Asthma Update

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INTRODUCTION

Management of acute asthma exacerbations has evolved over recent decades, with an expanding body of research driving advances in therapeutics. Asthma is a heterogeneous chronic inflammatory condition with variable phenotype, influenced by genetic and environmental determinants. Although differences in response to therapy may occur, standard treatment has been defined in the National Asthma Education and Prevention Program (NAEPP) guidelines and involves inhaled bronchodilators and systemic corticosteroids (SCSs).\textsuperscript{1} Prompt recognition of severity and initiation of therapy are important goals.

KEYWORDS

- Acute
- Asthma
- Treatment
- Pediatric
- Emergency

KEY POINTS

- Acute asthma management involves prompt recognition of severity and treatment using short-acting \(\beta\)-agonists (SABAs), anticholinergics, and systemic corticosteroids (SCSs).
- Children with severe exacerbations should receive high-dose SABAs mixed with ipratropium bromide as well as SCSs.
- Children with less-severe exacerbations may benefit from SCSs based on chronic asthma severity reflecting significant airway inflammation.
- Patients not improving after multiple high-dose SABA treatments should receive adjunctive therapy, such as intravenous (IV) magnesium.
- Many children treated for asthma in the emergency department (ED) have significant morbidity and infrequent primary asthma care; prescription of inhaled corticosteroids (ICSs) is appropriate.

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Funding Source: None.
Conflicts of Interest: K.A.N., Spouse employed at Vertex Pharmaceuticals, Inc; J.J.Z., None.
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http://dx.doi.org/10.1016/j.pcl.2013.06.003
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Despite advances in chronic and acute care, asthma remains a major public health issue. It is important to appreciate its epidemiology, including the significant disease burden and health disparities according to race and socioeconomic status. There are aspects of chronic care beyond the ED visit, including prescription of controller therapy and access to primary asthma care, that are also important considerations. This article discusses current recommendations and evidence for acute asthma management.

**EPIDEMIOLOGY**

According to recent United States statistics, lifetime prevalence of asthma is estimated at 13% of all children, with 6.7 million experiencing active disease. More than 3.5 million children have greater than or equal to 1 exacerbation per year, resulting in approximately 600,000 ED visits. Children younger than 4 years have the highest rates of ED visits, ambulatory visits, and hospitalizations. Asthma is uncommonly diagnosed before 12 months of age, and some clinicians hesitate to diagnose asthma in children younger than 24 months, when the diagnosis relies on history and symptoms and overlaps with transient viral bronchiolitis. A diagnosis of asthma is appropriate, however, if a child has compatible history of recurrent episodes of cough, respiratory distress, and wheezing, suggesting the characteristic features of airway obstruction, bronchial hyper-responsiveness, and airway inflammation.

Asthma disproportionately affects minority children, those in urban areas, and those of lower socioeconomic status. Puerto Rican children in the United States have the highest prevalence, at 19.2%. Black children have the highest rates of both ED visits and death, however. Moreover, with regard to preventative care, minority children have fewer ambulatory visits compared with white children and lower rates of controller medication use.

**DIFFERENTIAL DIAGNOSIS**

Asthma is characterized clinically by a pattern of periodic episodes of cough, wheeze, respiratory distress, and reversible bronchospasm. Although wheezing is the most obvious symptom, asthma may also present as cough without significant wheeze. Asking a family about typical symptoms for a child can provide clarification. Pulmonary function testing can identify airway obstruction in children able to complete it (usually children older than 5 years), although often a clinical diagnosis is made.

Considering the symptoms common for asthma are nonspecific, an appropriate differential diagnoses list should be considered. A diagnosis of asthma during the first episode of wheezing can be challenging, and clinical presentation overlaps with bronchiolitis in young children.

**SEVERITY ASSESSMENT**

Rapid determination of severity is important to direct appropriate therapy. Severity is a spectrum—mild, moderate, severe, and impending respiratory failure. Clinical scores using predominantly subjective measures, such as the pediatric asthma severity score, have been shown valid and reliable. The NAEPP guidelines recommend objectively measuring airway obstruction using spirometry or peak expiratory flow rate (PEFR), although this may be impossible in young or severely ill children. In assessing severity
and formulating treatment plans, patient history and response to medications already used for that exacerbation should be considered.

INITIAL STANDARD THERAPY

The main goals of acute asthma treatment are 2-fold—to rapidly reverse broncho-spasm and to treat underlying airway inflammation. Severity-based treatment should be initiated as soon as possible.

**Short-acting β-Agonist**

**Albuterol or levalbuterol**

Inhaled SABAs cause bronchodilation of airway smooth muscle through activation of β₂-adrenergic receptors (Table 2). Albuterol is the most commonly used SABA, a racemic mixture of 2 enantiomers—(R)-albuterol (binds β₂-receptor and causes bronchodilation plus adverse effects of tachycardia and tremor) and (S)-albuterol (thought to have detrimental effect on airway function). Levalbuterol is a purified form of the (R)-enantiomer, marketed as an alternative with fewer adverse effects than racemic albuterol. Studies comparing racemic albuterol and levalbuterol have not consistently reported superiority over racemic albuterol, however, in improved pulmonary function or clinical outcomes,¹¹⁻¹⁴ raising questions about cost effectiveness. The updated NAEPP guidelines list levalbuterol as an option for SABA treatment at half the dose of (racemic) albuterol.¹

**Delivery device**

Albuterol can be administered using metered dose inhalers (MDIs) that have either valved holding chambers (spacer) or nebulizers; use of each requires proper technique. Although there are potential differences in lung deposition between devices, in general, studies of clinical outcomes have found equivalency or favor MDI with spacer due to shorter ED length of stay (LOS) and less tachycardia.¹⁵⁻²¹ Although

<table>
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<tr>
<th>Differential diagnosis</th>
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<td>Upper respiratory tract infection with wheezing</td>
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<td>Bronchiolitis</td>
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<td>Pneumonia</td>
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<td>Pneumothorax</td>
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<td>Congenital cardiac abnormality with heart failure</td>
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<tr>
<td>Congenital pulmonary abnormality</td>
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<td>Foreign body</td>
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<tr>
<td>Cystic fibrosis</td>
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<td>α₁-Antitrypsin deficiency</td>
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<td>Gastroesophageal reflux disease</td>
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<td>Tracheoesophageal fistula</td>
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<td>Allergic reaction/anaphylaxis</td>
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<td>Vocal cord dysfunction</td>
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<td>Toxic exposure</td>
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nebulizers have traditionally been the preferred devices, MDI with spacer may be considered an option for children with mild and moderate exacerbations (see Table 2).

Data on MDI with spacer use for severe asthma are limited. Patients with severe exacerbations have significant lower airway obstruction, which limits drug deposition in the lung, and higher overall doses using nebulizer are often necessary.

**Continuous nebulized SABA treatment**
Continuous nebulized albuterol treatment is recommended for patients with severe exacerbations or poor response to intermittent or back-to-back dosing (see Table 1).
Ipratropium Bromide

Ipratropium bromide causes bronchodilation by blocking muscarinic cholinergic receptors (see Table 2). It is associated with lower admission rate for children with severe exacerbations and may reduce ED LOS.\textsuperscript{24–26} Multidose protocols are associated...
Corticosteroids

Corticosteroids block formation of potent inflammatory mediators and reduce airway inflammation. SCSs are proved effective for moderate and severe exacerbations and should be administered as early as possible for maximum benefit (see Table 2).27,28 One systematic review found the reduction in hospitalization rate was most significant after 2 hours, which may be an important consideration when assessing response to therapy.27 Another review found that SCSs reduced relapse visits, a major ED quality outcome.28 Adverse events were similar between study groups in these reviews.27,28 Patients with mild exacerbations should receive SCSs if they have incomplete response to inhaled SABA.

For many ED patients, the potential benefits of SCSs outweigh the potential harms, including patients who have recently completed an SCS course but have recurrence of symptoms. Although SCS courses have been reported to be associated with alteration in bone metabolism and bone mineral density, they were not associated with increased fracture rates.29–31 Patients requiring more than 1 course of SCS in 6 months should be prescribed ICSs.

Route, dosing, duration

Oral administration of SCSs is the preferred route because of similar bioavailability compared with the parenteral route and less pain (see Table 2). Patients with severe exacerbations or significant vomiting may require parenteral administration. Intramuscular (IM) dexamethasone is an option. Studies report similar outcomes with IM dexamethasone compared with oral prednisone.32,33 The current recommended dose of oral prednisone or prednisolone is 1 mg to 2 mg per kg (maximum 60 mg) per day for 3 to 10 days (NAEPP). In a recent study, a 3-day course of prednisone had similar outcomes compared with a 5-day course.34 One or 2 days of oral dexamethasone is reported to have similar ED relapse rates and less vomiting compared with multiple days of prednisolone and may be considered an option, although current studies are limited due to differences in protocols and variable dexamethasone and prednisolone dosing.35–37

Inhaled corticosteroid

ICSs are beneficial for long-term asthma control, and administration during acute exacerbations may also be effective but research has some limitations. Systematic reviews have found single-dose ICS protocols similar to SCSs for some outcomes, whereas multidose protocols were associated with greater early (within 60 minutes) PEFR improvement and reduction in hospitalization rate, although these studies had significant heterogeneity.38,39 At this point, results of studies do not support replacing SCSs with ICSs in ED management of acute exacerbations.

Studies have also not found ICSs superior to SCSs for immediate post-ED outcomes.40,41 Considering the beneficial effects in chronic asthma, however, initiation or continuation of ICSs along with a short course of OCS at time of discharge should be considered.

REASSESSMENT

Careful reassessment should be conducted after initial treatment, taking into consideration the timing of SCS dosing (Table 3). If response to treatment is incomplete or poor, further treatment with SABAs is indicated. Patients with severe exacerbations
require close monitoring and reassessment to determine response and need for adjunctive therapies.

ADJUNCTIVE THERAPIES

Adjunctive therapies are usually administered in addition to (but not instead of) inhaled bronchodilators, and timing may vary according to severity. Anticipating their need is essential to avoid delays in care. Most patients requiring adjunctive therapy will require hospitalization, and many of these therapies should be administered in an ICU setting.

Magnesium Sulfate

Magnesium sulfate is associated with improved pulmonary function and reduced hospitalization rate. Its mechanism of action is unclear but it is thought to cause bronchodilation by decreasing intracellular calcium concentration resulting in respiratory smooth muscle relaxation. It is most commonly administered as a single IV bolus, and a dose-response effect has been reported. The recommended dose is 50 mg/kg to 75 mg/kg (maximum 2 g). There is limited pediatric data on inhaled magnesium sulfate and systematic reviews report no clear benefit. In practice, most clinicians hospitalize patients who require magnesium.

Helium-oxygen–Delivered SABA

Heliox is a mixture of helium and oxygen, thought to improve drug delivery in obstructed airways due to its lower density and airflow resistance. A recent systematic review found that delivery of aerosolized medication with heliox may improve outcomes in severe exacerbations. The commonly used mixtures (helium:oxygen) are 70:30 or 80:20, and use in patients with significant hypoxemia is, therefore, limited.

Systemic (Injected) β-Agonists

Epinephrine, given subcutaneously or IM, should be considered an option for severe exacerbations, particularly as initial treatment of patients with significant airway obstruction when delivery of inhaled medications to the lower airways may be limited. Terbutaline may be administered subcutaneously and is also commonly administered as a continuous IV infusion, although pediatric studies evaluating such protocols are limited.
Noninvasive Ventilatory Support

Noninvasive ventilatory support bilevel positive airway pressure may benefit patients tiring from increased work of breathing and with impending respiratory failure. Pediatric studies are limited but suggest it is generally well tolerated and may reduce need for ICU admission. In practice, most patients who require biphasic positive airway pressure are treated in ICU settings.

Other Medications

Aminophylline and theophylline are not recommended for routine exacerbations. They are usually reserved for ICU settings and patients not responsive to other adjunctive therapies. Although studies suggest possible benefit in pulmonary function, LOS did not differ and there were more adverse events, such as vomiting, compared with β-agonists.

Montelukast, a leukotriene receptor antagonist, is an effective controller medication for chronic asthma, but pediatric studies have not consistently shown effectiveness for oral or IV montelukast in the ED.

Ketamine is a dissociative anesthetic that is an option during rapid sequence induction for intubation of children with asthma in respiratory failure. It has not, however, been found associated with added benefit during standard acute therapy.

CHEST RADIOGRAPHS

Use of chest radiographs (CXRs) during ED visits with wheezing diagnoses varies in the United States, estimated between 14% and 56% of such visits. Studies seeking to identify predictors of pathologic CXRs (most frequently pneumonia) among children with wheezing have shown that fever, hypoxia, and focal rales or wheezing may be indicators. In a study of children of all ages with wheezing who had CXR for possible pneumonia, 4.9% of CXRs showed pneumonia.

In children with first-time wheezing episodes, rates of pathologic CXRs ranged from 6% to 24% with similar predictors as described previously. In a prospective study of young children with bronchiolitis, the rate of CXRs inconsistent from bronchiolitis was less than 1%. The potential risks of CXR include radiation exposure and false-positive results, leading to unnecessary antibiotic therapy. In general, a high threshold for imaging is appropriate for patients with typical asthma exacerbation given the low rate of abnormality.

CLINICAL PRACTICE GUIDELINES

Implementation of clinical practice guidelines for acute asthma is associated with improved efficiency and quality of care, including shorter time to SABAs and SCSs, increased rates of SCSs, decreased LOS, lower hospitalization rate, and fewer prescription errors.

POST–EMERGENCY DEPARTMENT CARE

Improving Preventive Therapy

Poor adherence to prescribed ICSs is well documented in patients seeking asthma care in EDs, and studies have reported up to two-thirds of children presenting to EDs have persistent chronic asthma severity, indicating poor long-term control. A majority of children treated in EDs, however, are not prescribed ICSs.
The NAEPP guidelines recommend ED providers consider initiating controller medications to appropriate patients.\(^1\) A brief assessment of asthma control can assist clinicians in identifying such patients—assess impairment (>2 d/wk of asthma symptoms or SABA use or 1 to 2 nighttime awakenings due to asthma per month) and risk (>1 SCS course in last 6 mo or >3 acute wheezing episodes lasting >1 d each in last 12 mo).\(^1\)

**Written Asthma Care Plans**

Written asthma care plans are associated with improved outcomes, including increased adherence to ICSs.\(^75,76\) Although discharge instructions should include information regarding care after the acute visit, this is an opportunity for clinicians to provide appropriate care plans to assist patients with future exacerbations and to encourage partnership with primary care physicians and ongoing discussions of home asthma care.

**Follow-up After an Acute Visit**

Primary care physician visits, both follow-up after the ED and periodically to monitor asthma control, are important for optimal care, because studies have shown that NAEPP guideline-based asthma care reduces morbidity.\(^77,78\) Patients discharged from EDs should have primary care physician follow-up visits within 2 to 4 weeks. Unfortunately, studies have shown unacceptably poor follow-up rates in urban populations.\(^79,80\) Interventions, such as scheduling follow-up at the time of an ED visit, can improve adherence.\(^79\)

**SUMMARY**

- Acute asthma management involves prompt recognition of severity and treatment using SABAs, anticholinergics and SCSs.
- Children with severe exacerbations should receive high-dose SABAs mixed with ipratropium bromide as well as SCSs.
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**REFERENCES**


