Pediatric Emergency Medicine Reports

The Practical Journal of Pediatric Emergency Medicine

Volume 18, Number 4 / April 2013 **www.ahcmedia.com**

Authors:

Ronald M. Perkin, MD, MA, Professor and Chairman, Department of Pediatrics, Brody School of Medicine at East Carolina University, Greenville, NC.

Matthew R. Ledoux, MD, Division Chief, Division of Pediatric Critical Care and Sedation Services, Brody School of Medicine, East Carolina University, Greenville, NC.

Peer Reviewer:

Christopher J. Haines, DO, FACEP, FAAP, Associate Professor of Pediatrics and Emergency Medicine, Drexel University College of Medicine, Director, Department of Emergency Medicine, Medical Director, Critical Care Transport Team, St. Christopher's Hospital for Children, Philadelphia, PA.

Statement of Financial Disclosure

To reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Dietrich (editor), Dr. Skrainka (CME question reviewer), Dr. Perkin (author), Dr. Ledoux (author), Dr. Haines (peer reviewer), Ms. Mark (executive editor), and Ms. Hamlin (managing editor) report no relationships with companies related to the field of study covered by this CME activity.

AHC Media

Acute Severe Asthma

Asthma is a common problem in the emergency department (ED), with many children having significant exacerbations. The ED physician must be prepared with a versatile approach to rapidly stabilize the patient. This article comprehensively reviews the approach to a child with acute severe asthma, emphasizing management alternatives.

— Ann M. Dietrich, MD, Editor

Introduction

Asthma is the most common chronic pediatric respiratory disease and remains one of the most common reasons children in the United States require hospitalization. Acute exacerbations of asthma can be life-threatening. While most of these acute exacerbations can be managed successfully in the emergency department, a few children with severe exacerbations may require admission to the intensive care unit. These severe exacerbations have been referred to as status asthmaticus, acute severe asthma, life-threatening asthma, or near-fatal asthma.[1-5] The following review explores the current understanding of epidemiology, physiology, and treatment of acute severe asthma in children.

Definition

The exact definition of acute severe asthma or status asthmaticus varies between authors.[1] For this article, the authors define acute severe asthma as a wheezing patient who does not respond to initial doses of inhaled bronchodilators.

Risk Factors

Although few children have life-threatening asthma episodes, these episodes may be associated with potential mortality, a high morbidity, and a high cost of treatment.[3]

There appear to be two clinical subsets of children who die from acute severe asthma.[3,6] The first group of children with fatal asthma has a long history of poorly controlled asthma, often with a previous history of respiratory failure. In these children, death occurs secondary to acute respiratory failure and asphyxia or complications associated with mechanical ventilation.[6-8] Pathologic examination in these children reveals extensive bronchial mucous plugging, edema, and eosinophilic infiltration of the airways. In the second group, the children have only a mild history of asthma, experience the sudden onset of bronchospasm, and can rapidly progress to cardiac arrest and death. If recognized and managed early, these children respond to beta-adrenergic agonists and mechanical ventilatory support better than children with the slow-onset fatal asthma.[3,6,9,10] Pathologic examination in this rapidly fatal group of children shows empty airways devoid of mucous plugging with a greater proportion of neutrophils rather than eosinophils.[3,6,9,10] Although the existence of this second type of fast onset has been controversial, many studies have shown a high percentage of

Executive Summary

- Pulsus paradoxus is a valuable clinical sign of disease severity in children with asthma.
- Hypoxemia appears to be an independent risk factor for both hospitalization and increased length of stay.
- While antibiotics are not recommended in the therapy of acute asthma, recent evidence suggests that antibiotic therapy targeted to patients with evidence of atypical bacterial infection may confer additional advantage to standard therapy alone.
- Unfortunately, the majority of studies in children with exacerbations of asthma suggest that there is not a clinical benefit to the use of levalbuterol versus racemic albuterol.
- The use of intravenous terbutaline is not recommended by the current National Asthma Education Program Expert Panel Report.

death occurring within one to two hours of onset of symptoms.[3,6-13] Some of these studies reveal an overrepresentation of obese children and African-American children in this rapidly progressive, type 2 cohort, which invites speculation about an alternative pathophysiology or possible health care disparities in this group of children.[3,14] These studies indicate the need to recognize children at risk for sudden asphyxial asthma. Accordingly, several authors have attempted to define risk factors for children who die from asthma.[3,6,15,16] (*See Table 1.*) Patients who have had a life-threatening episode of asthma should receive ongoing care from a physician who specializes in asthma.[8,15]

Table 1. Risk Factors for Potentially Fatal Asthma

- History of previous attack with:
  - — Severe, rapid progression of symptoms
  - — Respiratory failure requiring endotracheal intubation and ventilatory support*
  - — Pediatric intensive care unit admission
- Attacks precipitated by food allergy
- Denial or failure to perceive the severity of illness
- Noncompliance
- Lack of social support network (dysfunctional family)
- Non-white children (especially African-American and Hispanic children)

*May include noninvasive positive pressure ventilation

Adapted from: Reference 6.

Pathogenesis/ Pathophysiology

Asthma is now considered a disease of inflammation. During the past two decades, tremendous gains have been made with regard to the understanding of asthma.[6,17-19] Asthma frequently begins during childhood and is often associated with atopy, the genetic susceptibility to produce IgE specific to common airborne allergens. Atopic children respond to these airborne allergens with a T helper type 2 (Th2) immune response. Th2 cells produce interleukin (IL)-4, IL-5, IL-6, IL-9, and IL-13 and are involved in activating B cells for the production of immunoglobulins, particularly IgE. Th2 responses stimulate antibody-mediated responses and activation of mast cells and eosinophils. All of these factors result in the main pathophysiologic components of the asthmatic response — airway inflammation, bronchial airway hyper-responsiveness, airway remodeling, and reversible airway obstruction.

"Severe airway obstruction resulting from inflammation, bronchoconstriction, and excessive mucus production is at the heart of the gas exchange abnormalities and symptomatology in children with acute severe asthma."[6] The increase in airway resistance leads to an increase in the work of breathing and reductions in FEV_1 and FEV_1/FVC.[6,20] In acute severe asthma, transpulmonary pressures greater than 50 cm H_2O are not uncommon.[19] As the degree of airway obstruction worsens, expiration becomes active rather than passive; air flow rates are low and expiratory times become progressively longer. Inspiration often occurs before termination of the previous expiration, resulting in air-trapping and lung hyperinflation and, because of this, residual volume and functional residual capacity is increased.[20]

Air-trapping and lung hyperinflation lead to an intrinsic positive end-expiratory pressure (PEEPi), or auto-PEEP, a phenomenon also termed dynamic hyperinflation. Dynamic hyperinflation has several adverse effects in the cardiovascular and respiratory systems. The increased lung volumes shift tidal breathing to a less compliant portion of the pressure volume curve. In addition, flattening of the diaphragm produces additional mechanical disadvantage.[21] Dynamic hyperinflation also results in premature closure of

the airways, which produces a further increase in air resistance, thereby worsening gas exchange. These factors collectively increase the work of breathing and increase the physiologic dead space. The gas exchange abnormalities produced by dynamic hyperinflation result in ventilation-perfusion mismatch.[6]

The effects of dynamic hyperinflation on cardiorespiratory interactions are quite complex.[22] Right ventricular afterload is increased by a combination of factors, including lung hyperinflation (increased pulmonary vascular resistance), hypoxic pulmonary vasoconstriction, and acidosis. During expiration, the increase of intrathoracic pressure secondary to dynamic hyperinflation impedes systemic venous return, worsening left ventricular preload. During inspiration, the exaggerated negative intrathoracic pressure required to overcome airway resistance increases left ventricular afterload.[6,22] These changes can be detected clinically as an increase in the pulsus paradoxus.[23,24] Pulsus paradoxus is a valuable clinical sign of disease severity in children with asthma.[1,24]

Clinical Presentation and Assessment

The onset of asthma symptoms may result from exposure to "triggers" such as exercise, air pollutants, weather conditions, viral infections of the upper respiratory tract (particularly rhinovirus and respiratory syncytial virus), or allergen exposure, all of which increase inflammation in the lower airways.[2]

The presentation of acute severe asthma varies by severity, asthmatic trigger, and patient age.[2] This variability often leads to poor recognition of the severity of illness, which, in turn, results in greater morbidity.[25,26] The clinical examination can be misleading, and key clinical features must be taken into consideration when assessing a patient with acute asthma. [5,25-27] (*See Table 2.*)

The immediate assessment of patients with acute asthma exacerbations should include the degree of respiratory distress (ability to speak, respiratory rate, use of accessory muscle, air entry, inspiratory:expiratory ratio), degree of hypoxia (cyanosis, pulse oximetry, level of consciousness), and cardiovascular status (heart rate and rhythm, pulsus paradoxus, blood pressure).

Accessory muscle use, wheeze, and tachypnea might diminish as the patient tires.[5] This may be misinterpreted as an improvement, when in fact the patient has worsened. Clinicians must pay close attention to these changes.

There are many "asthma scores" based on these observations that have been developed to assess the

Table 2. Markers of Acute Severe Asthma

- Inability to speak in full sentences or unable to speak at all (infants will have shorter periods of crying and will have difficulty or will stop feeding)
- Drowsy/confused/altered level of consciousness
- Seated upright; unable to lie supine
- Respiratory rate is elevated (bradypnea is an ominous sign)
- Use of accessory muscles, tracheal tugging, head bobbing
- Loud wheeze; quiet chest is ominous sign
- Tachycardia; bradycardia is ominous sign
- Pulsus paradoxus (> 15 mmHg drop with inspiration); absence may indicate fatigue
- Decreased FEV_1 or PEFR < 40% of best or predicted
- Oxygen saturation < 90% in room air

Table 3. Assessing Asthma Severity
Becker Asthma Score

Score	Respiratory Rate (per min)	Wheezing	I/E Ratio	Accessory Muscle Use
0	< 30	None	1:1.5	None
1	30-40	Terminal expiration	1:2	1 site
2	41-50	Entire expiration	1:3	2 sites
3	> 50	Inspiration and entire expiration	> 1:3	3 sites or neck strap muscle use

Score ≤ 4 = mild
Score > 4 to < 7 = moderate
Score ≥ 7 = severe (needs PICU)

Source: Reference 29

Table 4. Asthma Severity

Parameter*	Mild	Moderate	Severe	Imminent Respiratory Arrest
Breathlessness	Walking Can lie down	Talking (infant: shorter cry/difficult feeding); Prefers sitting	At rest (infant will stop feeding) Hunched over	
Talks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy/confused
Respiratory rate	Increased	Increased	Increased	Bradypnea
Accessory muscles and suprasternal retractions	Usually not	Usually	Usually	Paradoxical movement
Wheeze	Moderate (end expiration)	Loud	Usually loud	Absence of wheeze
Pulse/min	< 100	100-120	> 120	Bradycardia
Pulsus paradoxus (mm HG)	Absent (< 10)	10-25	> 25	Absence suggests respiratory muscle fatigue
PEFR (after bronchodilator)	> 80%	60-80%	< 60%	
PaO2 on room air and/or PaCO2 (mm Hg)	Normal (need not be tested)	< 45	> 45	
Saturation	> 95%	91-95%	90% or less	

*The presence of several parameters, but not necessarily all, indicates the severity of the attack
PEFR = peak expiratory flow rate

Source: Reference 30.

severity of the asthma exacerbation; at least 18 different "asthma scores" are available.[3,28,29] The Becker asthma score is a quick assessment of severity by using respiratory rate, wheezing, inspiratory:expiratory ratio, and accessory muscle use.[30] (*See Table 3.*) A score greater than 4 is considered moderately severe status asthmaticus, while a patient with a score of 7 or greater may be admitted to the pediatric intensive care unit (PICU). A more detailed asthma score provided by the National Heart, Lung, and Blood Institute is given in Table 4.[31] The emergency physician also needs to consider the wide range of potential complications, as attention to these problems when assessing and managing acute asthma might significantly improve outcome.[5] (*See Table 5.*)

Pulse oximetry may be useful to differentiate between patients who are likely to improve with therapy and those who are likely to progress to respiratory failure.[6] An increase in oxygen saturation following albuterol nebulization predicts patients who are likely to improve, and respiratory failure rarely occurs in patients with an initial oxygen saturation greater than 92%.[6] The degree of hypoxemia significantly correlates with the degree of airway obstruction, as determined by FEV_1.[32] Furthermore, hypoxemia appears to be an independent risk factor for both hospitalization and increased length of stay.[33-35]

Hypoxemia is multifactorial in origin, resulting from a combination of factors including ventilation-perfusion mismatch, alveolar hypoventilation, and hypercarbia. Significant hypoxemia, however, is relatively uncommon in children with acute severe asthma.[6,19,35] Therefore, the presence of significant hypoxemia should alert the physician to search for some additional underlying cause, such as atelectasis secondary to mucous plugging, pneumonia, or pneumothorax.[5,6]

The degree of airway obstruction is rapidly determined by assessment of pulmonary function using the FEV_1 and the peak expiratory flow rate (PEFR). Although FEV_1 is considered to be the more reliable test, the PEFR is more easily obtained. Unfortunately, the correct performance of both tests is extremely dependent on the patient's cooperation and effort; the values obtained may vary widely and may not be reliable. PEFR and FEV_1 less than 30-50% of predicted, or of

the patient's personal best, indicate severe airflow obstruction.[6,27] If the child is in significant distress, the use of pulmonary function tests may need to be deferred.

Monitoring carbon dioxide levels, invasively or non-invasively, might be useful. Although initial $PaCO_2$ may be below normal levels, a progressive increase in $PaCO_2$ is considered an early warning sign of severe airway obstruction and impending respiratory failure.[6]

Metabolic acidosis is well described in patients with acute severe asthma.[36,37] One reported cause of metabolic acidosis is accumulation of lactic acid, presumably from a prolonged and marked increased work of breathing; additional factors include tissue hypoxia secondary to oxygen supply/demand imbalance in respiratory muscles, dehydration accompanying acute severe asthma from poor oral intake and increased insensible losses, and decreased cardiac output associated with hyperinflation.[6] These causes are often labeled as type A and represent impairment in oxygen delivery as the cause of lactic acidosis. Other authors have shown that lactic acidosis is common in acute severe asthma but is primarily type B lactic acidosis, which occurs in the presence of normal oxygen delivery.[36] Type B lactic acidosis is often seen with the use of beta-adrenergic agents to treat acute severe asthma, which leads to derangements in glucose metabolism and the development of type B lactic acidosis.[36,38,39] Support for this mechanism includes clinical observations demonstrating a resolution of lactic acidosis with decreasing or discontinuation of bronchodilator therapy.[36] Lactic acidosis developing during acute severe asthma is important to recognize because the compensatory hyperventilation that ensues to maintain body pH may lead to increased dyspnea. Lactic acid-induced hyperventilation has been mistaken as a sign of worsening airway obstruction, leading to inappropriate escalation of bronchodilator therapy, and has contributed to respiratory failure and the institution of mechanical ventilation.[36]

Table 5. Asthma Complications

- Pneumothorax
- Pneumomediastinum
- Pneumopericardium
- Pulmonary interstitial emphysema
- Pneumoretroperitoneum
- Cardiac arrhythmias
- Myocardial ischemia
- Mucous plugging
- Atelectasis
- Pneumonia
- Electrolyte imbalance (hypokalemia, hypomagnesemia, hypophosphatemia)
- Lactic acidosis
- Hyperglycemia

The mechanism for lactic acidosis during acute severe asthma is important to determine because effective treatment must address the underlying cause. If it is determined that the lactic acidosis is primarily type B associated with normal oxygen delivery and in the presence of adequate ventilation, a reduction in beta-adrenergic therapy may be appropriate.[36]

Hypokalemia is the most common electrolyte abnormality in children with acute severe asthma and is a well-recognized complication of beta-agonist administration.[38,40,41] In addition, glucocorticoids used in the management of asthma can result in unwanted mineralocorticoid effects, leading to hypokalemia.[40,41]

Serum potassium levels should be monitored and, if needed, replaced if sufficiently low. Oral supplementation should be avoided due to the patient's respiratory distress and supplementation should be given intravenously.

Another common abnormality seen is hyperglycemia. Treatment with beta-agonists and systemic steroids has been associated with changes in glucose metabolism.[42] The resultant hyperglycemia may result in osmotic diuresis and dehydration; this would be aggravated by utilization of intravenous fluid supplements containing glucose, a common practice during hospitalization of children.

Complicating the hyperglycemia, fluid balance abnormalities are also seen in children with acute severe asthma, and these children are often dehydrated because of increased insensible fluid losses from the respiratory tract, coupled with poor oral intake of fluids. Dehydration may produce thicker, more tenacious bronchial secretions, leading to worsening bronchial mucous plugging. Although the majority of children require intravenous fluid rehydration, an inappropriate type of fluid (hypotonic or glucose-containing) or overzealous fluid administration may lead to fluid retention and pulmonary edema.[6,42-45] Children with acute severe asthma may have elevated plasma antidiuretic hormone levels and are at risk for hyponatremia and fluid overload if given large volumes of hypotonic fluid.[44-46] In addition, the high negative transpulmonary pressures associated with acute severe asthma promote fluid accumulation around the respiratory bronchioles, leading to pulmonary edema and worsening respiratory status.[6,47]

Management

Any child with acute severe asthma requires cardiorespiratory monitoring and close attention to fluid

Table 6. Grades of Evidence of Interventions in Acute Severe Asthma

Grade A
• Oxygen should be administered to maintain peripheral oxygen saturation between 0.89 to 0.95
• Use inhaled β2-agonists as primary bronchodilators
• Give steroids in all cases of acute asthma
Grade B
• Add nebulized ipratropium bromide
Grade C
• A single dose of magnesium sulfate can be used
Grade D
• A single dose of intravenous montelukast should be considered

The quality of the evidence was given a grade of A, B, C, or D for high, moderate, low, and very low, respectively.

Adapted from: Reference 4

balance and neurologic status. A comfortable and supportive environment can ameliorate the situational anxiety, although hypoxemia and anxiety will also lead to agitation and restlessness. Sedatives should be avoided in the nonintubated patient with acute severe asthma, as it may cause hypoventilation and worsen the respiratory distress leading to failure.

There has been a great deal of interest in phenotypic classification of severe or difficult to treat asthma.[4] Although childhood asthma is generally an allergic, eosinophilic inflammatory disease, many patients with severe asthma have significant neutrophil inflammation.[4,48,49] Neutrophilic inflammation may be due to chronic infection with organisms such as *Mycoplasma* or *Chlamydia*.[50,51] While antibiotics are not recommended in the therapy of acute asthma, this recent evidence suggests that antibiotic therapy targeted to patients with evidence of atypical bacterial infection may confer additional advantage to standard therapy alone.[50,51] Additional use of antibiotics involves using macrolide antibiotics as immunomodulatory drugs that can reduce neutrophil inflammation and decrease asthma severity and the need for corticosteroids.[4,50]

Oxygen Therapy

Hypoxemia is always present in life-threatening asthma and is a major contributing factor to asthma death.[4,52] The administration of supplemental oxygen is considered standard therapy for children with acute severe asthma/status asthmaticus.[6,31] (*See Table 6.*) While oxygen therapy is essential, unregulated oxygen therapy, the provision of high amounts of oxygen beyond what is necessary to obtain physiologic oxygen saturation levels, has been shown to be unnecessary and potentially harmful.[4,53,54] Giving 100% oxygen can depress compromised ventilation and increase the partial pressure of carbon dioxide ($PaCO_2$). Therefore, some authors have recommended that only sufficient oxygen be administered to maintain peripheral oxygen saturation (SpO_2) between 89-94%.[4] It must be remembered that some bronchodilators, particularly the beta-agonists, reduce hypoxic pulmonary vasoconstriction and, thus, worsen hypoxemia by increasing V/Q mismatch.[6] Therefore, these medications should be administered concurrently with supplemental oxygen.[6,52]

Systemic Corticosteroids

With the recognition that airway inflammation plays a prominent role in the pathophysiology of acute severe asthma, corticosteroids are standard treatment for children with acute severe asthma. (*See Table 6.*) Based on the wealth of available evidence, expert opinion and published guidelines recommend the administration of corticosteroids in the management of acute severe asthma/status asthmaticus within the initial 48 hours of treatment.[2,6,31] A 2003 Cochrane Database review supports improved outcomes for children who receive corticosteroids early in their emergency department course.[55] Corticosteroids speed the resolution of airflow obstruction, potentiate the effects of beta-agonist therapy, and have the potential to decrease hospitalization for sicker patients.

The optimal dosing of systemic corticosteroids for children with acute severe asthma remains an unresolved issue.[6,56] Several studies suggest that high-dose corticosteroid therapy offers few advantages over low-dose corticosteroids in the treatment of acute severe asthma.[6] Typically, oral or intravenous corticosteroids (e.g., methylprednisolone) have been given at a dose of 1-2 mg/kg as frequently as every 6 hours during an acute severe asthma attack. Although corticosteroids are often administered intravenously, data do not show that this is more effective than oral steroids, and there are no data that show that giving prednisone 2 mg/kg/day (80 mg maximum for older children and adults) is less effective than higher doses.[4] (*See Table 7.*) Oral steroids are generally not recommended for children with acute severe asthma and impending respiratory failure because of the increased risk of intubating a patient with a full stomach.

Table 7. Common Drugs and Doses in Acute Severe Asthma

Corticosteroids

- Usually administered intravenously
- Methylprednisolone: 2-4 mg/kg/day, with a maximum dose of 60 mg/day (adult maximum 125 mg/day)

Beta-agonist (Albuterol)

- Hourly or continuously delivered albuterol via nebulizer
- Hourly: 0.15 mg/kg every hour (minimum 2.5 mg; maximum 5 mg)
- Continuous: 0.3-0.5 mg/kg/hour up to 20 mg/hr (consider 10 mg/hr for children who weigh 5-10 kg; 15 mg/hr for children who weigh 10-20 kg; and 20 mg/hr for children who weight > 20 kg)

Beta-agonist (Terbutaline)

- Continuous intravenous infusion
- Loading dose: 2-10 mcg/kg
- Infusion dose: 0.5 mcg/kg/min; dose may be increased by 0.1-0.2 mcg/kg/min every 15-30 min; doses up to 10 mcg/kg/min have been reported

Ipratropium bromide

- 250 mcg/dose for children < 20 kg; 500 mcg/dose for children ≥ 20 kg
- Consider 3 doses given every 4-8 hours

Magnesium sulfate

- 50-75 mg/kg (max dose 2 grams given every 4-6 hours)
- Optimal magnesium level 4-5.5 mg/dL

Aminophylline

- Aminophylline is the ethylenediamine salt of theophylline; pharmacokinetic parameters are those of theophylline; 100 mg aminophylline = 80 mg theophylline
- Monitoring parameter: theophylline level; recommend level < 15 mcg/mL (see text)
- Loading dose (inpatients not currently receiving aminophylline or theophylline): 5-6 mg/kg (based on aminophylline) over 20-30 minutes
- Continuous infusion follows, and dose depends on patient age and desired level
- Suggested infusion rates:
  - 6 months-1 year: 0.7 mg/kg/hr aminophylline
  - 1-9 years: 1.2 mg/kg/hr aminophylline
  - 10-16 years: 0.9 mg/kg/hr aminophylline
- Metabolism is influenced by multiple medications
- Effect as a respiratory muscle inotrope is dose-dependent; lower doses are effective

Leukotriene Modifiers

- Montelukast (Singulair) oral tablets
- Dose:
  - 1-5 years: 4 mg po QD
  - 6-14 years: 5 mg po QD

Significant side effects may occur with the use of steroids, particularly if used at a high dose; these include hyperglycemia, hypertension, and acute psychosis.[2,57] Prolonged steroid use may cause immunosuppression, hypothalamic-pituitary-adrenal axis suppression, osteoporosis, myopathy, and weakness.[2,4,58,59]

Currently available evidence does not support the use of inhaled steroids in lieu of systemic corticosteroids.[6] While it is most common to discontinue inhaled corticosteroids in patients with acute severe asthma, the concomitant use of inhaled steroids along with systemic steroids may provide

additional benefit for some, but not all, patients.[60,61]

Beta-Adrenergic Agonists

Table 7 provides details on the bronchodilators currently used in the management of acute severe asthma. Beta-2-adrenergic receptor agonists have emerged as the single most potent class of bronchodilator available.[26,62] Non-selective agonists such as isoproterenol or epinephrine are associated with a higher incidence of significant side-effects (i.e., myocardial ischemia) and are often not used.[6,62,63]

Subcutaneous epinephrine has been used for decades for the treatment of acute severe asthma.[6,62] The use of subcutaneous epinephrine has fallen out of favor because of the widespread availability, ease of administration, and efficacy of the newer beta-adrenergic agonists such as albuterol. However, subcutaneous/IM epinephrine continues to have a role in the treatment of critically ill children with impending respiratory failure secondary to acute severe asthma.[64-66] Subcutaneous/IM administration of epinephrine should be considered in children who are rapidly decompensating despite inhaled beta-adrenergic agonists and in children who are unable to cooperate with inhalation therapy secondary to anxiety, altered mental status, or apnea.[6] Subcutaneous epinephrine (0.01 mg/kg) may be administered every 20 minutes for three doses. Severe airflow obstruction may be relieved by subcutaneous/IM epinephrine to a degree sufficient to allow adequate delivery of aerosolized beta-adrenergic agonists to the distal airways, thereby allowing these agents to take effect.

For the majority of patients with acute severe asthma, inhaled beta-adrenergic agonists have superior efficacy compared with subcutaneous epinephrine.[1,6] Furthermore, although the duration of action appears to be dose-dependent, sequential inhalation of these agents (most commonly albuterol) produces a more rapid, greater improvement in airway obstruction than nebulizing higher doses less frequently.[6,67] Based on the available evidence, the consensus is that frequent albuterol nebulization should be considered standard therapy for children presenting with acute severe asthma.[6,31] (*See Table 6.*)

Several studies have compared the efficacy of small-volume nebulizers versus metered-dose inhalers (MDI) with spacers for the treatment of acute asthma exacerbation in children.[68] Although nebulizers allow for the concurrent administration of supplemental oxygen, some studies have suggested close to 90% of the drug is lost to the atmosphere.[1,6,64] The available evidence suggests that there are no differences between MDIs with spacers compared with nebulizers, and either option appears reasonable in the emergency department setting.[68,70] However, evidence is growing that the use of an MDI with a valved holding chamber is more effective than nebulized albuterol in young children with moderate to severe asthma exacerbations.[1,4,71]

Recent studies have evaluated the use of Breath Actuated Nebulizer (BAN).[72,73] These studies have revealed that BANs allow for a lower amount of albuterol while decreasing asthma severity scores, decreasing length of stay in the emergency department, and reducing the rate of hospitalization.[73] A BAN may prove to be an acceptable alternative to conventional nebulizer use.[73]

Continuous albuterol nebulization has been shown to be more effective in children with acute severe asthma and impending respiratory failure.[1,62,74,75] Continuous nebulization provides sustained stimulation of the beta-adrenergic receptors in the airways, thereby preventing the rebound bronchospasm that can occur with intermittent nebulization.[6] Although continuous nebulization of albuterol can be safely done, it should be done only in a closely monitored setting. Side effects occur with beta-agonists and include hypokalemia, cardiac arrhythmias, cardiac ischemia, tremor, ventilation-perfusion mismatch, lactic acidosis, and increased mucus secretion.[1,2,4,6,62] It is important to remember that beta receptors in the lung are down regulated and rapidly saturated with the use of inhaled beta-agonists.[4] This may result in no clinically beneficial effect of higher doses of beta-agonists but increasing side effects.[4,76]

Albuterol exists as a 50:50 mixture of two mirror-image enantiomers: the active R-albuterol and S-albuterol. Previously thought to be an inert compound, S-albuterol may exaggerate airway hyperresponsiveness and result in bronchoconstriction; it may also have a proinflammatory effect.[1,70,77] It appears that administration of only the R-enantiomer of albuterol would be an appropriate treatment rationale. Levalbuterol (Xopenex R) is pure R-albuterol and is available for nebulization. Unfortunately, the majority of studies in children with exacerbations of asthma suggest that there is not a clinical benefit to the use of levalbuterol versus racemic albuterol.[1,78-80] No recommendation regarding the use of the much more expensive levalbuterol in children with acute severe asthma can presently be made.[1,6]

Intravenous beta-agonists should be considered in patients unresponsive to treatment with continuous nebulization, as well as those for whom nebulization is not feasible (i.e., intubated patients, patients with prohibitively poor air entry). Decreased tidal volume and/or near complete airway obstruction in severe status asthmaticus may prevent effective aerosolized bronchodilator delivery. Terbutaline is the current intravenous beta-agonist of choice in the United States, while other countries use albuterol intravenously. Most adverse effects of beta-agonists in asthma are of cardiovascular nature, including tachycardia, increased QTc interval, dysrhythmia, hypertension, as well as hypotension. Induced severe hypokalemia may precipitate arrhythmias. Neither albuterol nor terbutaline, however, is known to cause clinically significant cardiac toxicity when used for pediatric status asthmaticus.[81,82]

The use of intravenous terbutaline is not recommended by the current National Asthma Education Program (NAEP) Expert Panel Report.[31]

Anticholinergic Therapy

The autonomic nervous system is involved in the regulation of airway smooth muscle tone and mucus secretion. The parasympathetic nerve fibers, which are confined to the larger, central airways, stimulate bronchoconstriction and mucus secretion (mediated through the neurotransmitter acetylcholine).[6] In contrast, the sympathetic nerve fibers are distributed more peripherally in the smaller airways and stimulate bronchodilation. This dual-innervation suggests that a therapeutic strategy aimed at both the cholinergic and adrenergic pathways would be beneficial in the treatment of acute severe asthma. Indeed, this is the case, and, when used in conjunction with beta-agonists, anticholinergic agents are now standard of care in the treatment of acute asthma in children.[1,4,6] (*See Table 6.*) A Cochrane review strongly suggests significant clinical benefit to the concomitant use of a beta-agonist and inhaled anticholinergic for treating acute severe asthma, and some studies have indicated an added benefit with minimal risk in the most severely ill patients with asthma.[83,84] The most commonly used compound is ipratropium bromide, a quaternary derivative of atropine. (*See Table 7.*)

Magnesium

Magnesium is safe, and a meta-analysis has shown that when given systematically, it confers additional benefit in the treatment of life-threatening asthma.[85] Magnesium might be effective in acute asthma through a variety of mechanisms.[5,6]

Magnesium administration may serve to replace an underlying magnesium deficiency. Multiple studies have shown that patients with acute severe asthma have underlying hypomagnesemia, and frequent beta-agonist therapy has been demonstrated to result in decreased magnesium levels.[6]

Magnesium may act as a pharmacologic agent via one of several mechanisms.[5,6] It is clear that magnesium acts principally as a calcium antagonist, directly inhibiting calcium uptake in smooth muscle cells, thereby resulting in smooth muscle relaxation. Magnesium acts at the neuromuscular junction by decreasing acetylcholine release, diminishing the depolarization action of acetylcholine, and depressing the excitability of smooth muscle membranes.[6,89,90] Magnesium decreases histamine release from mast cells.[90-92] Finally, magnesium decreases superoxide production by neutrophils, thereby producing anti-inflammatory properties.[90,91]

A single dose of intravenous magnesium sulfate administered to patients with severe acute asthma has been shown to be effective.[5]

Several small, prospective, randomized, controlled trials comparing intravenous magnesium and placebo in children presenting to the emergency department with acute severe asthma have been performed.[91,93-96] Not all of these studies demonstrated beneficial effects with magnesium; a subsequent meta-analysis concluded that magnesium sulfate provides additional benefit to children with acute severe asthma when added to a regimen of frequent, nebulized beta-adrenergic agonists and corticosteroids.[92] Magnesium sulfate should be tried, at least a single dose, when respiratory failure is impending.[26,31] (*See Table 6.*)

The current dose and frequency of administration have not been adequately defined. (*See Table 7.*) There is evidence to suggest that increasing the serum magnesium level to greater than 4 mg/dL is necessary to produce bronchodilation.[26,97] Onset of action is within minutes and the effects last approximately 2 hours.[6,97] Side effects appear dependent upon serum magnesium concentration; mild effects include nausea, vomiting, facial flushing, and dry mouth. At serum magnesium levels greater than 12 mg/dL, loss of deep tendon reflexes, muscle weakness, and respiratory depression, as well as cardiac conduction defects, may be seen.[97]

Theophylline/ Aminophylline

Theophylline has been used as a bronchodilator for the treatment of asthma for many years and was once considered the bronchodilator of choice for the management of acute asthma.[100] The therapeutic effects of aminophylline in asthma include bronchodilation and improved diaphragmatic contraction.[101] Therapeutic effects occur at blood levels up to 20 mg/dL. Levels above this range may occur and cause toxic effects. These include diuresis, hypokalemia, insomnia, tachycardia, cardiac arrhythmias, convulsions, and sudden death.[101,102] In many centers, aminophylline has been supplemented by the use of beta-agonists for the treatment of acute severe asthma.

The NAEP Expert Panel has revised its original guidelines and concluded that methylxanthines are not recommended for treatment of hospitalized children with status asthmaticus.[31] However, current recommendations proscribing the use of theophylline are not based on analysis of treatment data in critically ill children with acute severe asthma.[6]

Theophylline offers several potential advantages for the treatment of acute severe asthma in the PICU population. Theophylline produces bronchodilation and improves air flow without adversely affecting ventilation-perfusion matching.[103] Theophylline's diuretic effect may reduce excess alveolar fluid and microvascular permeability.[6,103,104] Finally, theophylline increases respiratory drive, improves mucociliary clearance, reduces pulmonary vascular resistance, and improves contractility of the diaphragm, all of which may benefit the child with acute severe asthma.[101,103] For these reasons, there has been renewed interest in intravenous aminophylline.[101] Current guidelines assert that there may be a role for aminophylline in particularly severe asthma.[101] Aminophylline use in children may be appropriate if children have acute

severe asthma and the response to aggressive therapy (inhaled bronchodilators and glucocorticoids) is poor. This recommendation is based on limited data and further work is needed.[101,105] Avoidance of toxic theophylline levels is critical. (*See Table 7.*) One study recommends an intravenous loading dose of 7 mg/kg, followed by age-adjusted rates of 0.5-0.65 mg/kg/hr.[105] Theophylline levels are kept between 12-17 mg/mL.

Helium-Oxygen Mixtures

Helium-oxygen mixtures (heliox) are available in concentrations of 80% helium/20% oxygen and 70% helium/30% oxygen. Helium mixtures have a low density compared with air (the 80/20 mixture is approximately one-third the density of air).[26] Heliox is a temporary measure to reduce respiratory resistive work and forestall muscle fatigue until airway obstruction improves with conventional therapy.[26] Evidence suggests heliox is more effective for the sicker patient.[106] The beneficial effects of heliox seem most efficacious when used early in the disease course (less than 24 hours).[106] The addition of heliox to the treatment regimen for acute asthma is not warranted for all patients.[107] Patients requiring FiO_2 greater than 0.30 will not tolerate the use of heliox, as there is no way to titrate beyond the 70/30 mixture.

Heliox may also be effective as the driving gas for nebulized bronchodilators.[108,109] The low density of helium improves the deposition of aerosolized particles in the airways, which can lead to a more rapid response to treatment and more significant improvement in airway function.[26]

In the pediatric patient who requires conventional mechanical support of ventilation, heliox may assist in lowering peak inspiratory pressure (PIP) and improving blood gas pH and partial pressure of CO_2.[110] This benefit is lost once PIP is less than 30 cm H_2O.

Ketamine

Ketamine, a dissociative anesthetic agent, causes bronchodilation by a combination of factors, including drug-induced release of endogenous catecholamines, inhibition of vagal tone, and direct smooth muscle relaxation.[111] Although ketamine has been used successfully for the treatment of refractory bronchospasm in intubated patients, there is controversy concerning its use in non-intubated patients because it may cause increased pulmonary secretions and laryngospasm.[112-115] Literature exists supporting its use as an efficacious adjunct to standard therapy in the treatment of children with acute severe asthma and impending respiratory failure.[116-117]Ketamine should be used cautiously in unintubated patients and only in a monitored setting.

Leukotriene-Modifying Agents

The leukotrienes are biologically active fatty acids generated from arachidonic acid by the enzyme 5-lipoxygenase; 5-lipoxygenase generates leukotriene A4 (LTA4) from arachidonic acid. LTA4 is metabolized to LTC4, LTD4, and LTE4, which are referred to as the slow-reacting substances of anaphylaxis.[118-120] The leukotrienes produce bronchoconstriction, stimulate mucus secretion, decrease mucociliary clearance, increase vascular permeability, and recruit eosinophils and basophils into the airway, thereby perpetuating airway inflammation.[118] The leukotrienes are 1,000 times more potent than either histamine or methacholine in airway challenge tests.[121] Activation of the leukotriene pathways during acute asthma exacerbations, as determined by urinary LTE4 levels, appears to correlate with the degree of airway obstruction.[122]

Several different leukotriene-modifying agents are currently available, each working via different mechanisms. The leukotriene receptor antagonists (LTRA), montelukast and zafirlukast, are the only leukotriene-modifying agents approved for use in children. At present, the main indications for LTRA in pediatric asthma are as add-on therapy to inhaled corticosteroids or as initial controller therapy in children with mild asthma, especially those who cannot or will not use inhaled corticosteroids.[120]

There has been growing interest in using these agents for the treatment of acute severe asthma, although few studies exist.[120,123,124] (*See Table 6.*)

Mechanical Ventilation

Despite maximum medical therapy, mechanical ventilation may be needed to manage respiratory insufficiency resulting from airway obstruction and respiratory muscle fatigue in acute severe asthma.[4,125] Acute severe asthma leading to respiratory failure is an important cause of morbidity and mortality because of the high risk of barotrauma and cardiovascular instability associated with the positive pressure mechanical ventilation in these children.[6,126] The goal of mechanical ventilation in acute severe asthma is twofold: to provide sufficient gas exchange to ensure survival until reversal of airway obstruction is accomplished and to minimize complications associated with mechanical ventilation.

In an effort to unload the respiratory muscles during a severe asthma exacerbation, noninvasive mechanical ventilation using bilevel positive airway pressure (BiPAP) may be used.[5,127,128] The presence of air-trapping in the alveoli results in auto-positive end-expiratory pressure (auto-PEEP), which requires the patient to generate a higher negative inspiratory force to overcome the auto-PEEP and generate inspiratory flow. The addition of EPAP (end-expiratory pressure) should allow for equilibration of pressure between the mouth and the alveoli, reducing the amount of force the patient needs to generate to achieve inspiratory flow.[127] The use of an inspiratory pressure (IPAP) in BiPAP helps to reduce the work of the respiratory muscles.

Early initiation of noninvasive ventilation in addition to standard therapy may be effective in decreasing work of breathing in children with acute severe asthma.[127,128] It may be

safe and well tolerated by patients for at least 24 hours and may prevent the need for intubation.[128] Clinicians using noninvasive ventilation for acute severe asthma must be skilled in noninvasive ventilation and be aware of complications such as barotrauma and hemodynamic instability. These patients must be closely monitored; their condition may abruptly worsen, so the medical team must be ready for immediate intubation.[127]

There are few absolute indications for tracheal intubation in children with status asthmaticus (e.g., coma, cardiac arrest), although failure to maintain adequate oxygen saturations, a worsening metabolic acidosis, and decreasing mental status are all signs that respiratory arrest is imminent. The decision to tracheally intubate should be based on the clinical examination and not the results of an arterial blood gas. These children should be considered high risk for intubation, and a rapid-sequence intubation technique should be performed by the most experienced physician available. Ketamine (2 mg/kg intravenous [IV]) is an excellent choice for an induction agent because of its bronchodilatory properties.[129] Neuromuscular blockade with either succinylcholine (if there are no contraindications to its use) or a nondepolarizing agent such as vecuronium or rocuronium produces acceptable conditions for laryngoscopy and tracheal intubation.[129]

These children will likely require high inspiratory pressures, so the use of a cuffed endotracheal tube is preferable.[6,126,130]

More than one-half of the complications in patients requiring mechanical ventilation for acute severe asthma occur at or around the time of tracheal intubation and include hypoxemia, hypotension, and cardiac arrest.[130] Hyperventilation should be avoided, and hypotension should improve with volume resuscitation and slowing the respiratory rate to avoid further air-trapping and dynamic hyperinflation. A tension pneumothorax should be considered if these measures fail to relieve hypotension and hypoxemia. In these cases, needle thoracentesis is life-saving.

The goal of mechanical ventilation is to obtain and maintain acceptable oxygenation, avoid complications, and allow time for the corticosteroids and bronchodilators to reduce the bronchospasm and inflammation.

Mechanical ventilation should not be targeted toward the results of an arterial blood gas.[6] Utilizing low tidal volumes and respiratory rates and tolerating the resultant hypercapnia dramatically reduces the frequency of barotrauma and death.[6,131] In children, strategies that use low tidal volumes (8-10 mL/kg or less), short inspiratory times (0.75-1.5 sec), long expiratory times, and lower than normal respiratory rates result in improved survival.[6,126,132] The degree of hypercapnia that can be safely tolerated is not known.[6,133]

The most appropriate mode of mechanical ventilatory support may differ among patients and their stage of illness. Pressure control, volume control, and pressure support have all been used in children with acute severe asthma.[3,19,125] Each mode of ventilation has its advantages and disadvantages. Most authors prefer pressure-controlled ventilation.[3,6] The use of positive end-expiratory pressure (PEEP) in these patients is controversial; however, low-level PEEP will minimize dynamic airway collapse and decrease trigger work in spontaneously breathing patients.[19,130]

The use of high-frequency oscillatory ventilation in children with respiratory failure secondary to status asthmaticus has been reported.[134] Extracorporeal life support may be life-saving in children with refractory acute severe asthma.[135,136]

Finally, inhaled nitric oxide has been utilized in children with refractory status asthmaticus.[137,138] The rapid improvement in ventilation described may be related to the action of inhaled nitric oxide as a bronchodilator, direct vascular effect, or both.

Volatile Anesthetics

Inhalational anesthetics are occasionally used for the treatment of status asthmaticus and acute respiratory failure.[6] The bronchodilatory properties of these agents are well-known, and proposed mechanisms include direct stimulation of the beta-adrenergic receptor, direct relaxation of bronchial smooth muscle, inhibition of the release and action of bronchoactive mediators (e.g., histamine, acetylcholine), and depression of vagally mediated airway reflexes.[139] Halothane appears to be particularly effective, although concerns regarding its potential toxicity, including direct myocardial depression, hypotension, and arrhythmias, have limited its use in this setting.[140] These adverse effects may be further potentiated in children with status asthmaticus who will have some degree of hypoxia, hypercapnia, and acidosis and who are frequently managed with the concomitant administration of beta-adrenergic agents and/or theophylline.[6]

The use of isoflurane in status asthmaticus and acute respiratory failure offers several advantages over halothane.[141] Isoflurane produces less myocardial depression and is less arrhythmogenic compared with halothane. Given its role as a general anesthetic, concomitant administration of sedation/analgesia and neuromuscular blockade is not necessary. Isoflurane has been used with some success in both children and adults with status asthmaticus refractory to conventional therapy.[141,142]

Summary/Conclusion

The burden of childhood asthma continues to rise, with increasing rates of asthma prevalence, severity, and death.[143] Background asthma management remains suboptimal in children needing hospitalization. This is despite our improved understanding of the pathophysiology of asthma and the availability of effective anti-inflammatory therapy.

Children will continue to present to the ED with acute severe asthma. The emphasis in treatment remains on the aggressive use of inhaled beta-agonist and steroid therapy to abort the acute attack and decrease

both the mortality rate and need for hospitalization. For children who fail to respond, adjunctive therapies and advances in ventilatory management can lead to improved outcomes in these patients.

References

1. Mannix R, Bachur R. Status asthmaticus in children. *Curr Opin Pediatr* 2007;19:281-287.
2. Saharan S, Lodha R, Kabra SK. Management of status asthmaticus in children. *Indian J Pediatr* 2010;77: 1417-1423.
3. Newth CJL, Meert KL, Clark AE, et al. Fatal and near-fatal asthma in children: The critical care perspective. *J Paediatr Resp Rev* 2012;161:214-221.
4. Rubin BK, Pohanka V. Beyond the guidelines: Fatal and near-fatal asthma. *Paediatr Resp Rev* 2012;13:106-111.
5. Holley AD, Boots RJ. Review article: Management of acute severe asthma and near-fatal asthma. *Emergency Medicine Australasia* 2009;21:259-268.
6. Wheeler DS, Page K, Shanley TP. Status asthmaticus, in Wheeler DS et al (eds.) *The Respiratory Tract in Pediatric Critical Illness and Injury.* London, Springer-Verlag, 2009:169-193.
7. Malmstrom K, Kaila M, Kajosaari M, et al. Fatal asthma in Finnish children and adolescents 1976-1998: Validity of death certificated and a clinical description. *Pediatr Pulmonol* 2007;42:210-215.
8. Triasih R, Duke T, Robertson CF. Outcomes following admission to intensive care for asthma. *Arch Dis Child* 2011;96:729-734.
9. Maffei FA, van der Jagt EW, Powers KS, et al. Duration of mechanical ventilation in life-threatening pediatric asthma: Description of an acute asphyxial subgroup. *Pediatrics* 2004;114(3):762-767.
10. Sedik HA, Barr RG, Clark S, et al. Prospective study of sudden-onset asthma exacerbations in children. *Pediatr Emerg Care* 2007;23(7):439-444.
11. Robertson CF, Rubinfeld AR, Bowes G. Pediatric asthma deaths in Victoria: The mild are at risk. *Pediatr Pulmonol* 1992;13:95-100.
12. Kravis, LP, Kolski GB. Unexpected death in childhood asthma. *Am J Dis Child* 1985;139(6):558-563.
13. Flether HJ, Ibrahim SA, Speight N. Survey of asthma deaths in the northern region, 1970-1985. *Arch Dis Child* 1990;65:163-167.
14. Jensen ME, Collins CE, Gibson PG et al. The obesity phenotype in children with asthma. *Paediatric Respiratory Reviews* 2011;12:152-159.
15. Bratton SL. Near fatal and fatal asthma in the PICU. *AAP Grand Rounds* 2012;28:46.
16. Wechsler ME, Shepard JO, Mark EJ. A 20-year-old woman with asthma a cardiorespiratory arrest. *N Engl J Med* 2007;356(20):2083-2091.
17. McFadden ER. Acute severe asthma. *Am J Resp Crit Care Med* 2003;168:740-759.
18. Busse WW, Lemanske RF. Asthma. *N Engl J Med* 2001;344(5):350-362.
19. Bohn D, Kisson N. Acute asthma. P*ediatr Crit Care Med* 2001;2(2):151-163.
20. Grover S, Jindel A, Bansal A, et al. Acute bronchial asthma. *Indian J Pediatr* 2011;78(11):1388-1395.
21. McCool FD, Tzelepis GE. Dysfunction of the diaphragm. *N Engl J Med* 2012;366(10):932-942.
22. Anas, NG, Bronicki RA. Cardiopulmonary interaction. *Pediatr Crit Care Med* 2009;10(3):313-322.
23. McGregor M. Pulsus paradoxus. *N Engl J Med* 1979;301(9):480-482.
24. Frey B, Freezer N. Diagnostic value and pathophysiologic basis of pulsus paradoxus in infants and children with respiratory disease. *Pediatr Pulmonol* 2001;31:138-143.
25. Lugogo NL, MacIntyre NR. Life-threatening asthma: Pathophysiology and management. *Respir Care* 2008;53(6):726-735.
26. Chipps BE, Murphy KR. Assessment and treatment of acute asthma in children. *J Pediatr* 2005;147:288-294.
27. Qureshi F. Management of children with acute asthma in the emergency department. *Pediatr Emerg Care* 1999;15(3):206-214.
28. Gorelick MH, Stevens MW, Schultz TR, et al. Performance of a novel clinical score, the Pediatric Asthma Severity Score (PASS), in the evaluation of acute asthma. *Acad Emerg Med* 2004;11:10-18.
29. Ducharme FM, Chalut D, Ploynick L, et al. The Pediatric Respiratory Assessment Measure: A valid clinical score for assessing acute asthma severity from toddlers to teenagers. *J Pediatr* 2008;152:476-480.
30. Becker AB, Nelson NA, Simons FE. The pulmonary index. Assessment of a clinical score for asthma. *Am J Dis Child* 1984;138:574-576.
31. National Heart, Lung and Blood Institute. Expert panel report 3: Guidelines for the diagnosis and management of asthma-full report 2007. Available at: www.nhlbi.nih.gov/guidelines/asthma.
32. Sok D, Komatsu MK, Curvalho KV, et al. Pulse oximetry in the evaluation of the severity of acute asthma and/or wheezing in children. *J Asthma* 1999;36:327-333.
33. Morray B, Redding G. Factors associated with prolonged hospitalization of children with asthma. *Arch Pediatr Adolesc Med* 1995;149:276-279.
34. Keogh KA, MacArthur C, Parkin PC, et al. Predictors of hospitalization in children with acute asthma. *J Pediatr* 2001;139:273-277.
35. Keahey L, Bulloch B, Becker AB, et al. Initial oxygen saturation as a predictor of admission in children presenting to the emergency department with acute asthma. *Ann Emerg Med* 2002;40:300-307.
36. Meert KL, McCaulley L, Sarnaik AP. Mechanism of lactic acidosis in children with acute severe asthma. *Pediatr Crit Care Med* 2012;13:28-31.
37. Yousel E, McGeady SJ. Lactic acidosis and status asthmaticus: How common in pediatrics? *Ann Allergy Asthma Immunol* 2002;89(6):585-588.
38. Assadi FK. Therapy of acute bronchospasm complicated by lactic acidosis and hypokalemia. *Clin Pediatr* 1989;28(6):258-260.
39. Koul PB, Minarik M, Totapally BR. Lactic acidosis in children with acute exacerbation of severe asthma. *Eur J Emerg Med* 2007;14:56-58.
40. Kolski GB, Cunningham AS, Niemec PW, et al. Hypokalemia and respiratory arrest in an infant with status asthmaticus. *J Pediatr* 1988;112:304-307.
41. Tsai WS, Wu CP, Hsu YJ, et al. Life-threatening hypokalemia in an asthmatic treated with high dose hydrocortisone. *Am J Med Sci* 2004;377:152-155.
42. Chawla S, Seth D, Cortez J. Asthma and hyperglycemia. *Clin Pediatr* 2007;46(5):454-457.
43. Beck CE. Hypotonic versus isotonic maintenance intravenous fluid therapy in hospitalized children: A systemic review. *Clin Pediatr* 2007;46(9):764-770.
44. Arisaka O, Shimura N, Hosaka A, et al. Water intoxication in asthma assessed by urinary arginine vasopressin. *Eur J Pediatr* 1988;148:137-169.
45. Singleton R, Moel DI, Cohn RA. Preliminary observation of impaired water excretion in treated status asthmaticus. *Am J Dis Child* 1986;140:59-61.
46. Iikura Y, Odajima Y, Akazama A, et al. Antidiuretic hormone in acute asthma in children: Effects of medication on serum levels and clinical course. *Allergy Proc* 1989;10(30):197-201.
47. Stalcup SA, Melins RB. Mechanical forces producing pulmonary edema in acute asthma. *N Engl J Med* 1977;297: 592-596.
48. Fahy JV. Eosinophilic and neutrophilic inflammation in asthma: Insights from clinical studies. *Proc Ann Thorac Soc* 2009;6:256-259.
49. Zhang X, Moilanen E, Kankaanranta H. Beclomethasone, budesonide and fluticasone propionate inhibit neutrophil apoptosis. *Eur J Pharmacol* 2001;431:365-371.
50. Blasi F, Consentini R, Tarsia P, et al. Potential role of antibiotics in the treatment of asthma. *Curr Drug Targets Inflamm Allergy* 2004;3:237-242.
51. Rolins DR, Benther DA, Martin RJ. Update on infection and antibiotics in asthma. *Curr Allergy Asthma Rep* 2010;10:67-73.

52. Inwald D, Roland M, Kuitert L, et al. Oxygen treatment for acute severe asthma. *BMJ* 2001;323:98-100.
53. Rodrigo GS, Rodriquez VM, Pereqali V, et al. Effects of short-term 28% and 100% oxygen on PaCO2 and peak expiratory flow rate in acute asthma: A randomized trial. *Chest* 2003;124:1312-1315.
54. Chien JW, Ciufo R, Novak R, et al. Uncontrolled oxygen administration and respiratory failure in acute asthma. *Chest* 2001;117:728-733.
55. Smith M, Iqbal SM, Rowe BH, et al. Corticosteroids for hospitalized children with acute asthma. *Cochrane Database Syst Rev* 2003;1:CD002886.
56. Zhang L, Medoza RA. Doses of systemic corticosteroids in hospitalized children with acute asthma: A systemic review. *J Paediatrics and Child Health* 2006;42:179-183.
57. Klein-Gitelman MS, Pachman LM. Intravenous corticosteroids: Adverse reactions are more variable than expected in children. *J Rheumatol* 1998;25: 1995-2002.
58. Mehta R, Fisher LE, Segeleon JE, et al. Acute rhabdomyolysis complicating status asthmaticus in children. *Pediatr Emerg Care* 2006;22(8):587-591.
59. Goh AYT, Chan PWK. Acute myopathy after status asthmaticus: Steroids, myorelaxants or carbon dioxide. *Respirology* 1999;4:97-99.
60. Rowe BH, Bota GW, Fabris L, et al. Inhaled budesonide in addition to oral corticosteroids to prevent asthma relapse following discharge from the emergency department: A randomized controlled trial. *JAMA* 1999;281:2119-2126.
61. Upham BD, Mollen CJ, Scarfone RJ, et al. Nebulized budesonide added to standard pediatric emergency department treatment of acute asthma: A randomized, double-blind trial. *Acad Emerg Med* 2011;18:665-673.
62. Biarent D. Therapeutic strategies in near fatal asthma in children. *Pediatr Pulmonology* 2001;23(Suppl):90-93.
63. Baren JM, Zorc JS. Contemporary approach to the emergency department management of pediatric asthma. *Emerg Clin N Am* 2002;20(1):115-138.
64. Kornberg AE, Zuckerman S, Welliver JR, et al. Effect of injected long-acting epinephrine in addition to aerosolized albuterol in the treatment of acute asthma in children. *Pediatr Emerg Care* 1991;7:1-3.
65. Safdar B, Cone DL, Phan KT. Subcutaneous epinephrine in the prehospital setting. *Prehosp Emerg Care* 2001;5:200-207.
66. Sharma A, Madan A. Subcutaneous epinephrine vs. nebulized salbutamol in asthma. *Indian J Pediatr* 2001;68: 1127-1130.
67. Robertson CF, Smith F, Beck R, et al. Response to frequent low doses of nebulized salbutamol in acute asthma. *J Pediatr* 1985;106:672-674.
68. Amirav I, Newhouse MT. Metered-dose inhaler accessory devices in acute asthma. *Arch Pediatr Adolesc Med* 1997;151: 876-882.
69. Rubilar L, Castro-Rodriquez JA, Girardi G. Randomized trial of salbutamol via metered-dose inhaler with spacer vs. nebulizer for acute wheezing in children less than 2 years of age. *Pediatr Pulmonol* 2000;29:264-269.
70. Scarfone RJ, Friedlaender EY. Beta-2 agonists in acute asthma: The evolving state of the art. *Pediatr Emerg Care* 2002;18:442-447.
71. Castro-Rodriquez JA, Rodrigo GJ. Beta-agonists through metered-dose inhaler with valved holding chamber versus nebulizer for acute exacerbation of wheezing asthma in children under 5 years of age: A systematic review with meta-analysis. *J Pediatr* 2004;145:172-177.
72. Titus MO, Eady M, King L, et al. Effectiveness of a breath-activated nebulizer device on asthma care in the pediatric emergency department. *Clinical Pediatrics* 2012;51(12):1150-1154.
73. Arunthari V, Bruinsma RS, Lee AS, et al. A prospective, comparative trial of standard and breath-actuated nebulizer: Efficacy, safety, and satisfaction. *Respiratory Care* 2012;57(8):1242-1247.
74. Craig VL, Bigos D, Brilli RJ. Efficacy and safety of continuous albuterol nebulization in children with severe status asthmaticus. *Pediatr Emerg Care* 1996;12(1):1-5.
75. Camargo CA, Spooner C, Rowe BH. Continuous versus intermittent beta-agonists for acute asthma. *Cochrane Database Syst Rev* 2003;4:CD0001115.
76. Rodrigo GJ, Rodrigo C. Continuous vs intermittent beta-agonists in the treatment of acute adult asthma: A systematic review with meta-analysis. *Chest* 2002;122:160-225.
77. Johnsson F, Rydberg I, Aberg G, et al. Effects of albuterol enantiomers on in vitro bronchial reactivity. *Clin Rev Allergy Immunol* 1996;14:57-64.
78. Hardasmalani MD, DeBari V, Bilhoney WG, et al. Levalbuterol versus racemic albuterol in the treatment of acute exacerbations of asthma in children. *Pediatr Emerg Care* 2005;21:415-419.
79. Ralston ME, Euwema MS, Knecht KR, et al. Comparison of levalbuterol and racemic albuterol combined with ipratropium bromide in acute pediatric asthma: A randomized, controlled trial. *J Emerg Med* 2005;19:29-35.
80. Qureshi, Zaritsky A, Welch C, et al. Clinical efficacy of racemic albuterol versus levalbuterol for the treatment of acute pediatric asthma. *Ann Emerg Med* 2005;46:29-36.
81. Chiang VW, Burns JP, Rifai N, et al. Cardiac toxicity of intravenous terbutaline for the treatment of severe asthma in children: A prospective assessment. *J Pediatr* 2000;137:73-77.
82. Carroll CL, Schramm CM. Protocol-based titration of intravenous terbutaline decreases length of stay in pediatric status asthmaticus. *Pediatr Pulmonol* 2006;41:350-356.
83. Rodrigo GJ, Castro-Rodriquez JA. Anticholinergics in the treatment of children and adults with acute asthma: A systemic review with meta-analysis. *Thorax* 2005;60:740-746.
84. Plotnick LH, Ducharme FM. Acute asthma in children and adolescents: Should inhaled anticholinergics be added to beta-agonists? *Am J Respir Med* 2003;2:109-115.
85. Rowe BH, Camargo CA. The role of magnesium sulfate in the acute and chronic management of asthma. *Curr Opin Pulm Med* 2008;14:70-76.
86. Kakish KS. Serum magnesium levels in asthmatic children during and between exacerbations. *Arch Pediatr Adolesc Med* 2001;155(2):181-183.
87. Zervas E, Papatheodoron G, Psathakis K, et al. Reduced intracellular magnesium concentrations in patients with acute asthma. *Chest* 2003;123:113-118.
88. Bodenhamer J, Bergstrom R, Brown D, et al. Frequent nebulized beta-agonists for asthma: Effects on serum electrolytes. *Ann Emerg Med* 1992;21:1337-1342.
89. Monem GF, Kisson N, De Nicola L. Use of magnesium sulfate in asthma in childhood. *Pediatr Ann* 1996;25(3):136-144.
90. Fawcett WJ, Haxby EJ, Male DA. Magnesium: Physiology and pharmacology. *British J Anaesthesia* 1999;83(2):302-320.
91. Ciaralllo L, Brousseau D, Reinert S. Higher-dose magnesium therapy for children with moderate to severe asthma. *Arch Pediatr Adoles Med* 2000;154: 979-983.
92. Cheuk DKL, Chau TCH, Lee SL. A meta-analysis on intravenous magnesium sulphate for treating acute asthma. *Arch Dis Child* 2005;90:74-77.
93. Ciarallo L, Sauer AH, Shannon MW. Intravenous magnesium therapy for moderate to severe pediatric asthma: Results of a randomized, placebo-controlled trial. *J Pediatr* 1996;129:809-814.
94. Devi PR, Kumar L, Sighi SC, et al. Intravenous magnesium sulfate in acute severe asthma not responding to conventional therapy. *Indian Pediatr* 1997;34: 389-397.
95. Gurken F, Haspolat K, Bosnak M, et al. Intravenous magnesium sulfate in the management of moderate to severe acute asthmatic children non-responding to conventional therapy. *Eur J Med* 1999;6: 201-205.
96. Scarfone RJ, Loiselle JM, Jotte MD, et al. A randomized trial of magnesium in the emergency department treatment of children with asthma. *Ann Emerg Med* 2000;36:572-578.
97. Noppen M, Vanmack L, Impens N, et al. Bronchodilating effect of intravenous

magnesium sulfate in acute severe bronchial asthma. *Chest* 1990;97:373-376.

98. Harker HE, Majcher TA. Hypermagnesemia in a pediatric patient. *Anesth Analg* 2000;91:1160-1162.

99. McGuire JK, Kulkerni MS, Baden HP. Fatal hypermagnesemia in a child treated with megavitamin/megamineral therapy. *Pediatrics* 2000;105(2):e18.

100. May C. History of the introduction of theophylline into the treatment of asthma. *Clinical Allergy* 1974;4:211-217.

101. Mitra A, Bussler D, Goodman K, et al. Intravenous aminophylline for acute severe asthma in children over two years receiving inhaled bronchodilators. *Evid-Based Child Health* 2006;1:101-146 (Cochrane Library).

102. Emerman CL, Devlin C, Connors AF. Risk of toxicity in patients with elevated theophylline levels. *Ann Emerg Med* 1990;19(6):643-648.

103. Montserrat JM, Barabera JA, Viegas C, et al. Gas exchange response to intravenous aminophylline in patients with a severe exacerbation of asthma. *Eur Respir J* 1995;8:28-33.

104. Bell M, Jackson E, Mi Z, et al. Low-dose theophylline increases urine output in diuretic-dependent critically ill children. *Intensive Care Med* 1998;24: 1099-1105.

105. Rean RS, Loftis LL, Albers GM, et al. Efficacy of IV theophylline in children with severe status asthmaticus. *Chest* 2001;119:1480-1488.

106. Gupta VK, Cheifetz IM. Heliox administration in the pediatric intensive care unit: An evidence-based review. *Ped Crit Care Med* 2005;6:204-211.

107. Rodrigo GJ, Pollack CV, Rodrigo C, et al. Heliox for non-intubated acute asthma patients. *Cochrane Database of Systematic Reviews* 2006;4:CD002884.

108. Kim IK, Phrampus E, Venkataraman S, et al. Helium/oxygen-driven albuterol nebulization in the treatment of children with moderate to severe asthma exacerbations: A randomized, controlled trial. *Pediatrics* 2005;116:1127-133.

109. Kim IK, Saville AL, Sikes KL, et al. Heliox-Driven albuterol nebulization for asthma exacerbations: An overview. *Respir Care* 2006;51(6):613-618.

110. Abd-Allah SA, Rogers MS, Terry M, et al. Helium-oxygen therapy for pediatric acute severe asthma requiring mechanical ventilation. *Pediatr Crit Care Med* 2003;4:353-357.

111. Strube PJ, Hallam PL. Ketamine by continuous infusion in status asthmaticus. *Anesthesia* 1986;41:1017-1019.

112. Rock MJ, Reyes de la Roche S, L'Hommedieu CS, et al. Use of ketamine in asthmatic children to treat respiratory failure refractory to conventional therapy. *Crit Care Med* 1986;14(5):514-516.

113. Hemming A, Mackenzie I, Finfer S. Response to ketamine in status asthmaticus resistant to maximal medical treatment. *Thorax* 1994;49(1):90-91.

114. Nehama J, Pass R, Bechtler-Karsh A, et al. Continuous ketamine infusion for the treatment of refractory asthma in a mechanically ventilated infant: A case report and review of the literature. *Pediatr Emerg Care* 1996;12(4):294-297.

115. Youseff-Ahmed MZ, Silver P, Ninkott L, et al. Continuous infusion of ketamine in mechanically ventilated children with refractory bronchospasm. *Intensive Care Med* 1996;22(9):972-976.

116. Sarma VJ. Use of ketamine in acute severe asthma. *Acta Anaesthesiol Scand* 1992;36(1):106-107.

117. Petrillo TM, Fortenberry JD, Linzer JF, et al. Emergency department use of ketamine in pediatric status asthmaticus. *J Asthma* 2001;38(8):657-664.

118. Drazen JM, Israel E, O'Byrne PM. Treatment of asthma with drugs modifying the leukotriene pathway. *N Engl J Med* 1999;340:197-206.

119. Bisqaard H. Leukotriene modifiers in pediatric asthma management. *Pediatrics* 2001;107:381-390.

120. Dumitra C, Chan SMH, Turcanu V. Role of leukotriene receptor antagonists in the management of pediatric asthma. *Pediatr Drugs* 2012;14(5):317-330.

121. Adelroth E, Morris MM, Hargreave FE, et al. Airway responsiveness to leukotrienes C4 and D4 and to methacholine in patients with asthma and normal controls. *N Engl J Med* 1986;315:480-484.

122. Green SA, Malica MP, Tanaka W, et al. Increase in urinary leukotriene LTE4 levels in acute asthma: Correlation with airflow limitation. *Thorax* 2004;59:100-104.

123. Dempsey OJ, Wilson AM, Sims EJ, et al. Additive bronchoprotective and bronchodilator effects of a single dose of salmeterol and montelukast in asthmatic patients receiving inhaled corticosteroids. *Chest* 2000;117:950-953.

124. Camargo CA, Smithline HA, Malice MP, et al. A randomized controlled trial of intravenous montelukast in acute asthma. *Am J Resp Crit Care Med* 2003;167: 528-533.

125. Sarnaik AP, Daphtory KM, Mart KL, et al. Pressure-controlled ventilation in children with severe status asthmaticus. *Pediatr Crit Care Med* 2004;5:133-138.

126. Cox RG, Barker GA, Bohn DJ. Efficacy, results, and complications of mechanical ventilation in children with status asthmaticus. *Pediatr Pulmonol* 1991;11(2):120-126.

127. Mayordomo-Colunga J, Medina A, Rey C, et al. Non-invasive ventilation in pediatric status asthmaticus: A prospective observational study. *Pediatr Pulmonol* 2011;46 949-955.

128. Basnet S, Mander G, Andoh J, et al. Safety, efficacy and tolerability of early initiation of non-invasive positive pressure ventilation in pediatric patients admitted with status asthmaticus: A pilot study. *Pediatr Crit Care Med* 2012;13:393-398.

129. Staple LE, O'Connell KJ. Pediatric rapid sequence intubation: An in-depth review. *Pediatric Emergency Medicine Reviews* 2013;18(1):1-11.

130. Werner HA. Status asthmaticus in children: A review. *Chest* 2001;119: 1913-1929.

131. Dariolo R, Perret C. Mechanical controlled hypoventilation is status asthmaticus. *Ann Rev Respir Dis* 1984;129:385-387.

132. Malmstrom K, Kaila M, Korhonen R, et al. Mechanical ventilation in children with severe asthma. *Pediatr Pulmonol* 2001;31:405-411.

133. Edmunds SM, Harrison R. Subarachnoid hemorrhage in a child with status asthmaticus: Significance of permissive hypercapnia. *Pediatr Crit Care Med* 2003;4:100-103.

134. Duval ELIM, vanVaght AJ. Status asthmaticus treated by high-frequency oscillatory ventilation. *Pediatr Pulmonol* 2000;30:350-353.

135. Tobias JP, Garrett JS. Therapeutic options for severe, refractory status asthmaticus: inhalational anesthetic agents, extracorporeal membrane oxygenation and helium/oxygen ventilation. *Pediatr Anaesth* 1997;7(1):47-57.

136. Mikkelsen ME, Pugh ME, Hansen-Flaschan JH, et al. Emergency extracorporeal life support for asphyxia status asthmaticus. *Respir Care* 2007;52(11):1525-1529.

137. Nakaqawa TA, Johnston SJ, Falkos SA, et al. Life-threatening status asthmaticus treated with inhaled nitric oxide. *J Pediatr* 2000;137:119-122.

138. Rishani R, El-Khatib M, Mrouch S. Treatment of severe status asthmaticus with nitric oxide. *Pediatr Pulmonol* 1999;28:451-453.

139. Hirshman LA, Edelstein G, Peetz S, et al. Mechanism of action of inhalational anesthetics on airways. *Anesthesiology* 1982;56:107-111.

140. O'Rouke PP, Crone PK. Halothane in status asthmaticus. *Crit Car Med* 1982;10:341-343.

141. Wheeler DS, Clapp CR, Ponaman ML, et al. Isoflurane therapy for status asthmaticus in children: A case series and protocol. *Pediatr Crit Care Med* 2000;1(1):55-59.

142. Johnston RG, Noseworthy TW, Friesen EG, et al. Isoflurane therapy for status asthmaticus in children and adults. *Chest* 1990;97(3):698-701.

143. Belessis Y, Dixon S, Thomsen A, et al. Risk factors for an intensive care unit admission in children with asthma. *Pediatr Pulmonol* 2004;37:201-209.

CME Questions

1. An episode of acute severe asthma is associated with:

   A. reduced functional residual capacity
   B. normal transpulmonary pressure

C. active expiration
D. prolonged inspiration
E. increased forced expiration volume fraction in 1 second (FEV_1)

2. Effects of dynamic hyperinflation are complex and include:
   A. increased preload
   B. reduced left ventricular afterload
   C. reduced physiologic dead space
   D. increased right ventricular afterload
   E. reduced pulsus paradoxus

3. Which of the following contributes to the acidosis that may be present in the patient with acute severe asthma?
   A. excessive dose of beta-adrenergic drugs
   B. dehydration
   C. reduced cardiac output
   D. mismatch of oxygen delivery to oxygen demand in respiratory muscles
   E. all of the above

4. Corticosteroids can have which of the following effects?
   A. antagonist to beta-adrenergic therapy
   B. decreased neutrophil survival
   C. hypoglycemia
   D. induced apoptosis of eosinophils
   E. hypotension

5. Regarding the use of steroids in the treatment of acute severe asthma, which of the following is true?
   A. The optimal dose is known.
   B. High-dose corticosteroid therapy offers few advantages over low-dose corticosteroid therapy.
   C. Data exist that demonstrate ineffectiveness of oral steroids.
   D. Inhaled steroids are as effective as systemic steroids.

6. Concerning the use of beta-agonists in the treatment of acute severe asthma, which of the following is true?
   A. Frequent albuterol nebulization should be considered standard therapy.
   B. Levalbuterol has been shown to be more beneficial than racemic albuterol.
   C. Use of intravenous terbutaline is recommended by the Expert Panel Report of the National Asthma Education Program.
   D. Subcutaneous epinephrine should be used as the initial bronchodilator of choice.

7. Magnesium may facilitate bronchodilation through which mechanism?
   A. calcium antagonist with resultant smooth muscle relaxation
   B. induced diuresis
   C. increased histamine from mast cells
   D. increased acetylcholine release at the neuromuscular junction

8. Which of the following effects of theophylline may be beneficial in the treatment of acute severe asthma?
   A. bronchodilation
   B. diuretic effect
   C. improved contractility of the diaphragm
   D. improved mucociliary clearance
   E. all of the above

9. Which of the following adjunctive measures may be helpful in the management of acute severe asthma?
   A. helium-oxygen gas mixture
   B. leukotriene receptor antagonist
   C. ketamine
   D. aminophylline
   E. all of the above

10. Concerning the use of positive pressure ventilation in acute severe asthma, which of the following is true?
   A. Non-invasive ventilation is not indicated.
   B. Provision of 100% oxygen is indicated and safe.
   C. One goal of ventilation is the maintenance of a normal pCO_2.
   D. Complications of tracheal intubation and positive pressure ventilation include hypotension and hypoxemia.

CME Instructions

HERE ARE THE STEPS YOU NEED TO TAKE TO EARN CREDIT FOR THIS ACTIVITY:

1. Read and study the activity, using the provided references for further research.

2. Log on to **www.cmecity.com** to take a post-test; tests can be taken after each issue or collectively at the end of the semester. *First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice, or renewal notice.*

3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.

4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.

5. **Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.**

Pediatric Emergency Medicine Reports

CME Objectives

Upon completion of this educational activity, participants should be able to:

- recognize specific conditions in pediatric patients presenting to the emergency department;
- describe the epidemiology, etiology, pathophysiology, historical and examination findings associated with conditions in pediatric patients presenting to the emergency department;
- formulate a differential diagnosis and perform necessary diagnostic tests;
- apply up-to-date therapeutic techniques to address conditions discussed in the publication;
- discuss any discharge or follow-up instructions with patients.

Pediatric Emergency Medicine Reports™ (ISSN 1082-3344) is published monthly by AHC Media, a division of Thompson Media Group LLC, 3525 Piedmont Road, N.E., Six Piedmont Center, Suite 400, Atlanta, GA 30305. Telephone: (800) 688-2421 or (404) 262-7436.

Senior Vice President/Group Publisher: Donald R. Johnston
Executive Editor: Shelly Morrow Mark
Managing Editor: Leslie Hamlin

GST Registration No.: R128870672
Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to ***Pediatric Emergency Medicine Reports***, P.O. Box 105109, Atlanta, GA 30348.

Back issues: $65. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Subscriber Information

Customer Service: 1-800-688-2421

Customer Service E-Mail Address: customerservice@ahcmedia.com
Editorial E-Mail Address: shelly.mark@ahcmedia.com
World-Wide Web page: http://www.ahcmedia.com

Subscription Prices

1 year with 30 ACEP, AMA, or AAP Category 1 credits: $439;
1 year without credit: $389;
Add $17.95 for shipping & handling
Multiple copies:
Discounts are available for group subscriptions, multiple copies, site-licenses or electronic distribution. For pricing information, call Tria Kreutzer at 404-262-5482.
One to nine additional copies: **$350 each;**
10 or more additional copies: **$311 each.**
Resident's Rate: **$194.50**
All prices U.S. only. U.S. possessions and Canada, add $30 postage plus applicable GST.

Accreditation

AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media designates this enduring material for a maximum of 30 *AMA PRA Category 1 Credits™*. Physicians should claim only credit commensurate with the extent of their participation in the activity.

Approved by the American College of Emergency Physicians for a maximum of 30.00 hour(s) of ACEP Category I credit.

This continuing medical education activity has been reviewed by the American Academy of Pediatrics and is acceptable for a maximum of 30.0 AAP credits. These credits can be applied toward the AAP CME/CPD Award available to Fellows and Candidate Members of the American Academy of Pediatrics.

This CME activity is intended for emergency and pediatric physicians.

It is in effect for 36 months from the date of the publication.
This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

Exclusive to our subscribers

Rapid Access Management Guidelines

Pediatric Emergency Medicine Reports

The Practical Journal of Pediatric Emergency Medicine

Acute Severe Asthma

Asthma Severity

Parameter*	Mild	Moderate	Severe	Imminent Respiratory Arrest
Breathlessness	Walking Can lie down	Talking (infant: shorter cry/difficult feeding); Prefers sitting	At rest (infant will stop feeding) Hunched over	
Talks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy/confused
Respiratory rate	Increased	Increased	Increased	Bradypnea
Accessory muscles and suprasternal retractions	Usually not	Usually	Usually	Paradoxical movement
Wheeze	Moderate (end expiration)	Loud	Usually loud	Absence of wheeze
Pulse/min	< 100	100-120	> 120	Bradycardia
Pulsus paradoxus (mm HG)	Absent (< 10)	10-25	> 25	Absence suggests respiratory muscle fatigue
PEFR (after bronchodilator)	> 80%	60-80%	< 60%	
PaO2 on room air and/or PaCO2 (mm Hg)	Normal (need not be tested)	< 45	> 45	
Saturation	> 95%	91-95%	90% or less	

*The presence of several parameters, but not necessarily all, indicates the severity of the attack
PEFR = peak expiratory flow rate

Source: Reference 30.

Assessing Asthma Severity Becker Asthma Score

Score	Respiratory Rate (per min)	Wheezing	I/E Ratio	Accessory Muscle Use
0	< 30	None	1:1.5	None
1	30-40	Terminal expiration	1:2	1 site
2	41-50	Entire expiration	1:3	2 sites
3	> 50	Inspiration and entire expiration	> 1:3	3 sites or neck strap muscle use

Score ≤ 4 = mild
Score > 4 to < 7 = moderate
Score ≥ 7 = severe (needs PICU)

Source: Reference 29

Risk Factors for Potentially Fatal Asthma

- History of previous attack with:
  - Severe, rapid progression of symptoms
  - Respiratory failure requiring endotracheal intubation and ventilatory support*
  - Pediatric intensive care unit admission
- Attacks precipitated by food allergy
- Denial or failure to perceive the severity of illness
- Noncompliance
- Lack of social support network (dysfunctional family)
- Non-white children (especially African-American and Hispanic children)

*May include noninvasive positive pressure ventilation

Adapted from: Reference 6.

Markers of Acute Severe Asthma

- Inability to speak in full sentences or unable to speak at all (infants will have shorter periods of crying and will have difficulty or will stop feeding)
- Drowsy/confused/altered level of consciousness
- Seated upright; unable to lie supine
- Respiratory rate is elevated (bradypnea is an ominous sign)
- Use of accessory muscles, tracheal tugging, head bobbing
- Loud wheeze; quiet chest is ominous sign
- Tachycardia; bradycardia is ominous sign
- Pulsus paradoxus (> 15 mmHg drop with inspiration); absence may indicate fatigue
- Decreased FEV_1 or PEFR < 40% of best or predicted
- Oxygen saturation < 90% in room air

Common Drugs and Doses in Acute Severe Asthma

Corticosteroids

- Usually administered intravenously
- Methylprednisolone: 2-4 mg/kg/day, with a maximum dose of 60 mg/day (adult maximum 125 mg/day)

Beta-agonist (Albuterol)

- Hourly or continuously delivered albuterol via nebulizer
- Hourly: 0.15 mg/kg every hour (minimum 2.5 mg; maximum 5 mg)
- Continuous: 0.3-0.5 mg/kg/hour up to 20 mg/hr (consider 10 mg/hr for children who weigh 5-10 kg; 15 mg/hr for children who weigh 10-20 kg; and 20 mg/hr for children who weight > 20 kg)

Beta-agonist (Terbutaline)

- Continuous intravenous infusion
- Loading dose: 2-10 mcg/kg
- Infusion dose: 0.5 mcg/kg/min; dose may be increased by 0.1-0.2 mcg/kg/min every 15-30 min; doses up to 10 mcg/kg/min have been reported

Ipratropium bromide

- 250 mcg/dose for children < 20 kg; 500 mcg/dose for children ≥ 20 kg
- Consider 3 doses given every 4-8 hours

Magnesium sulfate

- 50-75 mg/kg (max dose 2 grams given every 4-6 hours)
- Optimal magnesium level 4-5.5 mg/dL

Aminophylline

- Aminophylline is the ethylenediamine salt of theophylline; pharmacokinetic parameters are those of theophylline; 100 mg aminophylline = 80 mg theophylline
- Monitoring parameter: theophylline level; recommend level < 15 mcg/mL (see text)
- Loading dose (inpatients not currently receiving aminophylline or theophylline): 5-6 mg/kg (based on aminophylline) over 20-30 minutes
- Continuous infusion follows, and dose depends on patient age and desired level
- Suggested infusion rates:
  - 6 months-1 year: 0.7 mg/kg/hr aminophylline
  - 1-9 years: 1.2 mg/kg/hr aminophylline
  - 10-16 years: 0.9 mg/kg/hr aminophylline
- Metabolism is influenced by multiple medications
- Effect as a respiratory muscle inotrope is dose-dependent; lower doses are effective

Leukotriene Modifiers

- Montelukast (Singulair) oral tablets
- Dose:
  - 1-5 years: 4 mg po QD
  - 6-14 years: 5 mg po QD

Asthma Complications

- Pneumothorax
- Pneumomediastinum
- Pneumopericardium
- Pulmonary interstitial emphysema
- Pneumoretroperitoneum
- Cardiac arrhythmias
- Myocardial ischemia
- Mucous plugging
- Atelectasis
- Pneumonia
- Electrolyte imbalance (hypokalemia, hypomagnesemia, hypophosphatemia)
- Lactic acidosis
- Hyperglycemia

Grade of Evidence of Interventions in Acute Severe Asthma

Grade A

- Oxygen should be administered to maintain peripheral oxygen saturation between 0.89 to 0.95
- Use inhaled β2-agonists as primary bronchodilators
- Give steroids in all cases of acute asthma

Grade B

- Add nebulized ipratropium bromide

Grade C

- A single dose of magnesium sulfate can be used

Grade D

- A single dose of intravenous montelukast should be considered

The quality of the evidence was given a grade of A, B, C, or D for high, moderate, low, and very low, respectively.

Adapted from: Reference 4

Supplement to *Pediatric Emergency Medicine Reports*, April 2013: "Acute Severe Asthma." *Authors:* **Ronald M. Perkin, MD,** MA, Professor and Chairman, Department of Pediatrics, Brody School of Medicine at East Carolina University, Greenville, NC; and **Matthew R. Ledoux, MD**, Division Chief, Division of Pediatric Critical Care and Sedation Services, Brody School of Medicine, East Carolina University, Greenville, NC.