Management of Asthma in School-Aged Children and Adolescents

Sandy Durrani, MD

Abstract

Asthma is one of the most common childhood diseases in the world and a significant cause of morbidity and health care expenditures. United States and international evidence-based guidelines created and updated in the past 2 decades have significantly improved the consistency and effectiveness of asthma care in children. Assessing severity and monitoring control using the impairment and risk domains is fundamental to effective management. At every visit, the provider should assess environmental triggers and comorbid conditions, review inhaler technique and adherence, and provide an updated asthma action plan. Inhaled corticosteroids remain the preferred controller in persistent childhood asthma; however, especially in young children, a discussion should occur with caregivers regarding possible adverse effects. Similarly, if long-acting beta-2-agonists are added to inhaled corticosteroids at step 3 care and above, the risk of severe asthma-related events should be discussed. Indications for referral to an asthma specialist include difficult-to-treat asthma, step 4 care and above, risk factors for severe asthma related events, subtypes of asthma, and doubts of asthma diagnosis. [Pediatr Ann. 2014;43(8):e184-e191.]
Asthma is one of the most common childhood diseases encountered by health care professionals in the United States, with an estimated prevalence of 9.7%. Despite the availability of effective medications, childhood asthma remains a significant public health burden due to medication costs, frequent health care use (eg, urgent care or emergency department visits, hospitalizations), missed school, and missed work by caregivers. Globally, although rates of childhood asthma vary significantly, international surveys suggest there remains a substantial percentage of patients with poor asthma control in many countries. As a result, significant effort over the past 20 years has been made to provide an evidence-based asthma management approach to improve consistency and effectiveness of care by creating publically available guidelines published in the United States by the National Education and Prevention Program (NAEPP) Expert Panel Report (EPR) and internationally by the Global Initiative for Asthma (GINA). Although the last iteration of guidelines published by the NAEPP was in 2007, GINA guidelines are updated annually, with the most recent version published in 2014.

This review updates the health care professional on the principles of asthma care in the school-aged child and adolescent (ie, 6-18 years), primarily focusing on EPR recommendations. Management of preschool-aged wheeze/asthma is not covered in this review but is extensively reviewed by EPR and GINA guidelines.

**BASIC PRINCIPLES OF LONG-TERM MANAGEMENT OF CHILDHOOD ASThma**

Regardless of the patient’s age, the EPR cites the application of four essential components of care in the management of asthma:

1. Assessment and monitoring of asthma severity and control
2. Education
3. Control of environmental factors and comorbid conditions that affect asthma
4. Medications

**Assessment and Monitoring of Asthma Severity and Control**

The EPR recommends that pharmacologic therapy be initiated on the basis of asthma severity and control. Asthma severity, defined as the intrinsic intensity of the disease process, is most clearly assessed in a patient who is not currently on long-term controller therapy and can also be determined by the amount of medication needed to attain control. Asthma control is defined by the degree to which asthma symptoms are attenuated by treatment. Control is divided into three categories: well controlled, not well controlled, and very poorly controlled.

Asthma severity and control are further assessed within two major domains: impairment and risk. Impairment refers to the degree of current asthma symptoms and lung function. Impairment includes daytime symptoms, nighttime awakenings due to asthma, short-acting bronchodilator use, interference with normal activity, and lung function. Risk includes exacerbations, progressive loss of lung function, and side effects from medications.

Asthma severity is divided into two general classes: intermittent and persistent. Persistent childhood asthma is then further subdivided into mild, moderate, and severe. Children with intermittent asthma have few to no symptoms and normal lung function. These patients rarely have exacerbations; however, it is important for clinicians to remember that when exacerbations in intermittent asthmatics occur, they can be severe. In children with persistent asthma, there is a greater degree of impairment and risk. As children with persistent asthma develop more impairment (eg, daily symptoms, nighttime awakenings, obstruction on lung function) and greater risk (eg, increased frequency of exacerbations), they are classified with a higher degree of severity. Furthermore, increasing severity of asthma is characterized by the need for more medications to attempt to achieve disease control.

By assessing asthma severity and control within the context of impairment and risk, the clinician can thoroughly assess illness severity and effectively treat it. Once treatment is established, control should be assessed at frequent intervals using the previously discussed well-controlled, not well-controlled, and very poorly controlled categories. Control should be evaluated within the context of impairment and risk at every visit. Furthermore, validated tools, such as the Asthma Control Questionnaire or the Asthma Control Test, can be incorporated to objectively monitor control.

In a child or adolescent with uncontrolled asthma, a step-up approach (treatment escalation) should be attempted to decrease impairment and risk of exacerbation. Based on guidelines, when treatment is escalated, control should be re-evaluated in 2 to 6 weeks. Similarly, if an asthmatic child is assessed as well controlled, step-down treatment should be considered. There are currently no clear guidelines to aid health care professionals in step-down approaches. However, if a child is well controlled for 3 months, step-down therapy can be considered. Importantly, step-up and step-down treatment should also be performed with consideration of the heterogeneity of pediatric asthma. For example, some children develop increased risk of symptoms or more frequent exacerbations due to viruses (eg, school or day care attendance) or allergies (eg, seasonally due to pollens, perennial from pets). Similarly, if it is known that a child with allergies to cats or dogs will have a temporary increased exposure (eg, traveling to grandparents’ house, who have a dog), a short-term step-up...
approach can be used. Furthermore, asthma severity and control can also vary over time due to changes in treatment response or an intrinsic change in illness severity, such as loss of control after an exacerbation. It must be remembered by the health care professional that it requires considerable experience and a comprehensive understanding of the nuances of asthma care to appropriately achieve and maintain control in a child with asthma.6

Education

An often-underrecognized key component to effective care of a child with asthma is the establishment of a partnership in education between the health care professional and patient and/or caregiver. At the initial visit, education should include discussing the role of inflammation and what occurs during an asthma attack; explaining the differences between long-term and quick-relief medications; encouraging the development of patient skills, including appropriate inhaler technique; identifying precipitating factors (eg, environmental factors such as allergens or tobacco smoke); discussing self-monitoring (identifying increased symptoms and loss of asthma control); and encouraging the use of written asthma action plans.3

Adherence to medications remains a significant issue because the majority of patients with asthma are well controlled with low- to medium-dose inhaled corticosteroids (ICSs). Failure to address adherence in a child with uncontrolled asthma can lead to unnecessary escalations in medications, leading to an increased chance of adverse effects from medications.3,4 Similarly, every child and/or caregiver with asthma should be provided with an action plan. The addition of a written asthma action plan (tailed to the literacy levels of the patient and caregiver) has been shown to significantly decrease hospitalization and emergency department visits for asthma.7

### TABLE 1.
Assessment of Severity Using the Impairment and Risk Domains in Children Aged 5 to 11 Years, as Illustrated in the Expert-Panel Report 3 (EPR-3)3

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Classification of Asthma Severity (5–11 years of age)</th>
<th>Intermittent</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>≤ 2 days/week</td>
<td>≥ 2 days/week but not daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤ 2n/month</td>
<td>3–6n/month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-acting beta-blocker, against use for symptom control (not prevention of EIB)</td>
<td>≤ 2 days/week</td>
<td>≥ 2 days/week but not daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Normal limitation</td>
<td>Some limitation</td>
<td>Extremely limited</td>
<td></td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV1, between exacerbations</td>
<td>FEV1 &gt;80% predicated</td>
<td>FEV1 ≈ 60–80% predicated</td>
<td>FEV1 &lt; 60% predicated</td>
<td></td>
</tr>
</tbody>
</table>

Recommended Step for Initiating Therapy

<table>
<thead>
<tr>
<th>Step 1:</th>
<th>Step 2:</th>
<th>Step 3: medium-dose ICS option</th>
<th>Step 3: medium-dose ICS option, or step 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.</td>
<td>Frequency and severity may fluctuate over time for patients in any severity category.</td>
<td>Relative annual risk of exacerbations may be related to FEV1.</td>
<td></td>
</tr>
</tbody>
</table>

EIB = exercise-induced bronchoconstriction; FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity; ICS = inhaled corticosteroids.

Note: If greater intensity of exacerbation (eg, hospitalization, intensive care unit) consider higher degree of severity.

The Expert-Panel Report 3 is published by the US Department of Health and Human Services and is in the public domain. Figure 4-1b can be found in the full report.

### TABLE 2.
Assessment of Severity Using the Impairment and Risk Domains in Children Aged 12 Years and Older, as Illustrated in the Expert-Panel Report 3 (EPR-3)3

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Classification of Asthma Severity (≥12 years of age)</th>
<th>Intermittent</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>≤ 2 days/week</td>
<td>≥ 2 days/week but not daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal FEV1, FVC (% predicted)</td>
<td>80%–85%</td>
<td>65%–80%</td>
<td>45%–60%</td>
<td>30%–45%</td>
<td></td>
</tr>
<tr>
<td>Short-acting beta-blocker, against use for symptom control (not prevention of EIB)</td>
<td>≤ 2 days/week</td>
<td>≥ 2 days/week but not daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Normal limitation</td>
<td>Some limitation</td>
<td>Extremely limited</td>
<td></td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV1, between exacerbations</td>
<td>FEV1 &gt;80% predicated</td>
<td>FEV1 ≈ 60–80% predicated</td>
<td>FEV1 &lt; 60% predicated</td>
<td></td>
</tr>
</tbody>
</table>

Recommended Step for Initiating Therapy

<table>
<thead>
<tr>
<th>Step 1:</th>
<th>Step 2:</th>
<th>Step 3:</th>
<th>Step 4 or 5:</th>
</tr>
</thead>
<tbody>
<tr>
<td>In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.</td>
<td>Frequency and severity may fluctuate over time for patients in any severity category.</td>
<td>Relative annual risk of exacerbations may be related to FEV1.</td>
<td></td>
</tr>
</tbody>
</table>

EIB = exercise-induced bronchoconstriction; FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity.

Note: If greater intensity of exacerbation (eg, hospitalization, intensive care unit) consider higher degree of severity.

The Expert-Panel Report 3 is published by the US Department of Health and Human Services and is in the public domain. Figure 4-5 can be found in the full report.
Control of Environmental Factors and Comorbid Conditions That Affect Asthma

Dust mite, cockroach, rodent, and pet dander exposure have all been associated with worsening of asthma in children. Similarly, children with seasonal allergies (eg, trees, weeds, mold, and grass) are susceptible to exacerbations when pollen counts are high. As a result, allergy testing (ie, skin prick and/or in vitro immunoglobulin E [IgE] testing) is recommended in a child with persistent asthma to aid in identification, avoidance, and treatment of allergies. Allergy specialist consultation should be considered to facilitate testing and treatment.

Other important environmental triggers include smoke exposure and viruses. Active smoking by patients and passive smoke exposure from caregivers, most notably mothers, is associated with the development of asthma, as well as increased morbidity. Education and resources reducing passive smoke exposure and/or encouraging tobacco cessation should be provided. Children with asthma should also receive annual inactivated influenza vaccination.

Identification and treatment of comorbid conditions in childhood asthma are important because conditions such as gastroesophageal reflux, allergic rhinitis, sinusitis with or without nasal polyposis, aspirin-exacerbated respiratory disease, obesity, obstructive sleep apnea, paradoxical vocal fold motion, stress and depression, and allergic bronchopulmonary aspergillosis can affect management of asthma.

At every visit, the clinician should review environmental exposures and evaluate for comorbid conditions, especially if step-up therapy for uncontrolled asthma is considered.

Medications

The EPR designates two broad categories of asthma medications: quick-
relief medications and long-term control medications.²

Quick-Relief Medications
Quick-relief medications are used to treat acute symptoms and exacerbations, as well as to prevent symptoms in exercise-induced bronchospasm (EIB). Short-acting beta-2-agonists (SABAs) are bronchodilators that relax bronchial smooth muscle. SABAs can be used in all age groups and severities of asthma, with use greater than 2 times per week associated with uncontrolled asthma. Examples include albuterol and levalbuterol. Anticholinergics, such as inhaled ipratropium bromide, block muscarinic receptors and decrease vagal tone. Limited data exist for anticholinergics in pediatric asthma; however, some evidence suggests they can be used for exacerbations requiring emergency department–level care and as an alternative for those who cannot tolerate SABAs. Finally, oral systemic corticosteroids (OCSs), although not short acting, are used to treat moderate to severe exacerbations by reducing inflammation and airway dysfunction.³

Long-Term Control Medications
Long-term control medications are used daily to achieve control in a child with persistent asthma by reducing inflammation. ICSs are considered the mainstay of treatment in persistent childhood asthma. ICS anti-inflammatory effects are broad and include decreased type 2 helper T cells and decreased inflammatory cell migration and activation.⁵ ICS has been consistently found to be superior to all other controller medications in improving impairment and reducing exacerbations in childhood asthma.³,¹⁵⁻¹⁷ However, ICSs have not been found to alter the natural history of childhood asthma.¹⁶ Multiple preparations are available with low-, medium-, and high-dose options (Table 3).

Long-acting beta-2-agonists (LABAs), salmeterol and formoterol, are inhaled bronchodilators with a duration of action of at least 12 hours. These agents are used in combination with ICSs (Table 4) in children at step 3 care and above and should never be used as monotherapy due to safety concerns.³,⁴ Long-acting anticholinergic medications (eg, tiotropium) have been found to be beneficial in add-on therapy for moderate-to-severe asthma in adults¹⁸; its use in children warrants further study.

Leukotriene modifiers target leu-
kotriene-mediated inflammation from eosinophils, mast cells, and basophils. Medications in this class include leukotriene receptor antagonists (LTRAs; montelukast and zafirlukast) and leukotriene production inhibitors (5-lipoxygenase [5-LO] inhibitors; zileuton). LTRAs have an excellent safety profile and have been found to have a modest effect on lung function and symptoms; however, they are considered a second line/alternative agent for mild persistent asthma. In addition, LTRAs may be of benefit for EIB. Zileuton is only approved for patients aged 12 years and older and requires periodic liver function monitoring.

Mast cell stabilizers, such as cromolyn and nedocromil sodium, attenuate mediator release by blocking chloride channels and inhibiting subsequent inflammation and bronchospasm. These agents are safe, nonpreferred, alternative controllers in persistent asthma and EIB but are rarely used in practice due to limited availability in the United States.

Theophylline, a methylxanthine, has been found to be beneficial in controlling persistent asthma due to bronchodilator effects and modest anti-inflammatory effects. It is considered an alternative agent in step 2 care and above because ICSs have been found to be superior. In addition, due to concerns of toxicity, careful monitoring of serum levels (goal, 5-15 µg) is required, especially during illness or when other agents, such as macrolides, are added.

Immunomodulators are of increasing interest, especially in moderate to severe asthma. Omalizumab, or anti-IgE, is the only Food and Drug Administration (FDA)-approved agent in this category. A humanized monoclonal antibody, omalizumab binds IgE and, when used as add-on therapy, has been found to decrease exacerbations and corticosteroid use (inhaled and oral) and improve symptoms and quality of life. Although studies in children aged 5 years and older have shown efficacy, it is only approved in adolescents with allergic asthma aged 12 years and older at step 5 care and above. Any clinician who administers omalizumab should be prepared and equipped to identify and manage anaphylaxis.

Allergen-specific subcutaneous immunotherapy (SCIT) can be considered for children aged 5 years and older as an add-on therapy at steps 2 to 4 care. Meta-analyses have shown benefit, although most studies are per-
formed with a single allergen, whereas most patients have multiple sensitizations. Sublingual immunotherapy has recently been approved for allergic rhinitis treatment by the FDA but requires more study in children to evaluate its benefit in asthma.

**SPECIAL SAFETY CONSIDERATION FOR INHALED CORTICOSTEROIDS AND LONG-ACTING BETA-2-AGONISTS IN CHILDREN AND ADOLESCENTS**

The benefit of ICSs must be weighed against concerns regarding their effects on linear growth in young children. Although the risks are well balanced by the benefits, there may be a risk of decreased linear growth (approximately 1 cm) with low-dose ICSs. This occurs in the first few months of treatment, is generally not progressive, and is likely more associated with the use of ICSs in preschool-aged children. Unfortunately, there are no clear data on growth effects in children on moderate to high doses of ICSs for asthma. It is important to remember that growth in children is highly variable and influenced by multiple factors, including nutrition and hormonal status. Furthermore, children with poorly controlled asthma may have delayed growth. Regardless, regular monitoring of growth while a child is on ICSs using a stadiometer is important, and the EPR recommends titrating ICS doses to as low as required to control a child’s asthma.

The FDA placed a black box warning on all formulations containing LABA due to concern of an increased risk of asthma-related deaths. The EPR still recommends LABAs addition in step 3 care and above for adolescents (although not for children aged 5 to 11 years). In addition, if a child or adolescent requires LABA add-on, the benefits should be weighed against the small risk of severe exacerbations. Importantly, LABA standard dosing should not be exceeded, nor should LABAs be used in any formulation for acute symptoms. Similarly, LABAs should never be used as monotherapy.

**STEP-CARE APPROACH FOR SCHOOL-AGED CHILDREN AND ADOLESCENTS**

As stated previously, at any step in care, especially if asthma is uncontrolled, inhaler technique and adherence to medication should be assessed. In addition, a review of environmental exposures and an evaluation of comorbid conditions should be performed.

**Interruption of Asthma: Step 1**

Children with intermittent asthma have little to no impairment with normal activity and lung function. Exacerbations, although rare, can be severe. SABAs are recommended for acute symptoms as well as every 4 to 6 hours during an exacerbation or temporary loss of control for 24 hours. Prolonged regular SABA use for more than 1 day may require a short course of OCSs. Frequent OCS courses likely require a controller for uncontrolled persistent asthma.

Ipratropium is generally not recommended due to slower onset of action and unclear benefit. Mast cell stabilizers can also be considered at this step.

**Persistent Asthma**

**Step 2: Mild Persistent Asthma**

Children and adolescents with mild persistent asthma have symptoms during the day more than two times per week (not daily), nocturnal awakenings three to four times per month, and infrequent exacerbations with essentially normal lung function. As outlined previously, in children aged 5 to 11 years and adolescents aged 12 years or older, the EPR recommends low-dose ICSs as the preferred controller. For caregivers with concerns about adverse effects of ICSs (in particular linear growth effects), LTRAs may be a suitable alternative; however, treatment responsiveness and attainment of control should be closely monitored. Other controller possibilities include theophylline and mast cell stabilizers. In addition, in patients with allergic asthma, SCIT can be considered from steps 2 to 4.

**Step 3: Moderate Persistent Asthma**

Children with moderate persistent asthma have daily symptoms and SABA use, nocturnal awakenings more than once per week, some limitation of daily activities, and mild obstruction of lung function. In children aged 5 to 11 years, the EPR gives equal weight to (1) doubling ICS dose or adding LTRA (ICS + LTRA) and (2) adding LABA (ICS + LABA) due to LABA safety concerns. In adolescents aged 12 years or older, ICS + LABA is the preferred approach over doubling ICS or ICS + LTRA. A recent crossover study of children with uncontrolled mild persistent asthma confirmed that ICS + LABA was superior to medium-dose ICS or low-dose ICS + LTRA.

**Steps 4 to 6: Severe Persistent Asthma**

Children at this level of severity have continuous symptoms and SABA use with nightly awakenings, significant limitation of daily activities, and obstruction of lung function. The evidence for recom-
mendations at these steps is sparse due to lack of placebo-controlled trials given ethical concerns as well as relatively few
er patients to recruit into studies. At all ages, the addition of LABA is preferred with a step-wise increase in ICS dose with increased severity. Other alternatives include the addition of LTRA, 5-LO inhibitors, and theophylline. Omalizumab is another add-on option in patients aged 12 years and older with allergic sensitization to perennial allergens. Finally, the addition of OCS is recommended at step 6 level of care.3,5,6

ASTHMA SPECIALIST REFERRAL

In children and adolescents with the following indications or risk factors, a referral to an asthma specialist should be considered3,4:
- Difficult-to-control asthma, step 4 or above level of care, frequent exacerbations (more than two per year) or risk factors for asthma-related death (eg, previous intensive care unit admission or mechanical ventilation, anaphylaxis to food)
- Risk or evidence of treatment side effects (eg, concern for growth delay)
- Asthma subtypes (eg, aspirin-exacerbated respiratory disease, allergic bronchopulmonary aspergillosis)
- Doubts about asthma diagnosis

CONCLUSION

The development of national and international guidelines has significantly improved the quality of care of children and adolescents with asthma. The assessment of severity based on degree of impairment and risk helps to achieve and maintain control using a step-care approach. ICSs remain the first-line controller for children with persistent asth-

REFERENCES

15. Ng D, Salvio F, Hicks G. Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children. Cochrane Database Syst Rev. 2004(2):CD002314.