CHAPTER 44
Drugs for Asthma and Other Bronchoconstrictive Disorders

KEY TERMS
- Adrenergic drugs
- Anticholinergics
- Asthma
- Beta₂-adrenergic agonists
- Bronchitis
- Bronchospasm
- Corticosteroids
- Emphysema
- Hyperreactivity
- Leukotrienes
- Mast cells
- Occupational asthma
- Xanthine

LEARNING OBJECTIVES
After studying this chapter, you will be able to:
1. Describe the main pathophysiologic characteristics of asthma and other bronchoconstrictive disorders.
2. Discuss the uses and effects of bronchodilating drugs, including adrenergics, anticholinergics, and xanthines.
3. Differentiate between short-acting and long-acting inhaled beta₂-adrenergic agonists in terms of uses and nursing process implications.
4. Discuss the uses of anti-inflammatory drugs, including corticosteroids, leukotriene modifiers, and mast cell stabilizers.
5. Discuss reasons for using inhaled drugs when possible.
6. Differentiate between “quick relief” and long-term control of asthma symptoms.
7. Discuss the use of antiasthmatic drugs in special populations.
8. Teach patients self-care and long-term control measures.

Applying Your Knowledge
Lynne Albright is a 48-year-old woman who has adult-onset asthma. Her medications include zafirlukast and salmeterol/fluticasone (Advair) daily. She uses an albuterol inhaler as needed. Ms. Albright is a professor in women’s studies for a large university. You are the on-site nurse for the campus.

Introduction
The drugs described in this chapter are used to treat respiratory disorders characterized by bronchoconstriction, inflammation, mucosal edema, and excessive mucus production (asthma, bronchitis, and emphysema). Asthma is emphasized because of its widespread prevalence, especially in urban populations. Compared with Caucasians, African Americans and Hispanics have a higher prevalence and African Americans have a higher death rate from asthma. However, the differences are usually attributed to urban living and lesser access to health care rather than race or ethnic group. Occupational asthma (i.e., asthma resulting from repeated and prolonged exposure to industrial inhalants) is also a major health problem. Persons with occupational asthma often have symptoms while in the work environment, with improvement on days off and during vacations. Symptoms sometime persist after termination of exposure. Asthma may occur at any age but is especially common in children and older adults. Children who are exposed to allergens and airway
irritants such as tobacco smoke during infancy are at high risk for development of asthma.

**Asthma**

**Symptoms**

Asthma is an airway disorder characterized by bronchoconstriction, inflammation, and hyperreactivity to various stimuli. Resultant symptoms include dyspnea, wheezing, chest tightness, cough, and sputum production. Wheezing is a high-pitched, whistling sound caused by turbulent airflow through an obstructed airway. Thus, any condition that produces significant airway occlusion can cause wheezing. However, a chronic cough may be the only symptom for some people with asthma. Symptoms vary in incidence and severity from occasional episodes of mild respiratory distress, with normal functioning between “attacks,” to persistent, daily, or continual respiratory distress if not adequately controlled. Inflammation and damaged airway mucosa are chronically present, even when patients appear symptom free.

Acute symptoms of asthma may be precipitated by numerous stimuli, and hyperreactivity to such stimuli may initiate both inflammation and bronchoconstriction. Viral infections of the respiratory tract are often the causative agents, especially in infants and young children whose airways are small and easily obstructed. Asthma symptoms may persist for days or weeks after the viral infection resolves. In about 25% of patients with asthma, aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) can precipitate an attack. Some patients are allergic to sulfites and may experience life-threatening asthma attacks if they ingest foods processed with these preservatives (e.g., beer, wine, dried fruit). The U.S. Food and Drug Administration (FDA) has banned the use of sulfites on foods meant to be served raw, such as open salad bars. Patients with severe asthma should be cautioned against ingesting food and drug products containing sulfites or metabisulfites.

Gastroesophageal reflux disease (GERD), a common disorder characterized by heartburn and esophagitis, is also associated with asthma. Asthma that worsens at night may be associated with nighttime acid reflux. Although the precise mechanism of pulmonary symptoms of GERD in asthma is not known, there are suggestions that microaspirations or a vagally mediated, reflex type of bronchoconstriction may be involved. Asthma may also aggravate GERD, because antiasthma medications that dilate the airways also relax muscle tone in the gastroesophageal sphincter and may increase acid reflux. It has been suggested that in individuals with inadequate control of their asthma symptoms, a trial of an H2-blocker or proton-pump inhibitor therapy may be of benefit.

Additional precipitants may include allergens (e.g., pollens, molds), airway irritants and pollutants (e.g., chemical fumes, cigarette smoke, automobile exhaust), cold air, and exercise. Acute episodes of asthma may last minutes to hours.

**Pathophysiology**

Bronchoconstriction (also called bronchoctasis) involves strong muscle contractions that narrow the airways. Airway smooth muscle extends from the trachea through the bronchioles. It is wrapped around the airways in a spiral pattern, and contraction causes a sphincter type of action that can completely occlude the airway lumen. Bronchoconstriction is aggravated by inflammation, mucosal edema, and excessive mucus and may be precipitated by the numerous stimuli described above.

When lung tissues are exposed to causative stimuli, mast cells release substances that cause bronchoconstriction and inflammation. Mast cells are found throughout the body in connective tissues and are abundant in tissues surrounding capillaries in the lungs. When sensitized mast cells in the lungs or eosinophils in the blood are exposed to allergens or irritants, multiple cytokines and other chemical mediators (e.g., acetylcholine, cyclic guanosine monophosphate [GMP], histamine, interleukins, leukotrienes, prostaglandins, serotonin) are synthesized and released. These chemicals act directly on target tissues of the airways, causing smooth muscle constriction, increased capillary permeability and fluid leakage, and changes in the mucus-secreting properties of the airway epithelium.

Bronchoconstrictive substances are antagonized by cyclic adenosine monophosphate (cyclic AMP). Cyclic AMP is an intracellular substance that initiates various intracellular activities, depending on the type of cell. In lung cells, cyclic AMP inhibits release of bronchoconstrictive substances and thus indirectly promotes bronchodilation. In mild to moderate asthma, bronchoconstriction is usually recurrent and reversible, either spontaneously or with drug therapy. In advanced or severe asthma, airway obstruction becomes less reversible and worsens because chronically inflamed airways undergo structural changes (e.g., fibrosis, enlarged smooth muscle cells, enlarged mucous glands), called “airway remodeling,” that inhibit their function.

**National Asthma Education and Prevention Program (NAEPP)**

Because of asthma’s significance as a public health problem, the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) established the NAEPP. The NAEPP assembled a group of experts who established “Guidelines for the Diagnosis and Management of Asthma.” After nearly a decade, these guidelines (Box 44-1) were updated in 2007, including an expanded portion on childhood asthma. Further distinction is placed on the importance of classifying asthma severity and assessing asthma control. The guidelines are the current “standard of care” for adults and children with asthma and center around four essential components of asthma care: assessment and monitoring, patient education, control of factors contributing to asthma severity, and pharmacologic treatment. Additional information can be obtained from http://www.nhlbi.nih.gov.

**Chronic Bronchitis and Emphysema**

Chronic bronchitis and emphysema, commonly called chronic obstructive pulmonary disease (COPD), usually develop after long-standing exposure to airway irritants such as cigarette smoke. In these conditions, bronchoconstriction and
Establish and teach patients/parents/caregivers about quick relief measures and long-term control measures. Guide patients to identify and control environmental factors that aggravate asthma.

For acute attacks, gain control as quickly as possible (a short course of systemic corticosteroids may be needed); then step down to the least medication necessary to maintain control.

Review the treatment regimen every 1 to 6 months. If control is inadequate, the treatment regimen may need to be changed. For example, frequent or increasing use of a short-acting beta2 agonist may also be needed. Evaluate patients' medication techniques (e.g., correct use of inhalers), adherence, and environmental control measures.

Quick Relief for Acute Exacerbations

**Adults and children > 5 years:** Short-acting, inhaled, beta2 agonist, 2–4 puffs as needed. If symptoms are severe, patients may need up to 3 treatments at 20-minute intervals or a nebulizer treatment. A short course of a systemic corticosteroid may also be needed.

**Children 5 years and younger:** Short-acting beta2 agonist by nebulizer or face mask and spacer or holding chamber. Alternative: oral beta2 agonist. With viral respiratory infections, the beta2 agonist may be needed q4–6h up to 24 hours or longer and a systemic corticosteroid may be needed.

Long-Term Control

**Step 1 Mild Intermittent** (symptoms 2 days/week or less or 2 nights/month or less): No daily medication needed; treat acute exacerbations with an inhaled beta2 agonist and possibly a short course of a systemic corticosteroid.

**Step 2 Mild Persistent** (symptoms >2/week but <1×/day or >2 nights/month):

- **Low-dose inhaled corticosteroid**
- **Medium-dose inhaled corticosteroid**
- **High-dose inhaled corticosteroid**

**Step 3 Moderate Persistent** (symptoms daily and 1 night/week):

- **Adults and children > 5 years:** Low- to medium-dose inhaled corticosteroid and a long-acting beta2 agonist. Alternatives: increase corticosteroid dose or continue low to medium dose of corticosteroid and add a leukotriene modifier or theophylline.

- **Children < 5 years:** Low-dose inhaled corticosteroid and a long-acting beta2 agonist or medium-dose inhaled corticosteroid.

**Step 4 Severe Persistent** (symptoms continual during daytime and frequent at night):

- **Adults and children > 5 years:** High-dose inhaled corticosteroid and long-acting beta2 agonist and, if necessary, a systemic corticosteroid (2 mg/kg/d, not to exceed 60 mg/d). Reduce systemic corticosteroid when possible.

- **Children < 5 years:** Same as for adults and older children.

### Low (L), Medium (M), and High (H) Doses of Inhaled Corticosteroids:

<table>
<thead>
<tr>
<th>Corticosteroid</th>
<th>Adults (mcg)</th>
<th>Children (12 y and Younger) (mcg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone (42 or 84 mcg/puff)</td>
<td>L: 168–504</td>
<td>L: 84–336</td>
</tr>
<tr>
<td></td>
<td>M: 504–840</td>
<td>M: 336–672</td>
</tr>
<tr>
<td></td>
<td>H: &gt;840</td>
<td>H: &gt;672</td>
</tr>
<tr>
<td></td>
<td>H: &gt;480</td>
<td>H: &gt;320</td>
</tr>
<tr>
<td>Budesonide (200 mcg/ inhalation)</td>
<td>L: 200–600</td>
<td>L: 200–400</td>
</tr>
<tr>
<td></td>
<td>M: 600–1200</td>
<td>M: 400–800</td>
</tr>
<tr>
<td></td>
<td>H: &gt;1200</td>
<td>H: &gt;800</td>
</tr>
<tr>
<td>Budesonide inhalation suspension (child dose only)</td>
<td>L: 0.5 mg</td>
<td>L: 0.5 mg</td>
</tr>
<tr>
<td></td>
<td>M: 1.0 mg</td>
<td>M: 2.0 mg</td>
</tr>
<tr>
<td></td>
<td>H: &gt;800</td>
<td>H: &gt;800</td>
</tr>
<tr>
<td>Flunisolide (250 mcg/puff)</td>
<td>L: 500–1000</td>
<td>L: 500–750</td>
</tr>
<tr>
<td></td>
<td>H: &gt;2000</td>
<td>H: &gt;1250</td>
</tr>
<tr>
<td>Fluticasone aerosol (44, 110, or 220 mcg/puff)</td>
<td>L: 88–264</td>
<td>L: 88–176</td>
</tr>
<tr>
<td></td>
<td>H: &gt;660</td>
<td>H: &gt;440</td>
</tr>
<tr>
<td>Fluticasone powder (50, 100, or 250 mcg/puff)</td>
<td>L: 100–300</td>
<td>L: 100–200</td>
</tr>
<tr>
<td></td>
<td>M: 300–600</td>
<td>M: 200–400</td>
</tr>
<tr>
<td></td>
<td>H: &gt;600</td>
<td>H: &gt;400</td>
</tr>
<tr>
<td>Triamcinolone acetonide (100 mcg/puff)</td>
<td>L: 400–1000</td>
<td>L: 400–800</td>
</tr>
<tr>
<td></td>
<td>H: &gt;2000</td>
<td>H: &gt;1200</td>
</tr>
</tbody>
</table>

*Adapted from NAEPP Expert Panel Report 2 (NIH Publication No. 97-4051, 1997) and the Update on Selected Topics 2002 (NIH Publication No. 02-5075).*

**Definition**

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.”

**Goals of Therapy**

1. Minimal or no chronic symptoms day or night
2. Minimal or no exacerbations
3. No limitations on activities; for children, no school/parent’s work missed
4. Minimal use of short-acting inhaled beta2 agonist (<1 time per day, <1 canister/month)
5. Minimal or no adverse effects from medications

**General Recommendations**

- Establish and teach patients/parents/caregivers about quick relief measures and long-term control measures. Assist to identify and control environmental factors that aggravate asthma.
- For acute attacks, gain control as quickly as possible (a short course of systemic corticosteroids may be needed); then step down to the least medication necessary to maintain control.
- Review the treatment regimen every 1 to 6 months. If control is adequate and goals are being met, a gradual stepwise reduction in medication may be possible. If control is inadequate, the treatment regimen may need to be changed. For example, frequent or increasing use of a short-acting beta2 agonist may also be needed. Evaluate patients' medication techniques (e.g., correct use of inhalers), adherence, and environmental control measures.
inflammation are more constant and less reversible than with asthma. Anatomic and physiologic changes occur over several years and lead to increasing dyspnea, activity intolerance, and reduced quality of life. These conditions usually affect middle-aged or older adults.

**Drug Therapy**

Two general classifications of drugs are used for asthma management: long-term (prophylactic) control medications to achieve and maintain control of persistent asthma and quick relief (rescue) medications used during periods of acute symptoms and exacerbations. Specifically, two major groups of drugs used to treat asthma, acute and chronic bronchitis, and emphysema are bronchodilators and anti-inflammatory drugs. Bronchodilators are used to prevent and treat bronchoconstriction; anti-inflammatory drugs are used to prevent and treat inflammation of the airways. Reducing inflammation also reduces bronchoconstriction by decreasing mucosal edema and mucous secretions that narrow airways and by decreasing airway hyperreactivity to various stimuli. The drugs are described in the following sections; pharmacokinetic characteristics of inhaled drugs are listed in Table 44-1.

**Bronchodilators**

Table 44-2 lists routes and dosage ranges of the bronchodilators.

**Adrenergics**

Adrenergic drugs (see Chap. 17) stimulate beta₂-adrenergic receptors in the smooth muscle of bronchi and bronchioles. The receptors, in turn, stimulate the enzyme adenyl cyclase to increase production of cyclic AMP. The increased cyclic AMP produces bronchodilation. Some beta-adrenergic drugs (e.g., epinephrine) also stimulate beta₁-adrenergic receptors in the heart to increase the rate and force of contraction. Cardiac stimulation is an adverse effect when the drugs are given for bronchodilation. These drugs are contraindicated in patients with cardiac tachydysrhythmias and severe coronary artery disease; they should be used cautiously in patients with hypertension, hyperthyroidism, diabetes mellitus, and seizure disorders.

Epinephrine may be injected subcutaneously in an acute attack of bronchoconstriction, with therapeutic rescue effects in approximately 5 minutes and lasting for approximately 4 hours. However, an inhaled selective beta₂ agonist is the drug of choice in this situation. Epinephrine is also available without prescription in a pressurized aerosol form (e.g., Primatene). Almost all over-the-counter aerosol products promoted for use in asthma contain epinephrine. These products are often abused and may delay the patient from seeking medical attention. Patients should be cautioned that excessive use may produce hazardous cardiac stimulation and other adverse effects.

Albuterol and levalbuterol are short-acting beta₂-adrenergic agonists used for prevention and treatment of bronchoconstriction. These drugs act more selectively on beta₂ receptors and cause less cardiac stimulation than epinephrine. Most often taken by inhalation, they are also the most effective bronchodilators and the treatment of first choice to relieve acute asthma. Because the drugs can be effectively delivered by aerosol or nebulization, even to young children and to patients on mechanical ventilation, there is seldom a need to give epinephrine or other nonselective adrenergic drugs by injection.

The beta₂ agonists are usually self-administered by metered-dose inhalers (MDIs). Although most drug references still list a regular dosing schedule (e.g., every 4 to 6 hours),

<table>
<thead>
<tr>
<th>Table 44-1</th>
<th>Pharmacokinetics of Selected Inhaled Antiasthma Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic Name</strong></td>
<td><strong>Onset (min)</strong></td>
</tr>
<tr>
<td>Adrenergics</td>
<td></td>
</tr>
<tr>
<td>Albuterol</td>
<td>5</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td>5–10</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>30–48 COPD 120</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td></td>
</tr>
<tr>
<td>Ipratropium</td>
<td>1–3</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td></td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>Rapid</td>
</tr>
<tr>
<td>Budesonide</td>
<td>Immediate</td>
</tr>
<tr>
<td>Flunisolide</td>
<td>Slow</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>Slow</td>
</tr>
</tbody>
</table>
### Table 44-2: Drugs at a Glance: Bronchodilating Drugs

<table>
<thead>
<tr>
<th>Generic/Trade Name</th>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bronchodilators</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adrenergics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Albuterol</strong> (Proventil, Ventolin, AccuNeb)</td>
<td>Inhalation aerosol (90 mcg/actuation): 1–2 oral inhalations q4–6h; prevention of exercise-induced bronchospasm, 2 inhalations 1 min before exercise</td>
<td>Inhalation aerosol: 4 y and older (12 y and older for Proventil), same as adults</td>
</tr>
<tr>
<td></td>
<td>Inhalation solution via nebulizer, 2.5 mg 3–4 times daily (in 2.5 mL sterile saline, over 5–15 min)</td>
<td>Nebulizer solution, 12 y and older, same as adults; 2–12 y (AccuNeb), 1.25 mg 3–4 times daily, as needed, over 5–15 min</td>
</tr>
<tr>
<td></td>
<td>Regular tablets: PO 2–4 mg 3–4 times daily</td>
<td>Regular tablets: 12 y and older, same as adults; 6–12 y, 2 mg 3–4 times daily</td>
</tr>
<tr>
<td></td>
<td>Extended-release tablets: Proventil Repetabs PO 4–8 mg q12h, initially. Increase if necessary to a maximum of 32 mg/d, in divided doses, q12h.</td>
<td>Extended-release tablets: 12 y and older, same as adults; 6–12 y: PO 4 mg q12h initially; increase if necessary to a maximum of 24 mg/d, in divided doses, q12h.</td>
</tr>
<tr>
<td><strong>Epinephrine</strong> (Adrenalin, Bronkaid)</td>
<td>Aqueous solution (epinephrine 1:1000), Sub-Q 0.3–0.5 mg; dose may be repeated after 20 min if necessary for 3 doses Inhalation by inhaler, one or two inhalations 4–6 times per day Inhalation by nebulizer, 1–3 inhalations of 2.25% racemic epinephrine in 2.5 mL normal saline up to q3h</td>
<td>Aqueous solution (epinephrine 1:1000), Sub-Q 0.01 mL/kg q4h as needed. A single dose should not exceed 0.5 mL. Inhalation, same as adults for both inhaler and nebulizer</td>
</tr>
<tr>
<td><strong>Formoterol</strong> (Foradil)</td>
<td>Oral inhalation by special inhaler (Aerolizer), 12 mcg (contents of 1 capsule) twice daily, q12h</td>
<td>5 y and older, same as adults</td>
</tr>
<tr>
<td><strong>Levalbuterol</strong> (Xopenex, MDI: Xopenex HFA)</td>
<td>Nebulizer, 0.63–1.25 mg 3 times daily, q6–8h MDI: 1–2 puffs q4–6h</td>
<td>12 y and older, same as adults 6–11 y: Nebulizer, 0.31 mg 3 times daily, q6–8h MDI ≥4 y same as adults</td>
</tr>
<tr>
<td><strong>Metaproterenol</strong> (Alupent)</td>
<td>Inhalation,* 2–3 puffs (0.65 mg/dose), q3–4h; maximum dose, 12 inhalations/d</td>
<td>Inhalation, not recommended for use in children &lt;12 y</td>
</tr>
<tr>
<td><strong>Salmeterol</strong> (Serevent)</td>
<td>Inhalation powder: 1 inhalation (50 mcg) q12h</td>
<td>&lt;12 y, dosage not established Inhalation powder: 4 y and older, same as adults</td>
</tr>
<tr>
<td><strong>Terbutaline</strong></td>
<td>PO 2.5–5 mg q6–8h; maximum dose, 15 mg/d Sub-Q 0.25 mg, repeated in 15–30 min if necessary, q4–6h</td>
<td>PO 2.5 mg 3 times per day for children 12 y and older; maximum dose, 7.5 mg/d Sub-Q dosage not established</td>
</tr>
<tr>
<td><strong>Anticholinergics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ipratropium</strong> bromide (Atrovent)</td>
<td>Two inhalations (36 mcg) from the metered-dose inhaler 4 times per day</td>
<td>Dosage not established</td>
</tr>
<tr>
<td><strong>Tiotropium</strong> (Spiriva)</td>
<td>One tablet (18 mcg) in HandiHaler once daily</td>
<td>Dosage not established</td>
</tr>
<tr>
<td><strong>Xanthines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Short-acting theophylline</strong> (Aminophylline)</td>
<td>PO, 500 mg initially, then 200–300 mg q6–8h; IV infusion, 6 mg/kg over 30 min, then 0.1–1.2 mg/kg/h</td>
<td>PO, 7.5 mg/kg initially, then 5–6 mg/kg q6–8h; IV infusion, 6 mg/kg over 30 min, then 0.6–0.9 mg/kg/h</td>
</tr>
</tbody>
</table>
asthma experts recommend that the drugs be used when needed (e.g., to treat acute dyspnea or prevent dyspnea during exercise). If these drugs are overused, they lose their bronchodilating effects because the beta₂-adrenergic receptors become unresponsive to stimulation. This tolerance does not occur with the long-acting beta₂ agonists. Formoterol and salmeterol are long-acting beta₂-adrenergic agonists used only for prophylaxis of acute bronchoconstriction. They are not effective in acute attacks because they have a slower onset of action than the short-acting drugs (up to 20 minutes for salmeterol). Effects last 12 hours and the drugs should not be taken more frequently. If additional bronchodilating medication is needed, a short-acting agent (e.g., albuterol) should be used. The FDA has issued a BLACK BOX WARNING that initiating salmeterol in individuals with significantly worsening or acutely deteriorating asthma may be life-threatening.

Metaproterenol is a relatively selective, intermediate-acting beta₂-adrenergic agonist that may be given orally or by MDI. It is used to treat acute bronchospasm and to prevent exercise-induced asthma. In high doses, metaproterenol loses some of its selectivity and may cause cardiac and central nervous system (CNS) stimulation.

Terbutaline is a relatively selective beta₂-adrenergic agonist that is a long-acting bronchodilator. When given subcutaneously, terbutaline loses its selectivity and has little advantage over epinephrine. Muscle tremor is the most frequent side effect with this agent.

Anticholinergics

Anticholinergics (see Chap. 20) block the action of acetylcholine in bronchial smooth muscle when given by inhalation. This action reduces intracellular GMP, a bronchoconstrictive substance.

Ipratropium was formulated to be taken by inhalation for maintenance therapy of bronchoconstriction associated with chronic bronchitis and emphysema. Improved pulmonary function usually occurs in a few minutes. Ipratropium acts synergistically with adrenergic bronchodilators and may be used concomitantly. It improves lung function about 10% to 15% over an inhaled beta, agonist alone. Ipratropium may also be used to treat rhinorrhea associated with allergic rhinitis and the common cold. It is available as a nasal spray for such usage. Ipratropium is poorly absorbed and produces few systemic effects. However, cautious use is recommended in patients with narrow-angle glaucoma and prostatic hypertrophy. The most common adverse effects are cough, nervousness, nausea, gastrointestinal upset, headache, and dizziness.

Tiotropium (Spiriva) was approved to be taken once daily by inhalation for maintenance therapy of bronchoconstriction associated with chronic bronchitis and emphysema. Tiotropium has differences in its pharmacokinetic and pharmacologic properties that may make it superior to ipratropium as an anticholinergic agent. The primary adverse effect of tiotropium is dry mouth, though other effects include headache, dizziness, abdominal pain, constipation, diarrhea, flulike symptoms, and chest pain. Cautious use is recommended in patients with narrow-angle glaucoma.

Xanthines

The main xanthine used clinically is theophylline. Despite many years of use, the drug’s mechanism of action is unknown. Various mechanisms have been proposed, such as inhibiting phosphodiesterase enzymes that metabolize cyclic AMP, increasing endogenous catecholamines, inhibiting calcium ion movement into smooth muscle, inhibiting prostaglandin synthesis and release, or inhibiting the release of bronchoconstrictive substances from mast cells and leukocytes. In addition to bronchodilation, other effects that may be beneficial in asthma and COPD include inhibiting pulmonary edema by decreasing vascular permeability, increasing the ability of cilia to clear mucus from the airways, strengthening contractions of the
Diabetes, and decreasing inflammation. Theophylline also increases cardiac output, causes peripheral vasodilation, exerts a mild diuretic effect, and stimulates the CNS. The cardiovascular and CNS effects are adverse effects. Serum drug levels should be monitored to help regulate dosage and avoid adverse effects. Theophylline preparations are contraindicated in patients with acute gastritis and peptic ulcer disease; they should be used cautiously in those with cardiovascular disorders that could be aggravated by drug-induced cardiac stimulation.

Theophylline was formerly used extensively in the prevention and treatment of bronchoconstriction associated with asthma, bronchitis, and emphysema. Now it is considered a second-line agent that may be added in severe disease inadequately controlled by first-line drugs. Numerous dosage forms of theophylline are available. Theophylline ethylenediamine (aminophylline) contains approximately 85% theophylline and is the only formulation that can be given intravenously (IV). However, IV aminophylline is not recommended for emergency treatment of acute asthma because studies indicate little, if any, added benefit in adults or children. Oral theophylline preparations may be used for long-term treatment. Most formulations contain anhydrous theophylline (100% theophylline) as the active ingredient, and sustained-action tablets (e.g., Theochron) are more commonly used than other formulations. Theophylline is metabolized in the liver; metabolites and some unchanged drug are excreted through the kidneys.

**Applying Your Knowledge 44-1**

*How Can You Avoid This Medication Error?*

Ms. Albright is having difficulty breathing and visits the onsite clinic. You assist her in the administration of her inhaled bronchodilator, the Advair.

**Anti-Inflammatory Agents**

Table 44-3 provides routes and dosage ranges of anti-inflammatory antiasthmatic drugs.

**Corticosteroids**

Corticosteroids (see Chap. 23) are used in the treatment of acute and chronic asthma and other bronchoconstrictive disorders. They suppress the release of inflammatory mediators, block the generations of cytokines, and decrease the recruitment of airway eosinophils. Beneficial effects of suppressing airway inflammation include decreased mucus secretion, decreased edema of airway mucosa, and repair of damaged epithelium, with subsequent reduction of airway reactivity. Corticosteroids increase the number and sensitivity of beta2-adrenergic receptors, which restores or increases the effectiveness of beta2-adrenergic bronchodilators. The number of beta2 receptors increases within approximately 4 hours, and improved responsiveness to beta2 agonists occurs within approximately 2 hours.

In acute, severe asthma, a systemic corticosteroid in relatively high doses is indicated in patients whose respiratory distress is not relieved by multiple doses of an inhaled beta2 agonist (e.g., every 20 minutes for 3 to 4 doses). The corticosteroid may be given IV or orally, and IV administration offers no therapeutic advantage over oral administration. After the drug is started, pulmonary function usually improves in 6 to 8 hours. Most patients achieve substantial benefit within 48 to 72 hours and the drug is usually continued for 7 to 10 days. Multiple doses are usually given because studies indicate that maintaining the drug concentration at steroid receptor sites in the lung is more effective than high single doses. High single or pulse doses do not increase therapeutic effects; they may increase risks of developing myopathy and other adverse effects, however. In some infants and young children with acute, severe asthma, oral prednisone for 3 to 10 days has relieved symptoms and prevented hospitalization.

Corticosteroids are the most consistently effective long-term control medications for asthma. In chronic asthma, a corticosteroid is usually taken by inhalation, on a daily schedule. It is often given concomitantly with one or more bronchodilators and may be given with another anti-inflammatory drug such as a leukotriene modifier or a mast cell stabilizer. In some instances, the other drugs allow smaller doses of the corticosteroid. For acute flare-ups of symptoms during treatment of chronic asthma, a systemic corticosteroid may be needed temporarily to regain control.

In early stages of the progressive disease, patients with COPD are unlikely to need corticosteroid therapy. In later stages, however, they usually need periodic short-course therapy for episodes of respiratory distress. When needed, the corticosteroid is given orally or parenterally because effectiveness of inhaled corticosteroids has not been established in COPD (see Evidence-Based Practice Box 23-1: Efficacy of Corticosteroids on the Outcome in Patients With Acute Exacerbations of COPD).

In end-stage COPD, patients often become "steroid-dependent" and require daily doses because any attempt to reduce dosage or stop the drug results in respiratory distress. Such patients experience numerous serious adverse effects of prolonged systemic corticosteroid therapy.

Corticosteroids should be used with caution in patients with peptic ulcer disease, inflammatory bowel disease, hypertension, congestive heart failure, and thromboembolic disorders. However, they cause fewer and less severe adverse effects when taken in short courses or by inhalation than when taken systemically for long periods of time.

Beclomethasone, budesonide, flunisolide, fluticasone, mometasone, and triamcinolone are topical corticosteroids for inhalation. Most inhaled drugs are being reformulated (indicated with “HFA” secondary to the propellant being used). Topical administration minimizes systemic absorption and adverse effects. These preparations may substitute for or allow reduced dosage of systemic corticosteroids. In people with...
### Table 44-3

**Drugs at a Glance: Anti-Inflammatory Antiasthmatic Drugs**

<table>
<thead>
<tr>
<th>Generic/Trade Name</th>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Corticosteroids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Beclomethasone</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(QVAR)</td>
<td>Oral inhalation, two inhalations (0.84 mg/dose) three or four times daily; maximum, 20 inhalations/24 h</td>
<td>6–12 y: Oral inhalation, one or two inhalations three or four times per day; maximum dose, 10 inhalations/24 h</td>
</tr>
<tr>
<td><strong>Beclomethasone</strong></td>
<td>1 spray in each nostril 2–4 times/day or 2 sprays in each nostril twice daily (total dose 168–336 mcg/day)</td>
<td></td>
</tr>
<tr>
<td>(Beconase AQ)</td>
<td>Oral inhalation, 200–400 mcg twice daily</td>
<td>6 y: Oral inhalation 200 mcg twice daily</td>
</tr>
<tr>
<td><strong>Budesonide</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Pulmocort Turbuhaler)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Flunisolide</strong></td>
<td>Aerobid: Oral inhalation, two inhalations (0.50 mg/dose) twice daily, morning and evening; maximum dose, four inhalations twice daily (2 mg)</td>
<td>Aerobid: 6–15 y: Oral inhalation, two inhalations twice daily; maximum eight inhalations daily</td>
</tr>
<tr>
<td>(AeroBid, Aerospan-not interchangeable)</td>
<td>Aerospan: two inhalations twice daily; maximum eight inhalations daily</td>
<td>Aerospan: 6–11 y: Oral inhalation: one inhalation twice daily; maximum four times daily</td>
</tr>
<tr>
<td><strong>Fluticasone</strong></td>
<td>4 sprays in each nostril once daily (265 mcg/day)</td>
<td>12 y and older: Same as adults</td>
</tr>
<tr>
<td>(Flonase)</td>
<td>12 y and older: Same as adults</td>
<td>4–11 y: 1 spray in each nostril once daily; may increase to 2 sprays in each nostril for desired effect</td>
</tr>
<tr>
<td><strong>Fluticasone aerosol</strong></td>
<td>Aerosol, 88–440 mcg twice daily</td>
<td>Dosage not established</td>
</tr>
<tr>
<td>(Flovent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fluticasone powder</strong></td>
<td>Powder, 100–500 mcg twice daily</td>
<td>12 y and older: Same as adults</td>
</tr>
<tr>
<td>(Flovent Rotadisk)</td>
<td>4–11 y: Powder, 50–100 mcg twice daily</td>
<td></td>
</tr>
<tr>
<td><strong>Hydrocortisone sodium phosphate and sodium succinate</strong></td>
<td>IV 100–200 mg q4–6h initially, then decreased or switched to an oral dosage form</td>
<td>IV 1–5 mg/kg q4–6h</td>
</tr>
<tr>
<td><strong>Methylprednisolone sodium succinate</strong></td>
<td>IV 10–40 mg q4–6h for 48–72 h</td>
<td>IV 0.5 mg/kg q4–6h</td>
</tr>
<tr>
<td><strong>Mometasone</strong></td>
<td>Nasal inhalation two sprays (50 mcg/spray) in each nostril once daily</td>
<td>12 y and older: Same as adults</td>
</tr>
<tr>
<td>(Asmanex Twisthaler, Nasonex)</td>
<td>2–11 y: 1 spray (50 mcg) in each nostril once daily</td>
<td></td>
</tr>
<tr>
<td><strong>Prednisone</strong></td>
<td>PO 20–60 mg/d</td>
<td>PO 2 mg/kg/d initially</td>
</tr>
<tr>
<td><strong>Triamcinolone</strong></td>
<td>Oral inhalation, two (100 mcg/puff) inhalations 3 or 4 times per day or four inhalations twice daily; maximum dose, 16 inhalations (1600 mcg) 24 h</td>
<td>6–12 y: one or two (100 mcg/puff) inhalations 3 or 4 times per day or two to four inhalations twice daily; maximum dose, 12 inhalations/24 h</td>
</tr>
<tr>
<td>(Azmacort)</td>
<td>15 y and older: Same as adults</td>
<td>6–14 y: PO 5 mg once daily in the evening</td>
</tr>
<tr>
<td><strong>Zafirlukast</strong></td>
<td>PO 10 mg once daily in the evening or at bedtime</td>
<td>2–5 y: 4 mg once daily</td>
</tr>
<tr>
<td>(Accolate)</td>
<td>PO 20 mg twice daily, 1 h before or 2 h after a meal</td>
<td>12 y and older: Same as adults</td>
</tr>
<tr>
<td><strong>Mast Cell Stabilizers</strong></td>
<td></td>
<td>5–11 y: PO 10 mg twice daily</td>
</tr>
<tr>
<td><strong>Cromolyn</strong></td>
<td>Nebulizer solution, oral inhalation, 20 mg 4 times daily</td>
<td>2 y and older: Same as adults</td>
</tr>
<tr>
<td>(Intal)</td>
<td>Aerosol spray, oral inhalation, two sprays 4 times daily</td>
<td>5 y and older: Same as adults</td>
</tr>
</tbody>
</table>
Asthma who are taking an oral corticosteroid, the oral dosage is reduced slowly (over weeks to months) when an inhaled corticosteroid is added. The goal is to give the lowest oral dose necessary to control symptoms. Beclomethasone, flunisolide, and fluticasone also are available in nasal solutions for treatment of allergic rhinitis, which may play a role in bronchoconstriction. Because systemic absorption occurs in patients using inhaled corticosteroids (about 20% of a dose), high doses should be reserved for those otherwise requiring oral corticosteroids.

Hydrocortisone, prednisone, and methylprednisolone are given to patients who require systemic corticosteroids. Prednisone is given orally; hydrocortisone and methylprednisolone may be given IV to patients who are unable to take an oral medication.

**Applying Your Knowledge 44-2**

Ms. Albright has a friend who takes prednisone for his breathing problems. She asks why she isn’t taking the same medication. How should you respond?

**Leukotriene Modifiers**

Leukotrienes are strong chemical mediators of bronchoconstriction and inflammation, the major pathologic features of asthma. They can cause sustained constriction of bronchioles and immediate hypersensitivity reactions. They also increase mucus secretion and mucosal edema in the respiratory tract. Leukotrienes are formed by the lipoxygenase pathway of arachidonic acid metabolism (Fig. 44-1) in response to cellular injury. They are designated by LT, the letter B, C, D, or E, and the number of chemical bonds in their structure (e.g., LTB4, LTC4, and LTE4, also called slow releasing substances of anaphylaxis, or SRS-A, because they are released more slowly than histamine).

Leukotriene modifier drugs were developed to counteract the effects of leukotrienes and are indicated for long-term treatment of asthma in adults and children. The drugs help to prevent acute asthma attacks induced by allergens, exercise, cold air, hyperventilation, irritants, and aspirin or NSAIDs. They are not effective in relieving acute attacks. However, they may be continued concurrently with other drugs during acute episodes.

The leukotriene modifiers include three agents with two different mechanisms of action. Montelukast and zafirlukast are leukotriene receptor antagonists. Zafirlukast and montelukast improve symptoms and pulmonary function tests (PFTs), decrease nighttime symptoms, and decrease the use of beta2 agonist drugs. They are effective with oral administration, can be taken once or twice a day, can be used with bronchodilators and corticosteroids, and elicit a high degree of effects...
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patient adherence and satisfaction. However, they are less effective than low doses of inhaled corticosteroids.

Montelukast and zafirlukast are well absorbed with oral administration. They are metabolized in the liver by the cytochrome P450 enzyme system and may interact with other drugs metabolized by this system. Most metabolites are excreted in the feces. Zafirlukast is excreted in breast milk and should not be taken during lactation. The most common adverse effects reported in clinical trials were headache, nausea, diarrhea, and infection.

Mast Cell Stabilizers

Cromolyn and nedocromil stabilize mast cells and prevent the release of bronchoconstrictive and inflammatory substances when mast cells are confronted with allergens and other stimuli. The drugs are utilized as an alternative, but not preferred, medication for prophylaxis of acute asthma attacks in patients with mild persistent asthma; they are not effective in acute bronchospasm or status asthmaticus and should not be used in these conditions. Use of one of these drugs may allow reduced dosage of bronchodilators and corticosteroids and can be used prior to exercise or exposure to known allergens.

The drugs are taken by inhalation. Cromolyn is available in a metered-dose aerosol and a solution for use with a power-operated nebulizer. A nasal solution is also available for prevention and treatment of allergic rhinitis.

Mast cell stabilizers are contraindicated in patients who are hypersensitive to the drugs. They should be used with caution in patients with impaired renal or hepatic function. Also, the propellants in the aerosols may aggravate coronary artery disease or dysrhythmias.

Immunosuppressant

Monoclonal Antibody

Omalizumab (Xolair) works by binding to immunoglobulin E (IgE), blocking receptors on the surfaces of mast cells and basophils. This prevents IgE from attaching to the cells, thus preventing the release of substances in the body that can trigger an allergic reaction and preventing the development of inflammation. As an immunomodifier, omalizumab is indicated as adjunctive therapy in patients with allergic asthma whose symptoms do not respond adequately to inhaled steroids. Due to the risk of anaphylaxis the FDA has issued a BLACK BOX WARNING for omalizumab. The drug should only be administered to patients in a health care setting under direct medical supervision by provider who can initiate treatment of life-threatening anaphylaxis. Further discussion of this drug is found in Chapter 41.

Herbal and Dietary Supplements

Numerous preparations are promoted to relieve symptoms of asthma, and patients with asthma are increasingly using alternative and complementary therapies. Many herbal preparations are used traditionally, and tradition varies by culture. As with most herbal treatments, few clinical studies support their use though some herbs used are similar to asthma preparations in their chemical properties. For example, caffeine is a xanthine and therefore has bronchodilating effects similar to, but weaker than, those of theophylline. In addition to herbal preparations for the long-term treatment of asthma, vitamins and minerals are used frequently (i.e., vitamins C, B6, E, and magnesium, selenium).

In general, herbal and dietary therapies in asthma, as in other disorders, have not been studied in controlled clinical trials and should be avoided. Because asthma can result in death in a matter of minutes, patients should be counseled not to use dietary or herbal supplements in place of prescribed bronchodilating and anti-inflammatory medications. Delays in appropriate treatment can have serious, even fatal, consequences.

Applying Your Knowledge 44-3

Ms. Albright comes into the clinic and you suspect she is experiencing respiratory distress. You focus your assessment on what signs/symptoms?

Nursing Process

Assessment

Assess the patient’s pulmonary function.

■ General assessment factors include rate and character of respiration, skin color, arterial blood gas analysis, and pulmonary function tests. Abnormal breathing patterns (e.g., rate below 12 or above 24 per minute, dyspnea, cough, orthopnea, wheezing, “noisy” respirations) may indicate respiratory distress. Severe respiratory distress is characterized by tachypnea, dyspnea, use of accessory muscles of respiration, and hypoxia. Early signs of hypoxia include mental confusion, restlessness, anxiety, and increased blood pressure and pulse rate. Late signs include cyanosis and decreased blood pressure and pulse. Hypoxemia is confirmed if arterial blood gas analysis shows decreased partial pressure of oxygen (PO2).

■ In acute bronchospasm, a medical emergency, the patient is in obvious and severe respiratory distress. A characteristic feature of bronchospasm is forceful expiration or wheezing.

■ If the patient has chronic asthma, try to determine the frequency and severity of acute attacks; factors that precipitate or relieve acute attacks; antiasthmatic medications taken occasionally or regularly; allergies; and condition between acute attacks, such as restrictions in activities of daily living due to asthma.

nursing process continues on page 722
If the patient has chronic bronchitis or emphysema, assess for signs of respiratory distress, hypoxia, cough, amount and character of sputum, exercise tolerance (e.g., dyspnea on exertion, dyspnea at rest), medications, and nondrug treatment measures (e.g., breathing exercises, chest physiotherapy).

**Nursing Diagnoses**
- Impaired Gas Exchange related to bronchoconstriction and excessive mucus production
- Activity Intolerance related to impaired gas exchange and fatigue
- Risk for Injury: Severe bronchospasm with asthma and adverse effects with antiasthmatic drugs
- Noncompliance: Overuse of adrenergic bronchodilators
- Deficient Knowledge: Factors precipitating bronchoconstriction and strategies to avoid precipitating factors
- Deficient Knowledge: Accurate self-administration of drugs, including use of inhalers

**Planning/Goals**
The patient will
- Self-administer bronchodilating and other drugs accurately
- Experience relief of symptoms
- Avoid preventable adverse drug effects
- Avoid overusing bronchodilating drugs
- Avoid exposure to stimuli that cause bronchospasm when possible
- Avoid respiratory infections when possible

**Interventions**
Use measures to prevent or relieve bronchoconstriction when possible. General measures include those to prevent respiratory disease or promote an adequate airway. A specific monitoring plan should be in place, whether peak-flow or symptom monitoring. Some measures include the following:
- Use mechanical measures for removing excessive respiratory tract secretions and preventing their retention. Effective measures include coughing, deep breathing, percussion, and postural drainage.
- Help the patient identify and avoid exposure to conditions that precipitate bronchoconstriction. For example, allergens may be removed from the home, school, or work environment; cigarette smoke should be avoided when possible. When bronchospasm is precipitated by exercise, prophylaxis by prior inhalation of bronchodilating agents is better than avoiding exercise, especially in children.
- Assist patients with asthma to identify early signs of difficulty, including increased need for beta-adrenergic agonists, activity limitations, and waking at night with asthma symptoms.

**Evaluation**
- Monitor peak expiratory flow rate (PEFR) when indicated. Portable meters are available for use in clinics, physicians’ offices, and clients’ homes. This is an objective measure of airflow/airway obstruction and helps to evaluate the patient’s treatment regimen.
- Assist patients with moderate to severe asthma in obtaining meters and learning to measure PEFR. Patients with a decreased PEFR may need treatment to prevent acute, severe respiratory distress.
- Assist patients and at least one family member in managing acute attacks of bronchoconstriction, including when to seek emergency care.
- Try to prevent or reduce anxiety, which may aggravate bronchospasm. Stay with the patient during an acute asthma attack if feasible. Patients experiencing severe and prolonged bronchospasm (status asthmaticus) should be admitted or transferred to a hospital intensive care unit.
- With any patients who smoke cigarettes, encourage cessation of smoking and provide information, resources, and assistance in doing so. Emphasize the health benefits of improved respiratory function.
- In addition, provide appropriate patient teaching related to drug therapy (see accompanying display).

**Principles of Therapy**

**Drug Selection and Administration**
Choice of drug and route of administration are determined largely by the severity of the disease process and the patient’s response to therapy. Some guidelines include the following:
- A selective, short-acting, inhaled beta₂-adrenergic agonist (e.g., albuterol) is the initial drug of choice for acute bronchospasm.
- Because aerosol products act directly on the airways, drugs given by inhalation can usually be given in smaller doses and produce fewer adverse effects than oral or parenteral drugs.
- Ipratropium and tiotropium, the anticholinergic bronchodilators, are most useful in the long-term management of COPD. They are ineffective in relieving acute
General Considerations

- Asthma and other chronic lung diseases are characterized by constant inflammation of the airways and periodic or persistent labored breathing from constriction or narrowing of the airways. Antiasthmatic drugs are often given in combination to combat these problems. Thus, it is extremely important to know the type and purpose of each drug.
- Except for the short-acting, inhaled bronchodilators (e.g., albuterol), antiasthmatic medications are used long term to control symptoms and prevent acute asthma attacks. This means they must be taken on a regular schedule and continued when symptom free.
- When an asthma attack (i.e., acute bronchospasm with shortness of breath, wheezing respirations, cough) occurs, the only fast-acting, commonly used medication to relieve these symptoms is an inhaled, short-acting bronchodilator (e.g., albuterol). Other inhaled and oral drugs are not effective and should not be used.
- Try to prevent symptoms. For example, respiratory infections can precipitate difficulty in breathing. Avoiding infections (e.g., by good hand hygiene, avoiding people with infections, annual influenza vaccinations, and other measures) can prevent acute asthma attacks. If you are allergic to tobacco smoke, perfume, or flowers, try to avoid or minimize exposure.
- A common cause of acute asthma attacks is not taking medications correctly. Some studies indicate that one third to two thirds of clients with asthma do not comply with instructions for using their medications. Factors that contribute to noncompliance with drug therapy include long-term use, expense, and adverse effects. If you have difficulty taking medications as prescribed, discuss the situation with a health care provider. Cheaper medications or lower doses may be effective alternatives. Just stopping the medications may precipitate acute breathing problems.
- If unable to prevent symptoms, early recognition and treatment may help prevent severe distress and hospitalizations. Signs of impending difficulty include increased breathlessness, increased frequency of nighttime awakening, and evidence of inflammation in the airways. At this stage, bronchodilator inhalers may be effective and should be used.
- Keep adequate supplies of medications on hand. Missing a few doses of long-term control or “preventive” medications may precipitate an acute asthma attack; not using an inhaled bronchodilator for early breathing difficulty may lead to more severe problems and the need for emergency treatment or hospitalization.
- Be sure you can use your metered-dose inhalers correctly. According to several research studies, many patients do not.
- Drinking 2 to 3 quarts of fluids daily helps thin secretions in the throat and lungs and makes them easier to remove.
- Avoid tobacco smoke and other substances that irritate breathing passages (e.g., aerosol hair spray, antiperspirants, cleaning products, and automobile exhaust) when possible.

Self-Administration

- Follow instructions carefully. Better breathing with minimal adverse effects depends on accurate use of prescribed medications. If help is needed with metered-dose inhalers, consult a health care provider.
- Use short-acting bronchodilator inhalers as needed, not on a regular schedule. If desired effects are not achieved or if symptoms worsen, inform the prescribing physician. Do not increase dosage or frequency of taking medication. Overuse increases adverse drug effects and decreases drug effectiveness.
- If taking formoterol or salmeterol, which are long-acting, inhaled bronchodilators, do not use more often than every 12 hours. If constricted breathing occurs, use a short-acting bronchodilator inhaler between doses of a long-acting drug. Salmeterol does not relieve acute shortness of breath because it takes approximately 20 minutes to start acting and 1 to 4 hours to achieve maximal bronchodilating effects.
- If taking an oral or inhaled corticosteroid, take on a regular schedule, at approximately the same time each day. The purpose of these drugs is to relieve inflammation in the airways and prevent acute respiratory distress. They are not effective unless taken regularly.
- If taking oral theophylline, take fast-acting preparations before meals with a full glass of water, at regular intervals around the clock. If gastrointestinal upset occurs, take with food. Take long-acting preparations every 8 to 12 hours; do not chew or crush.
- Take zafirlukast 1 hour before or 2 hours after a meal; montelukast and zileuton may be taken with or without food. Take montelukast in the evening or at bedtime. This schedule provides maximum beneficial effects during the night and early morning, when asthma symptoms often occur or worsen.
- Use inhalers correctly:
  1. Shake well immediately before each use.
  2. Remove the cap from the mouthpiece.
  3. Exhale to the end of a normal breath.
  4. With the inhaler in the upright position, place the mouthpiece just inside the mouth, and use the lips to

Antiasthmatic Drugs

- Avoid excessive intake of caffeine-containing fluids such as coffee, tea, and cola drinks. These beverages may increase bronchodilation but also may increase heart rate and cause palpitations, nervousness, and insomnia with bronchodilating drugs.
- Take influenza vaccine annually and pneumococcal vaccine at least once if you have chronic lung disease.
- Inform all health care providers about the medications you are taking and do not take over-the-counter drugs or herbal supplements without consulting a health care provider. Some drugs can decrease beneficial effects or increase adverse effects of antiasthmatic medications. For example, over-the-counter nasal decongestants, asthma remedies, cold remedies, and antiseptic medications can increase the rapid heartbeat, palpitations, and nervousness often associated with bronchodilators. With herbal remedies, none are as effective as standard antiasthmatic medication, and they may cause serious or life-threatening adverse effects.

(continued on page 724)
A common regimen for treatment of moderate asthma is inhaled corticosteroids. In chronic disorders, inhaled corticosteroids should be used in a combination product with a long-acting beta_2 agonist. Cromolyn is used prophylactically, it is ineffective in acute bronchospasm. Theophylline is used less often than formerly and is now considered a second-line drug. Multidrug regimens are commonly used, and one advantage is that smaller doses of each agent can usually be given. This may decrease adverse effects and allow dosages to be increased when exacerbation of symptoms occurs. Available combination inhalation products include Combivent (albuterol and ipratropium) and Advair (salmeterol and fluticasone). Advair, which was developed to treat both inflammation and bronchoconstriction, was more effective than the individual components at the same doses and as effective as concurrent use of the same drugs at the same doses. In addition, the combination reduced the corticosteroid dose by 50% and was more effective than higher doses of fluticasone alone in reducing asthma exacerbations. The combination improved symptoms within 1 week. Additional combination products are likely to be marketed and may improve patient compliance with prescribed drug therapy.

**Drug Dosage**

Dosage of antiasthmatic drugs must be individualized to attain the most therapeutic effects and the fewest adverse effects. Larger doses of bronchodilators and corticosteroids (inhaled, systemic, or both) are usually required to relieve the symptoms of acute, severe bronchoconstriction or status asthmaticus. Then, doses should be reduced to the smallest effective amounts for long-term control.

Dosage of theophylline preparations should be based mainly on serum theophylline levels (therapeutic range is 5–15 mcg/mL; toxic levels are 20 mcg/mL or above). Blood for serum levels should be drawn 1 to 2 hours after immediate-release dosage forms and about 4 hours after sustained-release forms are taken. In addition, children and cigarette smokers usually need higher doses to maintain therapeutic blood levels because they metabolize theophylline rapidly, and patients with liver disease, congestive heart failure, chronic pulmonary disease, or acute viral infections usually need smaller doses because these conditions impair theophylline metabolism. For obese patients, theophylline dosage should be calculated on the basis of lean or ideal body weight because theophylline is not highly distributed in fatty tissue.

Patient Teaching Guidelines

- Form a tight seal or hold the mouthpiece approximately two finger-widths from the open mouth.
- While pressing down on the inhaler, take a slow, deep breath for 3 to 5 seconds, hold the breath for approximately 10 seconds, and exhale slowly.
- Wait 3 to 5 minutes before taking a second inhalation of the drug.
- Rinse the mouth with water after each use.
- Rinse the mouthpiece and store the inhaler away from heat.
- If you have difficulty using an inhaler, ask your physician about a spacer device (a tube attached to the inhaler that makes it easier to use).
Toxicity: Recognition and Management

With antiasthmatic drugs, signs and symptoms of overdose and toxicity are probably most likely to occur when patients with acute or chronic bronchoconstrictive disorders overdose bronchodilators in their efforts to relieve dyspnea. General management of acute poisoning includes early recognition of signs and symptoms, stopping the causative drug, and instituting other treatment measures as indicated. Specific measures include the following:

- Bronchodilator overdose. With inhaled or systemic adrenergic bronchodilators, major adverse effects are excessive cardiac and CNS stimulation. Symptoms of cardiac stimulation include angina, tachycardia, and palpitations; serious dysrhythmias and cardiac arrest have also been reported. Symptoms of CNS stimulation include agitation, anxiety, insomnias, seizures, and tremors. Severe overdoses may cause delirium, collapse, and coma. In addition, hypokalemia, hyperglycemia, and hypotension or hypertension may occur. Management includes discontinuing the causative medications and using general supportive measures. Emesis, gastric lavage, or activated charcoal may be useful with oral medications and using general supportive measures. Emesis, gastric lavage, or activated charcoal may be useful with oral drugs if benefit exceeds risk. For cardiac symptoms, monitor blood pressure, pulse, and electrocardiogram. Cautious use of a beta-adrenergic blocking drug (e.g., propranolol) may be indicated. However, a nonselective beta blocker may induce bronchoconstriction.

- Theophylline overdose. Signs and symptoms include anorexia, nausea, vomiting, agitation, nervousness, insomnia, tachycardia and other dysrhythmias, and tonic-clonic convulsions. Ventricular dysrhythmias or convulsions may be the first sign of toxicity. Serious adverse effects rarely occur at serum drug levels below 20 micrograms per milliliter. Overdoses with sustained-release preparations may cause a dramatic increase in serum drug concentrations much later (12 hours or longer) than the immediate-release preparations. Early treatment helps but does not prevent these delayed increases in serum drug levels.

In patients without seizures, induce vomiting unless the level of consciousness is impaired. In these patients, precautions to prevent aspiration are needed, especially in children. If overdose is identified within an hour of drug ingestion, gastric lavage may be helpful if unable to induce vomiting or vomiting is contraindicated. Administration of activated charcoal and a cathartic is also recommended, especially for overdoses of sustained-release formulations if benefit exceeds risk.

In patients with seizures, treatment includes securing the airway, giving oxygen, injecting IV diazepam (0.1–0.3 mg/kg, up to 10 mg), monitoring vital signs, maintaining blood pressure, providing adequate hydration, and monitoring serum theophylline levels until below 20 micrograms per milliliter. Also, symptomatic treatment of dysrhythmias may be needed.

- Leukotriene modifiers and mast cell stabilizers. These drugs seem relatively devoid of serious toxicity. There have been few reports of toxicity in humans and little clinical experience in managing it. If toxicity occurs, general supportive and symptomatic treatment is indicated.

Use in Special Populations

Use in Children

The American Academy of Pediatrics endorses the clinical practice guidelines established by the NAEP (see Box 44-1). In general, antiasthmatic medications are used in children and adolescents for the same indications as for adults. With adrenergic bronchodilators, recommendations for use vary according to route of administration, age of the child, and specific drug formulations. However, even infants and young children can be treated effectively with aerosolized or nebulized drugs. In addition, some oral drugs can be given to children as young as 2 years and most can be given to children 6 to 12 years of age.

With theophylline, use in children should be closely monitored because dosage needs and rates of metabolism vary widely. In children younger than 6 months, especially premature infants and neonates, drug elimination may be prolonged because of immature liver function. Except for preterm infants with apnea, theophylline preparations are not recommended for use in this age group. Children 6 months to 16 years of age, approximately, metabolize theophylline more rapidly than younger or older patients. Thus, they may need higher doses than adults in proportion to size and weight. If the child is obese, the dosage should be calculated on the basis of lean or ideal body weight because the drug is not highly distributed in fatty tissue. Long-acting dosage forms are not recommended for children younger than 6 years of age. Children may become hyperactive and disruptive from the CNS-stimulating effects of theophylline. Tolerance to these effects usually develops with continued use of the drug.

Corticosteroids are being used earlier in children as in adults and inhaled corticosteroids are first-line drugs for treatment of persistent bronchoconstrictive disorders. The effectiveness and safety of inhaled corticosteroids in children older than 3 years of age is well established; few data are available on the use of inhaled drugs in those younger than 3 years. Major concerns about long-term use in children include decreased adrenal function, growth, and bone mass. Most corticosteroids are given by inhalation, and dosage, type of inhaler device, and characteristics of individual drugs influence the extent and severity of these systemic effects.

Adrenal insufficiency is most likely to occur with systemic or high doses of inhaled corticosteroids. Dose-related inhibition of growth has been reported in short and intermediate studies, but long-term studies have found few, if any, decreases in expected adult height. Inhaled corticosteroids have not been associated with significant decreases in bone mass, but more studies of high doses and of drug therapy in adolescents are needed. Bone growth should be monitored closely in children taking corticosteroids. Although inhaled corticosteroids are the most effective anti-inflammatory medications available
for asthma, high doses in children are still of concern. The risk of high doses is especially great in children with other allergic conditions that require topical corticosteroid drugs. The risk can be decreased by using the lowest effective dose, administration techniques that minimize swallowed drug, and other antiasthmatic drugs to reduce corticosteroid dose.

Leukotriene modifiers have not been extensively studied in children and adolescents. With montelukast, the 10-milligram film-coated tablet is recommended for adolescents 15 years of age and older and a 4-milligram chewable tablet is recommended for children 2 to 5 years of age. Safety and effectiveness of zafirlukast in children younger than 12 years have not been established.

Cromolyn aerosol solution may be used in children 5 years of age and older, and nebulizer solution is used with children 2 years and older.

Use in Older Adults

Older adults often have chronic pulmonary disorders for which bronchodilators and antiasthmatic medications are used. As with other populations, administering the medications by inhalation and giving the lowest effective dose decrease adverse effects. The main risks with adrenergic bronchodilators are excessive cardiac and CNS stimulation.

Theophylline use must be carefully monitored because drug effects are unpredictable. On the one hand, cigarette smoking and drugs that stimulate drug-metabolizing enzymes in the liver (e.g., phenobarbital, phenytoin) increase the rate of metabolism and therefore dosage requirements. On the other hand, impaired liver function, decreased blood flow to the liver, and some drugs (e.g., cimetidine, erythromycin) impair metabolism and therefore decrease dosage requirements. Adverse effects include cardiac and CNS stimulation. Safety can be increased by measuring serum drug levels and adjusting dosage to maintain therapeutic levels of 5 to 15 micrograms per milliliter. If the patient is obese, dosage should be based on lean or ideal body weight because theophylline is not highly distributed in fatty tissue.

Corticosteroids increase the risks of osteoporosis and cataracts in older adults. Leukotriene modifiers usually are well tolerated by older adults, with pharmacokinetics and effects similar to those in younger adults. With zafirlukast, however, blood levels are higher and elimination is slower than in younger adults.

Use in Patients With Renal Impairment

Bronchodilating and anti-inflammatory drugs can usually be given without dosage adjustments in patients with impaired renal function. Beta agonists may be given by inhalation or parenteral routes. Theophylline can be given in usual doses, but serum drug levels should be monitored. Most corticosteroids are eliminated by hepatic metabolism, and dosage reductions are not needed in patients with renal impairment.

No data are available about the use of montelukast, and no dosage adjustments are recommended for zafirlukast.

Cromolyn is eliminated by renal and biliary excretion; the drug should be given in reduced doses, if at all, in patients with renal impairment.

Use in Patients With Hepatic Impairment

Montelukast and zafirlukast produce higher blood levels and are eliminated more slowly in patients with hepatic impairment. However, no dosage adjustment is recommended for patients with mild to moderate hepatic impairment.

Cromolyn is eliminated by renal and biliary excretion; the drug should be given in reduced doses, if at all, in patients with hepatic impairment.

Use in Patients With Critical Illness

Acute, severe asthma (status asthmaticus) is characterized by severe respiratory distress and requires emergency treatment. Beta$_2$ agonists should be given in high doses and as often as every 20 minutes for 1 to 2 hours (by MDIs with spacer devices or by compressed-air nebulization). However, high doses of nebulized albuterol have been associated with tachycardia, hypokalemia, and hyperglycemia. After symptoms are controlled, dosage can usually be reduced and dosing intervals extended. High doses of systemic corticosteroids are also given for several days, IV or orally. If the patient is able to take an oral drug, there is no therapeutic advantage to IV administration.

When respiratory function improves, efforts to prevent future episodes are needed. These efforts may include identifying and avoiding suspected triggers, evaluation and possible adjustment of the patient’s treatment regimen, and assessment of the patient’s adherence to the prescribed regimen.

Use in Home Care

Most of the drugs discussed in this chapter are used in the home setting; omalizumab should be administered only in the health care setting due to the risk of life-threatening anaphylaxis with administration. A major role of the home care nurse is to assist patients in using the drugs safely and effectively. Several studies have indicated that many people do not use MDIs and other inhalation devices correctly. The home care nurse needs to observe a patient using an inhalation device when possible. If errors in technique are assessed, further education may be needed. With inhaled medications, a spacer device may be useful, especially for children and older adults, because less muscle coordination is required to administer a dose. Adverse effects may be minimized as well.

For patients with asthma, especially children, assess the environment for potential triggers of acute bronchospasm, such as cigarette smoking. In addition, assist patients to recognize and treat (or get help for) exacerbations before respiratory distress becomes severe.

With theophylline, the home care nurse needs to assess the patient and the environment for substances that may affect metabolism of theophylline and decrease therapeutic effects or increase adverse effects. In addition, the nurse needs to reinforce the importance of not exceeding the prescribed dose, not crushing long-acting formulations, reporting adverse effects, and keeping appointments for follow-up care.
### Nursing Actions

#### Drugs for Asthma and Other Bronchoconstrictive Disorders

<table>
<thead>
<tr>
<th>Nursing Actions</th>
<th>Rationale/Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Administer accurately</strong></td>
<td></td>
</tr>
<tr>
<td>a. Be sure patients have adequate supplies of inhaled bronchodilators and corticosteroids available for self-administration. Observe technique of self-administration for accuracy and assist if needed.</td>
<td>To promote dissolution and absorption. Taking with food may decrease nausea and vomiting.</td>
</tr>
<tr>
<td>b. Give immediate-release oral theophylline before meals with a full glass of water, at regular intervals around the clock. If gastrointestinal upset occurs, give with food.</td>
<td>Sustained-release drug formulations should never be chewed or crushed because doing so causes immediate release of potentially toxic doses.</td>
</tr>
<tr>
<td>c. Give sustained-release theophylline q8–12h, with instructions not to chew or crush.</td>
<td>The bioavailability of zafirlukast is reduced approximately 40% if taken with food. Food does not significantly affect the bioavailability of montelukast and zileuton.</td>
</tr>
<tr>
<td>d. Give zafirlukast 1 hour before or 2 hours after a meal; montelukast and zileuton may be given with or without food.</td>
<td>This schedule provides high drug concentrations during the night and early morning, when asthma symptoms tend to occur or worsen.</td>
</tr>
<tr>
<td>e. Give montelukast in the evening or at bedtime.</td>
<td></td>
</tr>
<tr>
<td><strong>2. Observe for therapeutic effects</strong></td>
<td>Relief of bronchospasm and wheezing should be evident within a few minutes after giving subcutaneous epinephrine, or aerosolized adrenergic bronchodilators.</td>
</tr>
<tr>
<td>a. Decreased dyspnea, wheezing, and respiratory secretions</td>
<td></td>
</tr>
<tr>
<td>b. Reduced rate and improved quality of respirations</td>
<td></td>
</tr>
<tr>
<td>c. Reduced anxiety and restlessness</td>
<td></td>
</tr>
<tr>
<td>d. Therapeutic serum levels of theophylline (5–15 mcg/mL)</td>
<td>These signs and symptoms result from cardiac and central nervous system (CNS) stimulation.</td>
</tr>
<tr>
<td>e. Improved arterial blood gas levels (normal values: PO₂, 80 to 100 mm Hg; PCO₂, 35 to 45 mm Hg; pH, 7.35 to 7.45)</td>
<td>Ipratropium and tiotropium produce few adverse effects because they are not absorbed systemically.</td>
</tr>
<tr>
<td>f. Improved exercise tolerance</td>
<td>Theophylline causes cardiac and CNS stimulation. Convulsions occur at toxic serum concentrations (~20 mcg/mL). They may occur without preceding symptoms of toxicity and may result in death. IV diazepam (Valium) may be used to control seizures. Theophylline also stimulates the chemoreceptor trigger zone in the medulla oblongata to cause nausea and vomiting.</td>
</tr>
<tr>
<td>g. Decreased incidence and severity of acute attacks of bronchospasm with chronic administration of drugs</td>
<td>Inhaled corticosteroids are unlikely to produce the serious adverse effects of long-term systemic therapy (see Chap. 23).</td>
</tr>
<tr>
<td><strong>3. Observe for adverse effects</strong></td>
<td>These drugs are usually well tolerated. A highly elevated ALT and liver dysfunction are more likely to occur with zileuton.</td>
</tr>
<tr>
<td>a. With adrenergic bronchodilators, observe for tachycardia, dysrhythmias, palpitations, restlessness, agitation, insomnia.</td>
<td>Some of the cardiovascular effects are thought to be caused by the propellants used in the aerosol preparation.</td>
</tr>
<tr>
<td>b. With ipratropium and tiotropium, observe for cough or exacerbation of symptoms.</td>
<td></td>
</tr>
<tr>
<td>c. With xanthine bronchodilators, observe for tachycardia, dysrhythmias, palpitations, restlessness, agitation, insomnia, nausea, vomiting, convulsions.</td>
<td></td>
</tr>
<tr>
<td>d. With inhaled corticosteroids, observe for hoarseness, cough, throat irritation, and fungal infection of mouth and throat.</td>
<td></td>
</tr>
<tr>
<td>e. With leukotriene inhibitors, observe for headache, infection, nausea, pain, elevated liver enzymes (e.g., alanine aminotransferase [ALT]), and liver dysfunction.</td>
<td></td>
</tr>
<tr>
<td>f. With cromolyn, observe for dysrhythmias, hypotension, chest pain, restlessness, dizziness, convulsions, CNS depression, anorexia, nausea and vomiting. Sedation and coma may occur with overdose.</td>
<td></td>
</tr>
<tr>
<td><strong>4. Observe for drug interactions</strong></td>
<td>These drugs inhibit the metabolism of catecholamines. The subsequent administration of bronchodilators may increase blood pressure.</td>
</tr>
<tr>
<td>a. Drugs that increase effects of bronchodilators:</td>
<td>These drugs may decrease theophylline clearance and thereby increase plasma levels.</td>
</tr>
<tr>
<td>(1) Monoamine oxidase inhibitors</td>
<td></td>
</tr>
<tr>
<td>(2) Erythromycin, clindamycin, cimetidine</td>
<td></td>
</tr>
</tbody>
</table>

(continued on page 728)
Nursing Actions

**Drugs for Asthma and Other Bronchoconstrictive Disorders (continued)**

<table>
<thead>
<tr>
<th>NURSING ACTIONS</th>
<th>RATIONALE/EXPLANATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>b. Drugs that decrease effects of bronchodilators:</td>
<td>Lithium may increase excretion of theophylline and therefore decrease therapeutic effectiveness. This drug may increase the metabolism of theophylline by way of enzyme induction. These drugs may cause bronchoconstriction and oppose effects of bronchodilators.</td>
</tr>
<tr>
<td>(1) Lithium</td>
<td></td>
</tr>
<tr>
<td>(2) Phenobarbital</td>
<td></td>
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<tr>
<td>(3) Propranolol, other nonselective beta blockers</td>
<td></td>
</tr>
<tr>
<td>c. Drugs that alter effects of zafirlukast:</td>
<td>Increases blood levels Decrease blood levels</td>
</tr>
<tr>
<td>(1) Aspirin</td>
<td></td>
</tr>
<tr>
<td>(2) Erythromycin, theophylline</td>
<td></td>
</tr>
</tbody>
</table>

Key Concepts

- A specific monitoring plan for patients with asthma should be in place, whether through peak-flow or symptom monitoring.
- Two general classifications of drugs are used for asthma management: long-term control medications to achieve and maintain control of persistent asthma and quick relief medications used during periods of acute symptoms and exacerbations.
- Two major groups of drugs used to treat asthma, acute and chronic bronchitis, and emphysema are bronchodilators and anti-inflammatory drugs.
- A selective, short-acting, inhaled beta,2-adrenergic agonist (e.g., albuterol) is the initial rescue drug of choice for acute bronchospasm; subcutaneous epinephrine may also be considered.
- Because aerosol products act directly on the airways, drugs given by inhalation can usually be given in smaller doses and produce fewer adverse effects than oral or parenteral drugs.
- Asthma may aggravate GERD, because antiasthma medications that dilate the airways also relax muscle tone in the gastroesophageal sphincter and may increase acid reflux.
- Almost all over-the-counter aerosol products promoted for use in asthma contain epinephrine, which may produce hazardous cardiac stimulation and other adverse effects.
- Cigarette smoking and drugs that stimulate drug-metabolizing enzymes in the liver (e.g., phenobarbital, phenytoin) increase the rate of metabolism and therefore dosage requirements of aminophylline.
- Due to the risk of anaphylaxis the FDA has issued a BLACK BOX WARNING for omalizumab.
- The FDA has issued a BLACK BOX WARNING that initiating salmeterol in individuals with significantly worsening or acutely deteriorating asthma may be life-threatening.

Review and Application Exercises

**Short Answer Exercises**

1. What are some causes of bronchoconstriction, and how can they be prevented or minimized?
2. How do beta-adrenergic agonists act as bronchodilators?
3. What adverse effects are associated with bronchodilators, and how can they be prevented or minimized?
4. For what effects are corticosteroids used in the treatment of bronchoconstrictive respiratory disorders?
5. How does cromolyn act to prevent acute asthma attacks?
6. What are the main elements of treating respiratory distress from acute bronchospasm?
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**NCLEX-Style Questions**

7. The nurse notes that a patient’s serum theophylline level is 25 mcg/mL and that a scheduled dose of the medication is due. The nurse should
   a. Hold the scheduled dose, contact the health care provider, and assess the patient for signs of theophylline toxicity.
   b. Administer the dose as scheduled.
   c. Administer only half of the dose and repeat the theophylline level in 4 hours.
   d. Hold the dose until the next meal and administer at that time.

8. A patient, taking a short-acting inhaled bronchodilator and a steroid inhaler at the same scheduled time, asks the nurse if the order of administration of the inhalers matters. The best response by the nurse is
   a. “You should not take both inhalers at the same time.”
   b. “The short-acting inhaled bronchodilator should be used first, followed by the steroid inhaler.”
   c. “Either medication can effectively be used first.”
   d. “The steroid inhaler should be used first, followed by the short-acting inhaled bronchodilator.”

**Selected References**


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AU1 this sentence states that there are three leukotriene modifiers but only two are given below. Please advise