Childhood Asthma
A Guide for Pediatric Emergency Medicine Providers

Sarah Kline-Krammes, MD, Nirali H. Patel, MD*, Shawn Robinson, MD

INTRODUCTION
Asthma is a chronic inflammatory disease of the airways. The immunohistopathologic features of asthma are those of inflammation, and include neutrophils, eosinophils, mast cell activation, and epithelial cell damage.1 This inflammation causes airway obstruction that is at least partially reversible with medications.

PREVALENCE
Asthma prevalence in children increased steadily from 1980 to 1995, when it peaked at 7.5% (Fig. 1). Since 1997, asthma prevalence has remained stable.2 It affects every state, although the midwest, northeast, and southeast are disproportionately more affected than other regions of the United States. In addition, asthma affects minorities at a higher rate: Hispanic people have the highest risk and are 2.4 times more likely to have asthma compared with the general pediatric population. African-Americans, Native Americans, and Native Aleutians are 1.6 and 1.3 times more likely to be affected.

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Fig. 1. United States: asthma prevalence 2007.
with asthma. In addition, African-American children are 4 times more likely to die from asthma.  

Several theories exist to explain this discrepancy in prevalence. Children are more vulnerable to the effects of air pollution because their immune systems are still maturing and because they have increased minute ventilation per square meter of total body surface area compared with adults. As air pollution of ozone, nitrogen dioxide, sulfur dioxide, and carbon monoxide increases, the odds of developing wheezing in children also increases. In addition, the tendency for minorities to reside in densely populated urban regions and have increased exposure to higher levels of air pollution may be a contributing factor for their increase in asthma prevalence.

BURDEN OF DISEASE

The total cost to society of asthma is estimated at $56 billion dollars per year as of 2007. This cost includes morbidity productivity losses of $3.8 billion dollars and mortality productivity losses of $2.1 billion dollars. In pediatrics, the cost of treating asthma is also high, especially if the child requires intubation. Nearly 50% of all children who are intubated for status asthmaticus experience a complication (most commonly aspiration pneumonia, pneumothorax, and pneumomediastinum), and these complications translate to a hospital cost of $117,000 versus $38,000 for a visit with no complications. Most striking is the yearly cost of treating asthma per child. In 2005, the cost per year of health care for a child without asthma was $618. The same yearly cost of health care for a child with asthma was more than 60% higher, costing more than $1000. In addition, asthma is the leading cause of missed school days. Even if a child is not seeking care in a hospital setting, asthma may still affect a child’s ability to participate in school and the ability to sleep.

PATHOPHYSIOLOGY

Many studies have documented the relationship of histamine and/or leukotriene release with the inhalation of cold air, leading to bronchoconstriction. However, this does not account for the increased prevalence of asthma in the warmer regions of the southeast United States. A study in 2012 by Hayes and colleagues showed that bronchoconstriction increased among patients with asthma who inhaled hot air versus room air (112% vs 38% respectively) and was mediated by cholinergic reflexes that improved with use of ipratropium, suggesting an underlying seasonal or viral trigger.

Allergic asthma is considered to have a large inflammatory component. Allergens induce a cascade of events leading to interleukin release, mast cell degranulation, mucus hypersecretion, and neutrophilic inflammation, which ultimately contribute to steroid-resistant, severe asthma.

Certain polymorphisms causing structural changes have been associated with an accelerated decrease in lung function with asthma. Xiao and colleagues reported that the bronchial epithelial wall in asthmatics seemed to be damaged such that allergens passed through the epithelial wall, leading to immune activation and asthma exacerbation. Likewise, Lopez-Guisa and colleagues found that interleukin (IL) 3 and IL4 stimulated the production of transforming growth factor B2 and periostin, both of which promote airway remodeling.

Environment may have a contributing role in the development of asthma. Although the prevalence of asthma is increased in areas with high air pollution, a study conducted by Omland and colleagues found that being born and raised on a farm with high allergen exposures reduced the risk of asthma versus being raised in rural, nonfarm
environments. They also noted that exposure to dairy confinements, welding smoke, and tobacco smoke were all risk factors for asthma development. They therefore concluded that high exposure to potential allergens early in life may be protective against future development of asthma.

**HISTORY**

A detailed medical history is an important tool in the assessment of a wheezing child. Many children present to the emergency department (ED) with a first-time episode of wheezing. Although this is a common symptom of asthma, most of these children do not go on to develop asthma. A thorough history is essential in determining causes other than asthma in a first-time wheezing patient. Questions include age of patient, onset of symptoms, and associated symptoms. Sudden onset in symptoms may indicate foreign body aspiration (more common in toddlers with associated choking, cyanosis) or anaphylaxis (with associated urticaria, stridor, and hypotension). Fever with cough or congestion may indicate bronchiolitis (<2 years with first-time wheezing) or lower airway tract infection. More chronic symptoms such as failure to thrive, difficulty feeding, persistent wheezing, or failure to respond to short-acting beta agonists (SABAs) should concern the medical provider for underlying gastroesophageal reflux, cardiac disease/failure, thoracic masses, or cystic fibrosis. Historical clues that help distinguish those that are more suggestive of asthma are included in Box 1. Patients with a congenital cause for wheezing (vascular rings, cystic lung malformations) usually have a history of wheezing since birth without response to traditional asthma therapies like SABAs and corticosteroids.

When a patient with a history of asthma presents with wheezing, certain historical data can help characterize the underlying severity of asthma. This classification of asthma is based on current symptoms, use of SABAs, and interference with daily activity (Table 1).

Common symptoms of an asthma exacerbation include cough, wheezing, and some degree of respiratory distress. Young children may manifest shortness of breath as decreased activity or vocalizations. To help determine the severity of the exacerbation, it is important to ascertain the current usage of SABAs; compliance with controller medications; and the delivery mode of the medications, including spacer use. Assessment of risk factors of near-fatal asthma is critical because this may change the management of the current exacerbation (Box 2).

Predictors of severe asthma exacerbation remain multifactorial. A study in 2011 noted that experiencing persistent symptoms from asthma was related to having severe exacerbations; receiving inhaled corticosteroids (ICSs) was protective against a severe exacerbation. However, some predictors of a severe exacerbation were independent of persistent symptoms. These factors included young age, history of ED visits or hospitalizations in the past year, and history of greater than or equal to

<table>
<thead>
<tr>
<th>Box 1</th>
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<tbody>
<tr>
<td>History suggestive of asthma</td>
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<tr>
<td>More than 1 episode of wheezing per month</td>
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<tr>
<td>Triggers for wheezing (allergen, exercise, smoke, upper respiratory illness)</td>
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<tr>
<td>Previous bronchodilator use including response to therapy</td>
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<tr>
<td>Family history of asthma (especially in first-degree relative)</td>
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<tr>
<td>Atopy (allergic rhinitis, atopic dermatitis, or food allergy)</td>
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</table>
3 days of oral steroids in the prior 3 months. Thus, it is important to assess the underlying severity of disease as well as the risk of having a severe exacerbation.23

Recent studies have assessed the factors that may be associated with pediatric asthma-related ED visits. Previous studies indicated that age, race, insurance status, and average household income all played a role in predicting ED visits. However, a recent study showed that, after controlling for all variables, the only statistically significant predictor of a pediatric asthma-related ED visit was a previous asthma-related ED visit.24

**PHYSICAL EXAMINATION**

The physical examination of children with asthma brought to the ED begins with a rapid 30-second cardiopulmonary assessment as described by the American Heart Association.25 This assessment helps with a quick determination of general appearance, airway patency, effectiveness of respiratory effort, and adequacy of circulation. Vitals signs are also helpful in assessment of severity of exacerbation. Children presenting with hypoxia (less than 92%) are more likely to require aggressive treatment and require hospital admission. Severe exacerbations cause tachypnea, tachycardia, and sometimes pulsus paradoxus. Accessory muscle usage is more likely to indicate a severe exacerbation. Severe retractions, especially supraclavicular retractions, indicate a forced expiratory volume less than 50% of predicted. Poor air movement found on chest auscultation is a sign of impending respiratory failure. Patients presenting with agitation or depressed mental status may be approaching respiratory failure.21,22

Wheezing is the most common symptom associated with asthma in children aged 5 years and younger. Cough caused by asthma may be recurrent and/or persistent and is usually accompanied by wheezing episodes and breathing difficulties. Shortness of breath that is recurrent or occurs during exercise increases the likelihood of asthma.19 Cough-variant asthma can present as a dry harsh cough, usually worse at night; these patients often do not wheeze at all.

Physical examination findings can also help distinguish between other causes of cough and wheezing in children. Foreign body aspiration can present as unilateral wheezing. Wheezing secondary to a cardiac cause has hepatomegaly as an associated physical finding. Wheezing along with urticaria and uvular edema suggests anaphylaxis as the cause of wheezing. Wheezing along with signs of upper airway tract infection and fever indicates bronchiolitis.

**ASTHMA SCORES**

Pediatric asthma scores have been used to help classify severity of exacerbation. Most scores assess suprasternal retractions, air entry, and wheezing, and most also add respiratory rate and oxygen saturation. A study in 2008 showed that the Preschool Respiratory Assessment Measure (PRAM) was applicable to children between 2 and 17 years of age and was a feasible, reliable, valid, and responsive tool to measure asthma severity in a busy pediatric ED.26 Another tool, the Pediatric Asthma Severity Score (PASS) is a valid, reliable tool to measure asthma in the acute setting in children aged 1 to 18 years in a pediatric ED. The PASS score is limited because it only assesses 3 clinical measures: wheezing, prolonged expiration, and work of breathing. The Pediatric Asthma Score (PAS) is another measurement tool that includes measures of respiratory rate, oxygen saturation, auscultatory findings, retractions, and dyspnea. Kelly and colleagues27 in 2000 showed that the PAS showed good interobserver agreement and excellent face validity in the ED setting. The PAS allowed providers to have an objective understanding of the severity of each patient being cared
<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Intermittent</th>
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<th></th>
<th>Mild</th>
<th></th>
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<th>Moderate</th>
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<th>Severe</th>
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<tr>
<td></td>
<td>Ages 0–4 y</td>
<td>Ages 5–11 y</td>
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<td>Ages 0–4 y</td>
<td>Ages 5–11 y</td>
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<td>Ages 5–11 y</td>
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<td>Ages 0–4 y</td>
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<td>Impairment</td>
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<td>Symptoms</td>
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<tr>
<td>Nighttime awakenings</td>
<td>0</td>
<td>&lt;2 d/wk</td>
<td>&gt;2 d/wk but not daily</td>
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<td>≤2/mo</td>
<td>1–2/mo</td>
<td>3–4/mo</td>
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<td>Short-acting beta-2 agonist use for symptom control</td>
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<tr>
<td></td>
<td>≤2 d/wk</td>
<td>&gt;2 d/wk but not daily</td>
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<tr>
<td>Interference with normal activity</td>
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<tr>
<td>Lung Function</td>
<td>N/A</td>
<td>Normal FEV₁ between exacerbations</td>
<td></td>
<td>N/A</td>
<td>—</td>
<td>N/A</td>
<td>—</td>
<td>N/A</td>
<td>—</td>
<td></td>
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<tr>
<td>FEV₁, (predicted) or peak flow (personal best)</td>
<td>&gt;80%</td>
<td>&gt;80%</td>
<td>60%–80%</td>
<td></td>
<td></td>
<td>75%–80%</td>
<td></td>
<td></td>
<td>&lt;60%</td>
<td></td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>&gt;85%</td>
<td>&gt;80%</td>
<td>75%–80%</td>
<td></td>
<td></td>
<td>&lt;75%</td>
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</table>

Table 1
Determination of asthma severity in children

Classifying Asthma Severity and Initiating Therapy in Children

- Interimnet
  - Ages 0–4 y
  - Ages 5–11 y
- Mild
  - Ages 0–4 y
  - Ages 5–11 y
- Moderate
  - Ages 0–4 y
  - Ages 5–11 y
- Severe
  - Ages 0–4 y
  - Ages 5–11 y
<table>
<thead>
<tr>
<th>Risk</th>
<th>Exacerbations requiring oral systemic corticosteroids (consider severity and interval since last exacerbation)</th>
<th>0–1/y (see notes)</th>
<th>≥2 exacerbations in 6 mo requiring oral systemic corticosteroids, or ≥4 wheezing episodes in 1 y lasting &gt;1 d and risk factors for persistent asthma</th>
<th>—</th>
<th>—</th>
<th>—</th>
<th>—</th>
<th>—</th>
</tr>
</thead>
</table>

**Notes:**

- Level of severity is determined by both impairment and risk. Assess impairment domain by caregiver’s recall of previous 2 to 4 weeks. Assign severity to the most severe category in which any feature occurs.

- Frequency and severity of exacerbations may fluctuate over time for patients in any severity category. There are currently inadequate data to correlate frequencies of exacerbations with different levels of asthma severity. In general, more frequent and severe exacerbations (e.g., requiring urgent, unscheduled care; hospitalization; or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients with 2 or more exacerbations described may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

- *Abbreviations:* FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids; ICU, intensive care unit; N/A, not applicable.

for with an asthma exacerbation. This scoring system and corresponding clinical pathway resulted in a decreased length of stay, cost of hospitalization, and improved quality of care when used on the inpatient floors. In the same study, ED nurses preferred the PAS to peak flow measurements.

The PAS has been adapted for use in our institution including the ED, inpatient floors, pediatric intensive care unit (PICU), and transport settings (Table 2).

**DIFFERENTIAL DIAGNOSIS**

Asthma is the most common cause of chronic cough in children, although symptoms of cough, wheeze, and dyspnea can be the presenting symptoms for other diagnoses.

The differential diagnosis for first-time wheezing is broad and requires a thorough history and physical to make the appropriate diagnosis. Although the list can be extensive, it is important for the emergency medicine physician to initially consider and address life-threatening causes of wheezing as well as recognize causes that may need further evaluation. Partial airway obstruction from foreign body aspiration must be considered in toddlers with first-time wheezing that is of sudden onset, with a history of choking or gagging, and findings of unilateral wheezing. Although sudden in onset, anaphylaxis may have associated urticaria as well as a history of exposure to a possible allergen. Respiratory symptoms associated with first-time wheezing in infants may suggest bronchiolitis. History of inhalant use or exposure may indicate a chemical pneumonitis, whereas a history of hemoptysis may indicate pulmonary hemorrhage. Other life-threatening causes of first-time wheezing include cardiac disease and malformation, thoracic masses, or mediastinal masses. These patients often have a history of failure to thrive, feeding difficulties, and physical examination findings of murmur and hepatomegaly in cardiac failure. Wheezing secondary to structural anomalies may present with wheezing since birth, failure of improvement in symptoms following standard asthma treatment, and symptom severity that is associated with positional changes. Tracheomalacia or bronchomalacia caused by tracheal or main stem bronchi collapse manifests as cough and wheezing. In addition, symptoms caused by tracheomalacia improve with prone positioning and worsen with agitation or excitement because of increase in intrathoracic pressures. Right-sided aortic arch also causes mechanical compression of the airway resulting in wheezing.

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**Box 2**

**Characteristics of near-fatal asthma**

- Characteristics of a near-fatal asthma exacerbation
  - Doubling of beta agonist usage or using 1 or more metered-dose inhaler canister per month
  - African-American race
  - Adolescents
  - Hospital admission within the past year for asthma
  - Intensive care unit admission for asthma
  - Multiple ED visits within the last year for asthma
  - Oxygen saturations less than 91%
  - Psychological or psychosocial problems
  - Difficulty perceiving symptoms of a severe exacerbation

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Kline-Krammes et al
Gastroesophageal reflux in infants can present as wheezing that is exacerbated by feedings or infant positioning.

Patients who present with chronic cough or wheezing that does not improve with traditional asthma therapy also require a thoughtful differential diagnosis to ensure that the diagnosis is correct. Underlying congenital, immunologic, and infectious causes must be considered. Patients presenting with chronic cough along with multiple respiratory infections and symptoms of malabsorption should be evaluated for cystic fibrosis, primary ciliary dyskinesia, and cardiac disease. Chronic cough may be the presenting symptom of infectious causes such as pertussis or tuberculosis.

Parents often confuse other symptoms for wheezing. Patients with upper airway noises or stridor suggest a viral upper respiratory tract infection or croup as the cause. Vocal cord dysfunction is most common in adolescents and can be misdiagnosed as wheezing, although it is inspiratory stridor associated with chest or throat tightness. Habit cough may present as chronic cough not improving with traditional asthma therapy. Hyperventilation causes dyspnea that can be confused with asthma. Anxiety can also give the sensation of chest tightness resulting in a misdiagnosis of asthma.28,29

Box 3 summarizes important differential diagnoses to consider during the presentation of wheezing in the ED.

The distinguishing characteristic of asthma is the response to bronchodilator or corticosteroids when symptomatic. Knowledge of the natural history of asthma and

<table>
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<tr>
<th>Table 2</th>
<th>PAS and interpretation</th>
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<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Respiratory rate (breaths/minute)</td>
<td></td>
</tr>
<tr>
<td>Age 1–3 y</td>
<td>≤34</td>
</tr>
<tr>
<td>Age 4–5 y</td>
<td>≤30</td>
</tr>
<tr>
<td>Age 6–12 y</td>
<td>≤26</td>
</tr>
<tr>
<td>&gt;12 y</td>
<td>≤23</td>
</tr>
<tr>
<td>Oxygen requirement (%)</td>
<td>&gt;95 on room air</td>
</tr>
<tr>
<td>Retractions</td>
<td>None or intercostal</td>
</tr>
<tr>
<td>Dyspnea 1–4 y</td>
<td>Normal feeding, vocalization, and play</td>
</tr>
<tr>
<td>Dyspnea &gt;5 y</td>
<td>Counts to ≥10 in 1 breath; or speaks in complete sentences</td>
</tr>
<tr>
<td>Auscultation</td>
<td>Normal breath sounds, end-expiratory wheezes</td>
</tr>
<tr>
<td>Total PAS</td>
<td>Mild 5–7</td>
</tr>
</tbody>
</table>

Courtesy of Akron Children’s Hospital, Akron, OH.
response to treatment can guide clinicians in determining when to consider alternative diagnoses. Diagnostic testing or chest imaging may be required to help exclude other causes of wheezing or cough.

**DIAGNOSTIC EVALUATION**

Few diagnostic tools exist that help determine the diagnosis of asthma in the ED setting. In children, asthma is a clinical diagnosis. Diagnostic studies are used to help exclude other causes of wheezing or cough, to help recognize atypical presentations of asthma, and evaluate those patients who do not respond as expected to traditional asthma therapy.

**Pulse Oximetry**

The clinical assessment of hypoxemia relies on many factors. Under optimal conditions, an arterial blood saturation of approximately 75% is needed before central cyanosis is clinically detectable. Oxygen saturation is a sensitive indicator of disease severity in conditions associated with ventilation/perfusion mismatch like asthma. Oxygen saturations can be used to assess severity of disease and response to treatment. Mild asthma exacerbations are associated with oxygen saturations greater than 95%. Oxygen saturations less than 92% 1 hour after treatment correlate with an increased need for hospitalization. Therefore, pulse oximetry may be a useful tool during the management and disposition planning of an patient with asthma.

**Chest Radiograph**

For a child with known asthma who is responding as expected to traditional therapy, there is no evidence showing that chest radiographs change the management of asthma in children. Further, they are not helpful as a routine work-up of asthma in children in the ED. Children with an acute asthma exacerbation often have abnormal chest radiographs including hyperinflation, atelectasis, peribronchial thickening, and increased extravascular fluid. These findings do not play a role in directing patient management or assessing severity of exacerbation. A study in 2000 analyzed the clinical predictors of focal infiltrate on chest radiograph. Grunting and pulse oximetry less
than or equal to 93% was highly specific when diagnosing pneumonia in a wheezing infant and toddler. First-time wheezing, tachypnea, and fever were not associated with findings of infiltrate on chest radiograph. Chest radiographs can be used to help exclude other diagnoses of wheezing or cough, especially in patients with first-time wheezing. Acute-onset, unilateral wheezing suggests foreign body aspiration, and patients may show hyperinflation on chest radiographs. Chest radiographs may show a structural abnormality or mass in a patient with chronic wheezing that fails to respond to bronchodilator therapy. Chest radiograph in patients who present in extremis or with impending respiratory failure may help rule out complications from asthma such as pneumothorax or pneumomediastinum as well as other contributing causes for respiratory distress such as superimposed infection or cardiac disease. Although no clear guidelines exist, chest radiographs should be considered in the following instances: asymmetric wheezing, wheezing that fails to respond to bronchodilator therapy, or patients who present in extremis or with impending respiratory failure.

**Peak Expiratory Flow Measurements**

National guidelines for the treatment of asthma call for measures of peak expiratory flow rate as a valid and reproducible measure of airway obstruction and a guide for treatment plans. They are infrequently done in the ED setting and a 2004 study showed that only 64% of children eligible for peak flow measurements had it attempted in the ED. Most reports state that children less than 5 years old cannot reliably perform this maneuver, which is effort dependent and requires a significant degree of coordination. In the same study, less than half of the patients had a pre–peak flow and post–peak flow measurement obtained with bronchodilator treatment. Children with a more severe exacerbation as judged by asthma score or need for admission were less likely to be judged able to obtain a peak flow measurement.

Peak flow measurements are predicted based on the patient’s age, height, and gender. Patients who regularly perform peak flow measurements at home may know their personal best. Peak flow measurements correlate with the forced expiratory volume in 1 second (FEV₁), although there is more variability in peak flow measurements. A peak flow greater than 70% of expected is classified as a mild exacerbation. A peak flow between 40% and 70% is a moderate exacerbation, and less than 40% predicts a severe exacerbation. Both initial peak flow measurement and follow-up measures can help direct management and response to treatments. Patients with a peak flow less than 60% of predicted best after ED treatment are more likely to relapse in the outpatient setting. These measurements add to objective measures of severity of asthma exacerbation but are infrequently performed in the ED.

**MANAGEMENT**

Children with acute exacerbations should be rapidly assessed and triaged to a location in the ED where observation and frequent reassessment can be performed by medical and nursing staff. Reassessment of patients after each round of treatment is the most important aspect in the management of acute asthma exacerbations. Most children seen in the ED for asthma do not require hospital admission. In 2004, 754,000 children in the United States visited the ED for asthma and approximately 198,000 required hospital admissions. Regardless of disposition, the mainstay of asthma exacerbation treatment in the emergency room are SABAs, systemic corticosteroids, and ipratropium bromide. A summary of medication recommendations established by the National Heart, Lung, and Blood Institute (NHLBI) guidelines are shown in Table 3.
<table>
<thead>
<tr>
<th>Medication</th>
<th>Child Dose</th>
<th>Adult Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inhaled SABAs</strong></td>
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<tr>
<td>Albuterol</td>
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<tr>
<td>Nebulizer solution (0.63 mg/3 mL, 1.25 mg/3 mL, 2.5 mg/3 mL, 5.0 mg/mL)</td>
<td>0.15 mg/kg (minimum dose 2.5 mg) every 20 min for 3 doses then 0.15–0.3 mg/kg up to 10 mg every 1–4 h as needed, or 0.5 mg/kg/h by continuous nebulization</td>
<td>2.5–5 mg every 20 min for 3 doses, then 2.5–10 mg every 1–4 h as needed, or 10–15 mg/h continuously Only selective beta-2 agonists are recommended. For optimal delivery, dilute aerosols to minimum of 3 mL at gas flow of 6–8 L/min. Use large-volume nebulizers for continuous administration. May mix with ipratropium nebulizer solution</td>
<td></td>
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<tr>
<td>MDI (90 µg/puff)</td>
<td>4–8 puffs every 20 min for 3 doses, then every 1–4 h inhalation maneuver as needed. Use VHC; add mask in children &lt;4 y old</td>
<td>4–8 puffs every 20 min up to 4 h, then every 1–4 h as needed In mild to moderate exacerbations, MDI plus VHC is as effective as nebulized therapy with appropriate administration technique and coaching by trained personnel</td>
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<td><strong>Bitolterol</strong></td>
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<tr>
<td>Nebulizer solution (2 mg/mL)</td>
<td>See albuterol dose; thought to be half as potent as albuterol on mg basis</td>
<td>See albuterol dose Has not been studied in severe asthma exacerbations. Do not mix with other drugs</td>
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<tr>
<td>MDI (370 µg/puff)</td>
<td>See albuterol MDI dose</td>
<td>See albuterol MDI dose Has not been studied in severe asthma exacerbations</td>
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<tr>
<td><strong>Levalbuterol (R-Albuterol)</strong></td>
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<tr>
<td>Nebulizer solution (0.63 mg/3 mL, 1.25 mg/0.5 mL, 1.25 mg/3 mL)</td>
<td>0.075 mg/kg (minimum dose 1.25 mg) every 20 min for 3 doses, then 0.075–0.15 mg/kg up to 5 mg every 1–4 h as needed</td>
<td>1.25–2.5 mg every 20 min for 3 doses, then 1.25–5 mg every 1–4 h as needed Levalbuterol administered in one-half the mg dose of albuterol provides comparable efficacy and safety. Has not been evaluated by continuous nebulization</td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>MDI (45 µg/puff)</td>
<td>See albuterol MDI dose</td>
<td>See albuterol MDI dose</td>
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<tr>
<td>---------------------------</td>
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</tr>
<tr>
<td>Pirbuterol</td>
<td>See albuterol MDI dose; thought to be half as potent as albuterol on a mg basis</td>
<td>See albuterol MDI dose</td>
<td>Has not been studied in severe asthma exacerbations</td>
</tr>
</tbody>
</table>

**Systemic (Injected) Beta-2 Agonists**

<table>
<thead>
<tr>
<th>Drug</th>
<th>MDI (200 µg/puff)</th>
<th>See albuterol MDI dose</th>
<th>See albuterol MDI dose</th>
<th>—</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine 1:1000 (1 mg/mL)</td>
<td>0.01 mg/kg up to 0.3–0.5 mg every 20 min for 3 doses sq</td>
<td>0.3–0.5 mg every 20 min for 3 doses sq</td>
<td>No proven advantage of systemic therapy compared with aerosol</td>
<td></td>
</tr>
<tr>
<td>Terbutaline (1 mg/mL)</td>
<td>0.01 mg/kg every 20 min for 3 doses then every 2–6 h as needed sq</td>
<td>0.25 mg every 20 min for 3 doses sq</td>
<td>No proven advantage of systemic therapy compared with aerosol</td>
<td></td>
</tr>
</tbody>
</table>

**Anticholinergics**

<table>
<thead>
<tr>
<th>Drug</th>
<th>MDI (18 µg/puff)</th>
<th>See albuterol MDI dose</th>
<th>See albuterol MDI dose</th>
<th>—</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipratropium Bromide</td>
<td>4–8 puffs every 20 min as needed up to 3 h</td>
<td>8 puffs every 20 min as needed up to 3 h</td>
<td>Should use with VHC and face mask for children &lt;4 y old. Studies have examined ipratropium bromide MDI for up to 3 h</td>
<td></td>
</tr>
</tbody>
</table>

**Ipratropium with Albuterol**

<table>
<thead>
<tr>
<th>Drug</th>
<th>MDI (18 µg/puff)</th>
<th>See albuterol MDI dose</th>
<th>See albuterol MDI dose</th>
<th>—</th>
</tr>
</thead>
</table>
| Ipratropium with Albuterol | 1.5–3 mL every 20 min for 3 doses, then as needed | 3 mL every 20 min for 3 doses, then as needed | May be used for up to 3 h in the initial management of severe exacerbations. The addition of ipratropium to albuterol has not been shown to provide further benefit once the patient is hospitalized | (continued on next page)
Table 3 (continued)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Child Dose</th>
<th>Adult Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDI (each puff contains 18 µg ipratropium bromide and 90 µg of albuterol)</td>
<td>4–8 puffs every 20 min as needed up to 3 h</td>
<td>8 puffs every 20 min as needed up to 3 h</td>
<td>Should use with VHC and face mask for children &lt;4 y old</td>
</tr>
</tbody>
</table>

Systemic Corticosteroids

<table>
<thead>
<tr>
<th>Medication</th>
<th>Child Dose</th>
<th>Adult Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>1–2 mg/kg in 2 divided doses (maximum 60 mg/d) until PEF is 70% of predicted or personal best</td>
<td>40–80 mg/d in 1 or 2 divided doses until PEF reaches 70% of predicted or personal best</td>
<td>For outpatient “burst,” use 40–60 mg in single or 2 divided doses for total of 5–10 d in adults (children, 1–2 mg/kg/d maximum 60 mg/d for 3–10 d)</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes:

There is no known advantage for higher doses of corticosteroids in severe asthma exacerbations, nor is there any advantage for intravenous administration compared with oral therapy provided gastrointestinal transit time or absorption is not impaired.

The total course of systemic corticosteroids for an asthma exacerbation requiring an ED visit or hospitalization may last from 3 to 10 days. For corticosteroid courses of less than 1 week, there is no need to taper the dose. For slightly longer courses (eg, up to 10 days), there probably is no need to taper, especially if patients are concurrently taking ICSs.

ICSs can be started at any point in the treatment of an asthma exacerbation.

*Abbreviations:* MDI, metered-dose inhaler; PEF, peak expiratory flow; sq, subcutaneous; VHC, valved holding chamber.

*Children ≤12 years of age.*

OXYGEN

Children, and especially infants, are at risk for respiratory failure and develop hypoxemia more rapidly than adults. Therefore, monitoring of oxygen saturation is necessary.\textsuperscript{1,20,35} NHLBI guidelines recommend oxygen administration to maintain saturations greater than 90% (greater than 95% in pregnant women and in patients who have coexistent heart disease). SaO\textsubscript{2} is to be monitored until a clear response to bronchodilator therapy has occurred.\textsuperscript{1} Indiscriminate high-flow oxygen despite good saturations can lead to poorer outcomes.\textsuperscript{20,36}

SABAS

SABA is the most effective treatment of relieving bronchospasm and reversing airway obstruction. The most commonly used SABA in the United States is the beta-2 selective drug albuterol.\textsuperscript{37} Through its sympathomimetic effects, it exerts bronchodilating effects by relaxing airway smooth muscle and thus relieving bronchospasm. Secondary effects are enhancement of water output from bronchial mucous glands and improvement of mucociliary clearance.

Albuterol is available in 2 forms: albuterol or levalbuterol. Albuterol is a 50:50 mixture of R-enantiomers and S-enantiomers. The R-enantiomer is pharmacologically active and shows more potent binding to beta-2 receptors than the S-enantiomer. The S-enantiomer is pharmacologically inactive, has a longer elimination half-life, and may induce paradoxical bronchospasm, contributing to airway irritation.\textsuperscript{20} Levalbuterol consists solely of the R-enantiomer and is thought to provide maximum bronchodilating benefits and to minimize adverse side effects, including tachycardia and hypokalemia.\textsuperscript{20,38,39} Studies have shown mixed results, with some trials showing benefits in pulmonary function, reduction in hospital admission rate, and reduced side effects, whereas other studies have shown no difference.\textsuperscript{20,39–45} Current guidelines do not recommend using one rather than the other.

Albuterol has 2 common mechanisms of delivery: a metered-dose inhaler (MDI) with a spacer or nebulized solution typically via small-volume constant output jet nebulizers (SVN). A newer mechanism of delivery is breath-actuated nebulizer treatments, which are nebulizers that initiate aerosol production with the onset of inhalation, limiting the loss of aerosol during exhalation. A randomized control study conducted in the ED found that a breath-actuated nebulizer improved clinical asthma score, decreased respiratory rate, and decreased hospital admissions, but did not significantly affect length of stay in the ED.\textsuperscript{46} In mild to moderate asthma, an MDI with spacer has been shown to be at least equivalent, if not better, in efficacy to a nebulizer and is more cost-effective.\textsuperscript{20,47–51} Factors that influence delivery mechanism include patient cooperation, response to treatment via MDI, severity of exacerbation, and local protocols.\textsuperscript{20} Children less than 24 months old are thought to have a more difficult time with MDI and spacer. However, a double-blind, randomized, placebo-controlled clinical trial by Delgado and colleagues\textsuperscript{52} showed that MDI with spacers may be as efficacious as nebulizers in the ED treatment of wheezing in children from 2 to 24 months of age. Another double-blind, randomized equivalence trial of MDI with spacer versus nebulizer treatment in children 12 to 60 months of age found that the efficacy of albuterol administered via MDI and spacer was equivalent to nebulizer.\textsuperscript{53} The type of delivery system used may be determined by institution policy as well as provider preference and comfort.

Albuterol can be given as intermittent therapy every 20 minutes (up to 3 doses) or continuously for an hour depending on severity. Response to medication on reevaluation determines further frequency. Following reassessment, SABA can
be administered by MDI and spacer, 2 to 4 puffs, continuous or spaced to hourly based on severity (Fig. 2) or asthma score. Albuterol administered via nebulizer can be given at 0.15 to 0.3 mg/kg with a minimum of 2.5 mg and a maximum of 5 mg. The volume of albuterol is then diluted with normal saline for a total of 5 mL fluid per nebulized mask.\textsuperscript{20} With continuous nebulization, the recommended dose of albuterol is 0.5 mg/kg/h with the total hourly dose not to exceed 10 to 15 mg/h.\textsuperscript{1,20} Approximately 2% to 10% of albuterol given by nebulized treatment

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**MANAGEMENT OF ASTHMA EXACERBATIONS: \underline{EMERGENCY DEPARTMENT AND HOSPITAL-BASED CARE}**

<table>
<thead>
<tr>
<th>Initial Assessment (see figures 5-1, 5-3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEF or FEV, oxygen saturation, and other tests as indicated</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FEV, or PEF &gt;40% (Mild-to-Moderate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen to achieve SaO₂ &gt;90%</td>
</tr>
<tr>
<td>Inhaled SABA by nebulizer or MDI with valved holding chamber, up to 3 doses in first hour</td>
</tr>
<tr>
<td>Oral systemic corticosteroids if no immediate response or if patient recently took oral systemic corticosteroids</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FEV, or PEF &lt;40% (Severe)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen to achieve SaO₂ &gt;90%</td>
</tr>
<tr>
<td>High-dose inhaled SABA plus ipratropium by nebulizer or MDI plus valved holding chamber, every 20 minutes or continuously for 1 hour</td>
</tr>
<tr>
<td>Oral systemic corticosteroids</td>
</tr>
</tbody>
</table>

**Impending or Actual Respiratory Arrest**

| Intubation and mechanical ventilation with 100% oxygen |
| Nebulized SABA and ipratropium |
| Intravenous corticosteroids |
| Consider adjunct therapies |

<table>
<thead>
<tr>
<th>Admit to Hospital Intensive Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>(see box below)</td>
</tr>
</tbody>
</table>

**Repeat Assessment**

| Symptoms, physical examination, PEF, O₂ saturation, other tests as needed |

**Moderate Exacerbation**

<table>
<thead>
<tr>
<th>FEV, or PEF 40-69% predicted/personal best</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical exam: moderate symptoms</td>
</tr>
<tr>
<td>Inhaled SABA every 60 minutes</td>
</tr>
<tr>
<td>Oral systemic corticosteroids</td>
</tr>
<tr>
<td>Continue treatment 1-3 hours, provided there is improvement, make admitting decision in &lt;4 hours</td>
</tr>
</tbody>
</table>

**Severe Exacerbation**

<table>
<thead>
<tr>
<th>FEV, or PEF &lt;40% predicted/personal best</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical exam: severe symptoms at rest, accessory muscle use, chest retraction</td>
</tr>
<tr>
<td>History: high-risk patient</td>
</tr>
<tr>
<td>No improvement after initial treatment</td>
</tr>
<tr>
<td>Oxygen</td>
</tr>
<tr>
<td>Nebulized SABA + ipratropium, hourly or continuous</td>
</tr>
<tr>
<td>Oral systemic corticosteroids</td>
</tr>
<tr>
<td>Consider adjunct therapies</td>
</tr>
</tbody>
</table>

**Admit to Hospital Ward**

| Oxygen |
| Inhaled SABA |
| Systemic (oral or intravenous) corticosteroid |
| Consider adjunct therapies |
| Monitor vital signs, FEV, or PEF, SaO₂ |

<table>
<thead>
<tr>
<th>Admit to Hospital Intensive Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen</td>
</tr>
<tr>
<td>Inhaled SABA hourly or continuously</td>
</tr>
<tr>
<td>Intravenous corticosteroid</td>
</tr>
<tr>
<td>Consider adjunct therapies</td>
</tr>
<tr>
<td>Possible intubation and mechanical ventilation</td>
</tr>
</tbody>
</table>

**Key**

- FEV₁, forced expiratory volume in 1 second
- ICS, inhaled corticosteroid
- MDI, metered dose inhaler
- PCO₂, partial pressure of carbon dioxide
- PEF, peak expiratory flow
- SABA, short-acting beta₂-agonist
- SaO₂, oxygen saturation

**Fig. 2.** ED evaluation and management of asthma exacerbation. (From National Heart, Lung, and Blood Institute. Expert panel report 3: guidelines for the diagnosis and management of asthma. US Department of Health and Human Services, National Institutes of Health, National Heart, Lung, and Blood Institute. 2007. NIH Publication Number 08-5486.)
reaches the lung. An MDI gives 90 μg/puff, but the delivery is considered to be more efficient.37

Side effects of albuterol are common, but minor in severity. Sinus tachycardia is the most common side effect, but rarely causes serious problems. Other cardiovascular-related effects include palpitations, hypertension, and, rarely, ventricular dysrhythmias. Central nervous system side effects are secondary to stimulation and include tremors, hyperactivity, and nausea with vomiting. Metabolic side effects include hypokalemia and hyperglycemia. Periodic serum potassium levels should be monitored with long-term continuous use of SABA treatment.

**SYSTEMIC CORTICOSTEROIDS**

The overriding physiologic derangement in asthma is airway inflammation and corticosteroids are among the mainstays of treatment. Glucocorticoids suppress cytokine production, granulocyte-macrophage colony-stimulating factor, and inducible nitric oxide synthase activation (all important components of the underlying inflammatory cells), decrease airway mucous production, and attenuate microvascular permeability.21 The guidelines indicate use of steroid in asthma exacerbation when the patient does not completely respond to one inhaled beta agonist treatment, even if the patient is having a mild exacerbation.1 Systemic corticosteroids have been shown to decrease the need for hospital admission as well as the length of stay.20,54–56 A time series controlled trial on nurse initiation of oral systemic steroids in triage for moderate to severe asthma exacerbation in children 2 to 17 years of age showed earlier clinical improvement, decreased hospital admission rates, and earlier time to discharge in triage-administered steroids compared with systemic oral corticosteroid administration following physician assessment.57

Systemic corticosteroids may be given either orally or intravenously. Studies have showed that the effects of oral and intravenous (IV) steroids are equivalent.37,58 Advantages of oral dosing include ease of administration and decreased cost. IV steroids are indicated when a patient cannot tolerate oral medication, is too ill to take oral medication, or has intestinal issues affecting absorption of medication.1,20,35 Patients who vomit within 30 minutes of an oral dose should have dosing repeated.37 Side effects of systemic corticosteroids are more prevalent in the critically ill child because of duration and dose of medication, and include hyperglycemia, hypertension, and occasionally agitation related to steroid-induced psychosis.

Systemic corticosteroids begin to exert their effect in 1 to 3 hours and reach maximal effect within 4 to 8 hours.21 Oral prednisone or prednisolone is administered at a dose of 1 to 2 mg/kg once daily (maximum of 60 mg/d),20,59,60 typically for 3 to 5 days. The total course of systemic corticosteroids for an asthma exacerbation requiring an ED visit of hospitalization may last longer. For corticosteroid courses of less than 1 week, there is no need to taper the dose. For slightly longer courses (eg, up to 10 days), there probably is no need to taper, especially if patients are concurrently taking ICSs.1 IV steroids can be given as methylprednisolone, 2 mg/kg/d.21 An alternative to prednisone is dexamethasone. Dexamethasone is well absorbed orally and has the same bioavailability as when given parenterally, with the action lasting up to 72 hours after a single dose.61 Studies suggest that a 2-day course of oral dexamethasone at a dose of 0.6 mg/kg daily (maximum 16 mg) is as effective and well tolerated as a 5-day course of oral prednisone in adults and children.20,62–64 In addition, Qureshi and colleagues65 found that 2 doses of oral dexamethasone had fewer side effects with similar efficacy and better compliance compared with 5 doses of oral prednisone in children with acute
asthma. High doses of ICS may be considered in conjunction with oral corticoste-
roids in the ED. The data on ICS use in children are inconsistent and may be a result
of dosing inconsistency.1,66 One trial reporting greater efficacy for oral corticoste-
roids used a single high dose of an ICS (2 mg fluticasone), whereas a trial giving
multiple doses of budesonide (1.2 mg total) reported increased efficacy for the
inhaled route.67,68 Although the data are suggestive, a meta-analysis concluded
that evidence was insufficient for firm conclusions.69 ICSs in the ED management
of acute asthma exacerbations are currently not recommended as a replacement
for oral systemic corticosteroids because of lack of efficacy when used
alone.37,54,55,67,69–71

IPRATROPIUM BROMIDE

Ipratropium bromide, an anticholinergic agent, is also used in the treatment of severe
asthma exacerbation. Ipratropium promotes bronchodilation without inhibiting muco-
ciliary clearance, as with atropine. It also acts as a parasympatholytic, antagonizing
acetylcholine effects and ultimately impairing bronchial smooth muscle contraction.21
Adding multiple high doses of ipratropium bromide (0.5 mg nebulizer solution or 8
puffs by MDI in adults; 0.25–0.5 mg nebulizer solution or 4–8 puffs by MDI in children)
to a selective SABA produces additional bronchodilation, resulting in fewer hospital
admissions, particularly in patients who have severe airflow obstruction.1,72,73 It can
be administered every 30 minutes for up to 3 doses. The most common adverse ef-
facts are dry mouth, bitter taste, flushing, tachycardia, and dizziness.21 However,
because of inability to cross membranes from the lung to the systemic circulation,
there is no significant effect on the systemic system, including heart rate, even at
high doses.37,74

IV FLUIDS

Children presenting with severe or life-threatening asthma exacerbation are often
dehydrated secondary to poor oral intake as well as increased insensible losses
from increased minute ventilation. Appropriate fluid resuscitation is necessary; how-
ever, care should be used in avoiding overhydration, which may place these children
at risk for pulmonary edema secondary to microvascular permeability, increased left
ventricular afterload, and alveolar fluid migration associated with the inflammatory
lung process.21 Oral routes of hydration are preferable except in exacerbations with
the possibility of noninvasive ventilator support or endotracheal intubation.1

MAGNESIUM SULFATE

Magnesium sulfate is a bronchodilator that should be used in severe asthma. Magne-
sium sulfate acts through its role as a calcium channel blocker, ultimately inhibiting
calcium-mediated smooth muscle contraction and facilitating bronchodilation.21 Rec-
ommendations for use of IV magnesium sulfate include those whose FEV₁ fails to
improve to more than 60% of predicted in 1 hour following therapy,60 exacerbations
that remain in the severe category after 1 hour of intensive conventional therapy, or
life-threatening asthma.1 It has shown improved clinical asthma scores with minimal
side effects.20,75,76 It is also inexpensive, easily administered intravenously, and well
tolerated.37 A randomized control study also showed that IV magnesium sulfate ther-
apy within the first hour of hospitalization in children aged 2 to 15 years classified as
acute severe asthma had a reduced requirement for mechanical ventilation support
and had a statistically significant shorter PICU and hospital stay.77 However, not all in-
dividual studies have found positive results.1,78–80 The treatment has no apparent
value in patients who have exacerbations of lesser severity, and one study found that IV magnesium sulfate improved pulmonary function only in patients whose initial FEV₁ was less than 25% predicted, and the treatment did not improve hospital admission rates. If administered, a single IV dose of 25 to 75 mg/kg (maximum of 2 g) magnesium sulfate can be given over 20 to 30 minutes.

Nebulized magnesium is also available. A recent meta-analysis of 6 trials suggests that the use of nebulized magnesium sulfate in combination with SABA may result in further improvements in pulmonary function. A Cochrane Review found that 1 study from 3 trials suggested possible improvement in pulmonary function in those with severe exacerbations (FEV₁ <50% predicted). However, heterogeneity among the trials precluded definite conclusions. In addition, there is currently no good evidence that inhaled MgSO₄ can be used as a substitute for inhaled SABA. When used in addition to inhaled SABA (with or without inhaled ipratropium), there is currently no overall clear evidence of improved pulmonary function or reduced hospital admissions. Inhaled magnesium sulfate may be used as a diluent in place of normal saline (usually 2.5 mL of a 250 mmol/L solution) combined with albuterol and ipratropium bromide in the same mask. Magnesium levels do not need to be monitored if a single dose is given, but may be followed if repeated doses are considered. Side effects include hypotension, central nervous system depression, muscle weakness, and flushing. More serious side effects include cardiac arrhythmias, including complete heart block, respiratory failure caused by severe muscle weakness, and sudden cardiopulmonary arrest, but these are usually in the setting of very high serum magnesium levels.

**IV BETA AGONIST**

IV and subcutaneous administration of beta agonists in the management of acute severe asthma are controversial. It has been postulated that children presenting with acute severe asthma exacerbation do not optimally benefit from inhaled SABA therapy because of the inability of the medication to penetrate constricted airways. Systemic administration of a beta agonist may help dilate obstructed airways and improve the efficacy of inhaled beta agonist in severe asthma exacerbations. A double-blind, randomized controlled study in Australia showed more rapid improvement in patients who received a single bolus of IV albuterol in addition to nebulized albuterol than in those who received nebulized albuterol alone.

IV terbutaline, a selective beta-2 agonist, is available in the United States for IV or subcutaneous administration. It may be used in children with no IV access as an adjunct to inhaled SABA. Subcutaneous dosing is 0.01 mg/kg/dose with a maximum dose of 0.3 mg. This dose may be repeated every 15 to 20 minutes for up to 3 doses. IV terbutaline is started with a loading dose of 10 μg/kg over 10 min followed by continuous infusion at 0.1 to 10 μg/kg/min. The side effects include a risk of myocardial ischemia caused by selective beta agonist activity. Between 10% and 50% of asthmatics can have increased troponin I levels during terbutaline therapy. However, data are limited and monitoring cardiac-specific enzymes (creatine phosphokinase or troponin) may be of value in children who receive more than 1 dose of terbutaline.

Nonselective beta agonists such as ephedrine, epinephrine, and isoproterenol are rarely used because of their high side effect profile and availability of more selective IV or subcutaneous agents. The NHLBI guidelines do not recommend use of IV isoproterenol in the treatment of asthma because of the danger of myocardial toxicity.

At present, the NHLBI guidelines do not consider systemic beta agonist therapy to have advantage compared with inhaled SABA. A meta-analysis addressing this issue.
concluded that there was no evidence supporting the use of IV beta agonists compared with aerosol administration in the treatment of acute severe asthma. Data are also sparse on the benefit of adding an IV beta-2 agonist to high-dose nebulized therapy. Systemic beta-2 agonists should be only considered in patients with life-threatening asthma exacerbations who have failed to respond to maximal inhaled therapy and systemic corticosteroids.

**LEUKOTRIENE RECEPTOR ANTAGONISTS**

Leukotriene receptor antagonists (LTRAs) (montelukast, zafirlukast) have been shown to decrease symptoms of mild to moderate asthma exacerbations. Leukotriene pathways are activated in acute asthma, as shown in increases of urinary leukotriene excretion. LTRAs block the production of these natural mediators that are involved in bronchoconstriction. LTRAs are considered to have potential additive benefit in combination with inhaled SABA and corticosteroids. There is some evidence in the adult literature that IV administration may be effective in acute, severe asthma and this may be another route of rapid bronchodilation in life-threatening asthma. A randomized, double-blind, parallel-group pilot study of IV montelukast versus placebo in adults with moderate to severe asthma exacerbation showed significant improvement in FEV1 within 10 minutes of administration of montelukast. There was also a trend toward reduction of inhaled beta agonist use compared with the placebo. Although its role in acute asthma is now being explored, there are insufficient data to recommend it as a possible adjunct treatment.

**HELIOX**

Heliox, a blend of helium and oxygen (80% helium/20% oxygen), is less dense than air and improves air flow resistance in small airways by reducing turbulent flow and enhancing laminar gas flow, increasing carbon dioxide elimination, increasing expiratory flow, decreasing work of breathing, and enhancing particle deposition of aerosolized medication in distal lung segments. Hypoxemia is one of the limits of this therapy. A Cochrane Review concluded that existing evidence did not support the therapeutic use of heliox-driven albuterol in all patients presenting to the ED with status asthmaticus. However, the review only included 3 pediatric trials with a total of 82 patients. Of these, a prospective, randomized controlled, single-blind study conducted by Kim and colleagues in children 2 to 18 years of age with moderate to severe asthma showed that continuously nebulized albuterol delivery by heliox early in the course of care was associated with a greater degree of clinical improvement than delivery by oxygen. There was also a statistically significant difference in discharge rates at the 12-hour treatment point between the two groups. However, there was no statistically significant difference in ED discharge or PICU admission rates. Other pediatric studies have shown that there was no clinical benefit compared with standard therapy in the initial treatment of moderate to severe asthma in the ED. At this time, heliox is to be considered in patients with life-threatening asthma or those who are considered to have severe asthma after 1 hour of conventional therapy.

**NONINVASIVE MECHANICAL VENTILATION**

Mortality in mechanically ventilated children with life-threatening asthma is increased compared with children who do not need mechanical ventilation. Noninvasive positive
pressure ventilation (NIPPV) is an alternative to conventional mechanical ventilation and is used in 3% to 5% of critically ill asthmatic children.21 NIPPV is considered to be a temporizing measure that may help avoid intubation and improve outcomes in children with status asthmaticus.20,96–100 A Cochrane Review highlighted one trial that showed the benefit of NIPPV in hospitalization rates, number of patients discharged, FEV₁, forced vital capacity, and respiratory rates compared with medical therapy alone. However, they still concluded that data were insufficient and that NIPPV was still controversial therapy in severe asthma.101 More recently, multiple pediatric trials have shown NIPPV to be well tolerated, safe, and to have minimal complications in pediatric patients.97,102,103 A recent study also showed that bilevel positive airway pressure ventilation, a form of NIPPV, was well tolerated in pediatric patients weighing less than 20 kg with no major complications, including death or pneumothorax.104 NIPPV in the pediatric patient does require pediatric specific equipment (mask, ventilator), and pediatric respiratory therapists who can monitor the circuit.104 If NIPPV is available, a trial may be warranted before the institution of conventional mechanical ventilation.

INTUBATION
Tracheal intubation in the management of asthma exacerbation is absolutely indicated for patients who present with apnea or coma.1 However, intubation should be strongly considered for the following conditions: refractory hypoxemia, significant respiratory acidosis unresponsive to pharmacotherapy, worsening mental status,37 and exhaustion.1 Ventilation goals should include maintaining adequate oxygenation, allowing for permissive hypercarbia (moderate respiratory acidosis), and minute ventilation adjustment (peak pressure, tidal volume, and rate) to maintain an arterial pH of 7.2. Strategies should attempt to minimize hyperinflation and air trapping, which can be accomplished by using slow ventilator rates with prolonged expiratory phase, minimal end-expiratory pressure, and short inspiratory time. In addition, adjustment to ventilator rate, inspiratory and expiratory time, or positive end-expiratory pressure can be made to facilitate full expiration between breaths.21

DISPOSITION
Adequate evaluation of the severity of asthma exacerbation is important for the initial management of patients, as well as for assessing the clinical response and subsequent disposition. Clinicians often have varying degrees of experience in determining the severity of an asthma exacerbation. More objective tools such as peak flow and spirometry require trained personnel as well as a patient who has adequate coordination and comprehension.105 This requirement makes such tools more difficult to use in the pediatric population, especially in infants and toddlers. To standardize asthma management in the ED, the PAS score has been used. The authors’ institution’s PAS-based management is shown in Fig. 3 for reference.

No single measure is best for assessing severity or predicting hospital admission. Lung function measures (FEV₁ or peak expiratory flow) may be useful for children 5 years of age, but these measures may not be obtainable during an exacerbation. Pulse oximetry may be useful for assessing the initial severity; a repeated measure of pulse oximetry of less than 92% to 94% after 1 hour predicts the need for hospitalization. Children who have signs and symptoms after 1 to 2 hours of initial treatment and who continue to meet the criteria for a moderate or severe exacerbation have greater than an 84% chance of requiring hospitalization.1 If patients are being discharged, a written asthma action plan should be considered. Most guidelines
recommend the provision of a written discharge plan with instructions for medication and follow-up.\textsuperscript{1,26,60,106} Although there are limited data to firmly conclude that provision of an action plan is superior to none, there is clear evidence suggesting that symptom-based plans are superior to peak flow–based plans in children and adolescents.\textsuperscript{107} Use of written action plans significantly reduced acute care visits per child compared with control subjects. Children using plans also missed less school, had less nocturnal awakening, and had improved symptom scores.

Patients who have severe exacerbations and are slow to respond to therapy may benefit from admission to an intensive care unit (ICU), where they can be monitored closely and intubated if indicated.\textsuperscript{1,21}
SUMMARY

Pediatric asthma plays a significant role in health care costs as well as quality of life. Early treatment of asthma exacerbation is the best strategy for management and includes patient education, an asthma action plan, early recognition of worsening symptoms, and intensification of treatment. Despite this, asthma exacerbations may require urgent medical attention. In these cases, beta agonists, systemic corticosteroids, and ipratropium bromide remain the cornerstones of treatment. With life-threatening asthma, various adjunct therapy including IV magnesium, IV beta agonists, heliox, and NIPPV may be considered. Although morbidity secondary to asthma is significant, overall mortality remains low.

REFERENCES


