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Management Of Acute Asthma In The Pediatric Patient: An Evidence-Based Review

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CME Objectives

Upon completion of this article, you should be able to:

1. Discuss the pathophysiologic changes of acute asthma and how they relate to treatment.
2. Identify elements of the history and physical examination that will be helpful in assessing the child with an asthma exacerbation.
3. Review therapeutic options and adjunct therapies for acute asthma.

Prior to beginning this activity, see the back page for faculty disclosures and CME accreditation information

Abstract

Asthma is the most common chronic disease of childhood, with asthma exacerbations and wheezing resulting in more than 2 million emergency department visits per year. Symptoms can vary from mild shortness of breath to fatal status asthmaticus. Given the high prevalence of asthma and its potential to progress from mild to moderate to life-threatening, it is vital for emergency clinicians to have a thorough understanding of acute asthma management. Current evidence clearly supports the use of inhaled bronchodilators and systemic steroids as first-line agents. However, in those who fail to respond to initial therapies, a variety of adjunct therapies and interventions are available with varying degrees of evidence to support their use. This review focuses specifically on evaluation and treatment of pediatric asthma in the emergency department and reviews the current evidence for various modes of treatment.

Case Presentation

A 6-year-old girl with a history of asthma presents to your ED with difficulty breathing. She has had several days of dry cough, rhinorrhea, and low-grade fevers. Her mother reports that she developed rapid breathing late last night and needed multiple puffs from her albuterol metered-dose inhaler. The inhaler helped her breathe more comfortably at first, but now it seems to have little effect. For the last few hours, her symptoms have worsened considerably to the point where she can hardly speak. The mother briefly mentions that her daughter has had many ED visits for asthma, 2 lifetime admissions, but no intubations or admissions to the ICU. She uses only albuterol at home, as needed. Her doctor prescribed an inhaled corticosteroid that was to be used daily, but she ran out a few weeks ago. On exam, the patient is tachypneic with increased work of breathing, as evidenced by subcostal and intercostal retractions, head bobbing, and nasal flaring. On auscultation, you hear generally poor air entry throughout without wheezing and no focal area of crackles or decreased aeration. Her vital signs are notable for a respiratory rate of 58 breaths per minute, heart rate of 154 beats per minute, oxygen saturation of 92%, and temperature of 38.2°C. You start her on a nebulized albuterol and ipratropium treatment and a dose of oral steroids and decide to watch her closely. If the patient does not respond to this treatment, what other management strategies are in your arsenal? What diagnostic studies, if any, does this patient require? Should her fever change your plan?

Introduction

According to recent data from the Centers for Disease Control and Prevention, 1 out of 11 children in the United States has asthma. Moreover, 1 of 5 children with asthma presented to the emergency department (ED) for asthma-related care in 2009, and it is the most frequent cause of hospitalization in children in the United States, costing the nation billions of dollars annually.[1,2] The symptoms of asthma can vary widely, ranging from mild shortness of breath to fatal status asthmaticus. Timely and targeted intervention during an acute exacerbation can significantly decrease morbidity and mortality. Many emergency clinicians are challenged by managing patients with worsening asthma symptoms and safely determining their disposition. Given the high prevalence of asthma and its potential to progress from mild to moderate to life-threatening, it is vital for emergency clinicians to have a solid understanding of the management of acute asthma exacerbations.

Critical Appraisal Of The Literature

A literature search was performed in the PubMed database using multiple combinations of the search terms *acute asthma exacerbation, pharmacologic management, nonpharmacologic management, noninvasive ventilation, invasive mechanical ventilation, innovative asthma treatment, pediatric emergency department, pediatric intensive care,* and *outcomes.* Relevant articles were selected, reviewed, and included in the bibliography. Over 275 articles were reviewed, 244 of which are cited in this article.

Etiology And Pathophysiology

Asthma is a well-recognized syndrome characterized by bronchoconstriction and airway inflammation that results in airflow obstruction. Individuals with asthma have an intrinsic airway hyperresponsiveness that can be triggered by common environmental allergens, viruses, and pollutants.[3,4] Asthma exacerbations have an early bronchospastic phase, during which patients typically respond favorably to bronchodilators, and a later inflammatory phase due to an overly robust immune response, which is typically treated with corticosteroids.[5-7] During the early bronchospastic phase, there is a release of mast cell mediators (including histamine, prostaglandin D2, and leukotrienes LTC4, D4, and E4) that gives rise to mucosal edema, mucus secretion, and increased smooth-muscle tone, culminating in airway narrowing.[6-8] In the later inflammatory phase, the lung parenchyma is infiltrated with inflammatory cells and immune cells (particularly eosinophils, basophils, neutrophils, and helper T-cells) that potentiate mucosal edema, mucus secretion, and smooth-muscle contraction, resulting in worsening airway narrowing.[6,7,9] Inadequate anti-inflammatory therapy can lead to irreversible airway remodeling (characterized by airway thickening and fibrosis) and increased mucus secretion that results in increased airway hyperresponsiveness and obstruction.[3,4,7] Patients with more-severe disease or those who present late to medical attention may not respond well to bronchodilators and corticosteroids alone. In such cases, there are a variety of agents that can be utilized.

Differential Diagnosis

Wheezing is often the hallmark feature of acute asthma, but many other common and critical disease processes may resemble an asthma exacerbation, and alternate diagnoses must always be considered. **(See Table 1.)**

Infants and young children up to 24 months of age are vulnerable to viral bronchiolitis, which is a common imitator of asthma and may be difficult to distinguish, particularly since upper respiratory viral infections are common triggers for asthma exacerbations.[10] Infants (immunized or not) are susceptible to pertussis and may present with cough and respiratory distress. Congenital conditions such

as airway hemangiomas, tumors, papillomas, vascular rings/slings, and laryngomalacia/tracheomalacia may also present in this age group, typically as progressively worsening noisy breathing, wheezing, stridor, or respiratory distress. Wheezing may also be a consequence of congestive heart failure from congenital heart disease, arrhythmias, or myocarditis, and it is often seen in conjunction with failure to thrive secondary to increased work of breathing.[11-13] Older infants and young children may present with wheezing from an inhaled foreign body. Retropharyngeal abscess typically presents with stridor or dysphagia, but it may also present in young children with wheezing.[14] These children usually present as acutely ill with fevers and decreased neck movement. Foreign body aspiration should be considered in the differential diagnosis, particularly in infants and children with localized or unilateral wheezing or in patients who have little or no response to systemic corticosteroids and bronchodilators.[15]

Older children and adolescents may present with wheezing from a variety of etiologies. Infections such as viral or bacterial pneumonia may present with wheezing. Inflammatory processes such as hypersensitivity pneumonitis, vasculitis, or collagen vascular disease can also present among older children. Vocal cord dysfunction, psychogenic cough, and panic attack are common causes of apparent respiratory distress and are diagnoses of exclusion.[16-18] Pulmonary manifestations of cystic fibrosis and alpha 1-antitrypsin deficiency may also develop within this age group. Anaphylaxis must also be considered, as it can present at any age.

The differential diagnosis outlined here illustrates the concept that not all wheezing is due to asthma. Conversely, not all children with asthma wheeze. Classic teaching is that cough-variant asthma is an occult form of asthma in which the only sign or symptom is chronic cough.[19,20] This diagnosis should be considered in any patient with a cough lasting longer than 2 weeks without an obvious cause, especially if the cough is nonproductive, is nocturnal, is induced by exercise or cold air, or if there is a family or personal history of atopy. In patients with such symptoms, an empiric trial of bronchodilators may be considered.[21,22] While inhaled bronchodilators have been shown to improve symptoms, the role of corticosteroids in cough-variant asthma is controversial. Some authors argue that airway remodeling in the form of subepithelial-layer thickening is present in cough-variant asthma, and, therefore, early anti-inflammatory treatment may be beneficial;[23] however, other studies show that steroids are not useful. A randomized placebo-controlled trial of systemic corticosteroids for nonspecific cough showed no benefit over placebo.[21] No clear guidelines exist for the management of cough-variant asthma. Additional data in the pediatric population are necessary.

Table 1. Diagnoses That May Mimic Asthma

Acutely Life-Threatening Diagnoses

- Anaphylaxis
- Airway foreign body
- Pneumonia
- Bronchiolitis
- Pertussis
- Retropharyngeal abscess
- Congestive heart failure
- Cardiac arrhythmia (supraventricular tachycardia) with heart failure
- Airway tumor/hemangioma
- Anatomic abnormality of the airway (vascular ring, pulmonary arterial sling)
- Mediastinal mass
- Pulmonary embolism
- Vasculitis (Churg-Strauss, Wegener granulomatosis)
- Collagen vascular diseases (lupus, sarcoid)

Nonacutely Life-Threatening Diagnoses

- Laryngomalacia/tracheomalacia
- Vocal cord dysfunction
- Vocal cord paralysis
- Psychogenic cough
- Panic attack/hyperventilation
- Suppurative bronchitis
- Primary ciliary dyskinesia
- Gastroesophageal reflux disease
- Allergic bronchopulmonary aspergillosis
- Alpha 1-antitrypsin deficiency
- Cystic fibrosis

Prehospital Care

Emergency medical services (EMS) are an important part of the continuum of asthma management. The magnitude of EMS personnel's responsibility is great, and millions of patients with asthma are treated each year by EMS personnel.

The goals of prehospital care for a child experiencing an acute exacerbation include timely assessment and recognition of the severity of the exacerbation and initiation of appropriate treatment. The prehospital provider should promptly elicit an asthma history, including previous admissions to the intensive care unit (ICU) and previous intubations. In addition, swift evaluation of a child's work of breathing (including mental status, respiratory rate, and accessory muscle use) are keys to appropriately assessing the severity of the exacerbation. The presence of wheezing on auscultation is an important physical finding, but the absence of wheezing in very severe asthma exacerbations may be misleading.[24] The National Asthma Education and Prevention Program has published guidelines for the management of asthma in the prehospital setting. The guidelines identify 3 principle goals for treating asthma exacerbations: (1) correction of significant

hypoxemia by administering supplemental oxygen, (2) rapid reversal of airflow obstruction, and (3) reduction of the likelihood of recurrence of severe airflow obstruction by intensifying therapy.[25]

Inhaled beta agonists such as albuterol are first-line therapies for asthma exacerbations. They may be administered intermittently or continuously, and their safety profile is well established in the prehospital setting.[26] Inhaled anticholinergic agents (such as ipratropium) may be helpful in moderate-to-severe acute asthma and can be added to inhaled beta agonists for coadministration.[25] Although corticosteroids are a mainstay of asthma therapy, they are unlikely to benefit the patient in a prehospital setting, though they may be considered when transport times are prolonged.[26] Early corticosteroid administration has been demonstrated to decrease the need for hospitalization. Children in extremis may benefit from injectable bronchodilators such as epinephrine or terbutaline. Noninvasive ventilation may be helpful in avoiding mechanical ventilation, which should be used only as a last resort in children with respiratory failure.[27] Significant regional variability exists with regard to the scope of prehospital personnel practice.[26,27]

Emergency Department Evaluation

History

Upon arrival to the ED, it is essential for the emergency clinician to survey the severity of the child's underlying disease as well as the current exacerbation. Patients should be asked about exposures to triggers, including upper respiratory illnesses, pets, smoke, environmental allergens, changes in weather, or exercise.[27] Assessing the use of home medications (or the lack thereof) will help determine compliance and baseline control of the child's asthma. Children who use rescue medications more than twice per week, who experience nighttime symptoms more than twice per month, or who refill their rescue medications more than twice per year may be inadequately controlled. This is known as the "rule of 2s."[28] The number of ED visits, the most recent course of systemic steroids, and the total number of steroid courses within the last year can also help gauge the underlying level of control as well as the severity of the child's disease. It can also be helpful to ask parents about appropriate use of rescue medications to ensure that patients are using spacers and facemasks with metered-dose inhalers to optimize pulmonary delivery of medication. A recently increased use of rescue bronchodilators is a marker for increasing disease severity. If a child previously required admission to the hospital (particularly to the ICU), he is more likely to require subsequent admissions.[29,30]

Even children diagnosed with mild asthma can be at risk for life-threatening exacerbations. Markers for severe exacerbations include a doubling of beta agonist usage or an increased usage of metered-dose inhalers in the previous month.[31] Although young children are more likely to be diagnosed with asthma, adolescents and non-Hispanic black children are more likely to suffer fatal exacerbations.[32-34] Children presenting with life-threatening asthma exacerbations are also more likely to have been previously admitted, particularly within the last year.[29,35] Other risk factors for life-threatening exacerbations include admission to the ICU, history of intubation,[5] additional ED visits within the last year,[29] oxygen saturation < 91%,[36] and a longer history of asthma.[36,37]

Physical Examination

The physical examination is integral in the assessment of acute asthma, and vital signs can provide critical information about the child's respiratory status. Children presenting with oxygen saturations < 92% are significantly more likely to require aggressive treatment (including frequent bronchodilator therapy and systemic medications[38]) and may be more likely to require admission.[36,39-41] Children with severe exacerbations also often have tachypnea and tachycardia (although the presence of normal vital signs does not rule out a severe exacerbation). Distressed children often use accessory muscle groups to breathe. Retractions (particularly supraclavicular retractions) indicate a forced expiratory volume in 1 second (FEV1) < 50% of predicted[42] and should alert the practitioner to more-severe disease. On auscultation, expiratory wheeze or biphasic wheezing may be heard. The "silent chest," signifying severe obstruction, is an ominous sign. Patients with agitation or depressed mental status may be approaching respiratory failure.

There are a variety of standardized tools for objectively measuring the severity of an asthma exacerbation and the response to therapy. Although several have been validated, their practical utility in the ED setting has not been well established, and no single score is widely accepted as standard.[43] Most asthma scoring systems include objective measures such as oxygen saturations, respiratory rate, and heart rate,[44,45] but they also include subjective items such as wheezing, accessory muscle use, and inspiratory to expiratory (I:E) ratios.[46-48] Consistent use of an asthma score by all providers may help to standardize care within a department, but a widely accepted scoring system has not yet been adopted. The Pediatric Respiratory Assessment Measure (PRAM)[48] and the Acute Asthma Intensity Research Score (AAIRS) [49] are commonly used asthma scoring systems that are easily employed.

Diagnostic Studies

In the acute care setting, asthma is primarily a clinical diagnosis. Laboratory evaluation of children experiencing an acute exacerbation is generally not helpful.

Arterial Blood Gas Testing

Previously, evaluation of children with asthma routinely included arterial blood gas (ABG) testing and chest radiography; however, current national guidelines suggest a selective approach to diagnostic testing in acute asthma exacerbations.[50] The routine use of ABG testing in all children with acute asthma is not justified for several reasons. Less-invasive means of assessing respiratory status are widely available via pulse oximetry (for evaluating oxygenation)[51] and end-tidal carbon dioxide ($ETCO_2$) (for evaluating ventilation).[52,53] These are simple and painless methods of evaluating oxygenation and ventilation.[54,55] There is evidence that an initial oxygen saturation of < 90% predicts a substantially higher likelihood of poor outcome;[37] however, most children with exacerbations have a ventilation-perfusion mismatch and mild hypoxemia (> 90%) that is often made temporarily worse by inhaled beta-agonist treatment. Regardless of oxygen saturation early in the course, experts emphasize that serial pulse oximetry throughout the ED course plays a vital role, as it allows children who require admission for supplemental oxygen to be identified.[54,55]

Routine ABG measurement has also fallen out of favor because there are no set values for pH, partial pressure of carbon dioxide (PCO_2), or partial pressure of oxygen (PO_2) that are diagnostic for respiratory failure.[56] Mild-to-moderate hypoxemia (along with hypocapnia and respiratory alkalosis) are common ABG findings in severe acute asthma. If airflow obstruction is severe and unrelieved, there may be progression to hypercapnia and metabolic acidosis due to muscle fatigue and inability to maintain adequate alveolar ventilation as well as lactate production by the overuse of respiratory muscles.[57,58] Normalizing pH and PCO_2 values may be falsely reassuring, as this may be a sign of exhaustion and pending respiratory failure. Given the availability of noninvasive pulse oximetry and $ETCO_2$ monitoring coupled with the fact that there are no clearly defined blood gas values for respiratory failure, routine ABG on all asthma patients is unnecessary. However, in a child with severe, acute asthma, a rising PCO_2 is worrisome and is often predictive of respiratory failure.

Radiography

For most patients, chest x-rays are not helpful in the emergent assessment of asthma. Children with acute asthma often have abnormal chest radiographs that show a variety of findings, including hyperinflation, hypoinflation, atelectasis, or increased extravascular fluid.[59] These findings rarely affect patient management. Even among children who wheeze for the first time, chest x-rays are generally not helpful.[60] There is a small subset of children for whom a chest x-ray may be helpful. This includes children with fever > 39°C, hypoxia, focal abnormalities on examination, no family history of asthma, or those who respond less favorably than expected to bronchodilator therapy.[60-62] In addition, chest x-rays may be warranted in children with unilateral chest pain or differential wheezing in order to evaluate for a foreign body, pneumothorax, or pneumomediastinum.

Peak Expiratory Flow Measurement

Peak expiratory flow (PEF) measurement is an objective and, possibly, underutilized assessment tool in acute asthma.[29,63] Ideally, children with asthma would use peak flow meters at home to monitor their symptoms and would be familiar with their personal-best peak flows. If patients do not know their personal-best peak flow, predicted values can be calculated based on age, height, and gender. Patients with a peak flow > 70% of expected are classified as experiencing a mild exacerbation, patients with a flow between 40% and 70% of expected are experiencing a moderate exacerbation, and patients with a flow < 40% of expected are experiencing a severe exacerbation.[29] PEF does have a few limitations. While it has long been a mainstay of asthma management, PEF measurement is both effort- and technique-dependent and is, therefore, not suitable for use in children aged < 6 years or in those with developmental disabilities.[64-66] In addition, there is evidence that PEF readings may be unreliable in children with moderate-to-severe asthma. As air trapping increases, it causes the PEF to give a misleading reassurance of normal pulmonary function. Despite these shortcomings, PEF is generally reliable in children who are able to perform it and in those who are at the milder end of the diagnostic spectrum.[64,67] Both initial and follow-up measurements can be used to drive therapy in the ED and to objectively determine responses to these therapies.

Treatment

Inhaled beta agonists, often referred to as bronchodilators, have been firmly established as the standard first-line therapy in the treatment of children with asthma. **(See Table 2, page 6.)** The safety and efficacy of beta agonists in reversing bronchospasm and airway constriction have been well established,[69,70] although tremors, tachycardia, headache, and hypokalemia can occur.[71]

Albuterol

Albuterol, the most commonly used inhaled bronchodilator, can be administered with various aerosol-generating devices and methods (such as nebulization or a metered-dose inhaler with a spacer) with equal effectiveness in children who can use them correctly.[72-75] Newer nebulizer designs are breath-enhanced, are breath-actuated, or have rebreathing bags.[76] These new devices are engineered to deliver a higher percentage of respirable-range particles[77] and they limit the loss of aerosol during exhalation,[76] making them ideal for use in the emergency setting. A recent randomized controlled trial demonstrated that, while these new devices did not reduce the patient's time in the ED when compared to standard therapy, they significantly improved patients' clinical asthma scores and reduced admissions.[78] Recommended standard albuterol dosing is 0.15 to 0.3 mg/kg (up to 10 mg per treatment),[29,79,80] although standard doses of 2.5 to 5 mg nebulized albuterol (or 4-8 puffs of a metered-dose inhaler) have also been shown to be safe and effective.[79,81] Dosing for albuterol via breath-actuated nebulizer is as follows: 2.5 mg for children 5 kg to 10 kg; 5 mg for children > 10 to 20 kg; and 7.5 mg for children > 20 kg.[82] Due to improved delivery, children tend to require fewer repeat doses. For children with severe exacerbations, continuous nebulization of albuterol (0.5 mg/kg/h up to 20 mg/h) is more effective than intermittent treatments and results in more-rapid improvement and fewer hospitalizations.[84,84] In addition, continuous treatments are less labor intensive than multiple intermittent doses and may be more cost-effective.[79,84] A drawback to continuous therapy is that children may be assessed less frequently and side effects (such as tachycardia and jitteriness) are more pronounced. In addition, hypokalemia may develop; however, the clinical significance of albuterol-associated hypokalemia is unclear in the literature. Oral albuterol has not been shown to be effective in acute or chronic asthma management.[5]

Table 2. Common Asthma Medications And Their Recommended Dosages[68]

Medication	Drug Class	Mechanism of Action	Dosage	Considerations
Albuterol nebulized	Short-acting beta agonist	Bronchodilator	2.5-5 mg q20min x 3	First-line therapy
Albuterol metered-dose inhaler	Short-acting beta agonist	Bronchodilator	4-8 puffs q20min x 3	First-line therapy
Ipratropium	Anticholinergic	Reduces bronchoconstriction	250-500 mcg + beta agonist x 1-3	Acts synergistically with albuterol, not as a single agent
Racemic epinephrine	Inhaled beta agonist	Vasoconstrictor, reduces mucus, bronchodilator, pulmonary vasodilator, reduces airway edema	0.5 mL diluted in 3-5 mL NS, inhaled	Used primarily for croup and bronchiolitis
Epinephrine	Parenteral beta agonist	Bronchodilator	0.01 mg/kg IM or SQ (IM is preferred route) Max dose: 0.5 mg q5-15min	Reserved for severe exacerbations
Terbutaline	Parenteral beta agonist	Bronchodilator	IV: 2-10 mcg/kg loading dose, then 0.08-0.4 mcg/kg/min continuous infusion SQ: 0.01 mg/kg; max dose: 0.4 mg q15-20min x 3	Reserved for severe exacerbations
Aminophylline	Methylxanthine	Bronchodilator	5.7 mg/kg loading dose	No longer recommended for use in asthma
Prednisone	Corticosteroid	Reduces airway inflammation	1-2 mg/kg/day Max dose: 60 mg/day	Duration of treatment: 3-5 days
Methylprednisolone	Corticosteroid	Reduces airway inflammation	1 mg/kg divided q12h Max 1-time dose: 240 mg	Duration of treatment: 3-5 days
Dexamethasone	Corticosteroid	Reduces airway inflammation	0.6-1.0 mg/kg PO, IM, IV Max dose: 16 mg	May be equally efficacious at 0.15-0.3 mg/kg dose
Magnesium sulfate	Bronchodilator	Bronchodilator, smooth-muscle relaxation	25-75 mg/kg IV over 20 min Max dose: 2 g	Associated with hypotension
Montelukast	Leukotriene receptor antagonist	Nonsteroidal anti-inflammation	4, 5, or 10 mg, based on age Max dose: 10 mg/day	Not recommended for use in acute asthma

Abbreviations: IM, intramuscular; IV, intravenous; NS, normal saline; PO, by mouth; q, every; SQ, subcutaneous.

Levalbuterol

Levalbuterol is an inhaled beta agonist similar to albuterol. The difference is that regular (or racemic) albuterol is a 50:50 mix of the (R)-enantiomer and the (S)-enantiomer, whereas levalbuterol contains only the (R)-enantiomer. Prevailing opinion is that the (R)-enantiomer is the active isomer, whereas the (S)-enantiomer has little or no activity at the beta receptor.[85] Levalbuterol is administered via nebulization or a metered-dose inhaler, and it has been shown to be as effective as albuterol in relieving bronchospasm.[79,86] Results of in vitro studies have raised theoretical concerns that the (S)-enantiomer, rather than being inert, has detrimental effects in asthma, accounting for the adverse effects of beta-agonists (such as tachycardia and jitteriness).[87,88] Clinical studies have failed to show a benefit of levalbuterol over racemic albuterol in acute asthma exacerbations.[89,90] Studies have not shown a difference in hospitalization or ED length of stay for children treated with racemic albuterol versus levalbuterol.[86,89,90] Some studies have shown a modest decrease in tachycardia with levalbuterol, but no decreases in other side effects (tremor, vomiting, palpitations, or nervousness) have been shown.[89,90] In view of its clinical equivalence and considerably higher cost, levalbuterol cannot be recommended over albuterol.[91] It is reasonable to consider the use of levalbuterol in children with cardiac issues in whom a modest decrease in tachycardia may be beneficial; however, there is no scientific literature that supports this practice.

Anticholinergic Agents

Anticholinergic agents (such as ipratropium) have been shown to be a beneficial adjunct treatment for acute asthma. **(See Table 2.)** Ipratropium works by blocking cholinergic receptors and reducing bronchoconstriction. Although ineffective as monotherapy for patients with mild exacerbations, ipratropium coadministered with beta agonists can improve lung function and reduce hospitalization rates in children with moderate-to-severe exacerbations.[92-94] Typically, 2 or 3 doses of 250 to 500 mcg are added to an inhaled beta agonist and administered every 20 to 30 minutes (and later, as needed).[29,93] Ipratropium has only been shown to be effective in the acute setting. Studies of hospitalized children have failed to show any benefit to the addition of ipratropium to their treatment regimens.[29,95,96] Historically, ipratropium was contraindicated in patients with peanut and soy allergies because previous metered-dose inhaler formulations of ipratropium contained an inert preservative that caused anaphylaxis in patients with nut and soy allergies.[97] The current nebulized formulation does not contain this preservative, and it is safe for children with peanut and soy allergies.[98]

Epinephrine And Terbutaline

Nebulized epinephrine is an alpha and beta agonist that may be useful for acute asthma, though there is a paucity of literature on the topic. **(See Table 2.)** Inhaled racemic epinephrine has been used for years to treat obstructive airway conditions such as croup[99] and bronchiolitis.[100] In addition to its vasoconstrictive effects, epinephrine may also decrease mucus production and is an effective bronchodilator and pulmonary vasodilator.[101] Nebulized racemic epinephrine (0.5 mL diluted in 3-5 mL normal saline[68]) has been shown to be as effective and as safe as albuterol,[101] but the incidence of minor side effects (such as nasal discharge or cough) is increased with epinephrine.[103] Efficacy and safety of multiple doses of racemic epinephrine has not been established. Terbutaline is also an effective beta agonist. Although it is not available as a nebulized solution, some experts have nebulized the IV form at a standard dose of 5 mg with good results—but at a significantly higher cost than albuterol.[5,102,104]

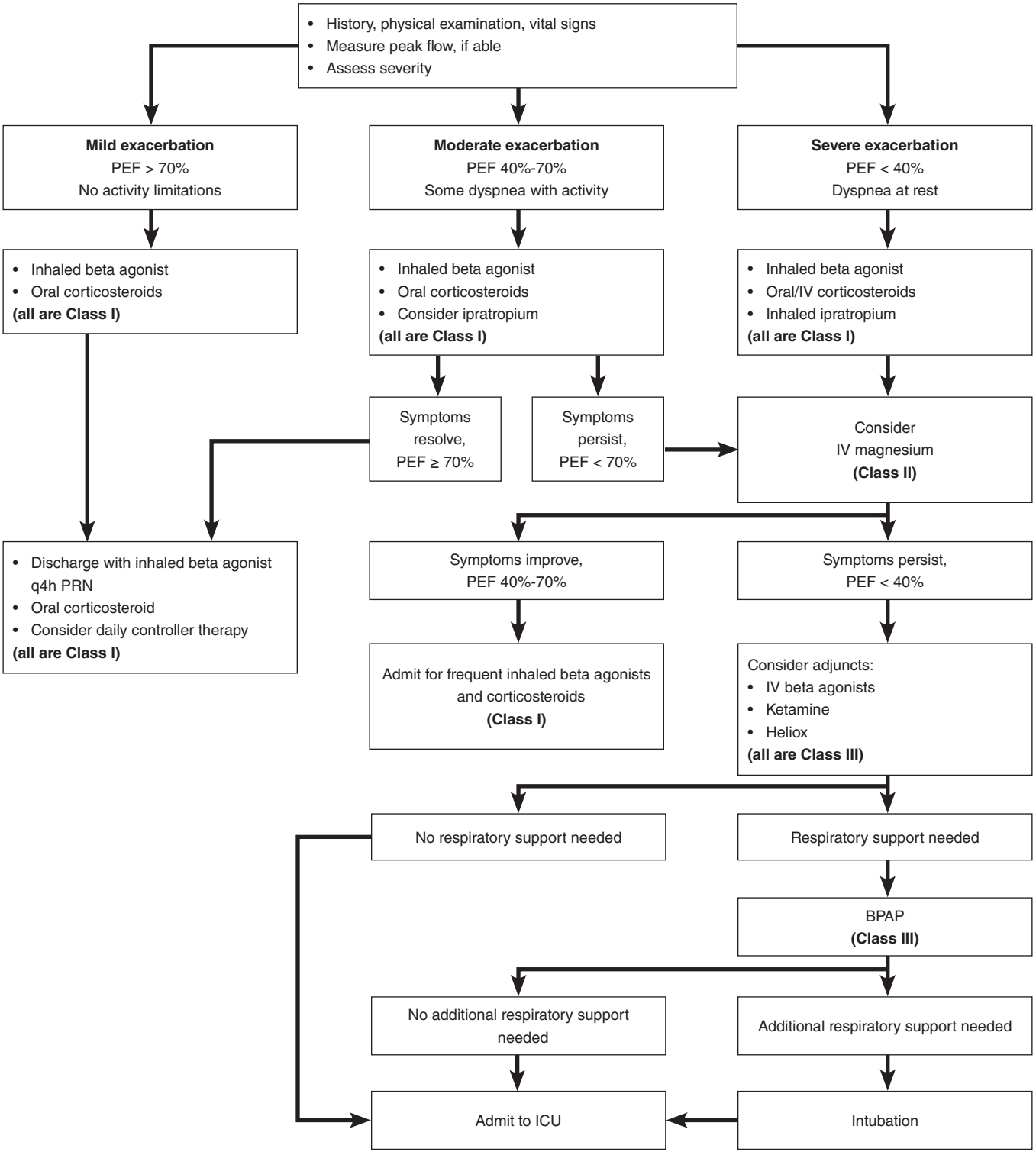
Parenteral Administration

Parenteral administration of beta agonists may be required for children with severe exacerbations in whom inhaled therapy is ineffective or infeasible.[105,106] In severe exacerbations, inspiratory flow may be too poor to allow for adequate drug delivery to the small airways,[79] and IV administration may be necessary to effectively provide beta-agonist therapy. A systematic review by the Cochrane Collaboration called into question the efficacy of parenteral beta agonists, but efficacy in the pediatric population remains unclear since too few pediatric clinical trials were identified.[107] Terbutaline and epinephrine are generally well tolerated.[108-110] Terbutaline can be administered subcutaneously (0.01 mg/kg) or intravenously (2-10 mcg/kg loading dose). Epinephrine can be given subcutaneously as well as intramuscularly (0.01 mg/kg); however, the intramuscular route is generally preferred due to better absorption. **(See Table 2.)** Major side effects are rare, but they can be significant, with arrhythmias, tachycardia, hypertension, and cardiac ischemia among the most serious.[105-107,111] Parenteral administration of beta agonists should be reserved for children who are unable to use or who are unresponsive to the inhaled route; these patients may require intubation and assisted ventilation.

Corticosteroids

Alongside inhaled beta agonists, systemic corticosteroids are a cornerstone of therapy for acute asthma.[112] **(See Table 2.)** Highly effective for both chronic and acute inflammation, corticosteroids work by suppressing inflammation at the cellular level. In addition, corticosteroids and beta agonists act synergistically. Steroids can increase the expres-

Clinical Pathway For Management Of Asthma In Children



Abbreviations: BPAP, bilevel positive airway pressure; ICU, intensive care unit; IV, intravenous; PEF, peak expiratory flow.

sion of beta agonist receptors and prevent their downregulation when beta agonists are administered.[113] Inhaled corticosteroids are commonly employed as daily controller therapy in persistent asthma with the goal of preventing an exacerbation, but there is inadequate evidence to recommend their use alone in acute asthma. Early guidelines advised doubling the doses of inhaled corticosteroid during asthma exacerbations, but this practice has not been found to be effective in preventing exacerbations.[114,115] In contrast, new evidence suggests that quadrupling the dose of an inhaled corticosteroid, starting at the first appearance of worsening symptoms, may obviate the need for systemic corticosteroids;[116-119] however, the current guidelines do not support this practice.[28]

While clinical improvement after the use of systemic corticosteroids is not immediate, their early use has been shown to decrease hospitalization rates in children with acute asthma exacerbations.[120,121] A recent clinical trial demonstrated that triage nurse initiation of an oral corticosteroid before physician assessment is associated with reduced times to clinical improvement and discharge and reduced admission rates in children presenting with moderate-to-severe acute asthma exacerbations.[122]

Corticosteroids have also been shown to decrease the rate of relapse.[123] Prednisone (1-2 mg/kg/day) is commonly used as oral outpatient therapy and, in short bursts, has minimal side effects. Noncompliance with 5 days of therapy is common.[124] Some experts have also advocated for shorter courses of corticosteroids, with good results and increased compliance.[125-128] Prednisone and prednisolone at 1 mg/kg/day have been shown to be as efficacious with fewer side effects. Alternatively, 1 dose of dexamethasone (0.6 -1.0 mg/kg up to a max of 16 mg, by mouth, IM, or IV) has been shown to be as effective as 5 days of prednisone, with the additional benefits of decreased vomiting and increased compliance.[129,130] Smaller doses of dexamethasone (0.15 mg/kg and 0.3 mg/kg) have been shown to be as effective as the standard dose (0.6 mg/kg) for the treatment of croup.[131-133] It is possible that these lower doses are also effective for the treatment of asthma; however, additional data are necessary. Although offering no benefits over oral administration with regard to onset of action or potency, corticosteroids such as methylprednisolone may also be administered intravenously if oral administration is not tolerated or is not feasible.[134]

Theophylline

Previously, oral theophylline and its IV form, aminophylline, were commonly used to treat asthma. **(See Table 2, page 6.)** Once routinely used as maintenance therapy for asthma, chronic use of theophylline in children is now rare, and its uses in the ED are limited. Aminophylline has not shown any benefit for children with mild or moderate asthma exacerbations, even among those requiring hospitalization.[135-138] In critically ill children who are refractory to other therapies, aminophylline may improve lung function over several hours to days,[139-142] but it has not been shown to acutely reduce symptoms, prevent intubation, avoid ICU admission, or decrease length of stay.[135,143-145] In fact, a recent study indicates that aminophylline increases critical care unit length of stay and time to improvement.[146] In addition, aminophylline may result in undesirable side effects, particularly vomiting, headache, abdominal pain, palpitations, and intractable seizures.[137,144] Given its narrow therapeutic range that requires repeated assessment of serum drug levels, its high incidence of toxicity, and its increased time to improvement, the adverse effects of aminophylline outweigh the potential benefits in the management of acute asthma.

Class Of Evidence Definitions

Each action in the clinical pathway section of *Pediatric Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Non-randomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. *JAMA*. 1992;268(16):2289-2295.

Magnesium

For children who present with severe asthma exacerbations and do not respond to initial therapies, IV magnesium sulfate may be a therapeutic option. **(See Table 2, page 6.)** Acting as a smooth-muscle relaxant, magnesium is thought to compete for the calcium channel, resulting in smooth-muscle relaxation and promotion of bronchodilation. Although a definite therapeutic benefit has yet to be proven,[147] several studies suggest that it may decrease hospital admissions and improve lung function in children with severe exacerbations.[148-153] Magnesium is generally well tolerated at 25 to 75 mg/kg over 20 minutes, and it has a good safety profile and minimal side effects.[149,150,154-156] Emergency clinicians should be aware that hypotension can result secondary to the smooth-muscle relaxation effect, but it is uncommon. Recently, investigators have been evaluating the use of inhaled magnesium.[157,158] A recent Cochrane review concluded that nebulized magnesium sulfate, in addition to a beta agonist, improved pulmonary function and decreased hospital admission rates in patients with severe asthma.[159] Other studies have concluded that inhaled magnesium alone does not demonstrate any benefit in improvement in lung function compared to inhaled beta agonists alone.[160,161] Additional data in the pediatric population are necessary.

Leukotriene Receptor Antagonists

Leukotriene receptor antagonists (LTRAs) are nonsteroidal anti-inflammatory agents that are used in the treatment of asthma. **(See Table 2, page 6.)** As mediators of inflammation, leukotrienes are minimally affected by corticosteroids,[162] and the addition of an oral LTRA (such as montelukast) to daily asthma treatment can improve lung function and reduce exacerbations for many children.[162,163] Although LTRAs have some bronchodilator effects,[164] the current available evidence does not support routine use of oral LTRAs in acute asthma. A recent randomized double-blind placebo-controlled study conducted on 583 adult patients with acute asthma showed a significant improvement in FEV1 within 60 minutes after a dose of IV montelukast compared to placebo;[165] however, another recent randomized double-blind placebo-controlled study conducted on 276 pediatric patients with acute asthma showed no significant change in FEV1 within 60 minutes after a dose of IV montelukast compared to placebo.[166] LTRAs are a novel area for research, and further studies are needed to assess whether IV treatment is beneficial in children in the acute setting and whether LTRAs can reduce the risk of hospital admission.[167]

Ketamine

Ketamine, a dissociative agent with amnestic properties primarily used in the emergency setting for procedural sedation, may be another useful adjunct for children with severe asthma exacerbations. **(See Table 3.)** Ketamine promotes bronchodilation and bronchorrhea,[168] which may aid in clearing mucus plugs. At low doses, it has not been shown to be effective at bronchodilatation,[169] but, at sedative doses, it has been reported to provide significant improvement in respiratory distress for some individuals with refractory, life-threatening exacerbations, and it may obviate the need for endotracheal intubation.[170-172] Ketamine must be used with caution, since side effects include hypoventilation, hypertension, laryngospasm, and emergence agitation.[168] Ketamine is an excellent choice of sedative for children requiring rapid sequence intubation for life-threatening asthma.[170-172]

Emergency clinicians giving ketamine should be knowledgeable about the unique actions of this drug and should be aware of its potential side effects. Unlike most agents commonly used for sedation, ketamine preserves cardiopulmonary stability. Upper-airway muscle tone and protective airway reflexes are maintained, and spontaneous respiration is preserved.[173] When administered intravenously, ketamine must be given slowly to prevent laryngospasm and transient respiratory depression.[174] Ketamine should be used with caution in patients with seizure disorders, as it may lower the seizure threshold.[175] Additionally, ketamine increases cerebral blood flow, which may heighten intracranial and intraocular pressures.[176] Unpleasant recovery reactions, also referred to as emergence reactions, have been well documented in the adult literature;[168] however, recent data suggest that these reactions are uncommon in children and teenagers, and they are typically mild.[167,169,177] There is no evidence of any benefit from the prophylactic administration of benzodiazepines in children receiving ketamine.[170,178] Ketamine is the drug of choice to sedate children who require rapid sequence intubation for life-threatening asthma.[179,180]

Heliox

Heliox is an inert, safe, low-density gas that may be beneficial for the child with refractory status asthmaticus.[181] **(See Table 3.)** Heliox is a mixture of helium and oxygen, and it promotes less-turbulent airflow through narrowed airways. It is believed that the increased laminar flow may reduce the work of breathing and promote inhaled drug delivery.[130,181] While current evidence does not support the use of heliox in children with mild-to-moderate symptoms,[182] there is evidence to suggest that heliox may improve respiratory distress and prevent respiratory failure in select children with severe obstruction, particularly when used early in the treatment course.[180,182-184] In children requiring significant oxygen supplementation, heliox can be challenging to utilize, as oxygen concentrations > 30% significantly reduce the efficacy of heliox.[181-184]

Bilevel Positive Airway Pressure

Although respiratory failure is infrequent in asthma, children experiencing severe asthma exacerbations occasionally deteriorate, and respiratory support may be required. Bilevel positive airway pressure (BPAP) ventilation can offer significant respiratory support to select children with status asthmaticus and may allow these children to avoid intubation.[185,186] **(See Table 3.)** For children in severe distress, BPAP may facilitate administration of inhaled beta agonists. BPAP is safe and is generally well tolerated, and it may improve oxygenation and decrease the work of breathing.[186-188] The minority of children who do not tolerate BPAP are younger, although no clear age cutoff is cited in the literature. In 1 study, only 12% of subjects were unable to tolerate BPAP, with a median age of 4.5 years and a range of 2 to 11 years of age.[182] Clear guidelines for its use are not yet established,[189] but for the child with a severe exacerbation that is refractory to other interventions, BPAP may offer an alternative to intubation if it is used in a timely fashion.

Table 3. Interventions To Consider Prior To Intubation

Intervention	Description	Action	Considerations
Ketamine	Dissociative amnestic agent	Central-acting sedative with bronchodilatory properties	Induction agent; may cause raised blood pressure, raised intraocular pressure, and laryngospasm Dose: 2-3 mg/kg IV or 3-6 mg/kg IM
Heliox	Helium and oxygen blended gas	Reduces turbulent flow of oxygen to lower airway and reduces work of breathing	Reserved only for select patients with severe obstruction; no benefit in mild-to-moderate exacerbation
BPAP	Bilevel positive airway pressure	Noninvasive ventilation increases oxygenation Increases delivery of inhaled beta agonists and reduces work of breathing	Recommended for use in patients refractory to all other treatments or in those with impending respiratory failure

Abbreviations: BPAP, bilevel positive airway pressure; IM, intramuscular; IV, intravenous.

Intubation

For children with refractory symptoms and impending respiratory failure, intubation may be necessary. **(See Table 4.)** All other therapies should be attempted and maximized prior to intubation.

Indications for intubation in children with status asthmaticus include cardiopulmonary arrest, severe hypoxia, or rapid deterioration in mental state. Intubation and mechanical ventilation should be considered in a child who responds poorly to initial therapy and shows a rising PCO_2.[190] Patients must be preoxygenated with 100% oxygen, and hypotension should be anticipated as a result of positive pressure ventilation. A cuffed endotracheal tube with the appropriate age-based diameter should be used.[191] The formula commonly utilized to calcu-

Table 4. Considerations For Intubation Of A Child With Asthma

Indications
- Poor response to therapy
- Rising CO_2 (PCO_2 > 50 mm Hg)
- Severe hypoxia (PO_2 < 60 mm Hg)
- Waning mental status or fatigue
- Impending respiratory arrest
- Cardiopulmonary arrest

Preparation Steps
- Preoxygenate
- Establish IV access
- Consider fluid bolus to prevent acute hypotension
- Endotracheal tube (internal diameter = [age in y ÷ 4] + 3.5)
- Begin rapid sequence intubation (ketamine, +/- atropine, paralytic)

Goals
- SaO_2 > 91%
- Permissive hypercarbia
- pH > 7.2

Settings
- SIMV; volume control mode to prevent barotrauma
- TV = 5-6 mL/kg
- Respiratory rate = half normal for age
- I:E ratio = 1:3
- PEEP = 0-3 cm H_2O

Complications
- Hypotension
- Desaturation
- Pneumothorax
- Subcutaneous emphysema
- Tension pneumothorax
- Cardiac arrest

Abbreviations: I:E, inspiration to expiration ratio; IV, intravenous; PCO_2, partial pressure of carbon dioxide; PEEP, positive end-expiratory pressure; PO_2, partial pressure of oxygen; SaO_2, arterial oxygen saturation; SIMV, synchronized intermittent mechanical ventilation; TV, tidal volume.

late cuffed ETT size is: (age in y ÷ 4) + 3.5.[192] Rapid sequence intubation should proceed with premedication (if indicated), a sedative or anesthetic, and a rapid-acting paralytic. Pretreatment can be given to attempt to attenuate the adverse effects of laryngoscopy and intubation. In infants and children aged < 8 years, atropine may be given to blunt the reflexive bradycardia that may result from vagal stimulation during endotracheal intubation. Lidocaine may also be given to patients of all ages to diminish the reflexive bronchospasm that may occur in those with reactive airway disease as well as to prevent increases in intracranial pressure in patients with intracranial pathology.[193] However, limited data exist to support the routine use of atropine and lidocaine for rapid sequence intubation.[194] Ketamine is the preferred induction agent in patients with severe asthma due to its bronchodilatory action.[179] **(See the Treatment section, page 10.)** Succinylcholine and rocuronium are the 2 most commonly preferred neuromuscular blockade agents for rapid sequence intubation in most children.[194,196] Succinylcholine has a high side-effect profile (including malignant hyperthermia, hyperkalemia, bradycardia, and prolonged blockade) due to a deficiency or absence of pseudocholinesterase. In contrast, rocuronium is generally safe and has very few side effects, so it is often the preferred agent; however, the prolonged duration of action of rocuronium must be weighed against the risk of side effects associated with succinylcholine.[195]

Risk Management Pitfalls For Acute Asthma In Children

(Continued on page 13)

1. **"She didn't wheeze, so she couldn't have had asthma."**
   Although asthma is the most common cause of wheezing in children aged > 2 to 3 years, there are multiple other causes that should be considered. In the pediatric population, bronchiolitis, airway foreign bodies, and laryngomalacia/tracheomalacia are other common asthma imitators that may be difficult to distinguish from a reactive airway asthma.

2. **"He was in respiratory distress, but he wasn't wheezing, so he must not have had asthma."**
   Some patients present with such severe exacerbations that they are unable to generate enough air movement to wheeze. In fact, the "silent lung" can be an ominous finding and generally requires aggressive treatment. Additionally, patients with cough-variant asthma may not present with wheezing, but they may present with a history of persistent cough, particularly at night.

3. **"She couldn't have had asthma because she didn't respond to inhaled albuterol."**
   Patients with severe exacerbations or prolonged symptoms prior to presenting to the ED may exhibit poor initial response to albuterol. For these patients, continued aggressive bronchodilator therapy for their asthma is critical. The addition of systemic corticosteroids is crucial, as corticosteroids and beta agonists act synergistically. Steroids can increase the expression of beta agonist receptors and prevent their downregulation when beta agonists are administered.

4. **"I ordered a chest x-ray because all patients who present in respiratory distress should have one."**
   For most patients with asthma, chest x-rays add little to the clinical assessment. Abnormal chest x-rays are common in children with acute asthma, but they rarely result in changes to management. Chest x-rays may be helpful in children with fever > 39°C, hypoxia, focal abnormalities on examination, no family history of asthma, or in those who respond less favorably than expected to bronchodilator therapy. Chest x-rays may also be warranted in children with unilateral chest pain or differential wheezing to evaluate for foreign body, pneumothorax, or pneumomediastinum.

5. **"I was reassured because her blood gas reading was normal."**
   Since pulse oximetry and $ETCO_2$ monitoring are now readily available, blood gases are generally unnecessary in acute asthma management. There are currently no laboratory values that define respiratory failure; it is a clinical diagnosis. Furthermore, patients are often able to compensate for severe distress until failure is imminent; thus, reliance on a blood gas finding may provide a false sense of security.

6. **"I didn't prescribe corticosteroids because they are not indicated in mild exacerbations."**
   Corticosteroids combat the inflammatory component of asthma and are an integral part of acute asthma management. Even for mild exacerbations, steroids have been shown

The goals of ventilation in status asthmaticus are to: (1) maintain adequate oxygenation, (2) permit mild hypercarbia, and (3) maintain an arterial pH of > 7.2 by adjusting minute ventilation (peak pressure, tidal volume, and rate). Typically, slow ventilator rates with a prolonged expiratory phase, minimal end-expiratory pressure, and short inspiratory time are used in order to minimize dynamic hyperinflation, air trapping, and barotrauma.[196,197] The use of positive end-expiratory pressure (PEEP) in the child with asthma receiving mechanical ventilation is controversial.[198] In older children, use the volume control mode (synchronized intermittent mechanical ventilation [SIMV]) with settings of tidal volume of 5 to 6 mL/kg, respiratory rate approximately half of the normal for age, inspiration to expiration (I:E) ratio of 1:3, and PEEP of 2 to 3 cm of H_2O. In infants, pressure-controlled ventilation may be used, with peak inspiratory pressure adjusted to achieve adequate ventilation; the settings of rate, I:E ratio, and PEEP are the same as above.

If an intubated and ventilated child begins to deteriorate, promptly evaluate for: (1) tube displacement and obstruction, (2) signs of pneumothorax, and (3) equipment failure.[193] The DOPE mnemonic (**d**isplacement of endotracheal tube, **o**bstruction of endotracheal tube, **p**neumothorax, **e**quipment failure) may help identify the problem so it can be rapidly reversed. **(See Table 5, page 14.)** The most frequent complications with ventilation in children

Risk Management Pitfalls For Acute Asthma In Children

(Continued from page 12)

to improve symptoms, decrease the rate of relapse, and decrease return visits to the ED. Corticosteroids are best given early in an exacerbation.

7. **"He couldn't tolerate oral steroids, so I gave him inhaled corticosteroids. They are just as effective."**
Although inhaled corticosteroids are paramount in the daily control of asthma, they offer little in its acute management. For exacerbations, systemic corticosteroids are required to treat inflammation. For patients who cannot tolerate oral steroids, dexamethasone may be given IM or IV. If compliance is an issue, a single dose of dexamethasone by mouth is equally as effective as a 3- to 5-day course of oral prednisolone.

8. **"Inhaled anticholinergics like ipratropium should be given alongside bronchodilators throughout an acute exacerbation."**
Anticholinergics provide beneficial adjunct treatment by blocking cholinergic receptors and reducing bronchoconstriction. Although ineffective as monotherapy, ipratropium coadministered with beta agonists can improve lung function and reduce hospitalization rates in children with moderate to severe exacerbations in the acute setting. Ipratropium is generally given in the first 24 hours of treatment. Studies of children with acute exacerbations have failed to show any benefit to the addition of ipratropium beyond the first 24 hours.

9. **"For patients in status asthmaticus who remain in severe distress despite continuous bronchodilators, systemic corticosteroids, and multiple other adjunct treatments such as magnesium and/or terbutaline and/or epinephrine, intubation is the next step in management."**
Ketamine, heliox, and BPAP may be effective noninvasive treatment options that may be available for children in refractory status asthmatics. Heliox, an inert, low-density mixture of helium and oxygen, promotes less turbulent airflow through narrowed airways, which reduces the work of breathing and promotes inhaled drug delivery. Although unlikely to be beneficial for children with mild-to-moderate symptoms, heliox may improve respiratory distress and prevent respiratory failure in select children with severe obstruction. In addition, BPAP ventilation can offer significant respiratory support to select children with status asthmaticus and may allow patients to avoid intubation and ICU admission.

10. **"Once a child with asthma is intubated, the ventilator management is routine."**
Children with life-threatening asthma are often challenging to ventilate, and strategies to promote exhalation are helpful. Prolonged expiratory times with small tidal volumes and slow ventilatory rates can help avoid progressive hyperinflation. High ventilatory pressure is best avoided, as it can result in barotrauma and pneumothorax. The ideal ventilator strategy in patients with asthma is characterized as "low and slow." Aim for low pressures and slow respiratory rates.

with asthma are hypotension, oxygen desaturation, pneumothorax/subcutaneous emphysema, and cardiac arrest.[199] If hypotension and/or hypoxemia do not rapidly respond to fluid administration and alteration in ventilatory pattern, tension pneumothorax must be considered. For children refractory to all other therapies, extracorporeal membrane oxygenation may be a last resort.[197,200]

Controversies And Cutting Edge

Researchers are continuously seeking innovative ways to prevent, assess, and treat acute childhood asthma. A vaccine has recently been developed that may be effective in preventing acute asthma by targeting one of the most critical mediators of asthma pathology, interleukin-13 (IL-13). The vaccine may be capable of neutralizing excessive endogenous IL-13, which could suppress the accumulation of eosinophils and inhibit total IgE levels. The hope is that this vaccine will successfully prevent airway inflammation and epithelial cell proliferation as seen in acute asthma, but more research is needed.[201]

Several cutting-edge biomarkers that may be able to quantify disease activity and/or predict exacerbations are currently being evaluated. Levels of exhaled nitric oxide, urinary leukotriene E4, and sputum eosinophils may soon be available as assessment tools that might permit more accurate treatment titration.[202-206]

New treatments are also under development, including therapies specifically targeting immunoglobulin E (IgE). Omalizumab, a monoclonal anti-IgE antibody, is approved for children aged > 12 years with moderate to severe asthma as part of their maintenance therapy, but it has yet to be studied in acute exacerbations.[207-210] Nebulized lidocaine has been demonstrated to inhibit bronchospasm, although the drug is associated with seizures and fatalities in overdose and is not currently being developed commercially for use in asthma.[211] In vitro studies have shown that nebulized heparin decreases inflammation, smooth-muscle proliferation, eosinophil recruitment, and fibrosis.[212-214] Whether heparin is clinically beneficial in the management of asthma is the subject of ongoing investigation.

In addition, numerous agents with anti-inflammatory properties have been studied in an effort to eliminate or decrease the underlying inflammation that characterizes chronic asthma. These agents include methotrexate,[215] cyclosporine,[216] colchicine,[217] hydroxychloroquine,[218] IV immunoglobulin,[219] macrolide antibiotics,[220] etanercept, and infliximab.[221,222] At present, no guidelines support the use of these agents, and additional data are necessary.

Many patients with asthma are sensitized to fungi such as *Aspergillus*, *Candida*, and *Trichophyton*.[223,226] A recent cross-sectional study found that almost 60% of patients with severe persistent asthma

Table 5. The DOPE Mnemonic For Sudden Deterioration Of The Intubated Child

D	**D**isplacement of endotracheal tube
O	**O**bstruction of endotracheal tube
P	**P**neumothorax
E	**E**quipment failure

Time- And Cost-Effective Strategies

1. **Avoid diagnostic testing for acute asthma.** Unless the diagnosis is in question, tests such as chest x-rays and blood gases rarely add to the clinical assessment of acute asthma. Measurements of pulmonary function other than peak flows are generally not feasible from the ED.
2. **Consider using dexamethasone instead of prednisolone/prednisone for acute exacerbations.** Corticosteroids are critical to the treatment of acute asthma and have been shown to decrease not only the need for admission but also the rate of relapse and return visits to the ED. Single-dose dexamethasone offers equivalent results compared to a 3- to 5-day course of prednisolone/prednisone and has the advantage of increased compliance and decreased cost.
3. **In the ED, initiate inhaled corticosteroids for daily controller therapy.** Prescribing inhaled corticosteroids as daily controller therapy for children with persistent asthma may decrease the frequency of exacerbations and the subsequent need for acute visits. While this practice is generally initiated in the outpatient setting, the ED provides another point of contact for patients with poorly controlled asthma and is an opportune setting to educate patients (and their parents) and start them on controller therapy.
4. **Consider using adjunct therapies for refractory acute asthma.** Although not routinely indicated, several adjunct therapies exist that may be helpful in children with severe asthma not responding to inhaled beta agonists and corticosteroids. Adjunct therapies such as magnesium, heliox, and BPAP in the ED have all been shown to be safe and well tolerated, and they may prevent admission to the ICU.

enrolled in the study had evidence of fungal sensitization.[225] Researchers hypothesize that exposure to these airborne fungi may lead to airway colonization, which may incite an ongoing allergic reaction. Prolonged antifungal treatment with itraconazole has demonstrated improvements in Asthma Quality of Life Questionnaire score (http://www.qoltech.co.uk/index.htm), morning peak flows, and total serum IgE levels; however, these improvements were not sustained after discontinuation of itraconazole.[224]

Finally, several nonpharmacologic approaches to asthma management have been proposed, including acupuncture, massage, breathing exercises, and dietary alterations.[226-234] Additionally, there is increasing evidence to support the use of traditional Chinese herbal therapy for asthma.[235,236] Clinical trials are currently being conducted in this area. At present, data from well-controlled trials regarding use of alternative forms of therapy in both acute and chronic settings are limited. As a result, it is difficult to compare these interventions with currently available forms of therapy or to make specific recommendations regarding their use.

Disposition

Determining who is safe to discharge and who requires hospitalization can be challenging in children with asthma exacerbations. Clearly, children with hypoxia or moderate-to-severe symptoms after treatment should be admitted. Peak flows are a helpful assessment tool in children who are able to perform them. Often, children with a posttreatment peak flow < 70% of expected will require admission, and peak flows < 40% may trigger admission to the ICU.[29] Even among children with a good initial response, factors such as the presence of wheezing for 2 or more days prior to presentation or a history of frequent recent acute asthma visits, fever, or severe persistent asthma may place them at risk for a poor short-term outcome.[237] For children who are stable for discharge, close follow-up with a primary care provider is essential. Interventions shown to increase short-term patient follow-up include free medications, transportation vouchers, assistance in scheduling appointments, and follow-up telephone coaching.[238,239]

Controller therapy is strongly recommended for children with persistent asthma. As mentioned earlier, inhaled corticosteroid therapy is the most common daily controller therapy and has been shown to improve asthma control with less need for rescue medications, fewer urgent visits, fewer hospitalizations, and fewer asthma deaths.[240-242] Despite the benefits, however, many children are not treated.[243,244] For some children, the ED may be the only point of contact with the medical system, and it is an appropriate place to initiate therapy in conjunction with a child's primary care provider.[244] Daily controller therapy is indicated in children reporting symptoms 2 or more days per week, using rescue medications 2 or more days per week, or experiencing nighttime symptoms 2 or more times per month. Inhaled corticosteroids (eg, budesonide or fluticasone) are generally preferred, but oral montelukast may be another option. For children already on inhaled corticosteroids but with persistent symptoms, the dose of inhaled corticosteroid may be increased or montelukast may be added to the daily regimen.[29]

Summary

Given the widespread prevalence of asthma and the frequency with which children present to the ED with exacerbations, pediatric emergency clinicians must be proficient in the assessment and management of asthma. Timely and aggressive use of inhaled beta agonists and systemic corticosteroids are the foundation of acute asthma treatment for most children, but several adjunct therapies, including magnesium, terbutaline, epinephrine, and heliox (at some institutions) are available in the ED to treat more severe exacerbations. Additionally, noninvasive BPAP is available to provide additional respiratory support for children progressing to ventilator failure as an effort to avoid endotracheal intubation and mechanical ventilation. In the uncommon case of impending respiratory failure, endotracheal intubation may be necessary. In such cases, ketamine conveniently provides both sedative and bronchodilatory effects. Although asthma is a common chief complaint in the ED and a significant chronic disease for many children, numerous opportunities for intervention are available.

Case Conclusion

You rapidly identified this child as having a severe asthma exacerbation needing aggressive management. You gave 2 doses of albuterol and ipratropium and started continuous albuterol. You also administered a dose of a corticosteroid. The patient continued to have poor air entry and severe distress characterized by subcostal retractions, intercostal retractions, nasal flaring, and head bobbing. You placed an IV and administered magnesium and a normal saline bolus. As you reassessed the patient frequently, you noted that her air entry improved modestly, but you appreciated diffuse wheezing. She continued to be quite tachypneic and appeared extremely anxious. You gave a dose of epinephrine IM and called the pediatric ICU in anticipation of escalating care to either BPAP or, possibly, intubation. You continued to monitor her closely, and you noted that her respiratory rate slowly decreased over the next hour, she had modest improvement in her work of breathing, and her anxiety lessened. After 2 hours, she was able to speak in full sentences and perform a peak flow, which was 50% of expected. You were able to transition her

from continuous albuterol nebulizers to intermittent treatments every 60 minutes, but her oxygen saturations remained 90% while on room air. You contacted her primary care provider and admitted her to the hospital for continued treatment of her acute asthma exacerbation. She remained hospitalized for 3 days, after which she was discharged on an increased dose of fluticasone as a daily controller medication.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study will be included in bold type following the references, where available. The most informative references cited in this paper, as determined by the author, will be noted by an asterisk (*) next to the number of the reference.

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1. The mainstays of acute asthma treatment include bronchodilation via beta agonists and anti-inflammation via corticosteroids. Inadequate anti-inflammatory therapy can lead to all of the following EXCEPT:
a. Increased mucus secretion
b. Increased airway hyperresponsiveness
c. Increased inspiratory time
d. Irreversible airway thickening

2. Risk factors for life-threatening exacerbations include all the following EXCEPT:
a. Presence of eczema and/or food allergies in addition to asthma
b. Multiple ED visits and admissions within the previous year
c. Prior admission to the ICU
d. Hypoxia

3. Respiratory failure in asthma is clearly defined based on age-specific blood gas results.
a. True
b. False

4. Which of the following diagnostic studies is indicated in the routine management of an acute asthma exacerbation?
a. Chest x-ray
b. Peak flow
c. ABG
d. Complete blood count with differential count

5. Compared to albuterol, levalbuterol has been shown to have a modest decrease in which of the following?
a. Tremor
b. Tachycardia
c. Nervousness
d. Palpitations

6. Increasing the dose of inhaled corticosteroids during an acute exacerbation is equally effective as a short course of systemic corticosteroids and is currently recommended.
a. True
b. False

7. For acute asthma exacerbations, all of the following are acceptable methods of administering systemic corticosteroids EXCEPT:
a. Oral prednisone
b. Oral dexamethasone
c. Inhaled fluticasone
d. IV methylprednisolone

8. For patients who fail to respond to inhaled bronchodilators and systemic steroids, evidence best supports the use of which adjunct therapy in the ED?
a. Magnesium sulfate
b. Aminophylline
c. Epinephrine
d. Terbutaline

9. **Heliox may be beneficial in a child with refractory status asthmaticus by:**
   a. Clearing mucus and debris from the distal airways
   b. Acting on the airway smooth muscle to promote bronchodilation
   c. Decreasing turbulent airflow through the airway
   d. Minimizing inflammation and edema of the airway

10. **For an intubated child with a severe asthma exacerbation, which of the following settings is appropriate?**
   a. A prolonged inspiratory time to help correct the I:E ratio
   b. A large tidal-volume to maximize air entry
   c. A slow ventilatory rate to minimize progressive hyperinflation
   d. A high pressure to overcome airway obstruction

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