthma* (e.g., symptom frequency and severity, exercise tolerance, hospitalizations, current medications). See figure 1-3 for a description of the levels of asthma severity or have the computer score your patient's severity.
- *Identify possible precipitating factors* (e.g., viral respiratory infections; exposure at home, work, day care, or school to inhalant allergens or irritants such as tobacco smoke). See Unit 2, Control of Factors Contributing to Asthma Severity, for more details.

Figure 1-1: Suggested Items for Medical History ↓

A detailed medical history of the new patient who is known or thought to have asthma should address the following items:

1. Symptoms

- Cough
- Wheezing
- Shortness of breath
- Chest tightness
- Sputum production

2. Pattern of Symptoms

- Perennial, seasonal, or both
- Continual, episodic, or both
- Onset, duration, frequency (number of days or nights, per week or month)
- Diurnal variations, especially nocturnal and on awakening in early morning

3. Precipitating and/or aggravating factors

- Viral respiratory infections
- Environmental allergens, indoor (e.g., mold, house-dust mite, cockroach, animal dander or secretory products) and outdoor (e.g., pollen)
- Exercise
- Occupational chemicals or allergens
- Environmental change (e.g., moving to new home; going on vacation; and/or alterations in workplace, work processes, or materials used) Irritants (e.g., tobacco smoke, strong odors, air pollutants, occupational chemicals, dusts and particulates, vapors, gases, and aerosols)
- Emotional expressions (e.g., fear, anger, frustration, hard crying or laughing)
- Drugs (e.g., aspirin; beta-blockers, including eye drops; nonsteroidal anti-inflammatory drugs; others)
- Food, food additives, and preservatives (e.g., sulfites)

- Changes in weather, exposure to cold air
- Endocrine factors (e.g., menses, pregnancy, thyroid disease)

4. Development of disease and treatment

- Age of onset and diagnosis
- History of early-life injury to airways (e.g., bronchopulmonary dysplasia, pneumonia, parental smoking)
- Progress of disease (better or worse)
- Present management and response, including plans for managing exacerbations
- Need for oral corticosteroids and frequency of use
- Comorbid conditions

5. Family history

- History of asthma, allergy, sinusitis, rhinitis, or nasal polyps in close relatives

6. Social history

- Characteristics of home including age, location, cooling and heating system, wood-burning stove, humidifier, carpeting over concrete, presence of molds or mildew, characteristics of rooms where patient spends time (e.g., bedroom and living room with attention to bedding, floor covering, stuffed furniture)
- Smoking (patient and others in home or day care)
- Day care, workplace, and school characteristics that may interfere with adherence
- Social factors that interfere with adherence, such as substance abuse
- Social support/social networks
- Level of education completed
- Employment (if employed, characteristics of work environment)

7. Profile of typical exacerbation

- Usual prodromal signs and symptoms
- Usual patterns and management (what works?)

8. Impact of asthma on patient and family

- Episodes of unscheduled care (emergency department, urgent care, hospitalization)
- Life-threatening exacerbations (e.g., intubation, intensive care unit admission)
- Number of days missed from school/work

- Limitation of activity, especially sports and strenuous work
- History of nocturnal awakening
- Effect on growth, development, behavior, school or work performance, and lifestyle
- Impact on family routines, activities, or dynamics
- Economic impact

9. Assessment of patient's and family's perceptions of disease

- Patient, parental, and spouse's or partner's knowledge of asthma and belief in the chronicity of asthma and in the efficacy of treatment
- Patient perception and beliefs regarding use and long-term effects of medications
- Ability of patient and parents, spouse, or partner to cope with disease
- Level of family support and patient's and parents', spouse's, or partner's capacity to recognize severity of an exacerbation
- Economic resources
- Sociocultural beliefs

Figure 1-2: Sample Questions for the Diagnosis and Initial Assessment of Asthma ↓

A "yes" answer to any question suggests that an asthma diagnosis is likely.

In the past 12 months, . . .

- Have you had a sudden severe episode or recurrent episodes of coughing, wheezing (high-pitched whistling sounds when breathing out), or shortness of breath?
- Have you had colds that "go to the chest" or take more than 10 days to get over?
- Have you had coughing, wheezing, or shortness of breath during a particular season or time of the year?
- Have you had coughing, wheezing, or shortness of breath in certain places or when exposed to certain things (e.g., animals, tobacco smoke, perfumes)?
- Have you used any medications that help you breathe better? How often?
- Are your symptoms relieved when the medications are used?

In the past 4 weeks, have you had coughing, wheezing, or shortness of breath:

- At night that has awakened you?
- In the early morning?
- After running, moderate exercise, or other physical activity?

Figure 1-3: Chronic Disease Severity ↓

Clinical Features before Treatment**

Goals of Asthma Treatment

- Prevent chronic and troublesome symptoms (e.g., coughing or breathlessness at night, in the early morning, or after exertion)
- Maintain (near) "normal" pulmonary function
- Maintain normal activity levels (including exercise and other physical activity)
- Prevent recurrent exacerbations of asthma and minimize the need for emergency department visits or hospitalizations
- Provide optimal pharmacotherapy with minimal or no adverse effects
- Meet patients' and families' expectations of and satisfaction with asthma care

	Symptoms**	**Nighttime Symptoms**	**Lung Function**
STEP 4 Severe Persistent	• Continual symptoms • Limited physical activity • Frequent exacerbations	• Frequent	• FEV_1 /PEF < 60% predicted • PEF variability >30%
STEP 3 Moderate Persistent	• Daily symptoms • Daily use of short-acting inhaled $beta_2$-agonists • Exacerbations affect activity • Exacerbations□ twice weekly; may last days	• >once weekly	• 60%<FEV_1/PEF<80% • PEF variability >30%
STEP 2 Mild Persistent	• Symptoms >2 times a week but <1 time a day • Exacerbations may affect activity	• >2 times a month	• FEV_1 /PEF > 80% predicted • PEF variability 20-30%
STEP 1 Mild Intermittent	• Symptoms < 2 times a week • Asymptomatic and normal PEF between exacerbations • Exacerbations brief (from a few hours to a few days); intensity may vary	• <2 times a month	• FEV_1 /PEF > 80% predicted • PEF variability <20%

* The presence of one of the features of severity is sufficient to place a patient in that category. An individual should be assigned to the most severe grade in which any feature occurs. The characteristics noted in this figure are general and may overlap because asthma is highly variable. Furthermore, an individual's classification may change over time.

** Patients at any level of severity can have mild, moderate, or severe exacerbations. Some patients with intermittent asthma experience severe and life-threatening exacerbations separated by long periods of normal lung function and no symptoms.

PHYSICAL EXAMINATION

The upper respiratory tract, chest, and skin are the focus of the physical examination for asthma. Physical findings that increase the probability of asthma include:

- *Hyperexpansion of the thorax,* especially in children; use of accessory muscles; appearance of hunched shoulders; and chest deformity.
- *Sounds of wheezing during normal breathing, or a prolonged phase of forced exhalation* (typical of airflow obstruction). Wheezing during forced exhalation is not a reliable indicator of airflow limitation. In mild intermittent asthma, or between exacerbations, wheezing may be absent.
- *Increased nasal secretion, mucosal swelling, and nasal polyps.*
- *Atopic dermatitis/eczema* or any other manifestation of an allergic skin condition.

PULMONARY FUNCTION TESTING (SPIROMETRY)

Spirometry measurements (FEV , FVC, FEV_1 /FVC) before and after the patient inhales a short-acting bronchodilator should be undertaken for patients in whom the diagnosis of asthma is being considered (Bye et al. 1992; Li and O'Connell 1996). This helps determine whether there is airflow obstruction and whether it is reversible over the short term (see Box 2 for further information). Spirometry is generally valuable in children over age 4; however, some children cannot conduct the maneuver adequately until after age 7.

Box 2-a: Importance of Spirometry in Asthma Diagnosis ↓

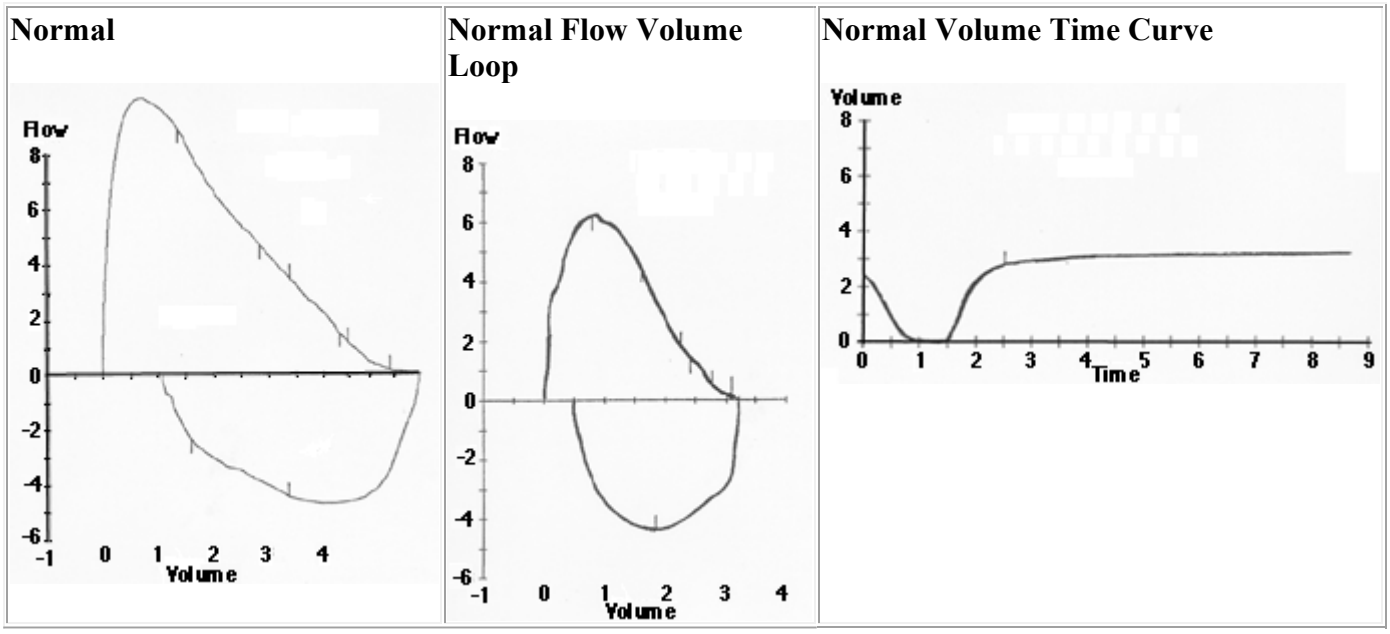
Objective assessments of pulmonary function are necessary for the diagnosis of asthma because medical history and physical examination are not reliable means of excluding other diagnoses or of characterizing the status of lung impairment. Although physicians generally seem able to identify a lung abnormality as obstructive (Russell et al. 1986), they have a poor ability to assess the degree of airflow obstruction (Shim and Williams 1980) or to predict whether the obstruction is reversible (Russell et al. 1986).

For diagnostic purposes, spirometry is generally recommended over measurements by a peak flow meter in the clinician's office because there is wide variability even in the best published peak expiratory flow reference values. Reference values need to be specific to each brand of peak flow meter, and such normative brand-specific values currently are not available for most brands. Peak flow meters are designed as monitoring, not as diagnostic, tools in the office (see Unit 1-Periodic Assessment and Monitoring). However, peak flow monitoring can establish peak flow variability and thus aid in the determination of asthma severity when patients have asthma symptoms and normal spirometry.

Spirometry typically measures the maximal volume of air forcibly exhaled from the point of maximal inhalation (forced vital capacity, FVC) and the volume of air exhaled during the first second of the FVC (forced expiratory volume in one second, FEV_1). Airflow obstruction is indicated by reduced FEV_1 and FEV_1 /FVC values relative to reference or predicted values. Significant reversibility is indicated by an increase of >12 percent and 200 mL in FEV_1 after inhaling a short-acting bronchodilator (American Thoracic Society 1991) (see figure 1-4 for examples of a spirometric curves for this test). A 2- to 3-week trial of oral corticosteroid therapy may be required to demonstrate reversibility. The spirometry measures that establish reversibility may not indicate the patient's best lung function.

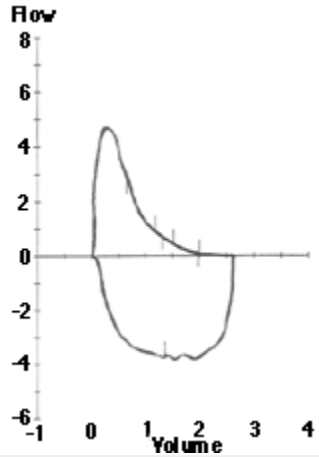
Figure 1-4: Sample Spirometry Curves ↓

NORMAL

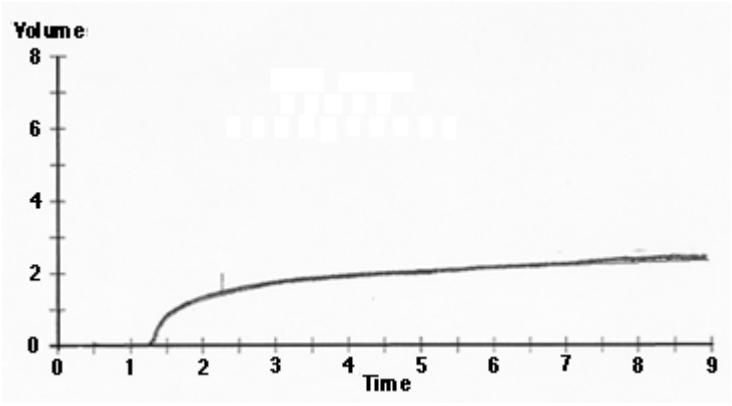


AIRWAY OBSTRUCTION

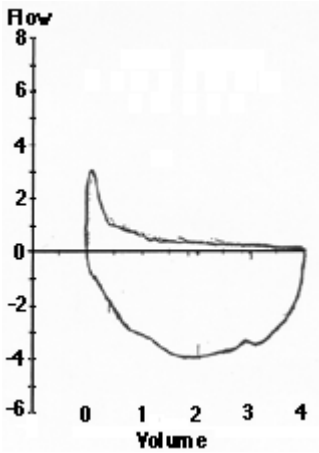
Mild Obstruction Flow Volume



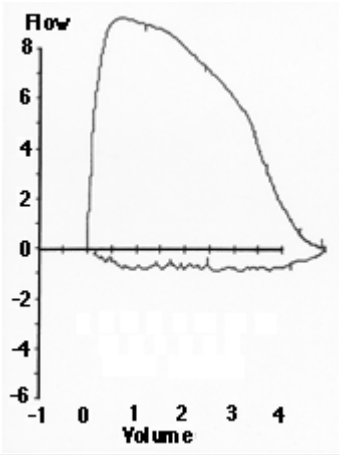
Mild Obstruction Volume Time Curve



Severe Obstruction Flow Volume



Variable Extrathoracic Upper Airway Obstruction



Fixed Upper Airway Obstruction

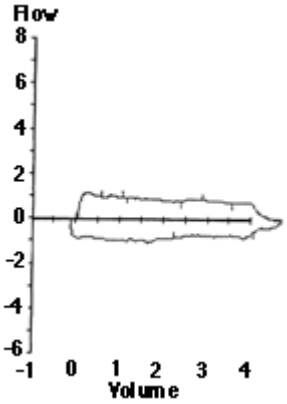


Figure 1-4a. Sample Spirometry Volume Time and Flow Volume Curves ↓

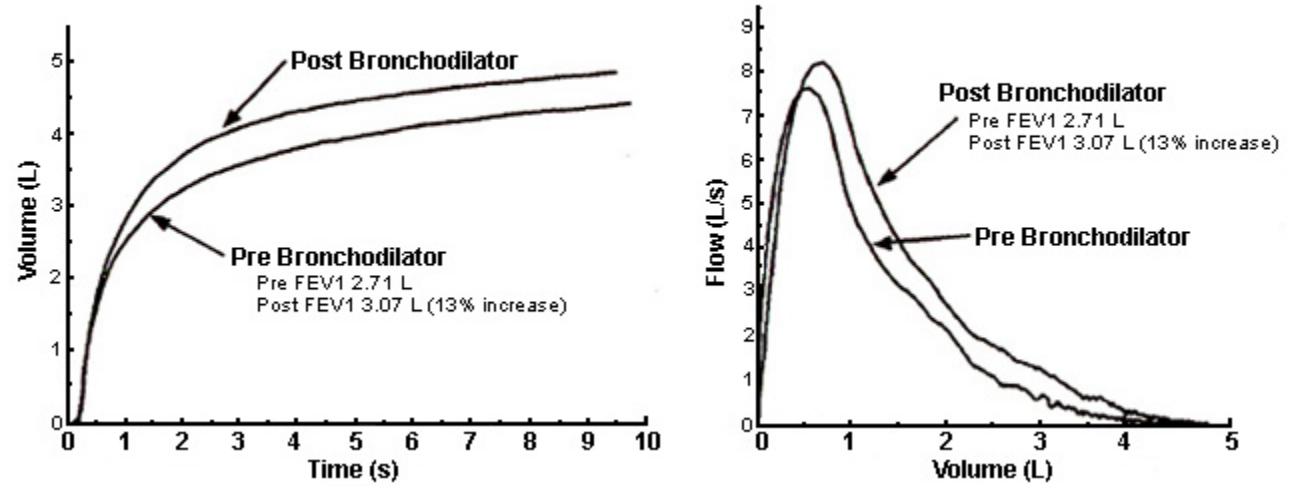


Figure 1-4b. Report of Spirometry Findings Pre and Post Bronchodilator ↓

Pre Bronchodilator				**Post Bronchodilator**			
Study: broncho Age: 59	ID: Height: 175 cm	Test date: 8/7/96 Sex: M	Time: 9:30 am System 7-20-17	Study: broncho Age: 59	ID: Height: 175 cm	Test date: 8/7/96 Sex: M	Time: 11:42 am System: 7-20-17
Trial 1 2 3 4 5	FVC 4.34 4.40 4.44 4.56 4.55	FEV_1 2.68 2.59 2.62 2.69 2.71	FEV_1/FVC% 61.8% 58.9% 58.9% 58.9% 59.6%	Trial 1 2 3 4 5	FVC 4.68 4.73 4.59 4.76 4.78	FEV_1 3.00 2.94 2.95 3.07 3.04	FEV_1/FVC% 64.0% 62.2% 64.3% 64.5
Best Values Predicted Values-1 LLN-2 Percent Predicted	4.56 4.23 3.10 107.8%	2.71 3.40 2.62 79.7%	59.4% 80.5% 69.9% 73.8%	Best Values Reference Values Difference (L) Difference (%)	4.78 4.56 0.22 4.8%	3.07 2.71 0.36 13.4%	64.3%
Interpretations: Pre-shift FEV_1/FVC are below normal range. The reduced rate which air is exhaled indicates obstruction to airflow. 1-Predicted values from Knudson, et al., *Am Rev Respir Dis*, 1983. 2-LLN is the Lower Limit of the Normal range (95th percentile)				Interpretation: Bronchodilator Response Significant increases in FEV_1, with bronchodilator (>12% increase after bronchodilator indicates a significant change).			

Abnormalities of lung function are categorized as restrictive and obstructive defects. A reduced ratio of FEV_1 /FVC (i.e., <65 percent) indicates obstruction to the flow of air from the lungs, whereas a reduced FVC with a normal FEV_1 /FVC ratio suggests a restrictive pattern. The severity of abnormality of spirometric measurements is evaluated by comparison of the patient's results with reference values based on age, height, sex, and race (American Thoracic Society 1991).

Although asthma is typically associated with an obstructive impairment that is reversible, neither this finding nor any other single test or measure is adequate to diagnose asthma. Many diseases are associated with this pattern of abnormality. The patient's pattern of symptoms (along with other information from the patient's medical history) and exclusion of other possible diagnoses also are needed to establish a diagnosis of asthma. In severe cases, the FVC may also be reduced, due to trapping of air in the lungs.

Office-based health care professionals who care for asthma patients should have access to spirometry, which is useful in both diagnosis and periodic monitoring. Spirometry should be performed using equipment and techniques that meet standards developed by the American Thoracic Society (1995). Correct technique, calibration methods, and maintenance of equipment are necessary to achieve consistently accurate test results. Maximal patient effort in performing the test is required to avoid important errors in diagnosis and management.

Training courses in the performance of spirometry that are approved by the National Institute for Occupational Safety and Health are available (1-800-35NIOSH). **When office spirometry shows severe abnormalities, or if questions arise regarding test accuracy or interpretation, the Expert Panel recommends further assessment in a specialized pulmonary function laboratory.**

ADDITIONAL STUDIES

Even though additional studies are not routine, they may be considered. No one test or set of tests is appropriate for every patient. However, the following procedures may be useful when considering alternative diagnoses, identifying precipitating factors, assessing severity, and investigating potential complications:

- *Additional pulmonary function studies* (e.g., lung volumes and inspiratory and expiratory flow volume loops) may be indicated, especially if there are questions about coexisting chronic obstructive pulmonary disease, a restrictive defect, or possible central airway obstruction. A *diffusing capacity test* is helpful in differentiating between asthma and emphysema in patients at risk for both illnesses, such as smokers and older patients.
- *Assessment of diurnal variation in peak expiratory flow over 1 to 2 weeks* is recommended when patients have asthma symptoms but normal spirometry (Enright et al. 1994). PEF is generally lowest on first awakening and highest several hours before the midpoint of the waking

day (e.g., between noon and 2 p.m.) (Quackenboss et al. 1991). Optimally, PEF should be measured close to those two times, before taking an inhaled short-acting beta -agonist in the morning and after taking one in the afternoon. A 20 percent difference between morning and afternoon measurements suggests asthma. Measuring PEF on waking and in the evening may be more practical and feasible, but values will tend to underestimate the actual diurnal variation.

- *Bronchoprovocation* with methacholine, histamine, or exercise challenge may be useful when asthma is suspected and spirometry is normal or near normal. For safety reasons, bronchoprovocation testing should be carried out by a trained individual in an appropriate facility and is not generally recommended if the FEV_1 is <65 percent predicted. A negative bronchoprovocation may be helpful to rule out asthma.
- *Chest X ray* may be needed to exclude other diagnoses.
- *Allergy testing* (see Unit 2).
- *Evaluation of the nose for nasal polyps and sinuses for sinus disease*.
- *Evaluation for gastroesophageal reflux* (Harding and Richter 1992) (see Unit 2). The usefulness of measurements of biomarkers of inflammation (e.g., total and differential cell count and mediator assays) in sputum, blood, or urine as aids to the diagnosis of asthma is currently being evaluated in clinical research trials.

DIFFERENTIAL DIAGNOSIS OF ASTHMA

Recurrent episodes of cough and wheezing are almost always due to asthma in both children and adults. Under-diagnosis of asthma is a frequent problem, especially in children who wheeze when they have respiratory infections. These children are often labeled as having bronchitis, bronchiolitis, or pneumonia even though the signs and symptoms are most compatible with a diagnosis of asthma. However, the clinician needs to be aware of other causes of airway obstruction leading to wheezing (see figure 1-5).

Figure 1-5: Differential Diagnosis Possibilities for Asthma ↓

<u>Infants and Children</u>

Upper airway diseases

- Allergic rhinitis and sinusitis

Obstruction involving large airways

- Foreign body in trachea or bronchus
- Vocal cord dysfunction
- Vascular rings or laryngeal webs

- Laryngotracheomalacia, tracheal stenosis, or bronchostenosis
- Enlarged lymph nodes or tumor

Obstructions involving small airways

- Viral bronchiolitis or obliterative bronchiolitis
- Cystic fibrosis
- Bronchopulmonary dysplasia
- Heart disease

Other causes

- Recurrent cough not due to asthma
- Aspiration from swallowing mechanism dysfunction or gastroesophageal reflux

Adults

- Chronic obstructive pulmonary disease (chronic bronchitis or emphysema)
- Congestive heart failure
- Pulmonary embolism
- Laryngeal dysfunction
- Mechanical obstruction of the airways (benign and malignant tumors)
- Pulmonary infiltration with eosinophilia
- Cough secondary to drugs (angiotensin-converting enzyme [ACE] inhibitors)
- Vocal cord dysfunction

There are two general patterns of wheezing in infancy: nonallergic and allergic. Nonallergic infants wheeze when they have an acute upper respiratory viral infection, but as their airways grow larger in the preschool years the wheezing disappears. Allergic infants also wheeze with viral infections, but they are more likely to have asthma that will continue throughout childhood. This group may have eczema, allergic rhinitis, or food allergy as other manifestations of allergy. Both groups may benefit from asthma treatment (see section on infants and young children in Unit 3-Managing Asthma Long Term).

Vocal cord dysfunction often mimics asthma. Patients with vocal cord dysfunction can present with recurrent severe shortness of breath and wheezing. Vocal cord dysfunction may even cause alveolar hypoventilation, with increases in Pco_2 that prompt urgent intubation and mechanical ventilation. Vocal cord dysfunction that mimics asthma is more common in young adults with psychological disorders. It should be suspected when physical examination reveals a

monophonic wheeze heard loudest over the glottis. Further evaluation by flow-volume curve revealing inspiratory flow limitation strongly supports the diagnosis of vocal cord dysfunction. Definitive diagnosis and exclusion of organic causes of vocal cord narrowing requires direct visualization of the vocal cords. Treatment with speech therapy that teaches techniques for relaxed throat breathing is often effective (Newman et al. 1995; Bucca et al. 1995; Christopher et al. 1983).

GENERAL GUIDELINES FOR REFERRAL TO AN ASTHMA SPECIALIST

Criteria for the referral of an asthma patient have been developed (Spector and Nicklas 1995; Shuttari 1995). **Based on the opinion of the Expert Panel, referral for consultation or care to a specialist in asthma care** (usually, a fellowship-trained allergist or pulmonologist; occasionally, other caregivers with expertise in asthma management developed through additional training and experience) **is recommended when:**

- Patient has had a life-threatening asthma exacerbation.
- Patient is not meeting the goals of asthma therapy (see Unit 1-Periodic Assessment and Monitoring) after 3 to 6 months of treatment. An earlier referral or consultation is appropriate if the caregiver concludes that the patient is unresponsive to therapy.
- Signs and symptoms are atypical or there are problems in differential diagnosis.
- Other conditions complicate asthma or its diagnosis (e.g., sinusitis, nasal polyps, aspergillosis, severe rhinitis, vocal cord dysfunction, gastroesophageal reflux, chronic obstructive pulmonary disease).
- Additional diagnostic testing is indicated (e.g., allergy skin testing, rhinoscopy, complete pulmonary function studies, provocative challenge, bronchoscopy).
- Patient requires additional education and guidance on complications of therapy or problems with adherence, or allergen avoidance occur.
- Patient is being considered for immunotherapy.
- Patient has severe persistent asthma, requiring step 4 care (referral may be considered for patients requiring step 3 care; see Unit 3-Managing Asthma Long Term). Patient requires continuous oral corticosteroid therapy or high-dose inhaled corticosteroids or has required more than two bursts of oral corticosteroids in 1 year.
- Patient is under age 3 and requires step 3 or 4 care (see Unit 3-Managing Asthma Long Term). When patient is under age 3 and requires step 2 care or initiation of daily long-term therapy, referral should be considered.
- Patient requires confirmation of a history that suggests that an occupational or environmental inhalant or ingested substance is provoking or contributing to asthma.
- Depending on the complexities of diagnosis, treatment, or the intervention required in the work environment, it may be appropriate in some cases for

the specialist to manage the patient over a period of time or co-manage with the primary care provider.

- In addition, patients with significant psychiatric, psychosocial, or family problems that interfere with their asthma therapy may need referral to an appropriate mental health professional for counseling or treatment. These characteristics have been shown to interfere with a patient's ability to adhere to treatment (Strunk 1987; Strunk et al. 1985).

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Section B: Periodic Assessment and Monitoring: Essential for Asthma Management

Key Points:

The goals of therapy are to:

- Prevent chronic and troublesome symptoms (e.g., coughing or breathlessness during the night, in the early morning, or after exertion)
- Maintain (near) "normal" pulmonary function
- Maintain normal activity levels (including exercise and other physical activity)
- Prevent recurrent exacerbations of asthma and minimize the need for emergency department visits or hospitalizations
- Provide optimal pharmacotherapy with least amount of adverse effects
- Meet patients' and families' expectations of and satisfaction with asthma care

Periodic assessments and ongoing monitoring of asthma are recommended to determine if the goals of therapy are being met. Measurements of the following are recommended:

- Signs and symptoms of asthma
- Pulmonary function
- Quality of life/functional status
- History of asthma exacerbations
- Pharmacotherapy
- Patient-provider communication and patient satisfaction

Clinician assessment and patient self-assessment are the primary methods for monitoring asthma. Population-based assessment is beginning to be used by managed care organizations.
Spirometry tests are recommended (1) at the time of initial assessment, (2) after treatment

is initiated and symptoms and PEF have stabilized, and (3) at least every 1 to 2 years. Patients should be given a written action plan based on signs and symptoms and/or PEF; this is especially important for patients with moderate-to-severe persistent asthma or a history of severe exacerbations. Patients should be trained to recognize symptom patterns indicating inadequate asthma control and the need for additional therapy. Recommendations on how and when to do peak flow monitoring are presented.

GOALS OF THERAPY

- The purpose of periodic assessment and ongoing monitoring is to determine whether the goals of asthma therapy are being achieved. The goals of therapy are as follows:
- Prevent chronic and troublesome symptoms (e.g., coughing or breathlessness during the night, in the early morning, or after exertion)
- Maintain (near) "normal" pulmonary function
- Maintain normal activity levels (including exercise and other physical activity)
- Prevent recurrent exacerbations of asthma and minimize the need for emergency department visits or hospitalizations
- Provide optimal pharmacotherapy with minimal or no adverse effects
- Meet patients' and families' expectations of and satisfaction with asthma care

ASSESSMENT MEASURES

The Expert Panel recommends ongoing monitoring in the six areas listed below to determine whether the goals of therapy are being met. The assessment measures for monitoring these six areas are described in this section and are **recommended based on the opinion of the Expert Panel**:

- Monitoring signs and symptoms of asthma
- Monitoring pulmonary function
    - Spirometry
    - Peak flow monitoring
- Monitoring quality of life/functional status
- Monitoring history of asthma exacerbations
- Monitoring pharmacotherapy
- Monitoring patient-provider communication and patient satisfaction
- References

Monitoring Signs and Symptoms of Asthma

Every patient with asthma should be taught to recognize symptom patterns that indicate inadequate asthma control (see figure 1-8, and Unit 4). Symptom monitoring should be used as a means to determine the need for intervention, including additional medication, in the context of an action plan (see Unit 4)..

Name: _____Date:_____

How many days in the past week have you had chest tightness, cough, shortness of breath, or wheezing (whistling in your chest)?	___0 ___1 ___2 ___3 ___4 ___5 ___6 ___7
How many nights in the past week have you had chest tightness, cough, shortness of breath, or wheezing (whistling in your chest)?	___0 ___1 ___2 ___3 ___4 ___5 ___6 ___7
Do you perform peak flow readings at home?	___ yes ___ no
If yes, did you bring your peak flow chart?	___ yes ___ no
How many days in the past week has asthma restricted your physical activity?	___0 ___1 ___2 ___3 ___4 ___5 ___6 ___7
Have you had any asthma attacks since your last visit?	___ yes ___ no
Have you had any unscheduled visits to a doctor, including to the emergency department, since your last visit?	___yes ___no
How many puffs of your short-acting inhaled $beta_2$ -agonist (quick-relief medicine) do you use per day?	_____ Average number of puffs per day
How many of your short-acting inhaled $beta_2$ -agonist inhalers did you go through over the past month?	_____ Number of inhalers in past month

What questions or concerns would you like to discuss with the doctor?

_____

_____

_____

How well controlled is your asthma in your opinion?	___ very well controlled ___ somewhat controlled ___ not well controlled
How satisfied are you with your asthma care?	___ very satisfied ___ somewhat satisfied ___ not satisfied

Figure 1-8 ↑

Symptoms and clinical signs of asthma should be assessed at each health care visit through physical examination and appropriate questions. This is crucial to optimal asthma care. A description of the important elements of an asthma-related physical examination can be found in Unit 1-Initial Assessment and Diagnosis, which also discusses the variability in the types of symptoms associated with asthma.

Detailed patient recall of symptoms decreases over time; therefore, **the Expert Panel recommends that any detailed symptoms history be based on a short (2 to 4 weeks) recall period.** For example, the clinician may choose to assess over a 2-week, 3-week, or 4-week recall period (see figure 1-6). Symptom assessment for periods longer than 4 weeks should reflect more global symptom assessment, such as inquiring whether the patient's asthma has been better or worse since the last visit and inquiring whether the patient has encountered any particular difficulties during specific seasons or events. Figure 1-6 provides an example of a set of questions that can be used to characterize both global (long-term recall) and recent (short-term recall) asthma symptoms. In addition, **any assessment of the patient's symptom history should include at least three key symptom expressions** :

- Daytime asthma symptoms (including wheezing, cough, chest tightness, or shortness of breath)
- Nocturnal awakening as a result of asthma symptoms
- Asthma symptoms early in the morning that are not improved 15 minutes after inhaling a short-acting beta$_2$ -agonist

Figure 1-6 ↓

Monitoring Signs and Symptoms

- (Global assessment) "Has your asthma been better or worse since your last visit?"
- (Recent assessment) "In the past 2 weeks, how many days have you:
    - Had problems with coughing, wheezing, shortness of breath, or chest tightness during the day?"
    - Awakened at night from sleep because of coughing or other asthma symptoms?"
    - Awakened in the morning with asthma symptoms that did not improve within 15 minutes of inhaling a short-acting inhaled beta2 -agonist?"
    - Had symptoms while exercising or playing?"

Monitoring Pulmonary Function

- **Lung Function**
  - "What is the highest and lowest your peak flow has been since your last visit?"
  - "Has your peak flow dropped below ___L/min (80 percent of personal best) since your last visit?"
  - "What did you do when this occurred?"
- **Peak Flow Monitoring Technique**
  - "Please show me how you measure your peak flow."
  - "When do you usually measure your peak flow?"

Monitoring Quality of Life/Functional Status

- "Since your last visit, how many days has your asthma caused you to:
  - Miss work or school?"
  - Reduce your activities?"
  - (For caregivers) Change your activity because of your child's asthma?"
- "Since your last visit, have you had any unscheduled or emergency department visits or hospital stays?"

Monitoring Exacerbation History

- "Since your last visit, have you had any episodes/times when your asthma symptoms were a lot worse than usual?"
- If yes - "What do you think caused the symptoms to get worse?"
- If yes - "What did you do to control the symptoms?"
- "Have there been any changes in your home or work environment (e.g., new smokers or pets)?"

Monitoring Pharmacotherapy

- **Medications**
  - "What medications are you taking?"
  - "How often do you take each medication?" "How much do you take each time?"
  - "Have you missed or stopped taking any regular doses of your medications for any reason?"
  - "Have you had trouble filling your prescriptions (e.g., for financial reasons, not on formulary)?"
  - "How many puffs of your short-acting inhaled $beta_2$ -agonist (quick-relief medicine) do you use per day?"

    - "How many _____ [name short-acting inhaled beta$_2$ -agonist] inhalers [or pumps] have you been through in the past month?"
    - "Have you tried any other medicines or remedies?"
- **Side Effects**
    - "Has your asthma medicine caused you any problems?"
        - shakiness, nervousness, bad taste, sore throat, cough, upset stomach
- **Inhaler Technique**
    - "Please show me how you use your inhaler."
- **Monitoring Patient-Provider Communication and Patient Satisfaction**
    - "What questions have you had about your asthma daily self-management plan and action plan?"
    - "What problems have you had following your daily self-management plan? Your action plan?"
    - "Has anything prevented you from getting the treatment you need for your asthma from me or anyone else?"
    - "Have the costs of your asthma treatment interfered with your ability to get asthma care?"
    - "How satisfied are you with your asthma care?"
    - "How can we improve your asthma care?"
    - "Let's review some important information:"
        - "When should you increase your medications? Which medication(s)?"
        - "When should you call me [your doctor, respiratory therapist, or nurse practitioner]? Do you know the after-hours phone number?"
        - "If you can't reach any of them, what emergency department would you go to?"

Monitoring Pulmonary Function

In addition to assessing symptoms, it is also important to periodically assess pulmonary function. The main methods are spirometry and peak flow monitoring. Regular monitoring of pulmonary function is particularly important for asthma patients who do not perceive their symptoms until airflow obstruction is severe. Currently, there is no readily available method of detecting the "poor perceivers." The literature reports that patients who had a near-fatal asthma exacerbation, as well as older patients, are more likely to have poor perception of airflow obstruction (Kikuchi et al. 1994; Connolly et al. 1992).

Spirometry

The Expert Panel recommends that spirometry tests be done (1) at the time of initial assessment; (2) after treatment is initiated and symptoms and peak expiratory flow (PEF) have stabilized, to document attainment of (near) "normal" airway function; and (3) at least every 1 to 2 years to assess the maintenance of airway function. Spirometry may be

indicated more often than every one to two years, depending on the clinical severity and response to management. Spirometry with measurement of the FEV_1 is also useful:

- As a periodic (e.g., yearly) check on the accuracy of the peak flow meter (Miles et al. 1995)
- When more precision is desired in measuring lung function (e.g., when evaluating response to bronchodilator or nonspecific airway responsiveness or when assessing response to a "step down" in pharmacotherapy)
- When PEF results are unreliable (e.g., in some very young or elderly patients or when neuromuscular or orthopedic problems are present) and the caregiver needs the quality checks that are available only with spirometry (Hankinson and Wagner 1993). For routine monitoring at most outpatient visits, measurement of PEF with a peak flow meter is generally a sufficient assessment of pulmonary function, particularly in mild intermittent, mild persistent, and moderate persistent asthma.

Peak Flow Monitoring

Peak expiratory flow provides a simple, quantitative, and reproducible measure of the existence and severity of airflow obstruction. PEF can be measured with inexpensive and portable peak flow meters. *It must be stressed that peak flow meters are designed as tools for ongoing monitoring, not diagnosis.* Because the measurement of PEF is dependent on effort and technique, patients need instructions, demonstrations, and frequent reviews of technique (see figure 1-7, the patient handout How To Use Your Peak Flow Meter). Peak flow monitoring can be used for short-term monitoring, managing exacerbations, and daily long-term monitoring. When used in these ways, the patient's measured personal best is the most appropriate reference value. Four studies (Woolcock et al. 1988; Ignacio-Garcia and Gonzalez-Santos 1995; Lahdensuo et al. 1996; Beasley et al. 1989) have found that comprehensive asthma self-management programs, in which peak flow monitoring was a component, achieved significant improvements in health outcomes. Thus far, the few studies that have isolated a comparison of peak flow and symptom monitoring have not been sufficient to assess the relative contributions of each to asthma management. The literature does suggest which patients may benefit most from peak flow monitoring. The Expert Panel concludes, on the basis of this literature and the Panel's opinion, that:

- **Patients with moderate-to-severe persistent asthma should learn how to monitor their PEF and have a peak flow meter at home.**
- **Peak flow monitoring during exacerbations of asthma is recommended for patients with moderate-to-severe persistent asthma to:**
    - **Determine severity of the exacerbation**
    - **Guide therapeutic decisions** (see Unit 3-Managing Exacerbations) **in the home, clinician's office, or emergency department**
- **Long-term daily peak flow monitoring is helpful in managing patients with moderate-to-severe persistent asthma to:**
    - **Detect early changes in disease status that require treatment**
    - **Evaluate responses to changes in therapy**

    - **Provide assessment of severity for patients with poor perception of airflow obstruction**
    - **Afford a quantitative measure of impairment**
- **If long-term daily peak flow monitoring is not used, a short-term (2 to 3 weeks) period of peak flow monitoring is recommended to:**
    - **Evaluate responses to changes in chronic maintenance therapy**
    - **Identify temporal relationship between changes in PEF and exposure to environmental or occupational irritants or allergens. It may be necessary to record PEF four or more times a day** (Chan-Yeung 1995).
    - **Establish the individual patient's personal best PEF**
- The Expert Panel does not recommend long-term daily peak flow monitoring for patients with mild intermittent or mild persistent asthma unless the patient/family and/or clinician find it useful in guiding therapeutic decisions. Any patient who develops severe exacerbations may benefit from peak flow monitoring.

Limitations of long-term peak flow monitoring include:

- Difficulty in maintaining adherence to monitoring (Reeder et al. 1990; Chmelik and Doughty 1994; Malo et al. 1993), often due to inconvenience, lack of required level of motivation, or lack of a specific treatment plan based on PEF
- Potential for incorrect readings related to poor technique, misinterpretation, or device failure

Whether peak flow monitoring, symptom monitoring, or a combination of approaches is used, the Expert Panel believes that self-monitoring is important to the effective self-management of asthma. The nature and intensity of self-monitoring should be individualized, based on such factors as asthma severity, patient's ability to perceive airflow obstruction, availability of peak flow meters, and patient preferences.

Figure 1-7 ↓

A peak flow meter is a device that measures how well air moves out of your lungs. During an asthma episode, the airways of the lungs usually begin to narrow slowly. The peak flow meter may tell you if there is narrowing in the airways hours—sometimes even days—before you have any asthma symptoms.

By taking your medicine(s) early (before symptoms), you may be able to stop the episode quickly and avoid a severe asthma episode. Peak flow meters are used to check your asthma the way that blood pressure cuffs are used to check high blood pressure. The peak flow meter also can be used to help you and your doctor:

- Learn what makes your asthma worse
- Decide if your treatment plan is working well

- Decide when to add or stop medicine
- Decide when to seek emergency care

A peak flow meter is most helpful for patients who must take asthma medicine daily. Patients age 5 and older are usually able to use a peak flow meter. Ask your doctor or nurse to show you how to use a peak flow meter.

How To Use Your Peak Flow Meter

Do the following five steps with your peak flow meter:

1. Move the indicator to the bottom of the numbered scale.
2. Stand up.
3. Take a deep breath, filling your lungs completely.
4. Place the mouthpiece in your mouth and close your lips around it. Do not put your tongue inside the hole.
5. Blow out as hard and fast as you can in a single blow.

Write down the number you get. But if you cough or make a mistake, don't write down the number. Do it over again. Repeat steps 1 through 5 two more times and write down the best of the three blows in your asthma diary.

Find Your Personal Best Peak Flow Number

Your personal best peak flow number is the highest peak flow number you can achieve over a 2- to 3-week period **when your asthma is under good control** . Good control is when you feel good and do not have any asthma symptoms.

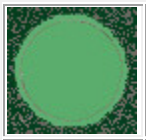
Each patient's asthma is different, and your best peak flow may be higher or lower than the peak flow of someone of your same height, weight, and sex. This means that it is important for you to find your own personal best peak flow number. Your treatment plan needs to be based on your own personal best peak flow number.

To find out your personal best peak flow number, take peak flow readings:

- At least twice a day for 2 to 3 weeks.
- When you wake up and between noon and 2:00 p.m.
- Before and after you take your short-acting inhaled $beta_2$ -agonist for quick relief, if you take this medicine.
- As instructed by your doctor.

The Peak Flow Zone System

Once you know your personal best peak flow number, your doctor will give you the numbers that tell you what to do. The peak flow numbers are put into zones that are set up like a traffic light. This will help you know what to do when your peak flow number changes. For example:

	**Green Zone** (more than ___ L/min [80 percent of your personal best number]) signals ***good control***. No asthma symptoms are present. Take your medicines as usual.
	**Yellow Zone** (between ___ L/min and ___ L/min [50 to less than 80 percent of your personal best number]) signals ***caution***. You must take a short-acting inhaled beta$_2$ -agonist right away. Also, your asthma may not be under good day-to-day control. Ask your doctor if you need to change or increase your daily medicines.
	**Red Zone** (below ___ L/min [50 percent of your personal best number]) signals a ***medical alert***. You must take a short-acting inhaled beta$_2$ -agonist (quick-relief medicine) right away. Call your doctor or emergency room and ask what to do, or go directly to the hospital emergency room. Record your personal best peak flow number and peak flow zones in your asthma diary.

Use the Diary To Keep Track of Your Peak Flow

Measure your peak flow when you wake up, *before* taking medicine. Write down your peak flow number in the diary every day, or as instructed by your doctor.

Actions To Take When Peak Flow Numbers Change*

- PEF goes between ___L/min and ___L/min (50 to less than 80 percent of personal best, **yellow zone**).
  - **ACTION:** Take a short-acting inhaled beta$_2$ -agonist (quick-relief medicine) as prescribed by your doctor.
- PEF increases 20 percent or more when measured before and after taking a short-acting inhaled beta$_2$ -agonist (quick-relief medicine)
  - **ACTION:** Talk to your doctor about adding more medicine to control your asthma better (for example, an anti-inflammatory medication).

It is the opinion of the Expert Panel that, regardless of the type of monitoring used, patients should be given a written action plan and be instructed to use it (see Unit 4). **The Panel believes it is especially important to give a written action plan to patients with moderate-to-severe persistent asthma and any patient with a history of severe exacerbations.** The action plan will describe the actions patients should take based on their signs and symptoms and/or PEF. The clinician should periodically review the plan, revise it as necessary, and confirm that the patient knows what to do if his or her asthma gets worse.

Recommendations on How To Monitor Peak Flow

The Expert Panel recommends that patients who are using a peak flow meter be instructed on how to establish their personal best peak expiratory flow (figure 1-7 above) and use it as the basis of their action plan (Unit 4). Meters used to measure PEF should meet American Thoracic Society recommendations for monitoring devices (American Thoracic Society 1995).

The patient's personal best PEF can be estimated after a 2- to 3-week period in which the patient records PEF two to four times per day. The personal best value is usually achieved in the early afternoon measurement after maximal therapy has stabilized the patient (Quackenboss et al. 1991). A course of oral corticosteroids may be needed to establish the personal best PEF. The patient's personal best value should be reassessed periodically to account for progression of disease in children and adults and for growth in children. Occasionally, a PEF value is recorded that is markedly higher than other values. This may be due to "spitting" (especially if the peak flow meter mouthpiece is small) or coughing into the peak flow meter, as well as other reasons that are not well understood. Therefore, caution should be used in establishing a personal best value when an outlying value is observed. Children with moderate-to-severe persistent asthma should repeat the short-term monitoring period every 6 months to establish changes in personal best PEF that occur with growth.

Patients requiring daily peak flow monitoring should measure their PEF on waking from sleep in the morning before taking a bronchodilator, if the patient uses a bronchodilator (Reddel et al. 1995; Morris et al. 1994). When the morning PEF is below 80 percent of the patient's personal best, PEF should be measured more than once a day (again, before taking a bronchodilator). This recommendation is based not on scientific data, but on the logic of reducing delays in treatment. The additional measurements of PEF during the day will enable patients to detect if their asthma is continuing to worsen or is improving after taking medication. If their asthma is worsening, they will have the opportunity to quickly respond to this. In addition, periodically having patients take their PEF first thing in the morning and in the early afternoon for 1 to 2 weeks will assess airflow variability, which is an indicator of the current level of the patient's asthma severity (see figure 1-3 above).

It is the Expert Panel's opinion that, in general, PEF below 80 percent of the patient's personal best before bronchodilator inhalation indicates a need for additional medication. PEF below 50 percent indicates a severe asthma exacerbation (see Unit 3 for recommended treatment). These cutpoints of 80 and 50 percent of the personal best are somewhat arbitrary. The emphasis is not on a specific PEF value but, rather, on a patient's change from personal best or from one reading to the next. Cutpoints should be tailored to individual patients' needs and PEF patterns.

Cutpoints may be easier to use and remember when they are adapted to a traffic light system (Lewis et al. 1984; Mendoza et al. 1988; Plaut 1995). In this system, for example, the green zone (80 to 100 percent of personal best) signals good control, the yellow zone (50 to less than 80 percent of personal best) signals caution, and the red zone (below 50 percent of personal best)

signals a medical alert. Because the yellow zone includes a wide spectrum of asthma severity, clinicians may consider recommending different interventions for a high yellow zone (e.g., 65 to less than 80 percent of personal best) and a low yellow zone (e.g., 50 to less than 65 percent of personal best).

The Expert Panel recommends that patients use the same peak flow meter over time and bring their peak flow meter for use at every follow-up visit. Using the same brand of meter is recommended because different brands of meters can give significantly different values (Jackson 1995; Enright et al. 1995; Hegewald et al. 1995; Sly et al. 1994; Miller et al. 1992) and because lung function varies across racial and ethnic populations. Thus, there is no universal normative standard for PEF. In addition, brand-specific normative values are not available for most peak flow meters.

Despite this variability across different brands of peak flow meters, measurements from the same meter and meters of the same brand are fairly consistent in measuring PEF (Jackson 1995; Enright et al. 1995; Hedgewald et al. 1995; Sly et al. 1994; Miller et al. 1992). Thus, once patients establish their personal best PEF on their own meter, they can obtain reliable and clinically meaningful readings of their PEF. However, at each visit, the patient's peak flow meter should be inspected. At least once a year, or any time there is a question about the validity of peak flow meter readings, PEF values from the portable peak flow meter and from laboratory spirometry should be compared.

When patients replace their peak flow meter, it is prudent to have them reestablish their personal best PEF with the new meter, regardless of whether the replacement meter is the same brand as the original. Action plan cutpoints also may need to be modified. The durability and consistency over time of peak flow meters have not been adequately studied to provide guidance on when a peak flow meter needs to be replaced.

Monitoring Quality of Life/Functional Status

To determine whether the goals of asthma therapy are being met, it is crucial to examine how the disease expression and control are affecting the patient's quality of life. Several dimensions of quality of life may be important to track, including physical function, role function, and mental health function. Several comprehensive survey instruments, such as the SF-36 (Stewart et al. 1988 for adult measure; Landgraf et al. 1996 for child measure), have been developed for general use for patient populations. In addition, a number of asthma-specific quality-of-life survey instruments have been developed (Creer et al. 1989; Hyland et al. 1991; Juniper et al. 1992; Marks et al. 1993; Richards and Hemstreet 1994), several of which appear promising. However, certain concerns preclude the Expert Panel from recommending the general adoption of these instruments at this time, such as the lack of experience with the use of the instruments in clinical practice and the time involved in administering the surveys. **The Expert Panel does recommend that at least several key areas of quality of life be periodically assessed for each person with asthma.** These include:

- Any missed work or school due to asthma

- Any reduction in usual activities (either home/work/school or recreation/exercise)
- Any disturbances in sleep due to asthma
- Any change in caregiver activities due to a child's asthma (for caregivers of children with asthma)

Figure 1-6 (above) provides a set of questions that the Expert Panel recommends for use in characterizing quality-of-life concerns for persons with asthma.

Monitoring History of Asthma Exacerbations

Exacerbations of asthma are characterized by periods of increased symptoms and reduced lung function, which may result in diminished ability to perform usual activities. Exacerbations may be brought on by exposures to irritants or sensitizers in the home, work, or general environment. Infections, certain medications, and a number of other medical conditions, as well as insufficient or ineffective therapy, also may trigger exacerbations (see Unit 2).

During periodic assessments, clinicians should question the patient and evaluate any records of patient self-monitoring (figures 1-8 and 1-9) **to detect exacerbations, both self-treated and those treated by other health care providers.** It is important to evaluate the frequency, severity, and causes of exacerbations. The patient should be asked about precipitating exposures and other factors. Specific inquiry into unscheduled visits to providers, telephone calls for assistance, and use of urgent or emergency care facilities may be helpful. Severity can be estimated by the increased need for oral corticosteroids. Control of asthma can be assessed by the increased need for short-acting $beta_2$ -agonist. Finally, any hospitalizations should be documented, including the facility, duration of stay, and any use of critical care or intubation. The clinician then can request summaries of all care received to facilitate continuity of care.

Figure 1-9 (example of patient diary) ↓

Date	Wheeze	Cough	Activity	Sleep	Quick Relief: Beta2-Agonist	Cromolyn/Nedocromil	Inhaled Steroids	Other - Inhaled	Oral Steroids	Theophylline	Peak Flow			Comments
											AM	PM	Other Times	

Wheeze	None = 0	Some = 1	Medium = 2	Severe = 3
Cough	None = 0	Occasional = 1	Frequent = 2	Continuous = 3
Activity	Normal = 0	Can run short distance or climb 3 flights of stairs = 1	Can walk only = 2	Missed school or work or stayed indoors = 3
Sleep	Fine = 0	Slept well, slight wheeze or cough = 1	Awake 2-3 times, wheeze or cough = 2	Bad night, awake most of the time = 3

Monitoring Pharmacotherapy

To ensure the effectiveness of pharmacotherapy, it is essential that the drug regimen be based on a sound rationale and that it be monitored on an ongoing basis. **Based on the opinion of the Expert Panel, the following factors should be monitored:**

- **patient adherence to the regimen,**
- **inhaler technique,**
- **level of usage of as-needed inhaled short-acting beta$_2$-agonist,**
- **frequency of oral corticosteroid burst therapy,**
- **changes in dosage of inhaled anti-inflammatory or other long-term-control medications, and side effects of medications**

(see assessment questions in figure 1-6).

It is also critical that the clinician determine that the patient is on the appropriate step of pharmacotherapy (see Unit 3-Managing Asthma Long Term) and has an up-to-date, written daily self-management plan and action plan.

Monitoring Patient-Provider Communication and Patient Satisfaction

Health care providers should routinely assess the effectiveness of patient/provider communication (see figure 1-6). Open and unrestricted communication among the clinician, the patient, and the family is essential to ensure successful self-management by the patient with asthma. Every effort should be made to encourage open discussion of concerns and expectation of therapy. See Unit 4 for specific strategies to enhance communication and patient adherence to the treatment plan.

Patients' satisfaction with their asthma care and resolution of fears and concerns are important goals and will increase adherence to the treatment plan (Haynes et al. 1979; Meichenbaum and Turk 1987). **Two aspects of patient satisfaction should be monitored: satisfaction with asthma control and satisfaction with the quality of care.** See figures 1-6, and 1-8 for examples of questions to use in monitoring patient satisfaction.

ASSESSMENT METHODS

Each of the key measures used in the periodic assessment of asthma (i.e., signs and symptoms, pulmonary function, quality of life, history of exacerbations, pharmacotherapy, and patient-provider communication and patient satisfaction) can be obtained by several methods. The principal methods include clinician assessment and patient (and/or parent or caregiver) self-assessment. In addition, population-based assessment of asthma care is being developed in the managed care field.

Clinician Assessment

Clinical assessment of asthma should be obtained via medical history and physical examination with appropriate pulmonary function testing. Optimal history assessment may be best achieved via a consistent set of questions (figure 1-6); physical examination for asthma is reviewed in Unit 1-Initial Assessment and Diagnosis. **Patients with mild intermittent or mild persistent asthma that has been under control for at least 3 months should be seen by a clinician about every 6 months.** This is a rough guideline based on the opinion of the Expert Panel. The exact frequency of clinician visits is a matter of clinical judgment. **Patients with uncontrolled and/or severe persistent asthma and those needing additional supervision to help them follow their treatment plan need to be seen more often.**

Patient Self-Assessment

Self-assessment by the patient and/or family is important to determine from *their* perspective whether the asthma is well controlled. Two methods are recommended: a daily diary (see figure 1-9 for an example) and a periodic self-assessment form to be filled out by the patient and/or family member at the time of the followup visits to the clinician (figure 1-8).

- The daily diary should include the key factors to be monitored at home: symptoms and/or peak flow, medication use, and restricted activity.

- The periodic self-assessment sheet completed at office visits is intended to capture the patient's and family's impression of asthma control, self-management skills, and overall satisfaction with care.

Patients are less likely to see completion of diaries and forms as a burden if they receive feedback from the clinician that allows them to see value in self-monitoring. Monitoring with a daily diary will be most useful to patients whose asthma is not yet under control and who are trying new treatments. It is also useful for those who need help identifying environmental or occupational exposures that make their asthma worse.

Population-Based Assessment

Asthma care is of increasing interest in various health care settings. Important regulatory organizations for the industry (e.g., the National Committee on Quality Assurance) have included the care of persons with asthma as a key indicator of quality of managed care. In this context, periodic population-based assessment of asthma care has begun to emerge as an issue for patients and their clinical providers. This type of assessment often uses population experience, such as hospitalization or emergency department visit rates, to examine care within different clinical settings and among different providers. Complex standardized population surveys (including lengthy health status instruments) are being tested experimentally in the managed care setting.

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Unit Two:

Control of Factors Contributing to Asthma Severity

Key Points:

Exposure of asthma patients to irritants or allergens to which they are sensitive has been shown to increase asthma symptoms and precipitate asthma exacerbations.

For at least those patients with persistent asthma on daily medications, the clinician should:

- Identify allergen exposures
- Use the patient's history to assess sensitivity to seasonal allergens
- Use skin testing or in vitro testing to assess sensitivity to perennial indoor allergens
- Assess the significance of positive tests in context of patients' medical history

Patients with asthma at any level of severity should avoid:

- Exposure to allergens to which they are sensitive.
- Exposure to environmental tobacco smoke.
- Exertion when levels of air pollution are high.
- Use of beta-blockers.
- Sulfite-containing and other foods to which they are sensitive.
- Aspirin and nonsteroidal anti-inflammatory drugs if they have a history of sensitivity; if they have severe persistent asthma, they should be counseled regarding the potential risk attendant with use of these drugs.

Patients should be treated for rhinitis, sinusitis, and gastroesophageal reflux, if present.

Patients with persistent asthma should be given an annual influenza vaccine.

For successful long-term asthma management, it is essential to identify and reduce exposures to relevant allergens and irritants and to control other factors that have been shown to increase asthma symptoms and/or precipitate asthma exacerbations. These factors fall into four categories: inhalant allergens, occupational exposures, nonallergic factors, and other factors. Ways to reduce the effects of these factors on asthma are discussed in this Unit.

INHALANT ALLERGENS

Exposure of an asthma patient to inhalant allergens to which the patient is sensitive increases airway inflammation and symptoms. Substantially reducing such exposure will result in

significantly reduced inflammation, symptoms, and need for medication (see a summary of the evidence in Box 1). **In the opinion of the Expert Panel, patients with asthma at any level of severity should be queried about exposures to inhalant allergens.**

Box 1 ↓

The association of asthma and allergy has long been recognized. Recent studies confirm that sensitization among genetically susceptible populations to certain indoor allergens such as house-dust mite, animal dander, and cockroach or to the outdoor fungus *Alternaria* is a risk for developing asthma in children (Peat et al. 1993, 1994; Sears et al. 1993a, 1993b; Sporik et al. 1990). Sensitization to outdoor pollens carries less risk for asthma (Sears et al. 1989), although grass (Reid et al. 1986) and ragweed (Creticos et al. 1996) pollen exposure has been associated with seasonal asthma. It is widely accepted that the importance of inhalant sensitivity as a cause of asthma declines with advancing age (Pollart et al 1989).

An allergic reaction in the airways caused by natural exposure to allergens has been shown to lead to an increase in inflammatory reaction, increased airway hyperresponsiveness (Boulet et al. 1983; Peroni et al. 1994; Piacentini et al. 1993), and increased eosinophils in bronchoalveolar lavage (Rak et al. 1991). Other research has demonstrated that asthma symptoms, pulmonary function, and need for medication in mite-sensitive asthma patients correlate with the level of house-dust mite exposure (Vervloet et al. 1991; Zock et al. 1994) and that reducing house-dust mite exposure reduces asthma symptoms, nonspecific bronchial hyperresponsiveness, and evidence of active inflammation (Peroni et al. 1994; Piacentini et al. 1993; Simon et al. 1994). Inhalant allergen exposure to seasonal outdoor fungal spores (Targonski et al. 1995; O'Hollaren et al. 1991) and to indoor allergens (Call et al. 1994) has also been implicated in fatal exacerbations of asthma. These reports emphasize that allergen exposure must be considered in the treatment of asthma.

The important allergens for children and adults appear to be those that are inhaled. Food allergens are not a common precipitant of asthma symptoms. Foods are an important cause of anaphylaxis in adults and children (Golbert et al. 1969; Sampson et al. 1992), but significant lower respiratory tract symptoms are uncommon even with positive double-blind food challenges (James et al. 1994).

Diagnosis—Determine Relevant Inhalant Sensitivity

Demonstrating a patient's relevant sensitivity to inhalant allergens will enable the clinician to recommend specific environmental controls to reduce exposures. It will also help the patient understand the pathogenesis of asthma and the value of allergen avoidance. **Given the importance of allergens and their control to asthma morbidity and asthma management, the Expert Panel recommends that patients with persistent asthma who require daily therapy be evaluated for allergens as possible contributing factors as follows** :

- **Determine the patient's exposure to allergens** (see relevant questions in figure 2-1).
- **Assess sensitivity to the allergens to which the patient is exposed.**

Figure 2-1 ↓

The association of asthma and allergy has long been recognized. Recent studies confirm that sensitization among genetically susceptible populations to certain indoor allergens such as house-dust mite, animal dander, and cockroach or to the outdoor fungus *Alternaria* is a risk for developing asthma in children (Peat et al. 1993, 1994; Sears et al. 1993a, 1993b; Sporik et al. 1990). Sensitization to outdoor pollens carries less risk for asthma (Sears et al. 1989), although grass (Reid et al. 1986) and ragweed (Creticos et al. 1996) pollen exposure has been associated with seasonal asthma. It is widely accepted that the importance of inhalant sensitivity as a cause of asthma declines with advancing age (Pollart et al 1989).

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- Use the patient's medical history which is usually sufficient, to determine sensitivity to seasonal allergens.

- Use skin testing or in vitro testing to determine the presence of specific IgE antibodies to the indoor allergens to which the patient is exposed year round (see figure 2-2 for a comparison of skin and in *vitro* tests). Allergy testing is the only reliable way to determine sensitivity to perennial indoor allergens (see Box 2 for further explanation).

(For selected patients with asthma at any level of severity, detection of specific IgE sensitivity to seasonal or perennial allergens may be indicated

as a basis for avoidance, for immunotherapy, or to characterize the patient's atopic status.)

Figure 2-2 ↓

Advantages of skin tests:	Advantages of RAST and other *in vitro* tests:
• Less expensive than *in vitro* tests	• Do not require knowledge of skin testing technique
• Results are available within 1 hour	• Do not require availability of allergen extracts
• More sensitive than *in vitro* tests	• Can be performed on patients who are taking medications that suppress the immediate skin test (antihistamines, antidepressants)
• Results are visible to the patient. This may encourage compliance with environmental control measures.	• No risk of systemic reactions
	• Can be done for patients with extensive eczema

Box 2 ↓

Determination of sensitivity to a perennial indoor allergen is usually not possible with a patient medical history alone (Murray and Milner 1995). Increased symptoms during vacuuming or bed making and decreased symptoms when away from home on a business trip or vacation are suggestive but not sufficient. Allergy skin or in vitro tests are reliable in determining the presence of specific IgE (Adinoff et al. 1990), but these tests do not determine whether the specific IgE is responsible for the patient's symptoms. That is why patients should only be tested for sensitivity to the allergens to which they are exposed and why the third step in evaluating patients for allergen sensitivity calls for assessing the clinical relevance of the sensitivity.

The recommendation to do skin or *in vitro* tests for patients with persistent asthma exposed to perennial indoor allergens will result in a limited number of allergy tests for about half of all asthma patients. This is based on the prevalence of persistent asthma and the level of exposure to indoor allergens. It is estimated that about half of all asthma patients have persistent asthma based on data on children in the United States (Taylor and Newacheck 1992) and on adults in Australia (Boston Consulting Group 1992). About 80 percent of the U.S. population is exposed to house-dust mites (Nelson and Fernandez-Caldas 1995), 60 percent to cat or dog, and a much

smaller percentage to both animals (Ingram et al. 1995). Cockroaches are a consideration only in the inner city and southern parts of the United States.

Skin or *in vitro* tests for patients exposed to perennial allergens are essential to justify the expense and effort involved in implementing environmental controls. In addition, patient adherence to maintaining environmental controls (e.g., with regard to pets) is likely to be poor without proof of the patient's sensitivity.

- **Assess the clinical significance of positive allergy tests in the context of the patient's medical history** (see figure 2-3).

Figure 2-3 ↓

- ***Animal Dander***. If there are pets in the patient's home and the patient is sensitive to dander of that species of animal, the likelihood that animal dander allergy is contributing to asthma symptoms is increased if answers to the following questions are affirmative. However, absence of positive responses does not exclude a contribution of animal dander to the patient's symptoms.
    - Do nasal, eye, or chest symptoms appear in a room where carpets are being or have just been vacuumed?
    - Do nasal, eye, or chest symptoms improve when away from home for a week or longer?
    - Do the symptoms become worse the first 24 hours after returning home?
- ***House-Dust Mites***. Mite allergy is more likely to be a contributing factor to asthma severity if answers to the following questions are affirmative. However, absence of a positive response does not exclude a contribution of mite allergen to the patient's symptoms.
    - Do nasal, eye, or chest symptoms appear in a room where carpets are being or have just been vacuumed?
    - Does making a bed cause nasal, eye, or chest symptoms?
- ***Outdoor Allergens (Pollens and Outdoor Molds).*** Contribution of pollens and outdoor molds in causing asthma symptoms is suggested by a positive answer to this question:
    - Is asthma consistently worse in spring, summer, fall, or parts of the growing season?

  Usually, if pollen or mold spores are causing increased asthma symptoms, the patient will also have symptoms of allergic rhinitis—sneezing, itching nose and eyes, runny and obstructed nose.

- ***Indoor Fungi (Molds)*.** Contribution of indoor molds in causing asthma symptoms is suggested by a positive answer to this question:
    - Do nasal, eye, or chest symptoms appear in damp or moldy rooms, such as basements?

Management—Reduce Exposure

The first and most important step in controlling allergen-induced asthma is to reduce exposure to relevant indoor and outdoor allergens. Effective ways patients can reduce their exposures to indoor and outdoor allergens are discussed below and summarized in figure 2-4, which also addresses irritants. Although these recommendations focus on the home environment, reductions in exposures to allergens and irritants are also appropriate in other environments where the patient spends extended periods of time, such as school, work, or day care. For information about companies that distribute products to help reduce allergen exposure, contact the Asthma and Allergy Foundation of America at 800-727-8462 or the Allergy and Asthma Network/Mothers of Asthmatics at 800-878-4403.

- *Animal Allergens.* All warm-blooded pets, including small rodents and birds, produce dander, urine, feces, and saliva that can cause allergic reactions (Swanson et al. 1985; de Blay et al. 1991a). No studies have been published on the effect of animal allergen avoidance on asthma symptoms; however, **based on the opinion of the Expert Panel, the following actions to control animal antigens are recommended:**
    - **If the patient is sensitive, remove the animal and products made of feathers from the home to eliminate exposure.**
    - **If removal of the animal is not acceptable:**
        - **Keep the pet out of the patient's bedroom.**
        - **Keep the patient's bedroom door closed.**
        - **Remove upholstered furniture and carpets from the home or isolate the pet from them to the extent possible.** Weekly washing of the pet may decrease the amount of dander and dried saliva the animal contributes to the environment (de Blay et al. 1991b; Klucka et al. 1995).
- *House-Dust Mite Allergen.* House-dust mites are universal in areas of high humidity (most areas of the United States) but are usually not present at high altitudes or in arid areas unless moisture is added to the indoor air. Mites depend on atmospheric moisture and human dander for survival. High levels of mites can be found in dust from mattresses, pillows, carpets, upholstered furniture, bed covers, clothes, and soft toys. The patient's bed is the most important source of dust mites to control. Recommended mite control measures are listed below (Platts-Mills et al. 1982).

  Essential actions **to control mites include:**

    - **Encase the mattress in an allergen-impermeable cover.**
    - **Encase the pillow in an allergen-impermeable cover or wash it weekly.**
    - **Wash the sheets and blankets on the patient's bed weekly in hot water.** A temperature of 130° F is necessary for killing house-dust mites.

  Desirable actions **to control mites include:**

- **Reduce indoor humidity to less than 50 percent.**
- **Remove carpets from the bedroom.**
- **Avoid sleeping or lying on upholstered furniture.**
- **Remove from the home carpets that are laid on concrete.**
- **In children's beds, minimize the number of stuffed toys and wash the toys weekly in hot water.**

Chemical agents are available for killing mites and denaturing the antigen; however, the effects are not dramatic and do not appear to be maintained for long periods. Therefore, use of these agents in the homes of house-dust mite-sensitive asthma patients should not be recommended routinely (Woodfolk et al. 1995). Vacuuming removes mite allergen from carpets but is inefficient at removing live mites.

- *Cockroach Allergen*. Cockroach sensitivity and exposure are common among patients with asthma who live in inner cities (Kang et al. 1993; Call et al. 1992). In an inner-city asthma study, asthma severity increased with increasing levels of cockroach antigen in the bedroom of sensitized children (Rosenstreich 1996). Although no studies have been published that report the effect of cockroach reduction on asthma symptoms, **it is the opinion of the Expert Panel that control measures need to be instituted when the patient is sensitive to cockroaches and infestation is present in the home.** Patients should not leave food or garbage exposed. Poison baits, boric acid, and traps are preferred to chemical agents because the latter can be irritating when inhaled by asthma patients. If chemical agents are used, the home should be well ventilated and the patient should not return to the home until the odor has dissipated.
- *Indoor Fungi (Molds)*. Indoor fungi are particularly prominent in humid environments and homes that have dampness problems. Children living in homes with dampness have increased respiratory symptoms (Cuijpers et al. 1995; Verhoeff et al. 1995), but the relative contribution of fungi, house-dust mites, or irritants is not clear. Because an association between indoor fungi and respiratory and allergic disease is suggested by some studies (Bjornsson et al. 1995; Smedje et al. 1996; Strachan 1988), measures to control dampness or fungal growth in the home may be beneficial.
- *Outdoor Allergens (Tree, Grass, and Weed Pollens and Seasonal Mold Spores)*. Patients can reduce exposure by staying indoors with windows closed in an air-conditioned environment (Solomon et al. 1980), particularly during the midday and afternoon when pollen and some spore counts are highest (Long and Kramer 1972; shortly after sunrise will result (Smith and Rooks 1954; Mullins et al. 1986). Conducting outdoor activities in less pollen exposure. These actions may not be realistic for some especially children.

Figure 2-4 ↓

Allergens: Reduce or eliminate exposure to the allergen(s) the patient is sensitive to, including:

- Animal dander: Remove animal from house or, at a minimum, keep animal out of patient's bedroom and seal or cover with a filter air ducts that lead to bedroom.
- House-dust mites:

    - Essential: Encase mattress in an allergen-impermeable cover; encase pillow in an allergen-impermeable cover or wash it weekly; wash sheets and blankets on the patient's bed in hot water weekly (water temperature of 130° F is necessary for killing mites).
    - Desirable: Reduce indoor humidity to less than 50 percent; remove carpets from the bedroom; avoid sleeping or lying on upholstered furniture; remove carpets that are laid on concrete.
- Cockroaches: Use poison bait or traps to control. Do not leave food or garbage exposed.
- Pollens (from trees, grass, or weeds) and outdoor molds: To avoid exposures, adults should stay indoors with windows closed during the season in which they have problems with outdoor allergens, especially during the afternoon.
- Indoor mold: Fix all leaks and eliminate water sources associated with mold growth; clean moldy surfaces. Consider reducing indoor humidity to less than 50 percent.

Tobacco Smoke: Advise patients and others in the home who smoke to stop smoking or to smoke outside the home. Discuss ways to reduce exposure to other sources of tobacco smoke, such as from day care providers and the workplace.

Indoor/Outdoor Pollutants and Irritants: Discuss ways to reduce exposures to the following:

- Wood-burning stoves or fireplaces
- Unvented stoves or heaters
- Other irritants (e.g., perfumes, cleaning agents, sprays)

Immunotherapy

Allergen immunotherapy may be considered for asthma patients when (1) there is clear evidence of a relationship between symptoms and exposure to an unavoidable allergen to which the patient is sensitive, (2) symptoms occur all year or during a major portion of the year, and (3) there is difficulty controlling symptoms with pharmacologic management either because the medication is ineffective, multiple medications are required, or the patient is not accepting of medication. This recommendation is based on the opinion of the Expert Panel and the evidence described below. If use of allergen immunotherapy is elected, it should be administered only in a caregiver's office where facilities and trained personnel are available to treat any life-threatening reaction that can, but rarely does, occur (AAAI Board of Directors 1994; Frew 1993).

Controlled studies of immunotherapy, usually conducted with single allergens, have demonstrated reduction in asthma symptoms caused by exposure to grass, cat, house-dust mite, ragweed, *Cladosporium*, and *Alternaria* (Reid et al. 1986; Malling et al. 1986; Creticos et al. 1996; Horst et al. 1990). A meta-analysis of 20 randomized, placebo-controlled studies has

confirmed the effectiveness of immunotherapy in asthma (Abramson et al. 1995). Few studies have been reported on multiple allergen mixes, which are commonly employed in clinical practice.

The course of allergen immunotherapy is typically of 3 to 5 years' duration. Reactions to immunotherapy, especially bronchoconstriction, are more frequent among patients with asthma, particularly those with poorly controlled asthma, compared with those with allergic rhinitis (Reid et al. 1993). For this reason, enthusiasm for the use of immunotherapy differs considerably among experts (Abramson et al. 1995; Canadian Society of Allergy and Clinical Immunology 1995; Frew 1993).

Assessment of Devices That May Modify Indoor Air

- **Vacuuming carpets once or twice a week is essential to reduce accumulation of house dust. Patients sensitive to components of house dust should avoid using conventional vacuum cleaners, and these patients should stay out of rooms where a vacuum cleaner is being or has just been used** (Murray et al. 1983). If patients vacuum, they can use a dust mask, a central cleaner with the collecting bag outside the home, or a cleaner fitted with a HEPA (high-efficiency particulate air) filter or with a double bag (Woodfolk et al. 1993).
- **Humidifiers and evaporative (swamp) coolers are *not* recommended for use in the homes of house-dust mite-sensitive patients with asthma.** These are potentially harmful because increased humidity may encourage the growth of both mold (Solomon 1976) and house-dust mites (Ellingson et al. 1995). In addition, humidifier problem if not properly cleaned because they can harbor and aerosolize mold spores (Solomon 1974).
- **Air conditioning during warm weather is recommended for asthma patients** because it allows windows and doors to stay closed, which prevents entry of outdoor allergens (Solomon et al. 1980). Regular use of central air conditioning also will usually control humidity sufficiently to reduce house-dust mite growth (Lintner and Brame 1993).
- **Use of a dehumidifier will reduce house-dust mite levels in areas where the humidity of the outside air remains high for most of the year** (Cabrera et al. 1995).
- **Indoor air-cleaning devices cannot substitute for the more effective measures described previously** (see Management—Reduce Exposure). However, air-cleaning devices (i.e., HEPA and electrostatic precipitating filters) have been shown to reduce airborne cat dander (de Blay et al. 1991b), mold spores (Maloney et al. 1987), and particulate tobacco smoke (Offermann et al. 1984). Air cleaners cannot significantly reduce exposure to house-dust mite and cockroach allergens because these heavy particles do not remain airborne (de Blay et al. 1991a). Most studies of air cleaners have failed to demonstrate an effect on asthma symptoms or pulmonary function (Nelson et al. 1988; Reisman et al. 1990; Warner et al. 1993; Warburton et al. 1994).
- Air-duct cleaning of heating/ventilation/air conditioning systems has been reported to decrease levels of airborne fungi in residences (Garrison et al. 1993). The effect on levels of house-dust mite or animal dander has not been studied. Limited evidence precludes the Expert Panel from making a recommendation in this area.

OCCUPATIONAL EXPOSURES

Early recognition and control of exposures are particularly important in occupationally induced asthma, because the likelihood of complete resolution of symptoms decreases with time (Chan-Yeung et al. 1987; Pisati et al. 1993). Occupational asthma is suggested by a correlation between asthma symptoms and work, with improvement when away from work for several days. Other indications of workplace exposure are listed in figure 2-5. The patient may fail to recognize the work relationship, because symptoms often begin several hours after exposure. Serial peak flow records at work and away from work can confirm the work association (Moscato et al. 1995).

Figure 2-5 ↓

Evaluation

Potential for workplace-related symptoms:

- Recognized sensitizers (e.g., isocyanates, plant or animal products).
- Irritants* or physical stimuli (e.g., cold/heat, dust, humidity).
- Coworkers may have similar symptoms.

Patterns of symptoms (in relation to work exposures):

- Improvement during vacations or days off (may take a week or more).
- Symptoms may be immediate (<1 hour), delayed (most commonly, 2 to 8 hours after exposure), or nocturnal.
- Initial symptoms may occur after high-level exposure (e.g., spill).

Documentation of work-relatedness of airflow limitation:

- Serial charting for 2 to 3 weeks (2 weeks at work and up to 1 week off work as needed to identify or exclude work-related changes in peak expiratory flow):
  - Record when symptoms and exposures occur.
  - Record when a bronchodilator is used.
  - Measure and record peak flow every 2 hours while awake.
- Immunologic tests
- Referral for further confirmatory evaluation (e.g., bronchial challenges)

Management

Work-aggravated asthma:

- Work with onsite health care providers or managers/supervisors.
- Discuss avoidance, ventilation, respiratory protection, tobacco smoke-free environment.

Occupationally induced asthma:

- Recommend complete cessation of exposure to initiating agent.

Workplace exposure to sensitizing chemicals or dusts can induce asthma, which often persists after the exposures are terminated (Chan-Yeung et al. 1987; Pisati et al. 1993). This should be distinguished from allergen- or irritant-induced aggravation of preexisting asthma. Acute exposure to irritant gases, dusts, or fumes can cause an asthma-like condition (reactive airway dysfunction syndrome) (Brooks et al. 1985).

Patient confidentiality issues are particularly important in work-related asthma. Because even general inquiries about the potential adverse health effects of work exposures may occasionally result in reprisals against the patient (e.g., job loss), asthma patients need to be informed of this possibility and be full partners in the decision to approach management regarding the effects or control of workplace exposures.

IRRITANTS

In the opinion of the Expert Panel, patients with asthma at any level of severity should be queried about exposures to irritants. Sample assessment questions are in figure 2-1.

Environmental Tobacco Smoke

Asthma patients should not smoke or be exposed to environmental tobacco smoke (Marquette et al. 1992). Tobacco smoke is the most important environmental indoor irritant and is a major precipitant of asthma symptoms in children and adults (Abbey et al. 1993; Greer et al. 1993; Jindal et al. 1994; Leuenberger et al. 1994). Jindal and colleagues (1994) found that exposure of adults to environmental tobacco smoke is associated with decreased levels of pulmonary function, increased requirements for medication, and more frequent absences from work. In addition, exposure to maternal smoke has been shown to be a risk factor for the development of asthma in infancy (Arshad and Hide 1992) and childhood (Frischer et al. 1992; Schmitzberger et al. 1993; Gortmaker et al. 1982; Henderson et al. 1995; Soyseth et al. 1995; Martinez et al. 1995; Agudo et al. 1994), although not for persistence of childhood asthma into adulthood (Roorda et al. 1993).

Indoor/Outdoor Air Pollution and Irritants

Asthma patients should avoid exertion or exercise outside to the extent possible when levels of air pollution are high. Increased pollution levels, particularly of respirable particulates (Abbey et al. 1993; Koenig et al. 1993; Pope et al. 1991; Walters et al. 1994; Schwartz et al. 1993; Ostro et al. 1995) and ozone (Abbey et al. 1993; Cody et al. 1992; Ponka 1991; Thurston et al. 1992; Ostro et al. 1995; Romieu et al. 1995; Kesten et al. 1995; White et al. 1994), but also of SO_2 (Moseholm et al. 1993) and NO_2 (Moseholm et al. 1993; Kesten et al. 1995), have been reported to precipitate symptoms of asthma (Abbey et al. 1993; Koenig et al. 1987; Moseholm et al. 1993; Pope et al. 1991) and to increase emergency department visits and hospitalizations for

asthma (Walters et al. 1994; Schwartz et al. 1993; Cody et al. 1992; Ponka 1991; Thurston et al. 1992; Romieu et al. 1995; Kesten et al. 1995; White et al. 1994).

Patients also should avoid exposure to fumes from unvented gas, oil, or kerosene stoves; wood-burning appliances or fireplaces (Ostro et al. 1994)**; sprays; and strong odors** because they irritate the lungs and can precipitate asthma symptoms.

OTHER FACTORS THAT CAN INFLUENCE ASTHMA SEVERITY

Rhinitis/Sinusitis

Treatment of upper respiratory tract symptoms is an integral part of asthma management. **Intranasal corticosteroids are recommended for the treatment of chronic rhinitis in patients with persistent asthma.** Antihistamine/decongestant combinations also may be used; they provide symptomatic relief but have not been shown to have a protective effect on the lower airways secondary to their action on the nose. Intranasal corticosteroids reduce nasal inflammation, obstruction, and discharge and have been shown to reduce lower airway hyperresponsiveness and asthma symptoms (Aubier et al. 1992; Watson et al. 1993; Corren et al. 1992; Welsh et al. 1987). Intranasal cromolyn has been shown to reduce symptoms of asthma during the ragweed season, but to a lesser extent than intranasal corticosteroids in the same study (Welsh et al. 1987).

Treatment of sinusitis includes medical measures to promote drainage (Zeiger 1992) **and the use of antibiotics when complicating acute bacterial infection is present** (Wald 1992; Gwaltnet al. 1992). In cases of subacute or chronic sinusitis, caregivers need to make a judgment regarding the appropriateness of antibiotic therapy. Antibiotic therapy was not shown to be of clear benefit in children who had nasal symptoms or cough for longer than 3 weeks and who had abnormal sinus x rays but no fever (Dohlman et al. 1993).

Asthma is commonly associated with perennial and seasonal rhinitis and sinusitis. Studies indicate that inflammation of the upper airway contributes to lower airway hyperresponsiveness and asthma symptoms (Watson et al. 1993; Corren et al. 1992; Welsh et al. 1987). The histopathology in the chronically thickened mucosa of the paranasal sinuses is similar to that in the nose and bronchi, with a primarily eosinophilic infiltrate that, in most patients, is notably lacking in neutrophils (Harlin et al. 1988; Demoly et al. 1994).

Gastroesophageal Reflux

Medical management of gastroesophageal reflux should be instituted for any patients with asthma complaining of frequent heartburn or pyrosis, particularly those with frequent episodes of nocturnal asthma. Medical management of gastroesophageal reflux includes:

- Avoiding food and drink within 3 hours of retiring (Nelson 1984)
- Elevating the head of the bed on 6- to 8-inch blocks (Nelson 1984)
- Using appropriate pharmacologic therapy (Hixson et al. 1992)

For patients who have persistent symptoms following optimal therapy, further evaluation is indicated.

For patients with poorly controlled asthma, particularly with a nocturnal component, investigation for gastroesophageal reflux may be warranted even in the absence of suggestive symptoms (Irwin et al. 1989). The symptoms of gastroesophageal reflux are common in both children and adults with asthma (Nelson 1984). Reflux during sleep can contribute to nocturnal asthma (Martin et al. 1982; Davis et al. 1983). Both medical (Ekstrom et al. 1989) and surgical (Perrin-Fayolle et al. 1989) therapy of gastroesophageal reflux have been reported to reduce the symptoms of asthma.

Aspirin Sensitivity

Adult patients with asthma should be questioned regarding precipitation of bronchoconstriction by aspirin and other nonsteroidal anti-inflammatory drugs. If they have experienced a reaction to any of these drugs, they should be informed of the potential for all these drugs to precipitate severe and even fatal exacerbations. Adult patients with severe persistent asthma or nasal polyps should be counseled regarding the risk of using these drugs. Usually safe alternatives to aspirin include acetaminophen or salsalate (Szczeklik et al. 1977; Settipane et al. 1995).

From 3 percent of patients with asthma seen in a private allergy practice (Chafee and Settipane 1974) to 39 percent of adults with asthma admitted to an asthma referral hospital (Spector et al. 1979) have been reported to experience severe and even fatal exacerbations of asthma after taking aspirin or certain other nonsteroidal anti-inflammatory drugs. The prevalence of aspirin sensitivity increases with increasing age and severity of asthma (Chafee and Settipane1974; Spector et al. 1979).

Sulfite Sensitivity

Patients who have asthma symptoms associated with eating processed potatoes, shrimp, or dried fruit or with drinking beer or wine should avoid these products (Taylor et al. 1988). These products contain sulfites, which are used to preserve foods and beverages. They have caused severe asthma exacerbations, particularly in patients with severe persistent asthma.

Beta-Blockers

Nonselective beta-blockers, including those in ophthalmological preparations, can cause asthma symptoms and should be avoided by asthma patients (Odeh et al. 1991; Schoene et al. 1984), although cardioselective beta-blockers, such as betaxolol, may be tolerated (Dunn et al. 1986).

Infections

Annual influenza vaccinations are recommended for patients with persistent asthma (Bell et al. 1978; CDC 1993). It is well established that viral respiratory infections can exacerbate

asthma, particularly in children under the age of ten (Busse et al. 1993). Respiratory syncytial virus, rhinovirus, and influenza virus have been implicated (Busse et al. 1993), with rhinovirus being implicated in the majority of the exacerbations of asthma in children (Johnston et al. 1995). The role of infections causing exacerbations of asthma also appears to be important in adults (Nicholson et al. 1993).

Viral infections are the most frequent precipitants of asthma exacerbations in infancy. In the majority of cases, young children are predisposed to have bronchial obstruction during viral infections because of very small airway size (Martinez et al. 1995) and will not have further exacerbations after infancy. However, chronic asthma also may start as early as the first year of life among infants with a family history of asthma, persistent rhinorrhea, atopic dermatitis, or high IgE levels. Early identification of these infants allows institution of environmental controls to reduce exposure to tobacco smoke, animal dander, and house-dust mites.

PREVENTING THE ONSET OF ASTHMA

Primary prevention of asthma (preventing initial development) is an accepted approach for occupational asthma (Venables 1994; Chan-Yeung et al. 1987) but remains unproven outside the workplace. Recent studies indicate that exposures to high levels of house-dust mite antigen (Sporik et al. 1990; Peat et al. 1993, 1994) and environmental tobacco smoke (Martinez et al. 1995; Kuehr et al. 1995) are associated with an increased incidence of asthma among infants. This suggests that reducing these exposures may result in reduction in the incidence of asthma. Prolonged breast feeding and avoidance of early introduction of allergenic foods have been reported to reduce eczema and food sensitization but not to reduce the prevalence of asthma (Zeiger 1994).

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Post Test Asthma Today

Select the ***best*** answer to each of the following items. Mark your responses on the Answer Form.

1. More than _____ people in the US have been diagnosed with asthma.

a. 500,000
b. 2 million
c. 17 million
d. 37 million

2. Asthma is the _____ most common cause of childhood hospitalizations under the age of 15.

a. first
b. second
c. third
d. fifth

3. Asthma treatment costs an estimated $_____, including direct and indirect expenditures each year.

a. 29 million
b. 800 million
c. 5 billion
d. 11.3 billion

4. Until recently, information on airway pathology in asthma has come largely from _____ which shows that both large and small airways often contain plugs composed of mucus, serum proteins, inflammatory cells, and cellular debris.

a. symptom analysis
b. anecdotal data
c. x-ray record analysis
d. post-mortem examination

5. _____ and biopsy provide new insight into mechanisms of airway disease and features that link altered lung function to a specific type of mucosal inflammation.

a. Laser technology
b. Lateral Radiograph analysis
c. Fiberoptic bronchoscopy
d. Fiberoptic bronchoscopy with lavage

6. It is recognized that specific adhesion _____, found in the vascular tissue, lung matrix, and bronchial epithelium, may be critical in directing and anchoring cells in the airway, thus causing the inflammatory changes noted.

a. allergens
b. proteins
c. calcium deposits
d. fomites

7. _____ is one of the strongest predisposing factors in the development of asthma.

a. Anemia
b. Atopy
c. High blood pressure
d. Anxiety

8. An important feature of asthma is an exaggerated _____ to a wide variety of stimuli. The propensity for airways to narrow too easily and too much is a major, but not necessarily unique, feature of asthma.

a. bronchoconstrictor response
b. endorphin
c. adrenalin
d. synaptic

9. Airway hyperresponsiveness can be measured by inhalation challenge testing with _____ or histamine, as well as after exposure to such nonpharmacologic stimuli as hyperventilation with cold dry air, inhalation of hypotonic or hypertonic aerosols, or after exercise.

a. xanthine
b. dopamine
c. methacholine
d. saline

10. Although inflammation can be used to describe a variety of conditions in various diseases, the inflammatory response in asthma has special features that include _____, mast cell degranulation, interstitial airway wall injury, and lymphocyte activation.

a. eosinophil infiltration
b. lung expansion
c. elevated PFTs
d. subnormal PFTs

11. Spirometry measurements (FEV , FVC, FEV_1 /FVC) before and after the patient inhales a _____ bronchodilator should be undertaken for patients in whom the diagnosis of asthma is being considered**.**

a. short-acting
b. long-acting
c. corticosteroid
d. xanthine

12. For diagnostic purposes, _____ is generally recommended over measurements by a peak flow meter in the clinician's office because there is wide variability even in the best published peak expiratory flow reference values.

a. bronchoscopy
b. spirometry
c. blow ball testing
d. radiographic analysis

13. _____ dysfunction often mimics asthma.

a. Lung expansion
b. Vocal cord
c. Cardiac
d. Cough

14. In addition to assessing symptoms, it is also important to periodically assess pulmonary function. The main methods are spirometry and _____.

a. blow ball testing
b. bronchoscopy
c. peak flow monitoring
d. radiographic analysis

15. Peak expiratory flow provides a simple, quantitative, and reproducible measure of the existence and severity of _____. PEF can be measured with inexpensive and portable peak flow meters.

a. asthma
b. eosinophil infiltration
c. lymphocyte activation
d. airflow obstruction

16. For successful long-term asthma management, it is essential to identify and reduce exposures to relevant allergens and irritants and to control other factors that have been shown to increase asthma symptoms and/or precipitate asthma exacerbations. These factors fall into four categories: _____, _____, _____, and other factors

a. inhalant allergens
b. nonallergic factors
c. occupational exposures
d. all the above

17. _____ may be considered for asthma patients when (1) there is clear evidence of a relationship between symptoms and exposure to an unavoidable allergen to which the patient is sensitive, (2) symptoms occur all year or during a major portion of the year, and (3) there is difficulty controlling symptoms with pharmacologic management

a. Bronchoscopy
b. PFT analysis
c. Allergen immunotherapy
d. All the above

18. _____ during warm weather is recommended for asthma patients

a. Strenuous exercise
b. Staying indoors
c. Air conditioning
d. Drinking cold liquids

19. _____ corticosteroids are recommended for the treatment of chronic rhinitis in patients with persistent asthma.

a. Intervenous
b. Inhaled
c. Intranasal
d. Liquid

20. Treatment of sinusitis includes medical measures to _____ and the use of antibiotics when complicating acute bacterial infection is present.

a. lower PF count
b. lower FEV rate
c. activate lymphocytes
d. promote drainage

21. _____ mediators can influence airway smooth muscle tone, modulate vascular permeability, activate neurons, stimulate mucus secretion, and produce characteristic structural changes in the airway.

a. Capsule-form
b. Cell-derived
c. Injected
d. Nasal spray form

22. _____ is needed in conducting the assessment for asthma.

a. A team approach
b. A respiratory therapist
c. Clinical judgment
d. None of the above

23. A "yes" answer to which question suggests that an asthma diagnosis is likely:

a. Have you had a sudden severe episode or recurrent episodes of coughing, wheezing (high-pitched whistling sounds when breathing out), or shortness of breath?
b. Have you had coughing, wheezing, or shortness of breath in certain places or when exposed to certain things (e.g., animals, tobacco smoke, perfumes)?
c. Have you had colds that "go to the chest" or take more than 10 days to get over?
d. All the above

24. Spirometry is generally valuable in children over age 4; however, some children cannot conduct the maneuver adequately until after age _____.

a. 5
b. 7
c. 9
d. 12

25. The peak flow meter also can be used to help you and your doctor:

a. Learn what makes your asthma worse
b. Decide when to add or stop medicine
c. Decide when to seek emergency care
d. All the above

26. When patients replace their peak flow meter, it is prudent to have them _____ with the new meter, regardless of whether with the replacement meter is the same brand as the original.

a. learn how to use
b. lower the settings
c. reestablish their personal best PEF
d. raise the settings

27. Determination of sensitivity to a perennial indoor allergen is usually not possible with

a. skin tests
b. *in vitro* tests
c. a patient medical history alone.
d. All the above

28. *Essential actions* to control mites found in the bed include:

a. Encase the mattress in an allergen-impermeable cover.
b. Encase the pillow in an allergen-impermeable cover or wash it weekly.
c. Wash the sheets and blankets on the patient's bed weekly in hot water.
d. All the above

29. _____ corticosteroids are recommended for the treatment of chronic rhinitis in patients with persistent asthma.

a. Intravenous
b. Capsule-form
c. Intranasal
d. All the above

30. Medical management of gastroesophageal reflux includes:

a. Avoiding food and drink within 3 hours of retiring
b. Elevating the head of the bed on 6- to 8-inch blocks
c. Using appropriate pharmacologic therapy
d. All of the above

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