

Long-Term Self-Management Plan for Persistent Asthma

Introduction: This long-term plan provides four benefits to the clinician and patient, who complete it together during an early visit and review it periodically. The chart: (1) reflects the step-up/step-down concept of pharmacotherapy; (2) enables patient and clinician to negotiate which medicines will be used and how often; (3) combines symptoms and/or peak flow monitoring as the basis for patient's adding or deleting medicines at home and self-adjusting doses; and (4) gives the patient a view of what the clinician recommends over the long-term—under what future circumstances the clinician intends that the regimen be increased or decreased.

Directions: The clinician writes the patient's medicines in the first column. Based on the symptoms and peak flow specified in the top row, the clinician then writes the doses and frequency of administration for each medication. (Some clinicians may prefer to print standard recommendations on the form to save time.)

Medication	At the FIRST sign of a cold or exposure to known trigger	If cough or wheeze is present	If cough or wheeze worsen	As soon as cough and wheeze have stopped	When there is no cough or wheeze for 2 weeks, even with activity	When there is no cough or wheeze for ____ months	Before exercise or physical activity	For rapidly worsening asthma (severe exacerbation)
		or peak flow is between 50 and 80% of personal best	or peak flow is below 50% of personal best	or peak flow is above 80% of personal best	or peak flow is above 80% of personal best for 2 weeks	or peak flow is above 80% of personal best for ____ months		
Times per day								

(Adapted from NHLBI 1995c).

This plan is provided as an example to clinicians.

Please note that the following long-term plan is included only as an example of how to fill out the plan. The treatment regimen itself does not correspond to recommendations made in the *Expert Panel Report II: Guidelines for the Diagnosis and Management of Asthma*.

Long-Term Self-Management Plan for Persistent Asthma (EXAMPLE ONLY)

Medication	At the FIRST sign of a cold or exposure to known trigger	If cough or wheeze is present or peak flow is between 50 and 80% of personal best	If cough or wheeze worsen or peak flow is below 50% of personal best	As soon as cough and wheeze have stopped or peak flow is above 80% of personal best	When there is no cough or wheeze for 2 weeks, even with activity or peak flow is above 80% of personal best for 2 weeks	When there is no cough or wheeze for ____ months or peak flow is above 80% of personal best for ____ months	Before exercise or physical activity	For rapidly worsening asthma (severe exacerbation)
Short-acting beta ₂ -agonist	2 puffs	2 puffs	2 puffs	2 puffs	0	0	2 puffs	2-4 puffs
Nonsteroidal anti-inflammatory	2 puffs	2 puffs	2 puffs	2 puffs	2 puffs	2 puffs	0	0
Inhaled corticosteroid	2 puffs	4 puffs	4 puffs	2 puffs	2 puffs	0	0	0
Antibiotic								
TIMES PER DAY	3	4 (every 4 hrs)	4 (every 4 hrs)	3	3	3	5-10 minutes before exercise	every 20 minutes for 3 doses*
Oral corticosteroid	0	0	2 mg/kg/day x 2 days then 1 mg/kg/day x 3 days	0	0	0	0	0

*If there is not a good response, seek emergency care immediately. If there is a good response return to the third column.

How To Use Your Peak Flow Meter

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.

Figure 1-7. Patient Handout (continued)

- 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.

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 beta₂-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 beta₂-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 beta₂-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 beta₂-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 beta₂-agonist (quick-relief medicine)
ACTION: Talk to your doctor about adding more medicine to control your asthma better (for example, an anti-inflammatory medication).

Adapted from *Nurses: Partners in Asthma Care*, National Asthma Education and Prevention Program, National Heart, Lung, and Blood Institute, 1995.

Introduction

Effective management of asthma relies on four integral components: **objective measures of lung function** not only to assess but also to monitor each patient's asthma; **pharmacologic therapy**; **environmental measures** to control allergens and irritants; and **patient education**. Part Two describes these critical elements of asthma management.

Goals of Therapy

Effective management of asthma has the following goals:

- Maintain (near) "normal" pulmonary function rates.
- Maintain normal activity levels (including exercise).
- Prevent chronic and troublesome symptoms (e.g., coughing or breathlessness in the night, in the early morning, or after exertion).
- Prevent recurrent exacerbations of asthma.
- Avoid adverse effects from asthma medications.

General Treatment Principles

Encompassing all components of effective asthma management are the following general treatment principles:

- **Asthma is a chronic condition with acute exacerbations.** Treatment requires a continuous care approach in order to control symptoms, prevent exacerbations, and reduce chronic airway inflammation.
- **Prevention of exacerbations is particularly important.** This includes avoiding triggers and allergens, especially in the indoor environment. It also includes around-the-clock medication treatment for many patients. Periodic assessment of these patients, especially with objective measures, will assure that their therapy is appropriate.
- **The treatment of asthma should be based on an understanding of the underlying pathophysiologic mechanisms.** Asthma therapy should include efforts to reduce underlying

inflammation in asthma and to relieve or prevent symptomatic airway narrowing. Such efforts should lead to reduction in airway hyperresponsiveness and help prevent irreversible airway obstruction.¹⁴ The increased appreciation of the importance of inflammation in the pathogenesis of asthma has led to this greater emphasis on the use of anti-inflammatory medication as first-line asthma therapy.

■ **Anticipatory or early interventions (facilitated by regular PEFR monitoring) in treating acute exacerbations of asthma reduce the likelihood of developing severe airway narrowing.**

Component 1

Objective Measures of Lung Function

Pulmonary function studies are essential for diagnosing asthma and for assessing the severity of asthma in order to make appropriate therapeutic recommendations. The use of objective measures of lung function is particularly important because subjective measures, such as patient symptom reports and physicians' physical examination findings, often do not correlate with the variability and severity of airflow obstruction.¹⁴

It is recommended that office spirometry be conducted in the initial assessment of all patients with, or being evaluated for, asthma and periodically thereafter as appropriate. Either spirometry or peak expiratory flow rate (PEFR) measured by a peak flow meter is recommended to assess the patient's response to therapy in the clinician's office, emergency department, and hospital. It is recommended that clinicians consider using home PEFR measurements to monitor the course of asthma and response to therapy in patients over 5 years old with moderate to severe asthma. For both spirometry and peak flow meter measurements, it is important to use correct techniques and equipment that meet established standards.^{6,7}

Spirometry

Pulmonary function is assessed by obtaining objective measurements of lung volumes or of flow rates produced with maximum expiratory effort. The most practical technique for obtaining these measurements is using a spirometer, which measures vital capacity, tidal volume, expiratory reserve volume, and inspiratory capacity. Most physicians' offices can successfully use an office spirometer. When office spirometry studies show abnormalities or complex questions arise, assessment in a specialized pulmonary testing facility should be considered.

Vital capacity is the most important measurement for assessing lung volume. Measurements of flow rate then determine whether any reduction in vital capacity is due to restriction or obstruction. (Abnormalities of lung function are categorized as restrictive and obstructive defects. Specific disease processes are associated with each type. Restrictive defects are often associated with parenchymal lung disease or limitation of chest wall movement. Obstructive defects result from impairment of airflow through the trachea and bronchi leading from the alveolar sacs.) Flow rates may be measured directly or determined by noting the volume expired over a period of time. Timed volumes measured on a spirometer include:

- **Peak expiratory flow rate (PEFR):** The maximum flow rate that can be generated during a forced expiratory maneuver with fully inflated lungs. PEFR is measured in liters per second and requires maximum effort for accuracy.
- **Forced vital capacity (FVC):** Total volume of air expired as rapidly as possible.
- **Forced expiratory volume 1 second (FEV₁):** The volume of air expired in 1 second from maximum inspiration.
- **Maximum midexpiratory flow rate (MMEF):** The slope of line between 25 percent and 75 percent of the forced expiratory volume.

Clinical decisions can in many cases be made with the use of spirometry alone:

- A reduced vital capacity and a normal flow rate are consistent with restrictive defect. Occasionally, the FEV₁ is reduced concomitantly with the reduction of the vital capacity. The flow rate can then be determined by assessing the percentage of the FEV₁ over the FVC: If there is no obstruction, this ratio is greater than 75 percent, and with severe restriction, the rate will approach 90 percent.

- A normal vital capacity with either impaired FEV₁ or impaired MMEF indicates pure obstruction. When the FEV₁ is severely reduced with clear evidence of obstruction (FEV₁/FVC ratio of less than 75 percent), the vital capacity can also be reduced due to severe obstruction alone.

- When the question of a mixed restrictive and obstructive defect occurs, further studies are necessary.

- When the maximum midexpiratory flow rate is the only abnormal finding, mild airflow obstruction is present, suggesting small airway disease.

Peak Expiratory Flow Rate Measurement

PEFR provides a simple, quantitative, reproducible measure of airway obstruction that can be obtained using either standard office peak flow meters or inexpensive, portable peak flow meters. PEFR measurements, when done with a good effort, correlate well with FEV₁ measured by spirometry.^{8,9} PEFR is an objective measurement analogous to the measurement of blood pressure with a sphygmomanometer.

PEFR measurement is a valuable clinical tool in the office, emergency department, and inpatient hospital service for helping to assess degree of airflow obstruction and severity, for monitoring response to therapy, for diagnosing exercise-induced asthma, and for detecting asymptomatic deterioration.¹⁰⁻¹¹ PEFR measurements, however, are not sufficient to make a diagnosis or

to fully evaluate physiologic impairment associated with asthma because PEFR is effort dependent and measures only large airway function.

When patients learn how to take PEFR measurements at home, the clinician's ability to provide effective treatment is improved. Daily monitoring of PEFR helps, for example, in detecting early stages of airway obstruction; assessing circadian (day-night) variations in lung function (which reflect degree of airway hyperresponsiveness);¹²⁻¹⁹ providing objective criteria in planning, initiating, or terminating treatment; facilitating communication between patient and clinician; and investigating specific allergens or school or workplace exposures that may exacerbate symptoms.^{20,21}

Interpreting PEFR measurements.

Because many patients' values are consistently higher or lower than average predicted norms (see Figure 3), it is important for each patient to establish a personal best PEFR value. This personal best value will be the standard against which subsequent measurements are evaluated by the patient and clinician. Personal best values can be established during a 2- to 3-week period in which the patient records PEFR measurements at least twice a day. The personal best is usually the highest PEFR measurement achieved in the p.m. measurement after a period of maximum therapy. A course of oral steroids may be needed to establish this personal best; and if the personal best is <80 percent of the predicted value, more aggressive therapy and continued daily monitoring are indicated. The personal best value should be reevaluated at least yearly to account for growth in children and progression of disease in children and adults. Further, peak flow meter measurements should be correlated periodically with office spirometry.

Using PEFR measurements at home to manage and monitor asthma. To integrate home PEFR monitoring into the treatment plan successfully, the clinician needs to explain how PEFR data are used to select and evaluate therapy. Regular supervision by the clinician is needed to ensure that the patient keeps PEFR

records up to date and takes appropriate action.

To help asthma patients use home PEFR monitoring, a system of PEFR zones may be useful.²²⁻²⁸ The zones can be established as a function of the patient's personal best or predicted value, whichever is highest. The emphasis is on the variability patients experience from their personal best or from one reading to the next rather than on isolated readings. It is recommended that daily measurements be made morning and evening—about 7 a.m. and 7 p.m. If the patient takes an inhaled medication, PEFR should be measured both before and after treatment. Taking PEFR measurements intermittently may lose the benefit of detecting early deterioration in lung function, but it may be preferred by some patients, particularly those with extremely stable asthma. If PEFR is measured only two or three times a week, both a.m. and p.m. readings on the same day are important.

When the zone system is adapted to a traffic light system, it is may be easier to use and remember.^{26,27}

- **Green (80 to 100 percent of personal best) signals all clear:** No asthma symptoms are present, and the routine treatment plan for maintaining control can be followed. For patients on chronic medications, consistent readings in the green zone may indicate an opportunity to consider a reduction in medications.

- **Yellow (50 to 80 percent of personal best) signals caution:** An acute exacerbation may be present, and a temporary increase in medication may be indicated. Alternatively, the overall asthma may not be under sufficient control, and maintenance therapy may need to be increased.

- **Red (below 50 percent personal best) signals a medical alert:** An immediate bronchodilator should be taken, and the clinician should be notified if PEFR measures do not return immediately and stay in yellow or green zones.

These zones are guidelines only; there are insufficient data to definitively establish zones for optimal therapy. Specific zones should be tailored by the clinician in recognition of each individual patient's circumstances.

Component 2 Pharmacologic Therapy

Discussion of this component of asthma management is in four parts: the pharmacologic properties of the medications used; the protocols for management of asthma as a chronic illness; the protocols for management of exacerbations of asthma; and the protocol for management of exercise-induced asthma.

The Medications

Pharmacologic therapy is used to treat reversible airflow obstruction and airway hyperresponsiveness. Medications include bronchodilators and anti-inflammatory agents; some drugs may act as both.

Whatever medication is used, it is essential for both patient and clinician to recognize that a poor or short-lasting response to treatment in the face of progressively worsening asthma mandates immediate, intensive medical care. An increased use of bronchodilators or the lack of an expected therapeutic response to a medication may be indications of diminished control of asthma. In fact, recent data suggest that increased use of bronchodilators is associated with increased asthma morbidity and mortality.¹ A decreasing therapeutic response may develop over a short period of time, or gradually during a period of days. Failure to appreciate the severity of asthma or an inadequate response to therapy are major risk factors for morbidity and mortality during exacerbations of asthma.

Anti-inflammatory Agents

Anti-inflammatory agents interrupt the development of bronchial inflammation and have a prophylactic or preventive action. They may also modulate or

terminate ongoing inflammatory reactions in the airways. These agents include corticosteroids, cromolyn sodium or cromolyn-like compounds, and other anti-inflammatory compounds.

Corticosteroids. The most effective anti-inflammatory drugs for the treatment of reversible airflow obstruction are corticosteroids. The primary mechanisms of action are interference with arachidonic acid metabolism and synthesis of leukotrienes and prostaglandins, prevention of directed migration and activation of inflammatory cells, and increased responsiveness of beta-receptors of airway smooth muscle. Corticosteroids can be administered parenterally, orally, or as aerosols.^{2,3} Dosages are suggested in Figures 4, 8, and 9 (see pages 20, 27, and 34) and on the charts that accompany the discussions of asthma management in following sections.

■ **Oral corticosteroid therapy.** Using oral corticosteroids in the early treatment of severe exacerbations of asthma prevents progression of the exacerbation, decreases the need for emergency department visits or hospitalizations, and reduces the morbidity of the disease. When oral corticosteroids are used to treat acute asthma, the onset of action occurs approximately 3 hours after administration with peak effectiveness occurring approximately after 6 to 12 hours.⁴

Oral or parenteral corticosteroids are, however, associated with many adverse effects in both short- or long-term therapeutic use.

—**Short-term** major adverse effects include reversible abnormalities in glucose metabolism, increased appetite, fluid retention, weight gain, rounding of the face, mood alteration, hypertension, peptic ulcer, and aseptic necrosis of the femur.

—**Long-term** oral corticosteroid therapy is limited by the risk of significant adverse effects that include osteoporosis, hypertension,

Cushing's syndrome, cataracts, myopathy, hypothalamic-pituitary-adrenal axis suppression, and, in rare instances, impaired immune mechanisms. Prolonged daily use of oral corticosteroids should thus be reserved for patients with severe asthma (despite use of high doses of inhaled corticosteroids).

Attempts to reduce dependence on oral corticosteroids should be made. For any patient requiring chronic therapy, a trial should be conducted to determine if the oral corticosteroids can be reduced or eliminated by the use of high-dose (two to four times the usual daily dose) inhaled corticosteroids. Other therapeutic regimens to reduce oral corticosteroid dependence—using troleandomycin, methotrexate, and gold—are still experimental and should be used only in selected patients under the supervision of an asthma specialist.

■ **Inhaled corticosteroid therapy.** Inhaled corticosteroids are safe and effective for the treatment of asthma.^{5,6} Because of the importance of airway inflammation in the pathogenesis of asthma, inhaled corticosteroids are being used as primary therapy for moderate and severe asthma. This approach not only provides symptomatic benefit but also reduces airway hyperresponsiveness.^{7,8} Dosages are suggested in Figures 4, 8, and 9 and the charts accompanying the discussions of asthma management in the following sections.

Concentrations per inhalation vary among the corticosteroid formulations beclomethasone, triamcinolone, and flunisolide. In the absence of complete data, the guidelines for total dosage may be applied. However, the relative anti-inflammatory, steroid-suppressive effects of these three distinct formulations have not been established.

Systemic adverse effects because of inhaled corticosteroid therapy are infrequent at doses currently approved in the United States. Long-term high-dose regimens of inhaled corticosteroids are being utilized, and long-term followup studies are under way. Local adverse effects of inhaled corticosteroid therapy

include oropharyngeal candidiasis, dysphonia, and occasional coughing resulting from upper airway irritation caused by inhaling the corticosteroid aerosol,¹⁰ but these adverse effects can be reduced or prevented by administering corticosteroids with a chamber or spacer and by rinsing the mouth after each use.

Cromolyn sodium. Administered prophylactically, cromolyn sodium inhibits early- and late-phase allergen-induced airway narrowing as well as acute airway narrowing after exercise and after exposure to cold dry air and sulfur dioxide. The mechanism of action is not fully understood, but it is considered that cromolyn sodium stabilizes and prevents mediator release from mast cells. Whether a patient will respond to cromolyn sodium can not be reliably predicted. A 4- to 6-week trial therapy may be required to determine efficacy in individual patients.^{1-4, 8, 10} Cromolyn sodium produces only minimal side effects, such as occasional coughing upon inhalation of the powder formulation.

Other anti-inflammatory compounds. Drugs that are being tested in clinical trials but not yet approved for the treatment of asthma in the United States include nedocromil sodium (which, in vitro, inhibits mediator release and inhibits and modulates allergen-induced hyperresponsiveness), antihistamines (which block acute bronchoconstrictor effects produced by inhaled histamine and in vitro may inhibit mediator release), and ketotifen (which has antihistaminic activity).

Bronchodilators

Bronchodilators act principally to dilate the airways by relaxing bronchial smooth muscle. They include beta-adrenergic agonists, methylxanthines, and anticholinergics.

Beta-adrenergic agonists (beta₂-agonists). Beta₂-agonists relax airway smooth muscle and may modulate mediator release from mast cells and basophils.^{12, 18} The desirable effects of beta-adrenergic agonists in asthma

therapy result from their action on beta₂-adrenergic receptors.

Inhaled beta₂-agonists are the medication of choice for treatment of acute exacerbations of asthma and for the prevention of exercise-induced asthma. Beta₂-agonists are also used chronically to aid in the control of persistent airway narrowing, although a recent report associates prolonged, regular administration (as opposed to as-needed use) of a potent inhaled beta₂-agonist with diminished control of asthma.¹ Therefore, exceeding three to four doses of inhaled beta₂-agonist on a daily regularly scheduled basis is not recommended.

Because asthma is an airway disease, inhaled beta₂-agonist therapy delivered directly to the airway is usually preferable to systemic oral therapy. Inhaled beta₂-agonist therapy, as compared to oral beta₂-agonist therapy, produces more bronchodilation; causes fewer systemic adverse effects such as cardiovascular stimulation, anxiety, and skeletal muscle tremor (although patients with preexisting cardiovascular disease, particularly the elderly, continue to be more likely to experience adverse cardiovascular reactions with inhaled therapy^{19, 20}); has a faster onset of action and similar duration of action; and achieves desired results at lower doses. Inhaled beta₂-agonists are available in metered-dose inhalers, dry-powder capsules, and compressor-driven nebulizers.

Methylxanthines. Theophylline is the principal methylxanthine used in asthma therapy. Although the precise mechanism is not clear (in vitro theophylline inhibits phosphodiesterases), theophylline serves as a mild-to-moderate bronchodilator, depending upon serum concentration.^{21, 22} When given in a sustained-release preparation, it has long duration of action and is thus particularly useful in the control of nocturnal asthma. When used in combination with usual doses of inhaled beta₂-agonists, theophylline may produce additional bronchodilation. In addition, theophylline may also reduce respiratory muscle fatigue²³ and possess some degree of anti-inflammatory activity.^{24, 25}

Theophylline has the potential for significant adverse effects, but these can generally be avoided by appropriate dosing and monitoring:

■ **Dosages** are suggested in Figures 4, 8, and 9 and on the charts accompanying the discussions of asthma management in the following sections. An optimal effect is produced by dosages that maintain a steady-state serum concentration of between 10 and 20 µg/mL. A more conservative approach is to aim for levels between 5 and 15 µg/mL,^{26, 27} a therapeutic range in which there appears to be a linear relation between log serum concentration and bronchodilator effect.

■ **Monitoring** of theophylline serum concentrations should be conducted when an asthma patient begins theophylline therapy and then at regular intervals of 6 to 12 months thereafter. It is also required when patients develop an adverse effect on their usual dose, when patients fail to exhibit the expected bronchodilator effect from an appropriate therapeutic regimen, when higher therapeutic levels are desired, and when conditions known to alter theophylline metabolism exist (see below).

Among points important to consider in relation to the use of theophylline are the following:

■ **Theophylline is eliminated from the body rapidly by some individuals**, especially children; sustained-release preparations are needed for chronic therapy.^{26, 28} Further, because preparations vary in intestinal transit time and in how they are affected by the presence of food (and its fat content) in the gut, physicians need to be familiar with the pharmacologic properties of the preparation selected in order to ensure efficacy.

■ **Theophylline clearance is reduced by several factors**, such as febrile illness, liver disease, congestive heart failure, and certain drugs (including cimetidine, quinoline, antibiotics, troleandomycin, and, to a lesser extent, erythromycin). These may reduce the elimination rate and allow toxic concentrations to develop. The dose of theophylline should be reduced in patients affected by these factors.

■ **The signs and symptoms of theophylline intoxication involve many different organ systems.** Serum concentrations under 15 µg/mL are generally not associated with theophylline toxicity. Gastrointestinal symptoms—nausea and vomiting—are the most common early events of toxicity. Seizures may occur that are not preceded by evidence of central nervous system stimulation. Children may experience behavioral disturbances because of central nervous system stimulation; however, a Food and Drug Administration review has concluded that current data do not support some earlier reports of theophylline's adverse effect on the learning of school children.²⁹ Cardiopulmonary effects include tachycardia, arrhythmias, and, occasionally, stimulation of the respiratory center (tachypnea). Diuresis and relaxation of the detrusor muscle (causing difficulty in urination in older men with prostatism) may occur. Important metabolic effects such as hyperglycemia and hypokalemia may also occur.

Anticholinergics. Inhaled anticholinergic agents produce bronchodilation by reducing intrinsic vagal tone to the airways. Such agents also block reflex bronchoconstriction caused by inhaled irritants. However, anticholinergic agents such as atropine have lost favor because of the length of time for onset of action and because of such local and systemic adverse effects as drying of respiratory secretions, blurred vision, and cardiac and central nervous system stimulation. Ipratropium is a quaternary derivative whose development has stimulated new interest in anticholinergic therapy.³⁰ Because of its very low bioavailability when inhaled, it lacks atropine's side effects. Some reports show it is effective during status asthmaticus when used in nebulized form in combination with beta₂-agonists.^{31,32} Its benefits in day-to-day management of asthma have not yet been established.

Management of Chronic Asthma

General Principles of Management

■ **Treat the underlying pathology of asthma.** Therapy should not merely alleviate symptoms but also prevent exacerbations and control chronic symptoms by reducing inflammation. First-line therapy should focus on preventing or reversing the airway inflammation that is a principal factor in the airway hyperresponsiveness that characterizes asthma and determines symptoms, disease severity, and possibly mortality.

■ **Tailor general therapy guidelines to individual patient needs.** Asthma is a disease that varies among patients. Further, the degree of severity for any individual may change from one season or year to the next. Therefore, specific asthma therapy—dictated by the severity of disease, medication tolerance, and sensitivity to environmental allergen—must be selected to fit the needs of individual patients.

The severity of asthma is often not appreciated by either patient or clinician on routine evaluation. However, by determining the extent to which activity is limited, by evaluating nighttime symptoms, and by assessing pulmonary function (by both spirometry and peak flow determinations), the clinician will be better able to begin appropriate therapy for a patient.

■ **Treat asthma triggers, associated conditions, and special problems.** Consideration of common asthma triggers is essential.

- Exposure to known *allergens and irritants* must be reduced or eliminated (see Component 3, Environmental Measures).
- Viral upper respiratory syndromes* can provoke exacerbations of asthma, especially in young children. Although there is no specific therapy, patients and parents of patients need to be vigilant in adhering to the regular asthma medication treatment plans and in being alert for early signs of

an acute exacerbation so that asthma medication may be started or increased immediately. Some patients, especially children, have an established pattern in which asthma deteriorates rapidly every time they have a viral respiratory infection. For these selected patients, it may be appropriate to institute a short course of oral corticosteroid therapy at the earliest sign of viral respiratory infection.

- Bacterial otitis and sinusitis* may be associated factors for asthma for all age groups. Even aggressive asthma therapy may fail if such infections are overlooked. Antimicrobial therapy (for 10 days to 3 weeks, depending on the chronicity of the patient's history of ear or sinus disease) is necessary if a bacterial infection is present in the airways, although it remains an adjuvant to primary asthma therapy.
- Influenza vaccinations and pneumococcal vaccine* should be considered for patients with moderate or severe asthma in order to avoid aggravation of asthma.
- Allergic and nonallergic rhinitis* should be treated with antihistamines, cromolyn sodium nasal spray, or topical nasal corticosteroids.
- Treatment of a known trigger prior to exposure*, with inhaled beta₂-agonist or cromolyn sodium or both, can prevent or diminish an asthmatic response. This is well demonstrated in relation to exercise (see the Exercise-Induced Asthma section). The same principles can be applied to other situations, including exposure to antigens (e.g., animal dander), cold air, or other irritants. However, because beta-agonists block symptoms during exposure, their use before antigen exposure may lead the patient to remain longer in the contaminated environment and increase the likelihood of symptoms occurring 4 to 6 hours later.