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CHAPTER 75

Asthma

Meredith Heltzer and Jonathan M. Spergel

Almost 5 million children in the United States have asthma,[1] and it is the most common reason for admission to pediatric hospitals.[2] Each year, asthma results in 10 million school absences,[2] 5500 deaths,[3] and 500,000 hospitalizations.[4,5] Appropriate asthma treatment prevents hospital admissions and emergency room visits, reduces the risk for death, and improves the quality of life for children with asthma.[4,6,7] The hospitalist is ideally situated to have a major impact on asthma by treating its acute manifestations, by implementing effective long-term therapy when indicated, and by diagnosing and managing any comorbidity that accompanies or exacerbates asthma (or both).

Asthma results from airway inflammation and smooth muscle dysfunction. It is defined by the National Heart, Lung, and Blood Institute (NHLBI) and World Health Organization as follows:

"A chronic inflammatory disorder of the airways in which many cells play a role, in particular, mast cells, eosinophils, and T lymphocytes. In susceptible individuals this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and in the early morning. These symptoms are usually associated with widespread but variable airway obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyperresponsiveness to a variety of stimuli."[4]

PATHOPHYSIOLOGY OF ASTHMA

The underlying cause of asthma is unknown, and the course of pediatric asthma is dynamic. Early in the course of the disease, airway inflammation, bronchial hyperreactivity, and loss of lung function are evident. Atopy and a family history of asthma are strongly correlated with asthma in childhood. Exposure to allergens activates mast cells and promotes inflammation and infiltration of the airway with neutrophils, eosinophils, and lymphocytes.[8] Whatever the cause, the inflammation results in airway hyperresponsiveness, which causes bronchoconstriction, edema, and mucous plugging, all of which contribute to bronchial obstruction. Chronically, collagen deposition below the epithelial basement membrane results in narrowing of the airway secondary to remodeling

ASTHMA EXACERBATIONS

An asthma exacerbation refers to an increase in a patient's respiratory symptoms above baseline as a result of increased airway obstruction. Status asthmaticus is continued or progressive airway obstruction despite bronchodilator therapy that results in sustained or worsening respiratory distress.[4]

Acute asthma exacerbations can be triggered by infectious respiratory illness, exposure to environmental allergens or irritants, exercise, cold air, or a combination of these factors. An asthma exacerbation involves either a slow onset of symptoms or a rapid decline in respiratory status. Persistent or acute allergen or irritant exposure promotes inflammation, bronchoconstriction, and airway hyperresponsiveness on an ongoing basis. Allergen exposure triggers a biphasic response. The "early response" occurs within minutes of allergen exposure and results in rhinorrhea, sneezing, itching of the eyes and nose, and bronchospasm secondary to release of histamine and other preformed mediators of inflammation. The "late-phase response" peaks 6 to 8 hours after allergen exposure with the development of eosinophilic inflammation and T-cell infiltration of the airway. During an exacerbation of asthma as a result of allergen exposure, both phases must be treated with medications to treat the symptoms of the early phase, as well as the subsequent inflammation of the late phase.[9]

Viral infections cause asthma symptoms by promoting eosinophilic or neutrophilic airway inflammation.[4] Viral-induced asthma exacerbations are common in children, and in fact a majority of acute asthma admissions are associated with viral infections in children and adults.[10,11] The risk for exacerbation of asthma can be modified by a patient's underlying inflammatory state and level of airway hyperreactivity. A patient with reduced airway inflammation because of adequate controller therapy is less likely to have a severe asthma flare when exposed to offending agents.

CLINICAL PRESENTATION

The presentation of acute asthma may vary, but all patients experience worsening airflow obstruction associated with respiratory distress. Patients often complain of shortness of breath, chest tightness, and wheezing. Some patients describe chest pain, cough, or fatigue. Caregivers may report observations of breathlessness, trouble speaking, decreased activity, retractions, rapid breathing, wheezing noises, or relentless cough.[12]

On physical examination, tachypnea is present, often accompanied by tachycardia. Pulse oximetry may reveal decreased oxygen saturation. There is evidence of increased respiratory effort, such as intercostal, supraclavicular, or subcostal retractions. Infants and young children may demonstrate nasal flaring or head bobbing. Paradoxical motion of the thoracoabdominal wall (i.e., expansion of abdominal girth with inspiration) is another useful sign of increased work of breathing. Auscultation of the chest frequently reveals wheezing and a prolonged expiratory phase. Rales or crackles are often heard and may shift in location over a period of minutes to hours ("migratory atelectasis"). Assessment of air movement is determined by the loudness of breath sounds in various areas of the chest and may also vary over time. Patients with poor air movement may have

minimal wheezing because the passage of air through the airway is what generates wheezing sounds. As air exchange improves, wheezing may become more pronounced. Conversely, patients with a deteriorating clinical course may have diminishing wheezing indicative of worsening air movement and perhaps respiratory insufficiency. Agitation and somnolence are worrisome signs and may indicate hypoxemia or hypercapnia with impending respiratory failure.

Some patients present without significant wheezing but with prominent cough as their manifestation of asthma, often referred to as "cough-variant" asthma. It is believed that the pathophysiology and response to treatment are similar to that for classic asthma.

DIFFERENTIAL DIAGNOSIS

Many conditions result in acute or chronic respiratory symptoms that mimic an asthma syndrome. Some of these conditions are discussed in the following text.

Anatomic abnormalities should be considered in young children with frequent episodes of cough or wheezing. Inhaled foreign bodies are most common in toddler-aged children (Chapter 79). These problems may manifest as cough, stridor, or wheezing. In all age groups, gastroesophageal reflux can mimic or contribute to underlying asthma (Chapter 101).[13,14] Cystic fibrosis is a genetic disorder that can also present with chronic cough or recurrent episodes of wheezing (Chapter 78).

Viral infections often cause wheezing in childhood as well. Respiratory syncytial virus is the most common cause of infantile bronchiolitis, but other respiratory viruses such as rhinovirus, parainfluenza virus, coronavirus, adenovirus, and influenza viruses are also common infectious agents.[15] Viral bronchiolitis is associated with edema, bronchospasm, and increased mucus production of the smaller airways, features that overlap with asthma (Chapter 66). Because these respiratory viral infections are known to precipitate asthma exacerbations, it may be difficult to determine whether the wheezing represents an isolated episode of bronchiolitis or an asthma exacerbation triggered by the respiratory virus.

Atypical respiratory infections with agents such as *Mycoplasma*, *Chlamydia pneumoniae*, and *Bordetella pertussis* or *parapertussis* can present with chronic cough. Coughing associated with these infections can persist for several months.

Functional disorders can coexist with or mimic asthma and include vocal cord dysfunction (VCD) and psychogenic cough. VCD usually presents in adolescence with upper airway (laryngeal) inspiratory or expiratory stridor, or both, which may be difficult to distinguish from lower airway wheezing. The diagnosis of VCD is confirmed by laryngoscopy demonstrating paradoxical adduction of the vocal cords during inspiration.[16-19] Psychogenic cough is a habitual cough that can also persist for months, and it often occurs after an acute respiratory illness.[20] Habitual cough has a characteristic sound described as barky or honking. The cough is exaggerated by stress or attention to the cough and disappears with sleep.[20] These features help distinguish this entity from cough-variant asthma. A key feature of VCD and psychogenic cough is lack of response to asthma therapy.[16-20] In addition, they are not associated with hypoxia.

Table 75-1 Questions to Ask Patients Who Present with Wheezing

Types of Symptoms
Cough
Wheeze
Shortness of breath
Chest tightness
Sputum production
Frequency of Symptoms
Daily, weekly, none
Perennial, seasonally
Do they have a night cough?
Do they cough with activity?
How often do they use their albuterol?
Severity of Symptoms
How often do they have flares of their asthma? How many times in the last year?
How many times have they used oral steroids? How many times in the last year?
How many emergency room visits?
How many visits to the hospital?
Have they ever been in the intensive care unit?

Table 75-2 Features That Place Patient at Risk for Severe Asthma

History of respiratory failure with asthma
Recent or multiple emergency department visits or hospitalizations (<6 months)
Daily oral steroid use at the time of exacerbations
Comorbid psychosocial conditions that interfere with administration of medications

EVALUATION

The initial evaluation of a patient presenting with an asthma exacerbation should include assessment of the acute respiratory symptoms, signs or symptoms of coexisting or precipitating conditions, and treatments initiated before presentation. A history should be obtained of the characteristics of the patient's asthma symptoms, the pattern and frequency of the symptoms, and any precipitating or aggravating factors, as well as features indicative of the severity and level of control of the asthma (Tables 75-1 and 75-2).[4]

The physical examination provides clues to the severity of the current illness, as well as the presence of comorbid conditions. Important physical parameters include the respiratory rate, work of breathing, air entry, wheezing, and oxygen saturation. Work of breathing refers to the use of accessory muscles of respiration and involves nasal flaring, abdominal retractions, and depth of respiration.

During an exacerbation of asthma, physical findings may vary and evolve with treatment or progression of the acute condition. A quiet or silent chest is a worrisome sign because

poor movement of air can be associated with respiratory insufficiency or failure. Asymmetry of auscultatory findings may indicate other conditions. Unequal breath sounds can be found with pneumonia, pleural effusion (especially in dependent regions of the lung), or atelectasis. Unilateral breath sounds may indicate an aspirated foreign body or pneumothorax on the side with diminished breath sounds[4] and may be accompanied by hyperresonance on that side, especially if significant air trapping is present.

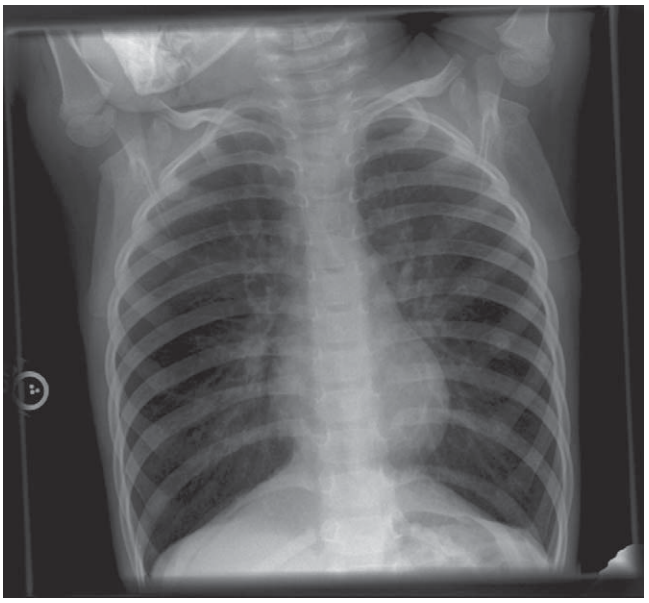
Chest radiographs are not typically needed for patients with known asthma and a straightforward asthma exacerbation.[21] Typical radiographic findings include hyperinflation, peribronchial thickening, and atelectasis (Fig. 75-1). Chest radiographs may be helpful when there is concern for pneumonia, pleural effusion, pneumothorax, pneumomediastinum, or foreign body aspiration.

A classification system for determining the severity of an asthma exacerbation in children 5 years of age or older is provided in Table 75-3. Patients in mild distress typically have slightly increased respiratory rates, may not use accessory muscles of respiration, and have end-expiratory wheezes with good air entry. Patients in severe distress are working hard to breathe, with inspiratory and expiratory wheezing, and are often hypoxic. Signs of impending respiratory failure are provided in Table 75-4. For infants and children younger than 5 years of age, clues to breathlessness include difficulty or reluctance to feed and changes in crying pattern (e.g., softer or shorter). Changes in vital signs in these younger patients must be interpreted in the context of normal values for the age range. Interestingly, paradoxical thoracoabdominal movement, a sign associated with severe respiratory distress in older children, may be seen in young children and infants, even in states of mild or moderate respiratory distress.

Objective measures for evaluation of acute asthma include pulmonary function testing, pulse oximetry, and arterial blood gases. Patients with exacerbations of asthma are at risk for hypoxemia. As a result, patients require frequent monitoring to ensure adequate oxygenation. Continuous pulse oximetry is recommended during a severe exacerbation, whereas intermittent oximetry may be acceptable as the clinical course improves.

Arterial blood gas parameters are typically obtained in critically ill patients and those with clinical deterioration or signs of respiratory insufficiency or failure. Arterial blood gases may reveal hypoxemia from ventilation-perfusion mismatch and respiratory alkalosis with hypocapnia secondary to hyperventilation. A normal or elevated partial pressure of carbon dioxide ($Paco_2$) may be the harbinger of respiratory failure[22] and may be associated with decreased blood pH because of respiratory acidosis.

Pulmonary function tests can be used to assess lung function even during an asthma exacerbation. Spirometric indices such as forced expiratory volume in 1 second (FEV_1) or the peak expiratory flow rate (PEFR) are most useful to assess the severity of asthma. However, because spirometry is often not readily available in the acute care setting, PEFR can be used instead. The hand-held peak flowmeter measures PEFR, and normal values have been established according to age, gender, and height[23] (Table 75-5). PEFR provides a measure of large-airway flow by measuring the rate of airflow in liters per minute. As a flare or asthma exacerba-



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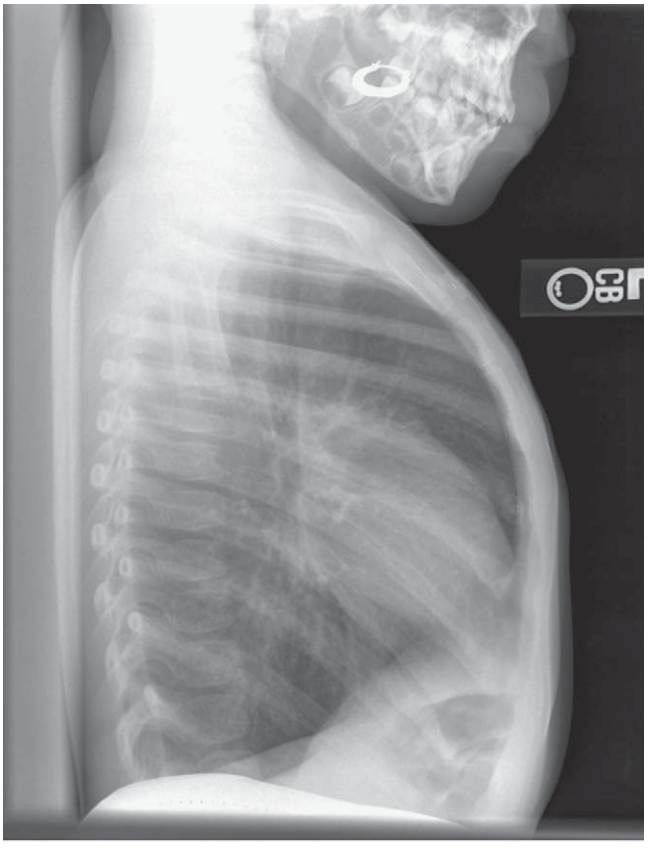

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Figure 75–1 **Typical radiographic findings of hyperinflation and peribronchial thickening in a patient with an acute asthma exacerbation. Flattening of the diaphragms is prominent in both the anteroposterior (A) and lateral (B) view. The lateral view demonstrates a widened anteroposterior diameter and increased prominence of the retrocardiac space.**

Table 75-3 Clinical Classification of Severity for Asthma Exacerbation

	Severity of Exacerbation			
	Mild	*Moderate*	*Severe*	*Impending Respiratory Failure*
Symptoms				
Breathlessness	While walking	While talking (infants: softer, shorter cry; difficulty feeding)	While at rest (infants: stop feeding)	
Positioning	Can lie down	Prefers sitting	Sits upright	
Speaks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
Signs				
Respiratory rate	Increased	Increased	Often >30/min	
Use of accessory muscles, suprasternal retractions	Usually not	Commonly	Usually	Paradoxical thoracoabdominal movement
Wheezing	Moderate, often only end expiratory	Loud, throughout exhalation	Usually loud, throughout inhalation and exhalation	Absence of wheezing
Pulse/min	<100	100-120	>120	Tachycardia or bradycardia
Pulsus paradoxus	Absent (<10 mm Hg)	May be present (10-25 mm Hg)	Often present (>25 mm Hg for an adult, 20-40 mm Hg for a child)	Absence suggests respiratory muscle fatigue
Functional Assessment				
PEF, % predicted or % personal best	80%	≈50%-80%	<50% of predicted or personal best	
Pa_{O_2} (on room air)	Normal (test not usually necessary)	>60 mm Hg (test not usually necessary)	<60 mm Hg, possible cyanosis	
And/or Pa_{CO_2}	<42 mm Hg	<42 mm Hg	>42 mm Hg, possible respiratory failure	
Sa_{O_2} (on room air) at sea level	>95%	91%-95%	<91%	

Asthma exacerbation usually includes several parameters, but not necessarily all. These parameters serve only as general guidelines because many have not been systemically studied.

Adapted from Moss MH, Gern JE, Lemanske RF Jr: Asthma in infancy and childhood. In Adkinson NF Jr, Yunginger JW, Busse WW, et al (eds): Middleton's Allergy Principles and Practice, 6th ed. Philadelphia, CV Mosby, 2003.

Available at *http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf.p107*.

Table 75-4 Indicators of Impending Respiratory Failure

Poor air movement or silent chest in combination with increased respiratory effort, decreased respiratory rate, or disorganized breathing pattern
Inability to speak
Inability to lie supine
Deteriorating mental status, lethargy, or agitation
Diaphoresis
Respiratory or cardiac arrest

tion worsens, PEFR typically becomes lower than baseline and may reflect the severity of the exacerbation. In patients presenting to an emergency room with an asthma exacerbation, FEV_1 is typically 30% to 35% of normal[24] and PEFR is less than 50% of normal. Monitoring PEFR can also assist in tapering medication during the recovery phase of an acute hospitalization. PEFR is effort and technique dependent, and therefore reliability remains a concern. It should be used in conjunction with other parameters of severity for assessment of patients (see Chapter 80).

TREATMENT

Exacerbations of asthma are treated with a combination of supportive therapy and pharmacologic interventions. Treatment is tailored to the severity of symptoms and adjusted according to the patient's response to therapy. Adequate hydration should be established and maintained either

Table 75-5 Predicted Average Peak Expiratory Flow (L/min): Normal Children and Adolescents

Height			Height			Height		
in	*cm*	Males and Females	*in*	*cm*	Males and Females	*in*	*cm*	Males and Females
43	109	147	51	130	254	59	150	360
44	112	160	52	132	267	60	152	373
45	114	173	53	135	280	61	155	387
46	117	187	54	137	293	62	157	400
47	119	200	55	140	307	63	160	413
48	122	214	56	142	320	64	162	427
49	124	227	57	145	334	65	165	440
50	127	240	58	147	347	66	168	454

This table is a guideline. National Heart, Lung, and Blood Institute guidelines suggest using a personal best as baseline values.
From Polgar G, Promahcat V: Pulmonary Function Testing in Children. Techniques and Standards. Philadelphia, WB Saunders, 1971.

orally or with intravenous fluids. Physiologic monitoring should include vital signs and pulse oximetry. Oxygen supplementation is provided to maintain oxygen saturation in a safe range. This range is widely debated, but most agree that levels greater than 91% are needed, and many target levels to greater than 93% to 95%.

Adrenergic Agonists

This class of medications works by stimulating the β_2-adrenergic receptor and causing activation of adenyl cyclase, which increases the production of cyclic 3′,5-adenosine monophosphate (cAMP). This increase in cAMP, depending on the site of stimulation, results in relaxation of bronchial smooth muscle, stimulation of skeletal and cardiac muscle, and inhibition of the release of inflammatory mediators through stabilization of the mast cell membrane. Albuterol is one of the short-acting β_2-adrenergic agents used as first-line therapy for an acute asthma exacerbation because of its ability to rapidly open the airways. Albuterol can be administered by nebulizer, either continuously or intermittently, or by metered-dose inhaler (MDI) with a spacer device. Studies have compared the amount of medication delivered to the lungs when given by MDI with spacer versus nebulizer.[25-27] The two modes are considered equivalent if the patient can use proper technique with the MDI-spacer method of delivery. Dosing information is provided in Table 75-6.

Paradoxical and transient worsening of hypoxia because of increased ventilation-perfusion mismatching can be seen with the administration of albuterol. The medication causes increased cardiac output, which leads to increased perfusion of unventilated lung.[28] Other side effects include sinus tachycardia, tremor, palpitations, headache, agitation, and ventricular irritability (e.g., ventricular premature contractions, ventricular tachycardia). In addition, because frequent or continuous dosing with adrenergic agents can lead to hypokalemia, patients receiving such treatment should have serum potassium levels checked periodically. Nonselective adrenergic agents (e.g., epinephrine) can also cause transient hyperglycemia and elevations in the neutrophil count as a result of demargination.

Albuterol is actually a racemic mixture of *R*-albuterol and *S*-albuterol, with a 50:50 ratio of these two stereoisomers. Levalbuterol (Xopenex) is made up of the *R*-isomer, which is thought to be the active component of the racemic product. However, *S*-albuterol has been found to have some bronchoconstrictive activity in select studies, but not in others, and demonstrates activation of eosinophils in vitro. In addition, *S*-albuterol is cleared much less rapidly, which can cause buildup of this isomer in vivo as opposed to the *L*-isomer. However, the vast majority of clinical studies and in vitro pharmacology data have shown no significant differences in cardiopulmonary side effects and tremor when comparing racemic with *R*-isomer albuterol.[29-31] One study found decreased rates of admission from an emergency department with the use of levalbuterol versus racemic albuterol.[32] Another study showed improved bronchodilation,[33] but these findings have not been confirmed in other studies.[29,30,34]

Terbutaline, a selective β_2-adrenergic agonist, and epinephrine, a nonselective adrenergic agonist, are used in asthmatics not responding to albuterol and corticosteroids or those who are deteriorating. These medications are given by subcutaneous injection or intravenous infusion. Bronchodilation is seen within 5 minutes of administration and can persist for 3 to 4 hours.[35,36] Terbutaline can also be given via continuous intravenous infusion by starting with a bolus and titrating the dose to the desired effect.

Dosing of β_2-adrenergic agonists and other bronchodilators is shown in Tables 75-6 and 75-7.

Corticosteroids

Corticosteroids are indicated for the initial treatment of status asthmaticus. They are potent anti-inflammatory medications that have been shown to hasten recovery, prevent recurrence,[37-41] and prevent hospitalizations.[42] Because of their mechanism of action, the effect of corticosteroids is not immediate. Steroids bind to the intracytoplasmic glucocorticoid receptor and translocate to the nucleus, where they effect RNA transcription in both positive and negative fashion through the transcription factors NF-κB and AP-1.

Table 75-6 **Dosages of Bronchodilators Commonly Used for Asthma Exacerbations**

Medications	Adult Dose	Child Dose	Onset of Action	Duration	Comments
Inhaled Short-Acting β_2-Agonists					
Albuterol nebulizer 5.0 mg/mL 2.5 mg/3 mL 1.25 mg/3 mL 0.63 mg/3 mL	2.5-5.0 mg every 20 minutes for 3 doses, then 2.5-10 mg every 1-4 hours as needed or 10-15 mg/hr continuously	0.15 mg/kg (minimum dose, 2.5 mg) every 20 minutes for 3 doses, then 0.15-0.3 mg/kg up to 10 mg every 1-4 hours as needed or 0.5 mg/kg/hr by continuous nebulization	15 minutes	3-4 hours	Only selective β_2-agonists are recommended. For optimal delivery, dilute aerosols to minimum of 4 mL at gas flow rates of 6-8 L/min
Albuterol via MDI 90 µg/puff	2-8 puffs every 20 minutes up to 4 hours, then every 1-4 hours as needed	2-8 puffs every 20 minutes for 3 doses, then every 1-4 hours	15 minutes	3-4 hours	As effective as nebulized therapy if patient is able to coordinate inhalation maneuver. A spacer or holding chamber should be used
Levalbuterol via nebulizer 0.31 mg/3 mL 0.63 mg/3 mL 1.25 mg/3 mL	Adults: 0.63 mg 3 times/day, may be increased to 1.25 mg	Children 6-11 years: 0.31 mg 3 times/day every 6-8 hours Children ≥12 years: 0.63 mg 3 times/day, may be increased to 1.25 mg	15 minutes	5-6 hours	0.63 mg of levalbuterol is equivalent to 1.25 mg of racemic albuterol in both efficacy and side effects Children 2-11 years: in a randomized, double-blind, single-dose, crossover study, doses ranging from 0.16 to 1.25 mg were used safely with clinically significant improvements in pulmonary function test values
Levalbuterol via MDI	1-2 puffs every 4-6 hours as needed	1-2 puffs every 4-6 hours as needed	5-10 minutes	3-6 hours	
Anticholinergics					
Ipratropium bromide Nebulizer solution (0.25 mg/mL)	0.5 mg every 30 minutes for 3 doses, then every 2-4 hours as needed	0.25 mg every 20 minutes for 3 doses, then every 2-4 hours	1-3 minutes	3-6 hours	May mix in same nebulizer with albuterol. Should not be used as first-line therapy. Should be added to β_2-agonist therapy
MDI (18 µg/puff)	2-8 puffs as needed	4-8 puffs as needed	1-3 minutes	3-6 hours	Dose in MDI is low and has not been studied in asthma exacerbations

MDI, metered-dose inhaler.

Adapted from National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report II: Guidelines for the Diagnosis and Management of Asthma (NIH Publication No. 96-4051). Bethesda, MD, U.S. Department of Health and Human Services, National Institutes of Health, 1997, 2002.

In general, steroids lead to down-regulation of inflammatory cytokines. Corticosteroids also activate histone deacetylase, which inhibits DNA transcription.[43] This change in transcription leads to increased expression of the β_2-adrenergic receptor and decreases in airway inflammation and mucus secretion. It can take several hours to reverse airway inflammation, and benefits are typically seen within 4 hours after the administration of corticosteroids.[38,39,44] Studies comparing oral and intravenous corticosteroids have found no significant differences in efficacy.[45,46] Oral steroids are typically preferred because intravenous access is not required.[45,47] Suggested dosing of corticosteroids is provided in Table 75-8.

Inhaled Anticholinergic Agents

Anticholinergic agents work by competitively inhibiting acetylcholine at the muscarinic junction to relieve the cholinergic-mediated bronchoconstriction. Nebulized atropine is associated with significant systemic absorption, but

Table 75-7 Systemic (Injected) Bronchodilators for Acute Asthma Exacerbations

Medications	Adult Dose	Child Dose	Onset of Action	Duration	Comments
β_2-Agonists					
Epinephrine 1 : 1000 (1 mg/mL) by IV infusion	0.3-0.5 mg every 20 minutes for 3 doses SC Loading dose: 2-10 µg/kg, followed by continuous infusion of 0.08-0.4 µg/kg/min; titrate dose by clinical response up to 6 µg/kg/min	0.01 mg/kg up to 0.3-0.5 mg every 20 minutes for 3 doses SC	1-3 minutes	30 minutes	No proven advantage of systemic therapy over aerosol
Terbutaline (1 mg/mL) by IV infusion	0.25 mg every 20 minutes for 3 doses SC Loading dose: 2-10 µg/kg followed by continuous infusion of 0.08-0.4 µg/kg/min; titrate dose by clinical response up to 6 µg/kg/min	0.01 mg/kg every 20 minutes for 3 doses, then every 2-6 hours as needed SC Loading dose: 2-10 µg/kg followed by continuous infusion of 0.08-0.4 µg/kg/min; titrate dose by clinical response up to 6 µg/kg/min	SC: 6-15 minutes	SC: 1.5-4 hours	

Table 75-8 Systemic Corticosteroids in the Setting of Asthma Exacerbations

Medication	Adult Dose	Child Dose (≤12 Years Old)	Onset of Action	Duration	Comments
Oral—prednisone/prednisolone IV—methylprednisolone	120-180 mg/day in 3-4 divided doses for 48 hours, then 60-80 mg/day until PEF reaches 70% of predicted or personal best	1 mg/kg every 6 hours for 48 hours, then 1-2 mg/kg/day (maximum, 60 mg/day) in 2 divided doses until PEF is 70% of predicted or personal best	1-4 hours (variable) 1-4 hours (variable)	12-36 hours	For outpatient burst for 3-10 days: Adult: use 40-60 mg in single or 2 divided doses Children: use 1-2 mg/kg/day with maximum of 60 mg/day
IM methylprednisolone 40 mg/mL 80 mg/mL	240 mg IM once	7.5 mg/kg IM once	1-4 hours (variable)	36-72 hours	IM should be used in place of a short burst of oral steroids in patients who are vomiting or if adherence is a problem

PEF, peak expiratory flow.

Adapted From National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report II: Guidelines for the Diagnosis and Management of Asthma (NIH Publication No. 96-4051). Bethesda, MD, U.S. Department of Health and Human Services, National Institutes of Health, 1997. Available at *http://www.nhlbi.nih.gov/guidelines/asthma/asthmafullrpt.pdf.*

anticholinergic medications such as ipratropium bromide have fewer side effects and less systemic absorption.[48]

The use of inhaled ipratropium in the initial phase of treatment has been shown to be effective in reducing the need for hospitalization. A few studies have found no benefit in comparison to β_2-agonists alone, whereas others have shown a slight advantage of one to three doses in the initial phase of an acute asthma exacerbation.[49] The role of ipratropium in hospitalized patients is less clear, but an initial study did not show clinical benefit.[50]

Combined administration of anticholinergic and β_2-agonist medications increases bronchodilation, although some controversy about this effect persists.[49,50] Nonetheless, many institutions use a combination of β_2-agonists and

anticholinergic medications during the initial phase of acute asthma exacerbations. Studies examining the use of anticholinergic medications as monotherapy have also been controversial. Dosing is listed in Table 75-6.

Nonstandard Therapies

If initiation of the aforementioned standard therapies does not improve the level of respiratory distress or if symptoms progress, additional interventions may be necessary. The clinical experience and expertise available at the particular institution should be considered in such decisions. Safe transfer to a facility able to provide critical care management should be anticipated, and arrangements should be expedited.

Magnesium Sulfate

Magnesium sulfate has been studied as a bronchodilator in severe asthma, with conflicting results.[51-54] Magnesium is thought to inhibit mast cell degranulation and increase bronchial dilation because of a decrease in calcium uptake by bronchial smooth muscle.[55] Its use is considered when a patient fails to improve or worsens despite treatment with continuous inhaled β_2-agonists, systemic corticosteroids, and inhaled anticholinergic agents.

Methylxanthines

Intravenous methylxanthines, such as aminophylline, were commonly used in the past to manage asthma exacerbations because of their ability to act directly on β-adrenergic receptors and relax bronchial smooth muscle. Concern regarding the toxicity and efficacy of this class of medication and the availability of newer agents have limited its use. Methylxanthines may help prevent acute airway hyperresponsiveness but do not appear to produce these effects chronically.[56-58] However, life-threatening events such as cardiac arrhythmia and seizures are associated with toxic levels of theophylline (>30 μg/mL). As a result, methylxanthines are recommended only as adjunctive therapy with close monitoring of serum concentrations and cardiac monitoring.

Studies examining the use of intravenous methylxanthines in children and adults with severe asthma have shown mixed benefit.[59-64] A recent Cochrane review found that theophylline in addition to β_2-agonists and glucocorticoids (with or without anticholinergics) improves lung function within 6 hours of treatment. However, there is no apparent reduction in symptoms, number of nebulized treatments, and length of hospital stay.[65]

Aminophylline requires a loading dose followed by a continuous infusion to reach and maintain a therapeutic level (see Table 75-9). Dosing is titrated according to serum level, clinical efficacy, and side effects.

Heliox

Heliox is a mixture of helium and oxygen used for inhalation. This agent is thought to improve airflow by creating gas with similar viscosity to air but with lower density, which in turn can increase ventilation and decrease work of breathing.[66-68] Heliox is indicated in patients with a refractory exacerbation of asthma in whom respiratory failure is impending. Patients with high oxygen requirements may not be able to tolerate heliox because they need a higher F_{IO_2} than a helium-oxygen mixture can provide. Heliox can also lower body temperature because of the high thermal conductivity of the mixture. Therefore, patients need to have their temperature monitored closely.

Dosing of nonstandard therapies is shown in Table 75-9, and adverse effects of medication are listed in Table 75-10.

Initial Treatment

The initial therapy for status asthmaticus has been outlined by the NHLBI guidelines (Fig. 75-2). In brief, patients are first treated with inhaled β_2-adrenergic agonists (e.g., inhaled albuterol), corticosteroids either orally or intravenously, and if needed, oxygen. Inhaled anticholinergics, such as ipratropium bromide, may be added for patients who do not demonstrate prompt improvement. Patients with significant improvement after these initial interventions may not require hospitalization.

Hospitalization is recommended for patients who continue to have moderately severe or severe symptoms after initial intervention. Treatment with inhaled albuterol (either every 1 to 2 hours by nebulizer or MDI with spacer or delivered continuously by nebulizer) and corticosteroid therapy (orally or, if not tolerated, intravenously) should be continued. Continuation of inhaled anticholinergic agents may be considered, although their benefit remains unproven.

If patients continue to deteriorate, they must be monitored for respiratory insufficiency and failure. An arterial blood gas measurement can be used to confirm the condition and should reveal decreased pH, elevated partial pressure of carbon dioxide (P_{ACO_2}), and an increased alveolar-arterial oxygen gradient. Pulse oximetry remains a poor monitoring device for early detection of respiratory failure. Oxygen saturation is initially maintained despite a significant degree of hypoventilation, and the addition of supplemental oxygen would further obscure evidence of respiratory failure from this device (Chapter 66). Patients with impending respiratory failure often need mechanical ventilatory support.

Tapering Hospital Therapy

After patients are stabilized and demonstrate improvement, therapies can be gradually reduced and withdrawn. Ongoing assessment of clinical parameters is performed, including the respiratory rate, work of breathing, auscultatory findings, and requirement for supplemental oxygen. If the patient remains comfortable with minimal signs of respiratory distress, the dosing of inhaled β_2-agonists is decreased. For patients receiving continuous inhaled β_2-agonist therapy, the dose may be reduced and then subsequently transitioned to intermittent treatments, usually every 2 hours. As the patient continues to improve, the interval between treatments can be extended. Similarly, the amount of supplemental oxygen is titrated to maintain oxygen saturation above the desired level and eventually discontinued. Systemic corticosteroids are continued throughout the exacerbation and maintained for several days after discharge from the hospital. If inhaled anticholinergic agents have been instituted, they are usually discontinued when albuterol begins to be tapered.

Many hospitals use clinical pathways, which are tools that detail a sequence of assessments and treatments for patients with various conditions.[69] Studies have shown that asthma clinical pathways shorten hospitalization and decrease the

Table 75-9 Nonstandard Therapies for Exacerbations of Asthma

Rights were not granted to include this table in electronic media.
Please refer to the printed publication.

need for readmission for up to 2 weeks after discharge.[70,71] An asthma clinical pathway allows multiple caregivers, including nurses, respiratory therapists, and doctors, to modify treatment based on structured assessments. The NHLBI guidelines (see Fig. 75-2) outline specific criteria that can be used to determine a patient's severity and frequency of therapy. It also provides criteria to assist in weaning treatments.

PEFR measurements may be useful to determine readiness for reduction in medication. If PEFR is at least 70% of baseline before a bronchodilator treatment (see Table 75-5), it is appropriate to space the frequency of the β_2-adrenergic agonist treatments. Technique and effort will affect measurement of PEFR; therefore, it should be used in conjunction with other clinical indicators of improvement.

Therapy after Discharge Home

Patients should be sent home on a regimen of oral corticosteroids, the duration of which depends on the length and severity of illness and the patient's frequency of exacerbations. In general, an isolated exacerbation is treated with oral corticosteroids for 5 days. However, if a patient was admitted to the hospital for an extended period, a prolonged course of corticosteroids will be required, followed by tapering doses. A taper is prescribed to prevent relapse of symptoms, as well as to prevent an addisonian crisis from adrenal suppression. The risk for an addisonian crisis is hypothetical and has not been demonstrated in any study.[72-74] In addition, patients receiving their second course of steroids in a month should undergo prolonged tapering as well. A typical taper involves keeping the patient at a full daily dose of corticosteroids until stable clinical status is achieved and then decreasing the dose by 30% to 50% daily. Patients who required admission to the hospital may not have been on an adequate treatment plan. Thus, hospitalization offers an opportunity to assess the overall treatment regimen. Patients should be evaluated according to the NHLBI guidelines shown in Table 75-11A and B and need their outpatient preventive treatment stepped up. Specific drug choices are outlined in Tables 75-12 through 75-14.

CONSULTATION

Outpatient referral to an asthma specialist (e.g., pulmonologist, allergist) is associated with reduced rates of emergency department visits[75] and is recommended for patients with the following scenarios[76-78]:

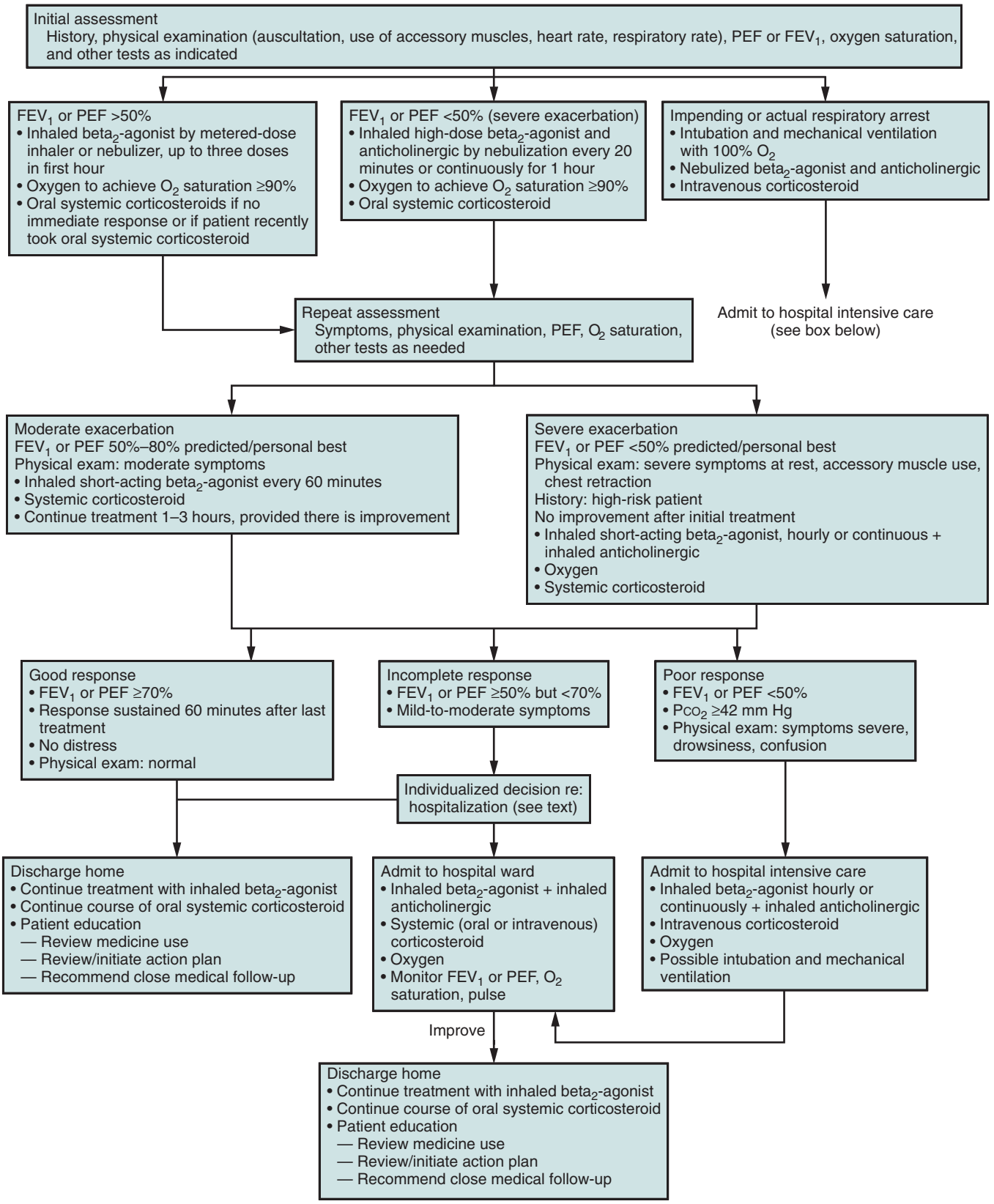

Figure 75–2 NHLBI hospital assessment and management of acute exacerbation. PEF, peak expiratory flow; FEV_1, forced expiratory volume in 1 second. Adapted from National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report II: Guidelines for the Diagnosis and Management of Asthma [NIH Publication No. 96-4051]. Bethesda, MD, U.S. Department of Health and Human Services, National Institutes of Health, 1997.

Table 75-10 Common Side Effects of Pharmacologic Therapies

Side Effect	Possible Causative Agent	Comment
Hypokalemia	Adrenergic agonists	Patients using prolonged hourly or continuous inhaled therapy or intravenous therapy should have serum potassium levels monitored
Tremor/agitation	Adrenergic agonists	Dose dependent
Hypertension	Corticosteroids, adrenergic agonists	May require reduction of dose, discontinuation of therapy, or addition of antihypertensive medication
Tachycardia, palpitations, ventricular premature contractions	Adrenergic agonists, aminophylline, theophylline	Usually dose dependent. Serum levels of methylxanthines should be monitored. The risk is increased with hypoxemia or acidemia
Hyperglycemia/glucosuria	Corticosteroids, adrenergic agonists	Resolves with completion or discontinuation of therapy
Emotional lability	Corticosteroids	Resolves with completion or discontinuation of therapy
Hyperphagia	Corticosteroids	Resolves with completion or discontinuation of therapy
Seizure	Theophylline, aminophylline	Serum levels of methylxanthines should be monitored. Risk is increased in the presence of acidosis
Elevated peripheral neutrophil count	Corticosteroids, adrenergic agonists (in particular, epinephrine)	May interfere with utility of the white blood count in assessing for infection

- Life-threatening asthma requiring admission to intensive care or a step-down unit
- Severe persistent asthma in a patient who has required a prolonged course of steroids or multiple courses of corticosteroids in 1 year
- Not meeting the goals of asthma therapy or not responding to treatment so that additional testing can be performed if necessary

Asthma specialists may be available to assist in the management of an acute asthma exacerbation as needed. Involving the specialist during a hospitalization may assist in transition after discharge. Critical care physicians should be contacted for all patients who may need management in an intensive care setting.

ADMISSION CRITERIA

Admission to the hospital is individualized and based on many factors. Hospitalization should be considered in patients with the following:

- Poor response to initial treatment
- Oxygen saturation less than 92% on room air
- Severe asthma with a relapsing course despite prolonged corticosteroid therapy
- Previous emergency visits during the current period of exacerbation
- Concern for noncompliance

Admission to an intensive care unit would be appropriate for patients with the following:

- Life-threatening or severe asthma that is unresponsive to initial therapy
- Inability to maintain oxygen saturation greater than 92% with supplemental oxygen
- Evidence of impending respiratory failure
- Inability to provide adequate monitoring outside an intensive care setting[79]

DISCHARGE CRITERIA

Patients are ready to go home when they have been successfully weaned to albuterol treatments every 4 to 6 hours. Before receiving a treatment, they should be able to breathe comfortably during ambulation or speaking. Wheezing may persist on examination, but it should not be audible without a stethoscope. A plan of care should include ongoing management of the current acute exacerbation and transition to maintenance therapy. Additionally, patients should leave with a plan of action for management of subsequent asthma exacerbations. Efforts should be coordinated with the primary care clinician and, if involved, the asthma specialist.

Before discharge, it is important to consider the environment to which the patient will return. Preventive management plans should be reviewed with the family, including identification of any potential comorbid conditions and triggers present in the environment. Table 75-15 highlights a discharge checklist that was created by the NHLBI panel.

PREVENTION

Educating the family about the pathogenesis of asthma, triggers, and medications is crucial for preventing exacerbations and admissions to the hospital. A patient who requires frequent admissions needs to have the treatment plan reassessed and be evaluated for comorbid conditions. Assessment of adherence to therapy and review of relevant drug delivery systems are important as well. For children experiencing symptoms on a daily basis, there are certain controllable environmental factors, such as exposure to allergens

Table 75-11A Stepwise Approach for Managing Infants and Young Children (5 Years and Younger) with Acute or Chronic Asthma

Classify Severity: Clinical Features Before Treatment or Adequate Control	**Symptoms/Day** **Symptoms/Night**	**Medications Required To Maintain Long-Term Control** **Daily Medications**
Step 4 **Severe Persistent**	Continual Frequent	• **Preferred treatment:** **– High-dose inhaled corticosteroids** **AND** **– Long-acting inhaled beta$_2$-agonists** AND, if needed, – Corticosteroid tablets or syrup long term (2 mg/kg/day, generally do not exceed 60 mg per day). (Make repeat attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids.)
Step 3 **Moderate Persistent**	Daily . 1 night/week	• **Preferred treatments:** **– Low-dose inhaled corticosteroids and long-acting inhaled beta$_2$-agonists** **OR** **– Medium-dose inhaled corticosteroids.** • Alternative treatment: – Low-dose inhaled corticosteroids and either leukotriene receptor antagonist or theophylline. If needed (particularly in patients with recurring severe exacerbations): • **Preferred treatment:** **– Medium-dose inhaled corticosteroids and long-acting beta$_2$-agonists.** • Alternative treatment: – Medium-dose inhaled corticosteroids and either leukotriene receptor antagonist or theophylline.
Step 2 **Mild Persistent**	. 2/week but , 1x/day . 2 nights/month	• **Preferred treatment:** **– Low-dose inhaled corticosteroid (with nebulizer or MDI with holding chamber with or without face mask or DPI).** • Alternative treatment (listed alphabetically): – Cromolyn (nebulizer is preferred or MDI with holding chamber) OR leukotriene receptor antagonist.
Step 1 **Mild Intermittent**	# 2 days/week # 2 nights/month	• **No daily medication needed.**

Quick Relief
All Patients

- Bronchodilator as needed for symptoms. Intensity of treatment will depend upon severity of exacerbation.
  - Preferred treatment: **Short-acting inhaled beta$_2$-agonists** by nebulizer or face mask and space/holding chamber
  - Alternative treatment: Oral beta$_2$-agonist
- With viral respiratory infection
  - Bronchodilator q 4–6 hours up to 24 hours (longer with physician consult); in general, repeat no more than once every 6 weeks
  - Consider systemic corticosteroid if exacerbation is severe or patient has history of previous severe exacerbations
- Use of short-acting beta$_2$-agonists .2 times a week in intermittent asthma (daily, or increasing use in persistent asthma) may indicate the need to initiate (increase) long-term-control therapy.

Step down
Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible.

Step up
If control is not maintained, consider step up. First, review patient medication technique, adherence, and environmental control.

Goals of Therapy: Asthma Control

- Minimal or no chronic symptoms day or night
- Minimal or no exacerbations
- No limitations on activities; no school/parent's work missed
- Minimal use of short-acting inhaled beta$_2$-agonist
- Minimal or no adverse effects from medications

Note

- The stepwise approach is intended to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- Classify severity: assign patient to most severe step in which any feature occurs.
- There are very few studies on asthma therapy for infants.
- Gain control as quickly as possible (a course of short systemic corticosteroids may be required); then step down to the least medication necessary to maintain control.
- Minimize use of short-acting inhaled beta$_2$-agonists. Overreliance on short-acting inhaled beta$_2$-agonists (e.g., use of approximately one canister a month even if not using it every day) indicates inadequate control of asthma and the need to initiate or intensify long-term-control therapy.
- Provide parent education on asthma management and controlling environmental factors that make asthma worse (e.g., allergies and irritants).
- Consultation with an asthma specialist is recommended for patients with moderate or severe persistent asthma. Consider consultation for patients with mild persistent asthma.

DPI, dry powder inhaler.

Adapted from National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Guidelines for the Diagnosis and Management of Asthma: Update on Selected Topics (NIH Publication No. 02-5075). Bethesda, MD, US Department of Health and Human Services, National Institutes of Health, 2002. Available at *http://www.nhlbi.nih.gov/guidelines/asthma/execsumm.pdf.*

Table 75-11B Stepwise Approach for Managing Asthma in Adults and Children Older Than 5 Years: Treatment

Classify Severity: Clinical Features Before Treatment or Adequate Control	Symptoms/Day Symptoms/Night	PEF or FEV_1 PEF Variability	Medications Required To Maintain Long-Term Control Daily Medications
Step 4 **Severe Persistent**	Continual Frequent	≤ 60% > 30%	• **Preferred treatment:** **– High-dose inhaled corticosteroids AND** **– Long-acting inhaled $beta_2$-agonists** AND, if needed, – Corticosteroid tablets or syrup long term (2 mg/kg/day, generally do not exceed 60 mg per day). (Make repeat attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids.)
Step 3 **Moderate Persistent**	Daily > 1 night/week	> 60% – < 80% > 30%	• **Preferred treatment:** **– Low-to-medium dose inhaled corticosteroids and long-acting inhaled $beta_2$-agonists.** • Alternative treatment (listed alphabetically): – Increase inhaled corticosteroids within medium-dose range OR – Low-to-medium dose inhaled corticosteroids and either leukotriene modifier or theophylline. If needed (particularly in patients with recurring severe exacerbations): • **Preferred treatment:** **– Increase inhaled corticosteroids within medium-dose range and add long-acting inhaled $beta_2$-agonists.** • Alternative treatment (listed alphabetically): – Increase inhaled corticosteroids within medium-dose range and add either leukotriene modifier or theophylline.
Step 2 **Mild Persistent**	> 2/week but < 1x/day > 2 nights/month	≥ 80% 20%–30%	• **Preferred treatment:** **– Low-dose inhaled corticosteroids.** • Alternative treatment (listed alphabetically): cromolyn, leukotriene modifier, nedocromil, OR sustained-release theophylline to serum concentration of 5–15 mcg/mL.
Step 1 **Mild Intermittent**	≤ 2 days/week ≤ 2 nights/month	≥ 80% < 20%	• **No daily medication needed.** • Severe exacerbations may occur, separated by long periods of normal lung function and no symptoms. A course of systemic corticosteroids is recommended.

Quick Relief
All Patients

- Short-acting bronchodilator: 2–4 puffs **short-acting inhaled $beta_2$-agonists** as needed for symptoms.
- Intensity of treatment will depend on severity of exacerbation; up to 3 treatments at 20-minute intervals or a single nebulizer treatment as needed. Course of systemic corticosteroids may be needed.
- Use of short-acting $beta_2$-agonists >2 times a week in intermittent asthma (daily, or increasing use in persistent asthma) may indicate the need to initiate (increase) long-term-control therapy.

Step down
Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible.

Step up
If control is not maintained, consider step up. First, review patient medication technique, adherence, and environmental control.

Goals of Therapy: Asthma Control

- Minimal or no chronic symptoms day or night
- Minimal or no exacerbations
- No limitations on activities; no school/work missed
- Maintain (near) normal pulmonary function
- Minimal use of short-acting inhaled $beta_2$-agonist
- Minimal or no adverse effects from medications

Note

- The stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- Classify severity: assign patient to most severe step in which any feature occurs (PEF is % of personal best; FEV_1 is % predicted).
- Gain control as quickly as possible (consider a short course of systemic corticosteroids); then step down to the least medication necessary to maintain control.
- Minimize use of short-acting inhaled $beta_2$-agonists. Overreliance on short-acting inhaled $beta_2$-agonists (e.g., use of approximately one canister a month even if not using it every day) indicates inadequate control of asthma and the need to initiate or intensify long-term-control therapy.
- Provide education on self-management and controlling environmental factors that make asthma worse (e.g., allergens and irritants).
- Refer to an asthma specialist if there are difficulties controlling asthma or if step 4 care is required. Referral may be considered if step 3 care is required.

Adapted from National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Guidelines for the Diagnosis and Management of Asthma: Update on Selected Topics (NIH Publication No. 02-5075). Bethesda, MD, US Department of Health and Human Services, National Institutes of Health, 2002. Available at *http://www.nhlbi.nih.gov/guidelines/asthma/execsumm.pdf*.

Table 75-12 **Preferred Treatment of Asthma According to Severity**

Severity	Preferred Treatment	Alternative Treatments	Comments
Intermittent	No daily medication needed		Severe exacerbations may occur, separated by long periods of no symptoms. Treat with a course of systemic corticosteroids
Mild persistent	Low-dose inhaled corticosteroid	Cromolyn Leukotriene modifier Nedocromil Sustained-release theophylline (level, 5-15 μg/mL)	
Moderate persistent	Low- to medium-dose inhaled corticosteroid *and* long-acting inhaled β_2-agonist	Increased inhaled corticosteroid within medium-dose range *or* low- to medium-dose inhaled corticosteroid and either a leukotriene modifier or theophylline	If exacerbations occur despite daily medication, increase the inhaled corticosteroid and add a long-acting inhaled β_2-agonist
Severe persistent	High-dose inhaled corticosteroids and long-acting inhaled β_2-agonists		

Adapted from Bacharier LB, Strunk RC: Asthma in older children. In Leung DYM, Sampson HA, Gehr RS, Szefler SJ (eds): Pediatric Allergy: Principles and Practice. Philadelphia, CV Mosby, 2003, p 416.

Table 75-13 **Usual Dosages for Long-Term Control Medications**

Medication	Dosage Form	Adult Dose	Child Dose
Inhaled Corticosteroids (see estimated daily dosages for inhaled corticosteroids)			
Systemic Corticosteroids			
Methylprednisolone	2-, 4-, 8-, 6-, 32-mg tablets	7.5-60 mg daily in a single dose in AM or qod as needed for control	0.25-2 mg/kg daily as single dose in AM or qod as needed for control
Prednisolone	5-mg tablets 5 mg/5 mL, 15 mg/5 mL	Short-course "burst" to achieve control: 40-60 mg/day as single or 2 divided doses for 3-10 days	Short-course "burst": 1-2 mg/kg/day, maximum of 60 mg/day, for 3-10 days
Prednisone	1-, 2.5-, 5-, 10-, 20-, 50-mg tablets 5 mg/mL, 5 mg/5 mL		
Long-Acting Inhaled β_2-Agonists (should not be used for symptom relief or for exacerbation; use with inhaled corticosteroids)			
Salmeterol	MDI: 21 μg/puff	2 puffs q12h	1-2 puffs q12h
	DPI: 50 μg/blister	1 blister q12h	1 blister q12h
Formoterol	DPI: 12 μg/single-use capsule	1 capsule q12h	1 capsule q12h
Combined Medication			
Fluticasone/salmeterol	DPI: 100, 250, or 500 μg/50 μg	1 inhalation bid; dose depends on severity of asthma	1 inhalation bid; dose depends on severity of asthma
Cromolyn and Nedocromil			
Cromolyn	MDI: 1 mg/puff	2-4 puffs tid-qid	1-2 puffs tid-qid
	Nebulizer: 20 mg/ampule	1 ampule tid-qid	1 ampule tid-qid
Nedocromil	MDI: 1.75 mg/puff	2-4 puffs bid-qid	1-2 puffs bid-tid
Leukotriene Modifiers			
Montelukast	4- or 5-mg chewable tablet 10-mg tablet	10 mg qhs	4 mg qhs (2-5 yr) 5 mg qhs (6-14 yr) 10 mg qhs (>14 yr)
Zafirlukast	10- or 20-mg tablet	40 mg daily (20-mg tablet bid)	20 mg daily (7-11 yr) (10-mg tablet bid)
Zileuton	300- or 600-mg tablet	2400 mg daily (give tablets qid)	
Methylxanthines (serum monitoring is important [serum concentration of 5–15 μg/mL at steady state])			
Theophylline	Liquids, sustained-release tablets, and capsules	Starting dose, 10 mg/kg/day up to 300 mg max; usual max, 800 mg/day	Starting dose, 10 mg/kg/day; usual max: <1 yr of age: 0.2 (age in wk) + 5 = mg/kg/day ≥1 yr of age: 16 mg/kg/day

DPI, dry powder inhaler; MDI, metered-dose inhaler.

Modified from National Heart, Lung, and Blood Institute, Executive Summary of NAEPP Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma: Update on Selected Topics (NIH Publication No. 02-5075). Bethesda, MD, US Department of Health and Human Services, National Institutes of Health, 2002.

Table 75-14 Estimated Comparative Daily Dosages for Inhaled Corticosteroids

	Low Daily Dose		Medium Daily Dose		High Daily Dose	
Drug	***Adult***	***Child****	***Adult***	***Child****	***Adult***	***Child****
Beclomethasone HFA 40 or 80 µg/puff	80-240 µg	80-160 µg	240-480 µg	160-320 µg	>480 µg	>320 µg
Budesonide DPI 200 µg/inhalation	200-600 µg	200-400 µg	600-1200 µg	400-800 µg	>1200 µg	>800 µg
Budesonide inhalation suspension for nebulization (child dose)		0.5 mg		1.0 mg		2.0 mg
Flunisolide 250 µg/puff	500-1000 µg	500-750 µg	1000-2000 µg	1000-1250 µg	>2000 µg	>1250 µg
Fluticasone						
MDI: 44, 110, or 220 µg/puff	88-264 µg	88-176 µg	264-660 µg	176-440 µg	>660 µg	>440 µg
DPI: 50, 100, or 250 µg/inhalation	100-300 µg	100-200 µg	300-600 µg	200-400 µg	>600 µg	>400 µg
Trlamcinolone acetonide 100 µg/puff	400-1000 µg	400-800 µg	1000-2000 µg	800-1200 µg	>2000 µg	>1200 µg

DPI, dry powder inhaler.
*Children ≤12 years of age.
Modified from National Heart, Lung, and Blood Institute: Executive Summary of NAEPP Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma: Update on Selected Topics (NIH Publication No. 02-5075). Bethesda, MD, US Department of Health and Human Services, National Institutes of Health, 2002.

Table 75-15 Hospital Discharge Checklist for Patients with Asthma Exacerbations

Intervention	Dose/Timing	Education/Advice	MD/RN Initials
Inhaled medications (MDI + spacer/holding chamber)	Select agent, dose, and frequency (e.g., albuterol)	Teach purpose Teach technique	
$Beta_2$-agonist	2-6 puffs q 3-4 hr prn	Emphasize need for spacer/ holding chamber	
Corticosteroids	Medium dose	Check patient technique	
Oral medications	Select agent, dose, and frequency (e.g., prednisone 20 mg bid for 3-10 days)	Teach purpose Teach side effects	
Peak flow meter	Measure AM and PM. PFF and record best of three tries each time	Teach purpose Teach technique Distribute peak flow diary	
Follow-up visit	Make appointment for follow-up care with primary clinician or asthma specialist	Advise patient (or caregiver) of date, time, and location of appointment within 7 days of hospital discharge	
Action plan	Before or at discharge	Instruct patient (or caregiver) on simple plan for actions to be taken when symptoms, signs, and PEF values suggest recurrent airflow obstruction	

Adapted from National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report II: Guidelines for the Diagnosis and Management of Asthma (NIH Publication No. 96-4051). Bethesda, MD, US Department of Health and Human Services, National Institutes of Health, 1997.

and cigarette smoke, that can cause symptoms and contribute to asthma exacerbations.[80] In addition, other factors, including gastroesophageal reflux, sinusitis, and others that might exacerbate asthma, should be explored and eliminated if possible (Table 75-16). If an allergic component is being considered, further evaluation can be arranged and environmental control measures recommended. Both passive and active cigarette smoking significantly increases the risk for asthma and worsens asthma symptoms.[81-88] As a result, no smoking should be permitted around asthmatics or in their home or family car. Physicians should provide assistance for caregivers to quit smoking.

Appropriate preventive medications based on daily symptoms and frequency of exacerbations should be maintained on a daily basis. These medications are essential for the prevention of asthma flares. Multiple studies have shown a

Table 75-16 Exacerbating Factors for Asthma and Control Measures

Factors That Worsen Asthma Severity	Control Measures
Animal dander	Remove the animal from the environment At a minimum, remove the pet from the bedroom
House dust mites	Encase mattress and pillows in an allergen-impermeable cover Wash bedding in hot water weekly at >130° F Remove carpets from the bedroom
Cockroaches	Exterminate! Do not leave garbage and food exposed
Pollen	During pollen season, stay indoors with windows closed, especially in the afternoon
Mold	Fix leaks, eliminate water sources Clean moldy surfaces
Cigarette/tobacco smoke	Encourage family members and caregivers to smoke outside and cease smoking
Sinusitis	Promote sinus drainage Antibiotic therapy when appropriate
Gastroesophageal reflux	No eating 3 hr before bedtime Elevate head of bed 6-8 inches Appropriate medications: H_2 receptor antagonist
Medications	No beta-blockers Aspirin and NSAIDs in combination with severe persistent asthma, nasal polyps, and aspirin sensitivity increase the risk for a reaction
Viral infections	Annual influenza vaccination
Irritants	Decrease exposure to wood-burning stoves, fireplaces, unvented stoves or heaters, perfumes, cleaning agents, sprays

NSAIDs, nonsteroidal anti-inflammatory medications.
Adapted from National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program Expert Panel II: Guidelines for the Diagnosis and Management of Asthma (NIH Publication No. 96-4051). Bethesda, MD, US Department of Health and Human Services, National Institute of Health, 1997.

strong negative correlation between hospital admission for asthma and the use of daily inhaled corticosteroids. Suggested doses and regimens have been established through national and worldwide collaboration between primary physicians, allergists, pulmonologists, and others. An example is seen in Tables 75-12 through 75-14.

Peak flowmeters can be helpful in managing asthma, if used appropriately.[89] However, studies comparing peak flow monitoring with symptom recognition show no benefit of peak flow–based action plans over those based on symptoms alone.[89-91] Peak flowmeters have numeric indicators that allow the creation of green, yellow, and red zones (see Table 75-5). Green represents the "good" or "all clear" zone and is 80% to 100% of a child's personal best. The yellow zone is 50% to 80% of the personal best and indicates a time when the family should be "cautious" because the child may be having or is at risk for asthma symptoms. Asthma reliever medications should be started and contact with the physician considered. The red zone is indicated by a PEFR less than 50% of normal; it is cause for concern and requires a visit to the emergency room or a call to the doctor.[4] Peak flow monitoring is typically helpful for children who are not good at recognizing symptoms of asthma. Current NHLBI guidelines recommend either a symptom-based or peak flow–based management plan.

Additional sources of support for families can include the Asthma and Allergy Foundation of America and Mothers of Asthmatics.

IN A NUTSHELL

- Asthma is a chronic disorder that results in airway inflammation and smooth muscle dysfunction and is manifested as recurrent episodes of wheezing, breathlessness, and chest tightness.
- Exacerbations can be triggered by a variety of stimuli, including respiratory infections, exposure to allergens or irritants, exercise, and cold air.
- Treatment of flares must be directed at decreasing airway inflammation and relieving bronchospasm while providing supportive care.
- The mainstay of pharmacologic therapy includes inhaled short-acting β_2-adrenergic agonist therapy and systemic corticosteroids. Supportive care includes supplemental oxygen if needed and maintenance of hydration.
- Many of the pharmacologic agents have significant side effects, and therefore appropriate monitoring is required.

- Patients with severe symptoms or those with moderately severe symptoms that fail to improve after initial therapy are candidates for admission to an intensive care setting.
- At the time of discharge, patients should have a clear plan for ongoing treatment of the acute exacerbation and transition to maintenance therapy. In addition, an action plan for subsequent exacerbations should be in place.

ON THE HORIZON

- Asthma is a chronic inflammatory disease that affects many Americans, and researchers are actively investigating new drugs and therapies to improve the quality of life of asthmatics. Drugs that modify the immune response are currently under active investigation. An example of one of these drugs is omalizumab, a recombinant humanized anti-IgE antibody. This drug binds circulating free IgE and consequently reduces the level of free IgE in the bloodstream and prevents it from binding to mast cell membrane receptors, thus curtailing the early and late asthmatic responses. Omalizumab has been found to reduce symptoms, exacerbations,[92] and the use of corticosteroids.
- New NHLBI Expert Panel guidelines on the diagnosis and treatment of asthma are expected in late 2006 or early 2007. The new guidelines are expected to emphasize daily symptom control in addition to preventing exacerbations in the management of asthma.

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