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Concepts and Clinical Practice

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59

Asthma

Taher T. Vohra and Richard M. Nowak

KEY CONCEPTS

- Inhaled and systemic steroid medications are effective in controlling airway inflammation and have important roles in the management of asthma exacerbations.
- Inhaled bronchodilators and systemic corticosteroids remain the mainstays of management for most acute asthma exacerbations.
- Acute severe asthma requires rapid identification. Treatment may use strategies not used in mild-to-moderate exacerbations, such as infusion of magnesium sulfate, use of non-invasive ventilation, and endotracheal intubation.
- Ventilator management in the intubated asthmatic is critical and includes lower tidal volumes (6 to 8 mL/kg) and low respiratory rates, often less than 10 per minute.
- A normal partial pressure of carbon dioxide (P_{CO_2}) in a pregnant patient represents hypercarbia.
- Elevated lactic acid levels are common in critically ill asthmatics and do not reflect deterioration or a poor prognosis.
- ED management of acute asthma is expanding (up to 24 hours) as more non-critically ill asthmatics are treated in observation units.
- Integration of discharged patients with acute asthma into chronic management strategies to prevent relapse requires physicians be familiar with controlling medications, such as inhaled corticosteroids and long-acting beta agonists.

FOUNDATIONS

Background and Importance

The word *asthma*, derived from the Greek ασυμα, signifies panting and was used initially as a synonym for "breathlessness." In 1698, Floyer published *A Treatise of the Asthma,* in which he attempted to differentiate asthma more clearly from other pulmonary disorders. Subsequent definitions of asthma highlight concepts of airway hyperresponsiveness, bronchospasm, reversible airway obstruction, and inflammation, emphasizing the many facets of this complex disease.

In 2017, it was estimated that 42.6 million Americans had been diagnosed with asthma by a health professional within their lifetime.[1] Asthma is more prevalent in children than adults, in females than males, and in African Americans and Puerto Ricans than whites or other Hispanics (Fig. 59.1). Asthma is also more prevalent in impoverished individuals and in the northeastern region of the United States (Fig 59.2).

African American adults had an ED visit rate for asthma nearly four times that of whites.[2] Over 3500 deaths due to asthma were reported in 2017 in the United States.[3,4] The female death rate from asthma was 1.3 times higher than males. African Americans were 2.5 to 3 times more likely to die from asthma than whites, Hispanics, and other races. Decreases in asthma death rates were noted from 2001 to 2007 but have remained steady from 2007 to 2017 (Fig. 59.3).[3] The highest death rate is reported among adults 65 years old and older, and the lowest among children 0 to 4 years old.

Industrialized nations have higher rates of asthma suggesting that urbanization and westernization correlate with increased asthma prevalence. Migrants who move from an area of low asthma prevalence to that of high prevalence assume increased asthma prevalence, suggesting that environmental factors play a role. Urban areas in the United States have high mortality rates associated with asthma, indicating that poverty and lack of access to medical care may also be major determinants of asthma complications.

Factors that contribute to asthma morbidity and mortality include under-treatment of acute episodes by emergency clinicians; overuse of prescribed or over-the-counter medications leading to delays in seeking treatment; failure of emergency clinicians to consider previous ED visits, hospitalizations, or life-threatening episodes of asthma; and failure to initiate corticosteroid therapy early in the course of an exacerbation. The cost of asthma care is a barrier to asthma management. African American and Hispanic adults identify costs related to seeking asthma care with a physician and the cost of asthma medications as significant impediments. Over-reliance on emergency facilities for all asthma care and lack of access or compliance with ongoing asthma care are other important factors contributing to morbidity and mortality from asthma.

Anatomy and Physiology

Asthma is a complex, immunologically mediated condition involving a variety of cellular and airway alterations. Airway inflammation and remodeling are the final common pathways that result in bronchospasm and limitation of airflow.

Asthma is a chronic respiratory disease characterized by periods of variable and recurring symptoms, airflow obstruction, and bronchial hyperresponsiveness that manifests clinically as attacks of impaired breathing. Asthma is an inflammatory disease. Repetitive episodes of acute superimposed on chronic airway inflammation are responsible for alterations in airway function and result in irreversible structural airway changes. Control of asthma symptoms ultimately depends on

ameliorating airway inflammation. Genetic, social, physiologic, and environmental factors influence the expression and control of asthma symptoms. Asthma is thus a complex interaction of the immune system, the environment, and genetic predispositions, which combine to alter airway structure and function. Successful emergency department (ED) management of asthma must address the multiple factors that result in airway dysfunction.

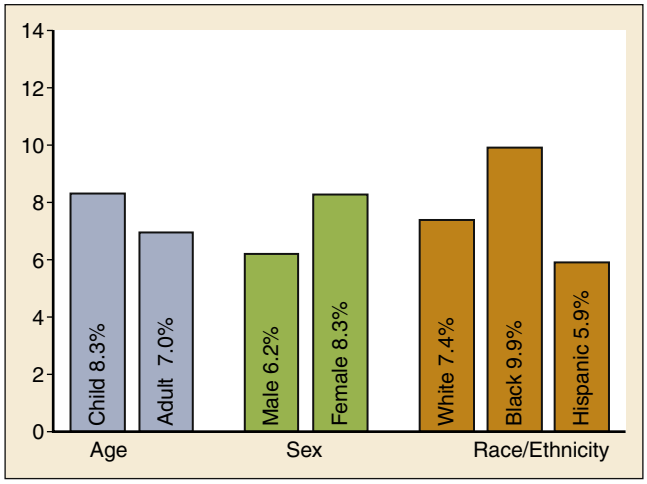

Fig. 59.1 Asthma Prevalence Percentages in 2017 by Age, Sex, and Race/Ethnicity in the United States. (From Centers for Disease Control and Prevention. Asthma: data, statistics, and surveillance. Available at: https://www.cdc.gov/asthma/data-visualizations/prevalence.htm.)

Compared with healthy individuals, patients with asthma show bronchial hyperreactivity (hyperresponsiveness) in response to various environmental and infectious stimuli (e.g., methacholine). Allergens (e.g., environmental, viruses, occupational) and non-allergic stimuli (e.g., exercise, aspirin-induced and menstrual-related asthma) induce bronchoconstriction via release of mediators and metabolites from inflammatory cells. Edema, inflammation, mucus production, and airway smooth muscle hypertrophy result in bronchoconstriction, airway obstruction, and airflow limitation. Recurrent episodes of airway inflammation result in permanent structural airway remodeling contributing to airway obstruction and hyperresponsiveness and decreases in response to therapy.

Autopsies of patients with fatal asthma reveal grossly inflated lungs that may fail to collapse on opening of the pleural cavities. Histologic examination reveals luminal plugs consisting of inflammatory cells, desquamated epithelial cells, and mucus. Marked thickening of the airway basement membrane, submucosal inflammatory cells, increased deposition of connective tissue, mucous gland hyperplasia, and hypertrophy of airway smooth muscle are also observed. Reports of slow-onset asthma fatalities reveal greater bronchial eosinophilia and basement membrane thickening when compared with rapid-onset fatal asthma. Reports of rapid-onset fatal asthma describe a greater number of degranulated mast cells and less mucus in the airway lumens, suggesting that terminal events may be dominated by bronchoconstriction without excessive luminal plugging.

Pathophysiology

Evidence that inflammation is a component of asthma physiology was initially derived from autopsy findings in patients with fatal asthma.

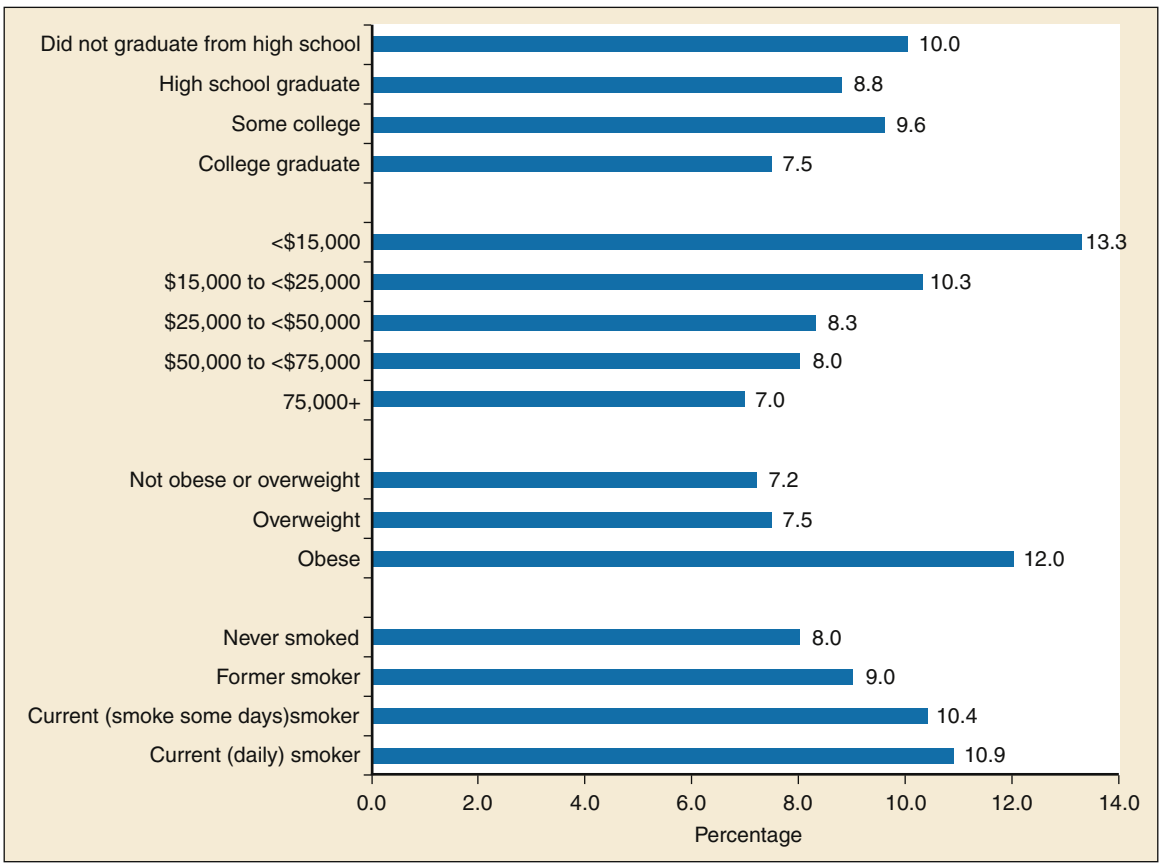

Fig. 59.2 Adult Asthma Prevalence Percent in 2017 by Education, Income, and Behavioral Risk Factors. (From Centers for Disease Control and Prevention. Asthma facts: CDC's National Asthma Control Program Grantees. Available at: https://www.cdc.gov/asthma/data-visualizations/prevalence.htm.)

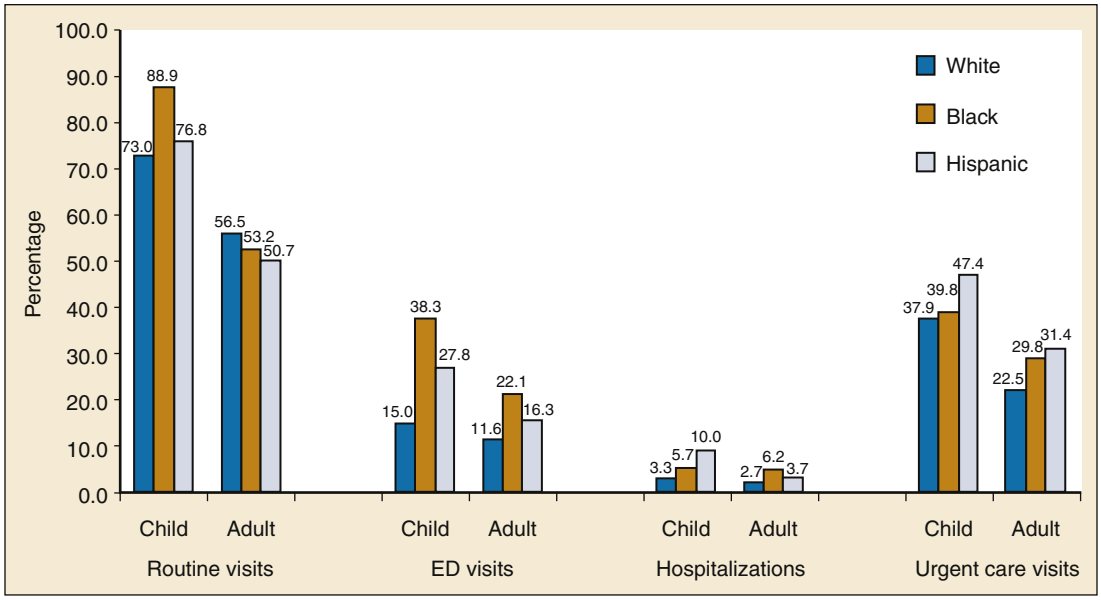

Fig. 59.3 Asthma Death Rates and Number of Deaths From 2007 to 2017. Thirty-five National Asthma Control Program (NACP) grantees. (Puerto Rico is excluded.) *Age-adjusted rate per million population. (From Centers for Disease Control and Prevention. Asthma facts: CDC's National Asthma Control Program Grantees. Available at: https://www.cdc.gov/asthma/data-visualizations/mortality-data.htm#anchor_1569599940376.)

The airways revealed infiltration by neutrophils, eosinophils, and mast cells and the presence of subbasement membrane thickening, loss of epithelial cell integrity, goblet cell hyperplasia, and mucous plugs. Bronchial biopsy findings in patients with even mild degrees of asthma also demonstrate inflammatory changes in the central and peripheral airways that correlate with disease severity. Inflammatory and chemotactic cytokines produced by both resident airway and recruited inflammatory cells are identified in bronchoalveolar lavage washings and pulmonary secretions.

Asthma has been divided into allergic and non-allergic types based on the presence or absence of immunoglobulin E (IgE) antibodies to common environmental antigens (pollen, dander, mites) and microbiologic antigens (bacteria, viruses). Exposure to microbes and allergens during childbirth, infancy, and childhood may confer a protective effect against atopy and suppress expression of the asthma phenotype later in life (known as the *hygiene hypothesis*). Regardless of the asthma type, a common feature is the presence of airway T-helper cells that release cytokines (e.g., interleukin [IL]-4, IL-5, and IL-13) that stimulate basophil, eosinophil, mast cell, and leukocyte migration to the airways and enhance IgE production. The result is amplification of the airway inflammatory response and, over time, irreversible airway remodeling. These complex cellular interactions clinically manifest as bronchospasm, mucus production, airway edema, and limitation of airflow.

Mast cells and eosinophils contain and release intracellular mediators and cytokines (histamine, prostaglandins, leukotrienes, tumor necrosis factor alpha [TNF-α]) that contribute to prolonged bronchial smooth muscle spasm, edema, and mucus production (Fig. 59.4). Airway epithelial cells are more than a passive barrier and produce pro-inflammatory mediators. Abnormal repair processes may further airway obstruction and contribute to airway remodeling.

Airway remodeling refers to the persistent structural changes in airways caused by repetitive or chronic airway inflammation. Microscopic remodeling features include epithelial thickening, subepithelial fibrosis, mucous gland metaplasia, increases in airway smooth muscle, angiogenesis, and loss of cartilage integrity. Airway remodeling occurs very early in asthma (childhood) and may precede clinical symptoms. Remodeling features are prominent in patients with severe asthma. Basement membrane thickening may be protective by preventing inflammatory cells and proteins from entering the airway submucosa through a damaged epithelium. Simultaneously, this process may be counterproductive by reducing the elasticity of the small airways. Airway remodeling induced by chronic inflammation may lead to the development of chronic irreversible airflow limitation and increased asthma mortality.

Genetics is playing an ever-increasing role in the understanding of asthma pathophysiology.[5] Heritability estimates vary between 35% and 95% for asthma and 30% and 66% for bronchial hyperresponsiveness. The first Genome Wide Association Study (GWAS) identified a novel asthma susceptibility locus on chromosome 17q21 and two large meta-analyses of asthma GWASs identified four gene loci considered robustly associated asthma susceptibility genes. Environmental influences (e.g., allergens, pollutants, tobacco, and occupational exposures) are associated with asthma, and the interaction of genetic variability and environmental factors may allow prediction of future disease risk, expression, and severity and response to therapies.[6]

CLINICAL FEATURES

Signs and Symptoms

Most patients with acute asthma have a constellation of symptoms, including cough, dyspnea, and wheezing. Slow-onset asthma with progressive deterioration over at least 6 hours (usually days) occurs in over 80% of cases. This type has a female predominance, is triggered by upper respiratory tract infections, and has an airflow inflammation mechanism that results in a slower response to treatment. Sudden-onset asthma with rapid deterioration in less than 6 hours occurs in less than 20% of cases. This type has a male predominance, is triggered by respiratory allergens, exercise, and psychosocial stress, and has a bronchospastic cause resulting in more severe airway obstruction with a faster response to therapy.

On initial history, questions should include possible triggers, onset of symptoms, and severity of symptoms, especially as compared with

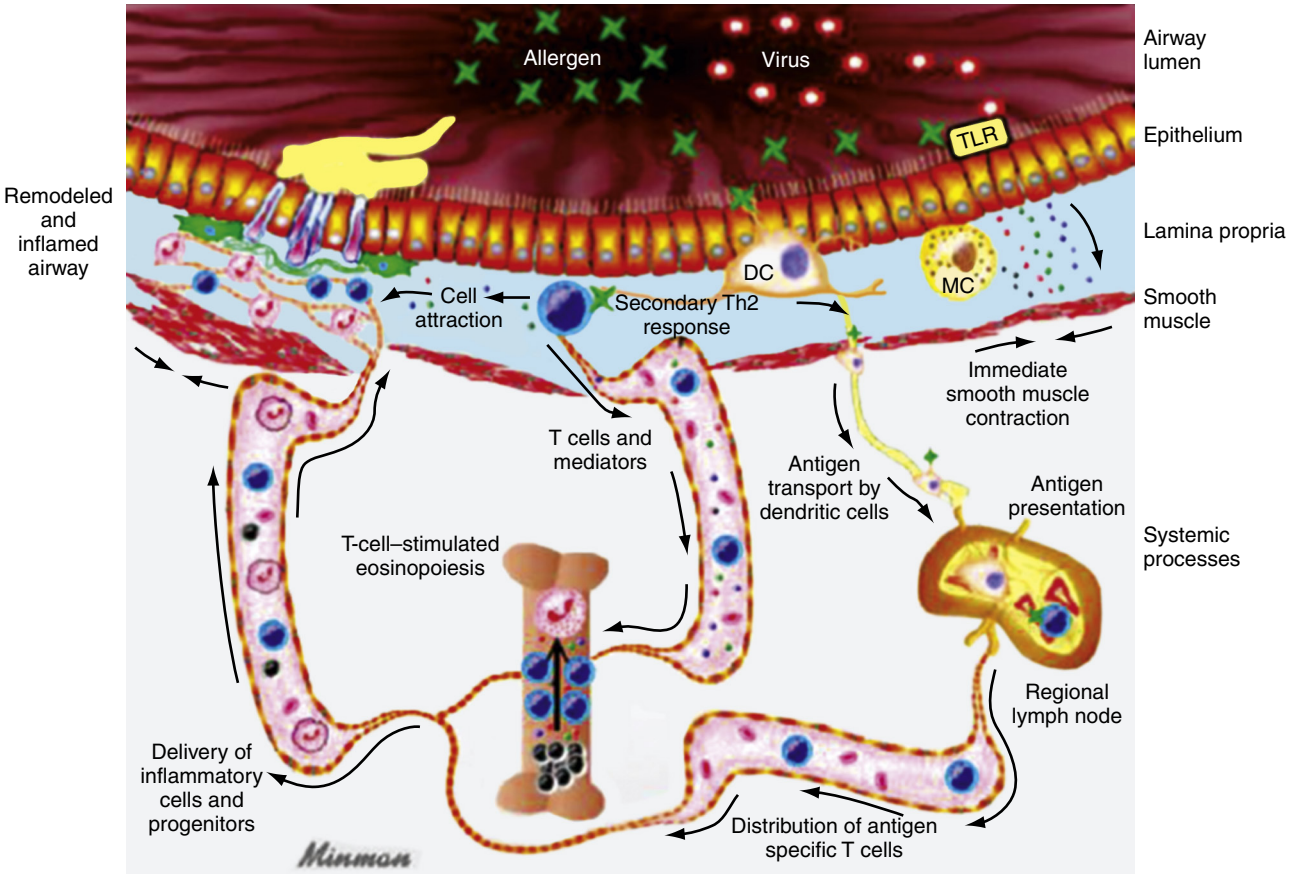

Fig. 59.4 The Physiologic Mechanism of Asthma. *DC,* Dendritic cell; *MC,* mast cell; *Th2,* T-helper 2; *TLR,* toll-like receptor. (From Murphy DM, O'Byrne PM. Recent advances in the pathophysiology of asthma. *Chest.* 2010;137:1417.)

previous exacerbations. Comorbidities should be identified, especially those that may be worsened by systemic corticosteroids such as diabetes, peptic ulcer disease, hypertension, and psychosis.[7] All current asthma medications should be noted, including times and amounts recently used, and any potential asthma aggravators, such as aspirin or nonsteroidal antiinflammatory drugs (NSAIDs), beta-blockers (including topical agents used for glaucoma), and angiotensin-converting enzyme inhibitors. Cardioselective and nonselective beta-blocker use increases hospitalizations and ED visits. There are inter-individual differences in the dyspnea perceived by asthmatic patients for the same level of airway narrowing. Patients with a blunted perception of dyspnea ("poor perceivers") have more ED visits, hospitalizations, and near-fatal and fatal asthma attacks.

Patients with mild or moderate acute asthma usually speak in sentences or phrases and may have a normal or slightly elevated pulse and respiratory rates. They also will usually have a normal oxygen saturation. Patients with severe acute asthma typically speak only one to two words at a time, may be agitated or restless and hunched forward, may be tachypneic or tachycardic, and may be hypoxic. Patients with altered level of consciousness such as confusion or drowsiness, silent chest on exam, poor respiratory effort or elevated paCO2 have life-threatening or near-fatal asthma.[7,8]

Wheezing does not define the presence, severity, or duration of asthma. It correlates poorly with the degree of functional derangement and may be absent when maximal effort produces minimal airflow. Physical examination may help to identify such complications of asthma as pneumonia, pneumothorax, or pneumomediastinum.

BOX 59.1 Risk Factors for Death From Asthma

Asthma History

A history of near-fatal asthma requiring intubation and mechanical ventilation
Hospitalization or ED visit for asthma in the past year
Currently using of having recently stopped using oral corticosteroids (a marker of event severity)
Not currently using inhaled corticosteroids
Over-use of SABAs, especially use of more than one cannister monthly
Poor adherence with asthma medications and/or poor adherence with (or lack of) a written asthma action plan

Other Factors

Psychosocial problems
Psychiatric disease
Food allergy in a patient with asthma

Risk Factors

Asthma exacerbations are more common in females. Additionally, specific risk factors for exacerbations include a history of one or more exacerbations in the past year, poor adherence to a plan or uncontrolled symptoms, incorrect inhaler use, chronic sinusitis, or smoking. Ethnicity and socioeconomic status are also predictors of exacerbations with African Americans having higher rates of ED visits and hospitalizations than Caucasians or Hispanics.[2] Risk factors for death from asthma are also important to determine and are listed in Box 59.1.[7,8]

Specific Contexts

The following conditions are particularly challenging due to their overlap and contribution to asthma.

Cough Variant

Chronic cough may be the sole manifestation of the disease in cough-variant asthma. It is associated with airway hyperresponsiveness and may be present more often at night. Other conditions of chronic cough to consider would be angiotensin converting enzyme (ACE) inhibitors, gastroesophageal reflux disease (GERD), chronic sinusitis, postnasal drip, and inducible laryngeal obstruction.

Cigarette Smokers

One-third of patients who come to the ED with acute asthma are current cigarette smokers, and these patients have poorer asthma control and greater acute care needs than lifelong nonsmokers or former smokers. They may also have chronic obstructive pulmonary disease (COPD) which makes diagnosis and treatment more challenging. Ambiguity between COPD and asthma should prompt referral due to the worse outcomes of patients with asthma and COPD overlap.[8]

Athletes

Exercise-induced bronchoconstriction has been recognized since the first modern Olympic Games. The key stimulus is felt to be airway dehydration resulting from increased ventilation, increasing the osmolarity of the airway lining fluid. The increased osmolarity may trigger release of mediators (histamine, leukotrienes, prostaglandins) from airway inflammatory cells, resulting in smooth muscle contraction and airway edema.[9]

Prophylaxis for exercise-induced asthma includes environmental measures (face mask or nasal breathing to allow warming and humidification of cool dry air, pre-exercise warm-up, and avoidance of known allergens) and medications. Inhaled glucocorticoids are strongly recommended, and a short-acting inhaled beta-2 agonist used 5 to 10 minutes before exercise is effective in preventing exercise induced bronchoconstriction.[9] Long-acting beta agonists (LABAs) in combination with inhaled glucocorticoids are useful when low doses of inhaled glucocorticoids are ineffective. Pretreatment with cromolyn, leukotriene antagonists (montelukast), or an inhaled parasympatholytic (ipratropium) is also effective.

Perimenstrual Asthma

Perimenstrual asthma affects up to 40% of asthmatic women yet receives little emphasis in asthma treatment guidelines. The ratio of female-to-male asthma prevalence increases dramatically after puberty, and health care for asthma increases in the perimenstrual phase.

Elderly

Asthma can appear at any age, including the ninth decade, wheezing and dyspnea may be mis-ascribed by patients and physicians to heart failure, bronchitis, COPD, occupational lung disease, or poor exercise capacity. Older asthmatic patients (>55 years old) have higher morbidity and mortality.

Obesity

Due to respiratory symptoms associated with obesity overlapping with asthma, there may be misdiagnosis or underdiagnosis. Objective testing is important to diagnose asthma in this patient population accurately. Overweight (body mass index [BMI] of 25 kg/m^2 or more) asthmatics have poorer asthma control, higher admission rates, and a greater risk of complications, possibly secondary to a difference in the perception of dyspnea or response to asthma controller agents. However, obesity does not adversely influence the severity or the resolution of an acute exacerbation.

Aspirin-Exacerbated Respiratory Disease

Aspirin-exacerbated respiratory disease (AERD) was first described more than 100 years ago. Clinically, AERD includes the tetrad of nasal polyps, eosinophilic sinusitis, asthma, and sensitivity to cyclooxygenase (COX)-1 inhibitor drugs (e.g., aspirin). A detailed mechanism is shown in Fig. 59.5. NSAIDs also precipitate AERD. AERD is a common precipitant of life-threatening asthma; one survey notes that 25% of asthmatics who require mechanical ventilation have AERD. Patients with AERD should avoid aspirin and NSAIDs. ICS are the primary therapy in AERD. Oral corticosteroids may be needed, and leukotriene antagonists may be useful. Desensitization with aspirin can significantly improve symptoms. There is little evidence to justify managing patients with AERD differently than other patients with acute asthma except for avoidance of aspirin and NSAIDs.

DIFFERENTIAL DIAGNOSES

See Box 59.2.

Diagnostic Testing

Peak Expiratory Flow

The severity of airflow obstruction cannot be accurately assessed from symptoms and physical examination alone. Because physicians initially tend to underestimate the degree of airway obstruction in acute asthma, routine measurement of the peak expiratory flow (PEF) in liters per second should be part of ED assessment and monitoring. Any patient not able to perform peak flow measurement should be considered to have severe airway obstruction.

The same device should be used to assess an individual patient, and different portable meters should not be used interchangeably. PEF assessed as a percentage of previous personal best is the most useful measurement. PEF as a percentage of predicted values (available online) gives a reasonable estimate if personal best values are unknown. PEF < 50% is often used to categorize an acute severe asthma exacerbation, and less than 33% may signify life-threatening or near-fatal asthma.[7]

Pulse Oximetry

Oxygen saturation (SpO_2) should be measured using pulse oximetry to determine the efficacy of oxygen supplementation, especially in children that cannot perform PEF. SpO_2 should be maintained between 94% and 98%. If SpO_2 falls below 90%, it may signal the need for more aggressive therapy.[7]

Capnography

Capnography is an alternative technique to monitor for hypercapnia and respiratory failure and is effective in asthma. Capnographic waveform analysis can indicate improvements in airway diameter in acute asthma and has the advantage of being effort independent and providing continuous monitoring.

Blood Gas

Initially, in acute asthma exacerbations, stimulated hyperventilation leads to a fall in the partial pressure of carbon dioxide in arterial blood ($PaCO_2$). As airway obstruction increases, patients develop hypoventilation. With hypoventilation, the $PaCO_2$ normalizes and then increases with resulting hypercapnia and respiratory acidosis. Routine arterial blood gas (ABG) analysis is not indicated in acute asthma exacerbations. An ABG should be considered to identify hypercapnia if the SpO2 is <92% or the PEF is <50% of personal best or predicted value.

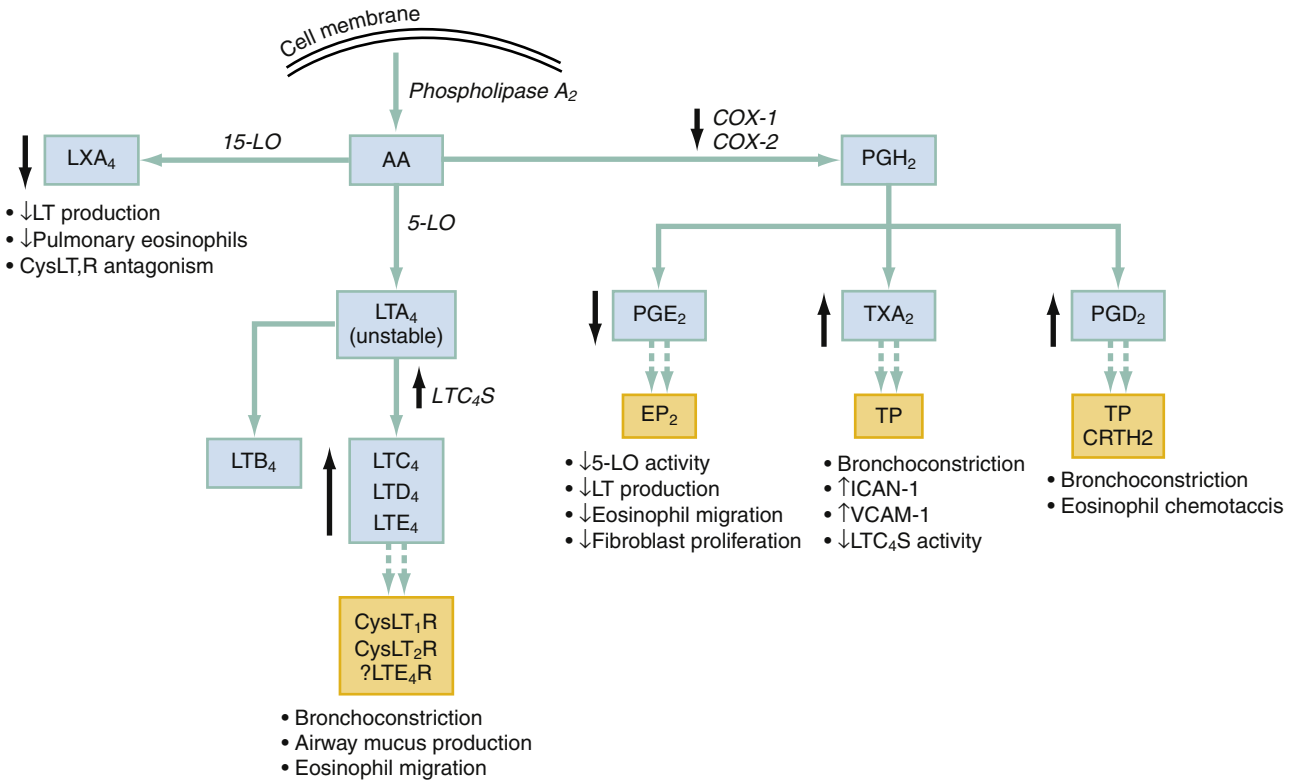

Fig. 59.5 Mechanism of aspirin-exacerbated respiratory disease (AERD). Inhibition of the enzyme cyclooxygenase *(COX)* decreases production of prostaglandin E_2 *(PGE_2).* PGE_2's inhibitory effect on 5-lipoxygenase *(5-LO)* is diminished resulting in increased production of leukotrienes (*LTC_4, LTD_4,* and *LTE_4)* causing bronchoconstriction, mucus production, and airway eosinophil migration. *5-LO,* 5 Lipoxygenase; *15-LO,* 15 lipoxygenase; *AA,* arachidonic acid; *COX-1,* cyclooxygenase 1; *COX-2,* cyclooxygenase 2; *CRTH2,* chemokine receptor-homologous Th2 lymphocytes; *$CysLT_1R$,* cysteinyl leukotriene T1R; *$CysLT_2R$,* cysteinyl leukotriene T2R; *EP_2,* E prostanoid 2 receptor; *LTA_4,* leukotriene A4; *LTB_4,* leukotriene B4; *LTC_4S,* leukotriene C4 synthetase; *LTC_4,* leukotriene C4; *LTD_4,* leukotriene D4; *LTE_4,* leukotriene E4; *LTE_4R,* leukotriene E4R; LXA_4, lipoxin A4; *PGD_2,* prostaglandin D2; *PGE_2,* prostaglandin E2; *PGH_2,* prostaglandin H2; *TP,* T prostanoid receptor; *TXA_2,* thromboxane A2. (From Laidlaw TM, Boyce JA. Pathogenesis of aspirin-exacerbated respiratory disease and reactions. *Immunol Allergy Clin North Am.* 2013;33[2]:195.)

BOX 59.2 The Differential Diagnosis of Asthma

- Cardiac conditions
  - Valvular heart disease
  - Congestive heart failure
- COPD exacerbation
- Pulmonary infection
  - Pneumonia
  - Allergic bronchopulmonary aspergillosis
  - Löffler syndrome
  - Chronic eosinophilic pneumonia
- Upper airway obstruction
  - Laryngeal edema
  - Laryngeal neoplasm
  - Foreign body
  - Vocal cord dysfunction
- Endobronchial disease
  - Neoplasm
  - Foreign body
  - Bronchial stenosis
- Pulmonary embolus
- Cystic fibrosis
- Carcinoid tumor
- Allergic/anaphylactic reaction
- Adverse drug reaction (ACE inhibitors)
- Miscellaneous conditions
  - Churg-Strauss syndrome
  - GERD
  - Hyperventilation with panic attack
  - Noncardiogenic pulmonary edema
  - Addison's disease
  - Invasive worm infection

ACE, Angiotensin-converting enzyme; *COPD,* chronic obstructive pulmonary disease; *GERD,* gastroesophageal reflux disease.

This will help identify possible respiratory acidosis and the need for airway management and ventilatory support. A venous blood gas (VBG) may also be considered as a screening tool for hypercapnia. A $PaCO_2$ on a VBG of less than 40 mm Hg likely excludes hypercapnia, however for an accurate measurement, one should obtain an ABG.[10]

Other Blood Testing

Leukocytosis is common with acute asthma exacerbation and does not necessarily indicate an acute superimposed pulmonary infection. Corticosteroids and catecholamines demarginate polymorphonuclear leukocytes after 1 to 2 hours, and patients on chronic steroid therapy may have normal or significantly elevated white blood cell counts.

Serum electrolytes are not altered unless the patient takes corticosteroids or diuretics or has cardiovascular disease and is receiving beta-2 agonist therapy. Frequent albuterol treatments can cause transient hypokalemia, hypomagnesemia, and hypophosphatemia, but this is rarely of clinical significance. The rare asthmatic on chronic theophylline therapy should have a level measured for possible toxicity. In the older asthmatic with cardiovascular comorbidities, measurement of the B-type natriuretic peptide (BNP) level may reveal unrecognized congestive heart failure. Hyperlactatemia is common in acute asthma and is thought to be secondary to albuterol therapy or the increased work of breathing. It is not associated with worse pulmonary function tests,

more hospitalizations, or relapse at one week. Overall, routine testing of the blood in an acute asthma exacerbation is not recommended.

Radiology

A chest radiograph (CXR) is of little value in most acute asthma exacerbations and should be restricted to patients with a suspected complicating cardiopulmonary process, such as pneumonia, pneumothorax, pneumomediastinum, subcutaneous emphysema, or congestive heart failure. Patients who do not respond to optimal therapy and require hospital admission have a higher likelihood of radiographically identifiable, unsuspected, clinically significant pulmonary complications of asthma.

Point of Care Ultrasound

The finding of an ultrasound comet-tail sign has high diagnostic accuracy in differentiating acute heart failure from COPD/asthma-related causes of acute dyspnea.

Electrocardiogram

The electrocardiogram (ECG) is selectively helpful in assessing patients with chest pain or a history of significant cardiovascular disease, in whom the asthma attack may be a physiologic stress test. In patients with severe asthma, the ECG may show a right ventricular strain pattern that reverses with improvement in airflow. All patients with severe hypoxemia should also receive cardiac monitoring.

In summary, the severity of airflow obstruction cannot be accurately judged by patients' symptoms, physical examination findings, and laboratory test results. Serial measurements of airflow obstruction with PEF is key for disease assessment and response to therapy (Table 59.1).

MANAGEMENT

Subacute lack of asthma control, defined as more than four outpatient visits or more than five short-acting beta-2 agonist prescriptions per year, is associated with an increased risk of acute asthma exacerbation. The ability to gauge the severity of an attack and present to the ED promptly is important, because patients who wait longer have worse asthma on presentation, more functional limitations, and are more likely to be admitted. Emergency medical services providers should provide albuterol inhalation therapy by protocol, and basic emergency medical technicians can be authorized to administer the patient's own inhaler. Further studies are needed to determine whether paramedics should be trained to administer continuous positive airway pressure ventilation in asthmatics with severe respiratory failure to decrease tracheal intubation and mortality rates.

The rapidity of the reversal of the acute airflow obstruction is directly predictive of the outcome. Effective bronchodilation often results in a decreased need for hospitalization with significant cost savings. As outlined in Tables 59.2 and 59.3, the severity of an attack as measured by peak flow measurement determines the aggressiveness of the therapy.

TABLE 59.1 Objective Findings in Asthma Assessment

Factor	Severe Asthma
Pulse rate (beats/min)	≥120
Respiratory rate (breaths/min)	≥30
Use of accessory muscles of respiration	If present, may indicate severe asthma; if absent, may have equally severe asthma in 50% of cases
ABG analysis (mm Hg)	Pa_{O_2} ≤ 60 or Pa_{CO_2} ≥ 42 indicates severe asthma; all other values difficult to interpret unless PEF known
Pulmonary function studies	PEF measures the degree of airflow obstruction; most useful in assessing severity and guiding treatment decisions

ABG, Arterial blood gas; Pa_{CO_2}, partial pressure of carbon dioxide in arterial blood; Pa_{O_2}, partial pressure of oxygen in arterial blood; *PEF,* peak expiratory flow rate.

Oxygen Administration

All patients should receive supplemental oxygen titrated to maintain arterial oxygen saturation between 94% and 98%, as titrated oxygen is associated with better physiologic outcomes than empiric high flow 100% oxygen therapy.[7]

Adrenergic Medications

Inhaled Beta2 Agonists

Inhaled short-acting beta-2 agonist (SABA) such as albuterol should be used in patients that present with acute asthma exacerbations. For patients with mild to moderate asthma, albuterol can be administered with a pressurized metered-dose inhaler (pMDI) with a spacer and is

TABLE 59.2 Initial Severity Assessments and Therapies in the Emergency Department

	Mild to Moderate	Severe
PEF (percentage predicted/personal best)	≥40%	Unable or <40%
Oxygen therapy	Maintain Sa_{O_2} ≥90%	Maintain Sa_{O_2} ≥90%
Nebulized Albuterol Solution		
Albuterol	2.5 mg every 20 min for up to three doses	5.0 mg every 20 min for three doses Continuous for 1 h if severe
Albuterol Metered-Dose Inhaler With Spacer		
Albuterol (90 µg/puff)	6–12 puffs every 20 min for up to three doses with supervision	Same for three doses (if able to do) with supervision
Ipratropium Therapy		
Nebulized solution	0.5 mg every 20 min for three doses (may mix with albuterol solution)	0.5 mg every 20 min for three doses (may mix with albuterol solution)
MDI (18 µg/puff) with spacer	8 puffs every 20 min for three doses	8 puffs every 20 min for three doses
Systemic Corticosteroids		
Oral (preferred)	40–50 mg of prednisone or prednisolone per day if no immediate response to albuterol	40 to 50 mg of prednisone or prednisolone per day
IV (unable to take orally or absorb)	125 mg of methylprednisolone per day	125 mg of methylprednisolone per day
IV magnesium sulfate	Not indicated	2 g over 20 min (or at rates of up to 1 g/min) if PEF ≤ 25% predicted

IV, Intravenous; *MDI,* metered-dose inhaler; *PEF,* peak expiratory flow rate; Sa_{O_2}, oxygen saturation in arterial blood.

TABLE 59.3 Response After 1 Hour of Initial Treatment

	Moderate Exacerbation	Severe Exacerbation
PEF (percentage predicted)	40%–69%	<40%
Oxygen therapy	Maintain Sa_{O_2} ≥90%	Maintain Sa_{O_2} ≥90%
Albuterol Therapy		
Racemic albuterol	Every 1–3 h, admit decision in <4 h	Every 1 h or continuous
Ipratropium therapy	Every 1 h or continuous	Every 1 h or continuous
Corticosteroids	Every 6–8 h	Every 6–8 h

PEF, Peak expiratory flow rate; *Sa_{O_2},* oxygen saturation in arterial blood.

more efficient and cost-effective than nebulization. However, for severe or near-fatal asthma, nebulization of beta-agonist is recommended over pMDI to allow for continuous administration, although there is a paucity of data to guide this recommendation. (see Table 59.2).

Long-Acting Beta-2 Agonists

Inhaled long-acting beta-2 agonists are medications used as the initial additional therapy to manage symptoms not adequately controlled by ICS alone. Salmeterol is a LABA with an onset of action of 20 minutes and thus is not a rescue medication. Formoterol is also a LABA that has an onset of action within minutes (similar to albuterol) and maximal effect within 2 hours. There is no difference in the efficacy of combination LABA/ICS inhalers compared to both medications in separate inhalers with good adherence. Regular use of LABAs without concomitant use of ICSs results in greater hospitalizations and asthma-related deaths, resulting in a black box warning on the package insert. There is no role for the use of LABA without the concomitant use of ICS.[7] In practice, combination inhalers are preferred to ensure LABAs and ICS are taken together. Due to the rapid onset of the medication, combination formoterol and ICS inhalers may be used as both controller and rescue medications. However, the role of these medications in the ED is limited amidst other readily available options.

Intravenous Beta2 Agonists

There is no evidence to support the routine use of intravenous beta-2 agonists.[8] There may be a limited role in ventilated patients or those in extremis, however, there is little evidence to support this.[7]

Subcutaneous Beta2 Agents

Terbutaline is a beta-2 adrenergic receptor agonist, administered subcutaneously. While terbutaline was previously used regularly for severe asthma, no evidence supports the use of subcutaneous adrenergic agents over aerosol delivery. It may be considered in patients who cannot adequately inhale albuterol or with severe bronchospasm unresponsive to other treatments.

Epinephrine

Epinephrine 0.3 mg given intramuscularly in addition to standard asthma therapy is recommended for patients with anaphylaxis or angioedema.

Corticosteroids

Steroids are an important part of acute and chronic asthma management. They reduce mortality, relapses, subsequent hospitalization, and the requirement for beta-2 agonist therapy.[7] They should be given as early as possible in an acute asthma exacerbation. There is no benefit to adding ICS to systemic steroids.

Systemic Corticosteroids

Corticosteroids are indicated for all patients with an acute asthma exacerbation. Early systemic corticosteroids are particularly important for patients who fail to achieve lasting improvement with the initial administration of SABA, were taking OCS when they developed the exacerbation, or have required OCS with past exacerbations.[8] Steroid effects begin within hours in acute asthma and peak at about 24 hours.

As studies have demonstrated that oral corticosteroids are equivalent to IV therapy, oral steroids are preferred unless the patient is very ill, is unable to swallow or is vomiting, or is thought to have impaired gastrointestinal transit or absorption. The recommended initial oral dose is usually 50 mg of prednisone.[7,8] If IV methylprednisolone is used, the dose is 125 mg/day in one or two divided doses until the switch to oral therapy or until PEF reaches 70% of predicted or personal best. Oral dexamethasone can alternatively be prescribed at a dose of 16 mg per day for 2 days.[11] Side effects of short-term (hours or days) steroid use include reversible increases in serum glucose (important in diabetics) and decreases in potassium, fluid retention with weight gain, mood alterations including psychosis, hypertension, peptic ulcers, aseptic necrosis of the femur, and rare allergic reactions.

Inhaled Corticosteroids

Use of high-dose ICS within 1 hour of arrival for acute asthma without systemic steroids reduces the need for hospitalization.[8] However, there is conflicting evidence regarding the role of ICS in addition to OCS in the setting of an acute exacerbation, and there is no known benefit to using ICS instead of OCS. ICS have an additional cost and no established dose and duration of treatment for patients in the ED. Therefore, we do not recommend routinely adding ICS to systemic steroids for the ED treatment of acute asthma exacerbations.

Corticosteroids and Discharged Patients

Discharged patients who receive systemic corticosteroids should continue oral out-patient therapy to control disease and prevent relapse. Any need for additional steroids should be determined at follow-up. An acceptable regimen is 40 to 50 mg of prednisone (or equivalent) in single daily dose for 5 to 7 days. Dose tapering to prevent asthma rebound or adrenal suppression is unnecessary unless the patient was already receiving systemic steroids or a prolonged course of therapy of more than 2 weeks is necessary. An alternative approach, if compliance or inability to obtain oral corticosteroids is an issue, is to give a single intramuscular dose of dexamethasone 10 mg, triamcinolone diacetate 40 mg, or methylprednisolone 160 mg before discharge.[12]

Patients with acute exacerbations of asthma may be on insufficient chronic controller medications. If the patient is not taking oral corticosteroids or ICS, the addition of ICS to the patient's regular asthma medications on discharge as a controller medication significantly reduces the risk of asthma-related death or hospitalization.[8] Patients with a moderate or severe exacerbation not taking any ICS should be given a prescription for an ICS containing medication. Patients already on ICS therapy should continue this home medication in addition to the prescribed short course of oral steroids.

Anticholinergic Medications

Anticholinergic drugs available for inhalation therapy are bronchodilators that override the smooth muscle constrictor and secretory effects of the parasympathetic nervous system, blocking reflex bronchoconstriction and reversing acute airway obstruction. Ipratropium bromide,

a quaternary derivative of atropine, is the preferred anticholinergic agent for acute asthma exacerbations. The maximum effect with inhaled ipratropium is 30 to 120 minutes after administration, lasting up to 6 hours. Its bronchodilatory potency is lower and onset of action slower than those of the beta-2 agonists and should not be used alone for acute attacks. For patients with moderate to severe exacerbations, emergency department treatment with a SABA and ipratropium was associated with fewer hospitalizations and greater improvement in PEF compared with SABA alone.[13] Treatment recommendations (see Table 59.2) include adding ipratropium (0.5 mg) with the first three albuterol treatments in severe acute asthma (PEF < 40% predicted). The equivalent MDI dose is approximately eight puffs (18 μg/puff) every 20 minutes for three doses.

Inhaled tiotropium bromide is a long-acting (>24 hours) anticholinergic agent. There is inconclusive evidence about the benefit of adding tiotropium for patients not responding to ICS plus LABA therapy as an outpatient. It is also unclear if there is any benefit to adding tiotropium to ICS compared to increasing the dose of ICS. There is no clear role for use of tiotropium for patients presenting to the emergency department with acute asthma exacerbations.[7]

Magnesium

Magnesium relaxes bronchial smooth muscle and dilates asthmatic airways in vitro. Mechanisms include calcium channel-blocking properties, inhibition of cholinergic neuromuscular transmission, stabilization of mast cells and T-lymphocytes, and stimulation of nitric oxide and prostacyclin. Intracellular magnesium levels are lower in acute asthma, and the level correlates with airway reactivity in chronic disease.

For adults with severe asthma attacks (PEF < 25%, predicted), adults and children with persistent hypoxia after initial treatment, and children with PEF < 60% after 1 hour of care, the addition of magnesium decreases the need for hospital admission.[14] The optimal dose and rates of infusion are unclear, but it is reasonable to administer 2 g of IV magnesium sulfate over 20 minutes to adult patients with severe refractory asthma while continuing aggressive inhalation therapy. For pediatric patients, a dose of 40 mg/kg/day (max of 2 g) of IV magnesium sulfate is recommended. Studies that excluded patients with severe asthma showed no benefit with use of IV or nebulized magnesium. Side effects of magnesium infusion are dose-related and include warmth, flushing, sweating, nausea and emesis, muscle weakness, loss of deep tendon reflexes, hypotension, and respiratory depression.

Methylxanthines

Theophylline is the main oral methylxanthine used to treat asthma, and a small subset of ambulatory patients may benefit from its chronic administration. IV methylxanthines are not recommended for acute disease as there is no demonstrated efficacy and increased adverse events.[8] However, there may be a limited role in patients with near-fatal asthma with a poor response to initial therapy.[7]

Leukotriene Modifiers

The cysteinyl leukotrienes (LTC_4, LTD_4, and LTE_4) are highly potent mediators of inflammation that play a large role in the pathogenesis of asthma. Leukotriene receptor antagonists (LTRAs) are used as controller medications. There is limited data regarding their efficacy in acute asthma management. Current recommendations do not support their use in the treatment of acute asthma in the emergency department.

Antibiotics

Bacterial, chlamydial, and mycoplasmal respiratory tract infections infrequently contribute to acute asthma. Antibiotics should generally be reserved for patients with clear objective evidence of infection. There may be a future role for procalcitonin to guide antibiotic use, but more studies are needed.[15]

Sedatives

Sedatives are contraindicated in acute disease because of their respiratory depression.

Ketamine

Ketamine is an IV dissociative anesthetic with potent bronchodilator effects. Studies suggest possible benefit when used in acute asthma, but no statistically significant findings have been reported. Further prospective work is needed. At present, ketamine is not recommended for acute asthma in the non-intubated patient.[7]

Heliox

Helium is an inert gas with one-eighth the density of nitrogen. When 60% to 80% helium is blended with 20% to 40% oxygen, the resulting gas mixture (heliox) has a threefold reduction in density compared with air. Heliox reduces the resistance associated with gas flow through airways with non-laminar flow and reduces respiratory muscle work; it also increases the diffusion of carbon dioxide and may improve alveolar ventilation. Heliox may decrease the work of breathing long enough to stop intubation by carrying bronchodilators to the distal airways and allowing anti-inflammatory agents time to achieve their effects. When heliox was compared to oxygen to drive nebulized delivery of beta-agonist therapies, an increase in PEF and a lower rate of hospitalization were observed. Patients with severe asthma receiving heliox nebulization of beta-2 agonists have more significant increases in PEF compared to those with mild to moderate asthma. Heliox has not been demonstrated to decrease the need for intubation in severe and resistant asthma, however. It is administered by nonrebreather mask and can also be used with mechanical ventilation. Emergency clinicians can consider heliox in cases of severe airflow obstruction (PEF < 30% predicted and a rapid onset of symptoms within 24 hours), a history of labile asthma or previous intubation, and inability to be adequately mechanically ventilated.

High-Flow Nasal Canula

Oxygen delivered via high-flow nasal canula (HFNC) can be used with hypoxemic patients. HFNC, with flow rates up to 60 L/min of warmed and humidified oxygen, provides high concentrations of oxygen, decreases respiratory work and may provide continuous positive airway pressure. The role in asthmatic adults is unknown, however, small studies have shown it reduces respiratory distress in children.[16] Further studies are warranted to determine overall efficacy.

Noninvasive Ventilation

Noninvasive ventilation (NIV) may benefit carefully selected patients with severe and resistant asthma. Continuous positive airway pressure improves oxygenation and reduces respiratory muscle fatigue by increasing functional residual capacity and lung compliance and supplying some of the inflating pressure required during inspiration. Biphasic positive airway pressure (BiPAP) provides continuous positive airway pressure but delivers higher pressure during inspiration than expiration. BiPAP allows speech and reduces the need for sedation as compared to intubation. Nebulized bronchodilators can be delivered through the BiPAP circuitry. BiPAP is well tolerated by children with status asthmaticus and may decrease the need for intubation and mechanical ventilation.[17] BiPAP may decrease the need for hospitalization, intubation, and ICU and hospital length of stay in adults with status asthmaticus.[18] There is limited evidence to routinely recommend NIV in patients with respiratory failure from severe asthma exacerbations.

NIV is not a substitute for endotracheal intubation and mechanical ventilation. A trial of NIV before intubation and mechanical ventilation can be considered in select patients by providers familiar with the use of NIV. Patients should have an alert mental status, intact airway reflexes, and ICU admission is mandatory. Intermittent ABG

monitoring to assess for worsening hypercapnia or respiratory acidosis during NIV identifies nonresponders that may need intubation.

Mechanical Ventilation

Endotracheal intubation and mechanical ventilation are required in 2% of all asthma exacerbations and 10% to 30% of those requiring ICU admission. Indications for intubation include coma, altered consciousness, cardiac or respiratory arrest, paradoxical breathing pattern, refractory hypoxemia, and failure of NIV. Some authors recommend threshold levels for intubation based on ABG results, but there is no evidence that ABG results provide better guidance regarding the need for intubation than overall clinical assessment.

Orotracheal rapid sequence intubation (RSI) with induction agents and muscle paralysis is preferred. A large endotracheal tube (≥8.0 mm for adults) facilitates airway suctioning, mucous plug removal, and bronchoscopy if needed later in the course. Ketamine (1 to 2 mg/kg) is the preferred agent for induction in RSI of the asthmatic patient because of its bronchodilatory and sympathetic stimulatory properties. Alternatively, propofol (1.5 to 2 mg/kg) offers rapid-onset deep sedation and possesses bronchodilatory properties, but its vasodilatory effects may cause hypotension, especially in the volume-depleted asthmatic. Succinylcholine (1.5 mg/kg) or a competitive neuromuscular blocking agent, such as rocuronium (1 mg/kg), can be used for intubation. Continued deep sedation with propofol, a long-acting benzodiazepine (e.g., lorazepam) or an opioid that does not release histamine (e.g., fentanyl) usually avoids the need for muscle paralysis. When bagging the patient after intubation, care must be taken to avoid hyperventilation.

A ventilator strategy providing adequate oxygenation and ventilation while minimizing hyperinflation, high airway pressure, barotrauma, and systemic hypotension must be instituted. Decreasing hyperinflation is the priority, rather than correcting hypercarbia and respiratory acidosis. Permissive hypercapnia is an appropriate technique. Low tidal volumes (6 to 8 mL/kg) keep airway pressures lower, thus reducing the risk of intrinsic positive end-expiratory pressure ("auto-PEEP"), stacking of ventilations, and barotrauma. Low ventilation rates (below 10 breaths/min) and high inspiratory flow rates (above 60 L/min) provide prolonged time for expiration. Oxygenation is maintained by titrating the fraction of inspired oxygen (Fio_2) as needed to maintain Spo_2 > 92%. Therapies such as IV hydration, inline beta-2 agonists and anticholinergics, IV corticosteroids, and magnesium to decrease airway pressure and airway obstruction are delivered simultaneously.

Continuous capnography is advisable. Moderate levels of hypercapnia are well tolerated and have few deleterious effects. Elevated carbon dioxide levels have vasodilatory effects on cerebral vessels. Cerebral blood flow reaches its maximum at a $Paco_2$ level of 120 mm Hg, which may increase intracranial pressure. Although there is no consensus on what constitutes a safe level of hypercapnia, $Paco_2$ levels above 100 mm Hg should be avoided.

Complications of mechanical ventilation in the asthmatic patient include hypoxemia, hypotension, nosocomial infections, and barotrauma. Hypotension is almost uniformly secondary to increased intrathoracic pressure with a subsequent decrease in venous return and cardiac output. Slowing the rate of mechanical ventilation or removing the patient from the ventilator for a short time (20 to 30 seconds) allows more time for expiration, thereby decreasing intrathoracic pressure. Volume depletion and medication effects (e.g., narcotic sedative agents) are other potential explanations for hypotension. Pneumothorax should be considered whenever sudden deterioration occurs or when hypotension is accompanied by a significant rise in peak inspiratory pressures on the ventilator. Although complications may occur, the use of mechanical ventilation in critically ill asthmatics is associated with low morbidity and mortality.

Extracorporeal Membrane Oxygenation

Extracorporeal membrane oxygenation (ECMO) is an invasive therapy that uses an artificial membrane to oxygenate and remove carbon dioxide. ECMO allows for gas exchange while using lung-protective ventilation strategies. Currently, there are no studies showing a clear indication for the use of ECMO in the asthmatic patient, however, registry data and case reports suggest a role in treating near fatal asthma in ventilated patients. If available, ECMO may be considered in asthmatic patients that are refractory to conventional ventilator management.[7]

Other and Future Therapies

In patients without dehydration or hypovolemia, the administration of fluids does not clear airway secretions. Mucolytics may worsen cough or airflow obstruction, and chest physical therapy is not beneficial. Infused enoximone (a phosphodiesterase III inhibitor) can cause significant bronchodilation. Specific cytokine antagonists, agonists, inhibitors of T-cell function, selective inducible nitric oxide synthetase inhibitors, and possibly gene-directed therapies may become novel treatments. Dexmedetomidine is a unique sedative that induces sleep but preserves respiratory drive and does not cause respiratory depression or change in airway patency. There may be a future role for the use of intravenous or intranasal dexmedetomidine for anxiolysis in asthma. Further studies are needed.[19]

There are currently biologic therapies available for the management of chronic asthma. Omalizumab, a recombinant humanized monoclonal anti-IgE antibody, is indicated for the treatment of severe allergic asthma. It has been shown to control symptoms in severe chronic asthmatic and may be an alternative for patients with poor compliance to ICS therapy.[20,21] Benralizumab, an antiinterleukin 5 receptor α monoclonal antibody, when given in the ED to severe nonresponding patients decreases future hospitalizations.[21]

SPECIAL SITUATIONS

Pregnancy

Asthma during pregnancy is extremely variable. During pregnancy, approximately one third of women have their asthma worsen, a third have their asthma improve, and a third have no change in their asthma symptoms. Approximately 11% to 18% of pregnant women will present to the emergency department with an asthma exacerbation and 62% of these will be admitted. Asthma exacerbation rates and hospitalizations are directly proportional to the degree of asthma control and baseline severity of disease. Maternal and neonatal outcome are excellent in patients with mild or moderate asthma. Severe asthma during pregnancy is associated with gestational diabetes and delivery before 37 weeks.[22]

The least amount of medication needed to maintain the pregnant asthmatic in the mild severity range is recommended. Acute exacerbations should be treated as in any nonpregnant patient. Pregnant asthmatics are less likely to receive systemic corticosteroids than nonpregnant asthmatics in the ED. Oral and IV steroids are safe during pregnancy and should be administered in a manner similar to nonpregnant patients. ICSs are not associated with adverse perinatal outcomes and are recommended for all pregnant patients with asthma (budesonide is preferred). Inhaled beta-2 agonists, ipratropium, magnesium sulfate, cromolyn, theophylline, and leukotriene antagonists are safe.[7] Acute asthma attacks are rare in labor likely due to endogenous steroid production. There are no contraindications to any asthma medication in the breast-feeding patient.

Near Fatal Asthma

Near fatal or life-threating asthma is used to describe acute severe asthma with clinical features such as altered consciousness level, exhaustion, poor respiratory effort, silent chest, hypotension, cyanosis,

a PEF <33% or hypoxia with a SpO_2 <92% or PaO_2 <60 mm Hg.[22a] Acute severe asthma does not require the patient to have severe asthma; rather it refers to acute episodes requiring immediate multimodal therapies to prevent progression to irreversible hypoxia and cardiopulmonary arrest. The terms status asthmaticus, near fatal asthma, and life-threatening asthma are all used to describe patients with different severity of acute severe asthma.

Risk factors for death from asthma have been identified (see Box 59.1). Other risk factors linked to near-fatal and fatal asthma include frequent use of inhaled beta-2 agonists, decreased use of corticosteroids, hospital admission for asthma treatment within the previous 12 months, low socioeconomic status, environmental exposures (air pollution, cigarette smoking), and psychosocial problems. Patients with near-fatal asthma are likely to depend on EDs for asthma management. Patients with fatal asthma commonly tend to be African American, live in inner-city areas, and are 15 to 34 years old. Less than 1% of asthmatics in the ICU die from their disease. Most deaths occur at home or on the way to the hospital, at night, and within 24 hours of the onset of symptoms.

Clinical Approach to Acute Severe Asthma

The patient with life-threatening or near fatal asthma appears agitated (hypoxemic), assumes an upright position, and appears to be in severe respiratory distress. Tachypnea, diaphoresis, and accessory muscle use are evident. Speech is fragmented into single or short bursts of syllables or words. Absence of wheezing indicates severe expiratory obstruction and minimal air movement. Peak expiratory testing is difficult for the patient to perform but when possible indicates severe expiratory obstruction. Alterations in consciousness and bradypnea indicate hypercarbia and impending respiratory arrest. No laboratory markers identify near fatal asthma.

Attempts to abort the episode include continuously nebulized beta-2 and anticholinergic agents (see Table 59.2). If parenteral adrenergic therapy is desired, terbutaline is preferred because of its beta-2 selectivity. IV magnesium sulfate may be of benefit. Oral prednisone 50 mg or IV methylprednisolone 125 mg should be administered. The use of additional therapies such as noninvasive or mechanical ventilation as described above may be necessary.

The American Heart Association recommendations for cardiopulmonary resuscitation in asthmatics indicate no difference from other cardiac arrest situations. Unrecognized barotrauma may cause cardiac arrest. Bedside ultrasound should be used to identify occult pneumothorax and to reveal nonpalpable cardiac contractions. Empirical bilateral tube thoracostomy should be performed if unexplained cardiac arrest occurs, especially in the context of dramatic increases in peak inspiratory pressure. ECMO may be indicated for severe asthma refractory to conventional therapies.

DISPOSITION

Asthmatic patients discharged from the ED have rates of relapse that vary from 11% over 3 days to 45% at 8 weeks. The relapse risk increases in those with numerous asthma-related ED visits within the previous year, more outpatient medications, and longer duration of symptoms before the ED visit. Other studies have also shown that insufficient improvement in peak flow measurements with hospital-based treatment is a risk factor for relapse.

Patients requiring extended care who are without life-threatening exacerbations, pregnancy, or complications of asthma can generally be treated in an observation unit with 8-week outcomes equal to those admitted to the hospital. Table 59.4 summarizes disposition guidelines based on PEF and other potential factors.

TABLE 59.4 Emergency Department Disposition Decision-Making Guidelines

	Good Response	Incomplete Response	Poor Response
PEF (% predicted/ personal best)	≥60%	40%–60%	<40%
Disposition Site			
Home	Yes	Consider based on risk factors (see Box 59.1)	No, continue therapy
Hospitalization	No	Consider based on risk factors (see Box 59.1)	Yes, if available and appropriate

Additional Factors With Increased Likelihood of Admission

- Female sex, older age, and non-white race
- Use of more than 8 beta agonist puffs in previous 24 h
- Severity of exacerbation (need for rapid medical intervention on arrival, respiratory rate >22, oxygen saturation <95%, final PEF <50% predicted
- Past history of intubations or asthma admissions
- Previous use of OCS

OCS, Oral corticosteroids; *PEF,* peak expiratory flow rate.

Asthma exacerbation does not end on discharge; airway inflammation and peripheral obstruction may take hours to days to resolve. Patients are likely to need continued beta-2 agonist therapy for a short time after the ED, and they should demonstrate the correct use of their inhalers. However, guidelines for the chronic use of inhaled beta-2 agonists recommend limited daily use only as a rescue therapy. A spacer should be used with any MDI. A patient using a portable, preloaded, multidose dry powder inhaler must be able to inhale from the mouthpiece in a rapid and forceful inhalation to total lung capacity.

Patients receiving systemic corticosteroids in the ED should continue these orally for 5 to 7 days. For patients with asthma symptoms less than twice per month, ED clinicians should consider discharging them with a low dose ICS-formoterol inhaler or having them take a low dose ICS whenever SABA is taken. If patients have asthma symptoms more than twice per month, they should be discharged with a low dose ICS-formoterol inhaler or taking a low dose ICS whenever SABA is taken. If the patient was not using controller medications before the acute visit and has characteristics of persistent asthma (symptoms or rescue therapy more than twice per week, interference with sleep more than twice per month, activity limitation caused by asthma or exacerbations requiring oral corticosteroids more than once in the past year), moderate-dose ICSs or a combination ICS and LABA should be started.[8]

Patients should contact their physician for asthma-related problems within the following 3 to 5 days and should make a follow-up medical appointment within 1 to 4 weeks. Interventions that include free medications, transportation vouchers, and appointment assistance significantly increase the likelihood that discharged asthma patients will obtain primary care follow-up. This assistance, however, may not affect long-term outcomes.

Patients managed by asthma specialists have fewer symptoms, less beta-agonist use, improved quality of life, reduced ED visits, and fewer hospitalizations than those managed by generalists. Patients

with severe persistent asthma or prior severe exacerbations should be referred to an asthma specialist.

The asthma patient should be provided with written education about discharge medications, medication adjustment if the condition is not improving (such action plans are not often created and when done are often inadequate), and a peak flow meter for daily measurements, especially for those who have difficulty perceiving airflow obstruction or who have symptoms of worsening asthma. At a minimum, focused education should address the difference between controller and rescue medications and the need for follow-up. Intervening in the ED during an acute asthma exacerbation with a web-based education tool may reduce future ED visits.[23] Smoking asthmatics have more respiratory symptoms, lower lung function, and more parenchymal abnormalities noted on chest computed tomography, so smoking cessation should be discussed.

The references for this chapter can be found online at ExpertConsult.com.

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CHAPTER 59: QUESTIONS AND ANSWERS

1. Which of the following is a risk factor for sudden death from asthma?

- **a.** A hospitalization for asthma in the past year but not within the past 30 days
- **b.** An emergency department (ED) visit for asthma in the past year but not within the past 30 days
- **c.** Current use of systemic corticosteroids
- **d.** Patient perception that the current exacerbation is very severe

Answer: c. Risk factors for sudden death are current or recent corticosteroid use, ED or hospitalization within the past 30 days, more than two hospitalizations for asthma in the past year, more than three ED visits for asthma in the past year, using more than two beta-agonist canisters per month, previous intubation or intensive care unit (ICU) visit, and difficulty perceiving symptoms or their severity.

2. A 23-year-old man with known severe asthma presents with an acute asthma flare over 2 hours. Physical examination reveals a well-developed man in marked respiratory distress. Heart rate is 120 beats/min, oxygen saturation is 90%, respiratory rate is 26 breaths/min, blood pressure is 140/92 mm Hg, and oral temperature is 98.7°F (37.2°C). Current medications are albuterol metered-dose inhaler (MDI) and fluticasone inhaler 500 µg twice daily. What therapy is recommended for this acute flare?

- **a.** Albuterol 2.5 mg nebulized, Ipratropium 0.5 mg, methylprednisolone 125 mg intravenously, and magnesium sulfate 2 g intravenously
- **b.** Epinephrine infusion at 5 µg/min
- **c.** Ipratropium 500 µg nebulized × three doses with methylprednisolone 125 mg intravenously
- **d.** Methylprednisolone 125 mg intravenously with salmeterol nebulized via continuous nebulization

Answer: a. Short-acting inhaled beta-agonists with ipratropium are the cornerstone of acute asthma management. Corticosteroids are indicated in any moderate or severe flare. Oral steroids are as efficacious as intravenous (IV) steroids if the patient can take oral medications. Magnesium sulfate may obviate the need for intubation or decrease hospital length of stay in severe cases. Salmeterol is a slow-onset, long-acting beta-2 agonist (LABA) not indicated in acute asthma management.

3. What is the medication combination of choice for the rapid sequence induction of an asthmatic?

- **a.** Etomidate/succinylcholine
- **b.** Ketamine/succinylcholine
- **c.** Midazolam/pancuronium
- **d.** Propofol/rocuronium

Answer: b. No choice is contraindicated. Ketamine is the sedative of choice because of its bronchodilatory effect. Propofol may have the same benefit, although less profoundly. Thiopental releases histamine, and etomidate does not bronchodilate. Succinylcholine releases trace amounts of histamine, but this is not known to cause any adverse effect. Rocuronium has an onset time similar to that of succinylcholine, no

histamine release, and a prolonged duration of action. Either succinylcholine or rocuronium is acceptable for rapid sequence intubation (RSI) in acute asthma.

4. Which of the following is a risk factor for death in patients presenting with an asthma attack?
   a. Currently taking theophylline
   b. Family history of asthma
   c. Presence of symptoms for 1 week
   d. Use of three albuterol metered-dose inhalers (MDIs) per month

Answer: d. The following are risk factors for death from asthma:

- Past history of sudden severe exacerbations
- Prior intubation for asthma
- Prior asthma admission to an intensive care unit (ICU)
- Two or more hospitalizations for asthma in the past year
- Three or more emergency department (ED) care visits for asthma in the past year
- Hospitalization or an ED care visit for asthma within the past month
- Use of more than two MDI short-acting beta-2 agonist canisters per month
- Current use of or recent withdrawal from systemic corticosteroids
- Difficulty perceiving severity of airflow obstruction
- Comorbidities such as cardiovascular diseases or other systemic problems
- Serious psychiatric disease or psychosocial problems
- Illicit drug use, especially inhaled cocaine and heroin

5. A 25-year-old woman presents with wheezing and shortness of breath from asthma. She was recently exposed to cigarette smoke. She denies cough and fever. You cannot get much more of a history from her at this time because she finds it difficult to speak in complete sentences. Her vital signs are blood pressure, 136/85 mm Hg; heart rate, 110 beats/min; respiratory rate, 32 breaths/min; and temperature, 99°F (37.2°C). Her oxygen saturation is 92%. Her PEF is 50% of predicted. On physical examination, you note bilateral wheezing, regular tachycardia, and accessory muscle use. The remainder of her examination is normal. Over the course of 1 hour, she receives supplemental oxygen, three doses of nebulized albuterol (5 mg) mixed with ipratropium (0.5 mg), and oral prednisone 50 mg. She now reports feeling somewhat better. She speaks in longer sentences but still cannot speak in complete sentences. A repeat peak flow measurement is now 60% of predicted. Otherwise, there are no changes on a repeat physical examination. You plan to admit her to your ED observation unit. What is an appropriate next step in the management of this patient?
   a. Additional nebulized albuterol
   b. Intravenous (IV) magnesium sulfate
   c. IV methylprednisolone (Solu-Medrol)
   d. Oral montelukast

Answer: a. This patient presents with a moderate-to-severe asthma exacerbation. She has responded to initial therapy but continues to have moderate symptoms. Additional adrenergic medications are indicated. Because she is tolerating nebulized medications and is responding, there is no need for IV or subcutaneous adrenergic agents, such as terbutaline. IV magnesium sulfate is a smooth muscle relaxant, but it is generally reserved for more severe asthma exacerbations. Oral and IV steroids have the same efficacy, and regardless of the route, only need to be administered every 6 to 8 hours. Montelukast is a leukotriene-modifying drug that is used in chronic management.