

# Pediatric Asthma for the Primary Care Practitioner



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## KEYWORDS

• Asthma • Pediatrics • Primary care practitioner • Guidelines

## KEY POINTS

- Asthma is a common chronic inflammatory disease of the airways.
- It is a complex disease, involving many different allergic, inflammatory, and environmental components.
- It is a disease for which patient and family education and a team-based approach are paramount for successful management.
- National Guidelines have been put forth by the National Heart, Lung and Blood Institute, which provide a helpful framework to begin to manage patients and to navigate the many medication choices available.
- It is only through diligent attention to control of asthma symptoms that improved quality of life and prevention of long-term sequelae are possible for the pediatric patient with asthma.

## INTRODUCTION

In the mid to late twentieth century, asthma was defined as a disease characterized by an increased responsiveness of the trachea and bronchi to various stimuli and manifested by widespread airway narrowing that changed in severity either spontaneously or as a result of treatment. This definition is no longer complete enough to define asthma in the twenty-first century.

Asthma affects at least 24 million individuals in the United States and is the most common chronic inflammatory disease of childhood (at least 7 million children are affected). In the pediatric world of medicine, males have a higher prevalence of asthma. African Americans and Puerto Ricans have the highest prevalence compared with whites and Mexican-Americans. Those who compose lower socioeconomic status are at increased risk, as are those in the Northeast United States.<sup>1</sup>

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By definition, asthma is the result of inflammation of the airways and narrowing of the airways, which is at least in part reversible. It occurs in paroxysms, causing symptoms of cough, wheezing, chest tightness, and difficulty breathing. Episodes are related to increased responsiveness of the airways to a variety of stimuli. Once believed to be entirely caused by bronchospasm of the smooth muscles lining the airways, asthma is viewed as a more complex chronic disease.

Medical information has greatly increased as science and biomedical research have enabled a more complete understanding of the disease processes of asthma. The incidence of disease has continued to increase, but the rate of acute attacks of asthma has remained constant over the past few years. According to the US Centers for Disease Control and Prevention 2006 National Health Interview Survey, there is a lifetime asthma prevalence of 13.5%.<sup>2</sup>

The components of asthma resulting in the symptoms and clinical expression of asthma include inflammation, edema (swelling), airway narrowing (secondary to edema, muscle thickening, and muscle contraction), airway plugging (secretions, inflammatory cells/debris), and basement membrane thickening caused by type IV collagen deposition.

The purpose of this article is to improve understanding of the basics and methods of the treatment of children with asthma.

## **PATHOPHYSIOLOGY OF ASTHMA**

Asthma is a chronic inflammatory disease of the airways, characterized by varying and recurrent symptoms of airway obstruction, hyperresponsiveness, and underlying inflammation.<sup>3</sup> Asthma manifests clinically as intermittent and recurrent wheezing or coughing.

In children, there are 2 main categories of asthma:

1. Recurrent wheezing (also called intrinsic asthma)
  - This typically arises from nonallergic causes
  - In early childhood, asthma is mostly caused by viral respiratory infections<sup>3</sup>
  - Can also be caused by aspirin/nonsteroidal antiinflammatory drug sensitivity
  - Some patients are also sensitive to environmental irritants, such as air pollutants, smoke, stress, exercise, and cold air
2. Chronic asthma (also called allergic or extrinsic asthma)
  - Mediated by a type 1 hypersensitivity reaction

Although there are distinct types of asthma, airway inflammation, hyperresponsiveness, and excess production of mucus are ubiquitous and are the result of a complex inflammatory response.

## **INFLAMMATORY RESPONSE**

### ***Inflammatory Cells and Their Roles***

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Lymphocytes, specifically T helper 1 (Th1) and T helper 2 (Th2), have distinct regulatory mechanisms that affect airway function.<sup>4</sup>

- A shift toward Th2 cells results in eosinophil recruitment and inflammation.
- Th2 release cytokines such as interleukin 4 (IL-4) and IL-5.
- Regulatory T cells, which normally inhibit Th2 cells and stimulate natural killer cells, are reduced, contributing to the lack of regulatory control over the Th2 response.
- Mast cells in the mucosa become activated from cross-linking of the increased IgE levels, and release histamine, leukotrienes C4/D4/E4 and prostaglandin D<sub>2</sub>.

- These inflammatory mediators cause bronchoconstriction, mucous production, and edema.

Generally, an increase in eosinophils correlates to increasing asthma severity.

Neutrophils are increased in the airways and sputum of severe asthmatics during exacerbations.

- Their pathologic role is uncertain, but neutrophils may explain a lack of response to corticosteroid therapy.
- They are the predominant cell type present in the airways of patients with nonallergic (intrinsic) asthma.<sup>5</sup>

Dendritic cells function as antigen-presenting cells, presenting the allergens from the airway to the regional lymph nodes.

- In the lymph nodes, these cells interact with regulatory T cells, resulting in the stimulation of Th2 cells from naive T cells.

Macrophages are present in the highest amounts in asthmatic airways and are activated by allergens to release inflammatory cytokines.

Airway smooth muscle cells also contribute to airway obstruction through generating their own proinflammatory cells.

- When the smooth muscle proliferates and hypertrophies, this response is accelerated, contributing to the disease process.

These inflammatory cellular infiltrates and exudates also obstruct the airways. They are capable of causing damage to the epithelium and even desquamation into the airway lumen.<sup>4</sup>

### ***Inflammatory Mediators and Their Roles***

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IgE is the antibody responsible for starting a type I hypersensitivity reaction.

- IgE attaches to high-affinity receptors on the cell surfaces.
- Mast cells express IgE receptors in large amounts, as well as basophils, dendritic cells, and lymphocytes.
- Clinical findings in the development of monoclonal antibodies to IgE support the understood role of IgE in asthma.

Chemokines (eotaxin) are expressed in airway cells and work to recruit inflammatory cells.

Cytokines control the inflammatory response in asthma and directly influence its severity.

- Th2 releases cytokines IL-4 and IL-5, which leads to eosinophil recruitment and the overproduction of IgE.
- Other Th2 cytokines include IL-1 and tumor necrosis factor  $\alpha$ , which amplify the inflammatory response, and granulocyte macrophage colony-stimulating factors, which promote eosinophil survival.

Leukotrienes C4/D4/E4 released by mast cells along with histamine and prostaglandin D<sub>2</sub> are potent bronchoconstrictors.

These inflammatory cells and mediators result in hyperresponsiveness, leading to bronchospasm and constriction of the airways, as well as mucous production and airway edema.

As mentioned earlier, it is hypothesized that an imbalance between Th1 and Th2 cells, resulting in a shift toward Th2 cytokine profiles, contributes to the disease process. There may be a loss of the reciprocal relationship between Th1 and Th2, an underexpression of Th1, or overexpression of Th2.<sup>6</sup>

Several factors favor the development of a protective Th1 phenotype, such as the presence of older siblings, early exposure to day care, a rural environment, and

infections such as tuberculosis, measles, or hepatitis A. Alternatively, a Western lifestyle, urban environment, house-dust mite sensitization, widespread antibiotic use, and diet can contribute to a Th2 phenotype, which can result in allergic diseases and asthma.

Respiratory infections during infancy have been associated with the development of asthma, as well. Respiratory syncytial virus (RSV) and parainfluenza virus cause bronchiolitis, which manifests similarly to childhood asthma.<sup>3</sup>

Although some studies show that such infections confer a risk (approximately 40%) of wheezing or asthma later in life,<sup>4</sup> evidence also shows that repeated viral infections, including RSV, can help develop a strong Th1 response and protect against asthma. Research is focused on understanding the innate and adaptive immune process and interplay with genes and environment.

## EPIDEMIOLOGY

Asthma is a common chronic disease, causing considerable morbidity. Current prevalence in the United States has been reported to be 8.2% up to 2010.<sup>1</sup> This prevalence includes 24.6 million people, 7.1 million of whom are children from birth to 17 years of age.

This statistic represents an overall increase in the prevalence of asthma since 2001, when current measures first began. In 2001, prevalence was 7.4% and remained fairly stable until recent increases to current prevalence of 8.2%.<sup>1</sup> Although the incidence of asthma has stabilized, the prevalence still remains at an all-time high.

Prevalence of asthma differs between multiple subgroups of the population.

- Prevalence of current asthma for children is higher overall, at 9.6%, than for adults, at 7.7%.
- Children ages 14 to 17 years have similar prevalence for both genders.
- Gender difference becomes reversed from childhood (11.3% of boys vs 7.9% of girls).
- During early adolescence, asthma prevalence declines steadily in boys and increases steadily for girls.
- Adult women have a higher prevalence of asthma overall, with 9.3% of women having asthma, compared with 7% of men.
- Current asthma prevalence is also higher for African Americans, Puerto Ricans, and those with family incomes lower than the federal poverty level.
- Prevalence for metropolitan and nonmetropolitan areas does not differ.
- Regional differences in prevalence are also noted, with higher rates in the Northeast and Midwest regions of the United States.<sup>1</sup>
- Prevalence of asthma attacks among people with asthma is 52%, as of 2009,<sup>7</sup> defined as patients having had at least 1 attack in the previous year.<sup>7</sup>
- Fifty-six percent of children with asthma reported attacks.<sup>7</sup>
- Forty-seven percent of adults with asthma reported attacks.<sup>7</sup>

Data from a 2008 aggregate report<sup>1</sup> show that children aged 5 to 17 years who suffered at least 1 asthma attack in the previous year were reported to have missed a total of 10.5 million days of school in that year. In addition, 5.5% of children with asthma reported activity limitations caused by their asthma.

Adults with asthma during the same period who also reported at least 1 attack in the previous year missed a total of 14.2 million work days, with 34% missing at least 1 day of work because of their asthma and 6% experiencing an activity limitation.<sup>1</sup>

Health care use and costs for asthma are high. In 2007, 13.9 million visits were made to physician offices for asthma, with 6.7 million of those visits including treatment of children with asthma.<sup>1</sup> This situation may represent some measure of appropriate disease

management, because periodic health maintenance visits for management are recommended. However, emergency department (ED) visits and hospital admissions for asthma represent adverse outcomes, and 1.75 million ED visits for asthma were reported during the same period; 640,000 of these were for children aged 0 to 17 years, and 157,000 hospital admissions were reported for children that year, with 185 deaths.<sup>1</sup>

In 2008, 96% of patients with a current asthma diagnosis reported that a health care team member provided education about proper inhaler use, but only 34% reported receiving a written asthma action plan with instructions about (1) increasing medication dosage, (2) changing medicines, or (3) when to call a medical provider and when to proceed to the ED for emergent care.

Sixty percent reported receiving education on recognizing personal signs and symptoms of an asthma attack. When compared with adults, children reported a higher rate of receiving asthma control instructions.<sup>6</sup>

Just as the cause of asthma is not understood, the complex role of asthma self-management, including environmental exposures, health care system access, and financial factors, is not well understood. Identifying any population-specific factors that contribute to asthma attacks or prevent their timely treatment can lead to targeted interventions for that population.<sup>7</sup>

## TREATMENT

### *Four Components of Asthma Care*

The clinical practice guidelines for diagnosis and management of asthma, as put forth by the National Heart Lung and Blood Institute Expert Panel Report 4, published in 2007, present 4 components for effective asthma care.<sup>6</sup>

- Component 1: measures of asthma assessment and monitoring
- Component 2: education and partnership in asthma care
- Component 3: control of environmental factors and comorbid conditions affecting asthma
- Component 4: pharmacologic management

### *Component 1: assessing and monitoring asthma severity, control, and responsiveness*

#### **Step 1: making the diagnosis**

Diagnosing the pediatric patient is the first step toward eliminating the symptoms and improving quality of life and preventing long-term sequelae.

- A detailed medical history and physical examination, with a focus on the upper respiratory tract, chest, and skin
- Spirometry use in conjunction helps diagnose asthma and rule out other diagnoses

Clinical features suggestive of asthma diagnosis<sup>4</sup>:

- History of episodic or chronic airway obstruction symptoms that are at least partially reversible
- Response to and duration of albuterol
- Spirometry before administration of bronchodilator:
  - FEV<sub>1</sub> (forced expiratory volume in first second of expiration) less than 80% predicted, FEV<sub>1</sub>/forced vital capacity less than 85%
- Spirometry after administration of bronchodilator:
  - FEV  $\geq$  9% from baseline, showing reversible airway obstruction
- Exclusion of alternative diagnoses

Ancillary studies may include a methacholine challenge in patients with symptoms suggestive of asthma but normal spirometry, chest radiograph to rule out congenital

malformations, sweat chloride test to rule out cystic fibrosis, barium swallow for patients with reflux, and allergy testing for environmental allergens in very young children.

In children younger than 5 years, the diagnostic process remains the same; however, spirometry may be unavailable. Asthma is a chronic condition, whereas nonatopic conditions like wheezy bronchitis and virus-induced wheezing tend to resolve by the age of 5 years.

**Step 2: assessing the severity** Although severity is most easily measured in a patient not on long-term treatment, if a patient is already receiving medication, the severity can be inferred from the amount of treatment needed to maintain control.

**Figs. 1 and 2**, from the Expert Panel,<sup>1</sup> show how to classify asthma severity in pediatric patients, based on age groups.

In patients not on long-term controller medications and for children of all ages, experiencing symptoms 2 days a week, or if the patient's classification changes

**Classifying severity in children who are not currently taking long-term control medication.**

| Components of Severity |                                                                                         | Classification of Asthma Severity<br>(Children 0–4 years of age)                                        |                                                                                                                                            |                 |                       |
|------------------------|-----------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|-----------------|-----------------------|
|                        |                                                                                         | Intermittent                                                                                            | Persistent                                                                                                                                 |                 |                       |
|                        |                                                                                         |                                                                                                         | Mild                                                                                                                                       | Moderate        | Severe                |
| Impairment             | Symptoms                                                                                | ≤2 days/week                                                                                            | >2 days/week but not daily                                                                                                                 | Daily           | Throughout the day    |
|                        | Nighttime awakenings                                                                    | 0                                                                                                       | 1–2x/month                                                                                                                                 | 3–4x/month      | >1x/week              |
|                        | Short-acting beta <sub>2</sub> -agonist use for symptom control (not prevention of EIB) | ≤2 days/week                                                                                            | >2 days/week but not daily                                                                                                                 | Daily           | Several times per day |
|                        | Interference with normal activity                                                       | None                                                                                                    | Minor limitation                                                                                                                           | Some limitation | Extremely limited     |
| Risk                   | Exacerbations requiring oral systemic corticosteroids                                   | 0–1/year                                                                                                | ≥2 exacerbations in 6 months requiring oral steroids, or ≥4 wheezing episodes/1 year lasting >1 day AND risk factors for persistent asthma |                 |                       |
|                        |                                                                                         | Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time. |                                                                                                                                            |                 |                       |
|                        |                                                                                         | Exacerbations of any severity may occur in patients in any severity category                            |                                                                                                                                            |                 |                       |

**Fig. 1.** Classification of asthma severity in children aged 0 to 4 years. EIB, exercise-induced bronchospasm. Level of severity is determined by both impairment and risk. Assess impairment domain by caregiver's recall of previous 2–4 weeks. Assign severity to the most severe category in which any feature occurs. At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral corticosteroids in the past 6 months, or ≥4 wheezing episodes in the past year, and who have risk factors for persistent asthma may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma. (From National Asthma Education and Prevention Program. Expert Panel report 3 (EPR3): guidelines for the diagnosis and management of asthma. Bethesda (MD): National Heart, Lung and Blood Institute; 2007. (NIH publication no 08-4051). Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>.)

**Classifying severity in children who are not currently taking long-term control medication.**

| Components of Severity |                                                                                         | Classification of Asthma Severity<br>(Children 5–11 years of age)                                                                                                                                                                                                                                                 |                                                                                                                             |                                                                                                                             |                                                                                                                           |
|------------------------|-----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
|                        |                                                                                         | Intermittent                                                                                                                                                                                                                                                                                                      | Persistent                                                                                                                  |                                                                                                                             |                                                                                                                           |
|                        |                                                                                         |                                                                                                                                                                                                                                                                                                                   | Mild                                                                                                                        | Moderate                                                                                                                    | Severe                                                                                                                    |
| Impairment             | Symptoms                                                                                | ≤2 days/week                                                                                                                                                                                                                                                                                                      | >2 days/week but not daily                                                                                                  | Daily                                                                                                                       | Throughout the day                                                                                                        |
|                        | Nighttime awakenings                                                                    | ≤2x/month                                                                                                                                                                                                                                                                                                         | 3–4x/month                                                                                                                  | >1x/week but not nightly                                                                                                    | Often 7x/week                                                                                                             |
|                        | Short-acting beta <sub>2</sub> -agonist use for symptom control (not prevention of EIB) | ≤2 days/week                                                                                                                                                                                                                                                                                                      | >2 days/week but not daily                                                                                                  | Daily                                                                                                                       | Several times per day                                                                                                     |
|                        | Interference with normal activity                                                       | None                                                                                                                                                                                                                                                                                                              | Minor limitation                                                                                                            | Some limitation                                                                                                             | Extremely limited                                                                                                         |
|                        | Lung function                                                                           | <ul style="list-style-type: none"><li>• Normal FEV<sub>1</sub> between exacerbations</li><li>• FEV<sub>1</sub> &gt;80% predicted</li><li>• FEV<sub>1</sub>/FVC &gt;85%</li></ul>                                                                                                                                  | <ul style="list-style-type: none"><li>• FEV<sub>1</sub> = &gt;80% predicted</li><li>• FEV<sub>1</sub>/FVC &gt;80%</li></ul> | <ul style="list-style-type: none"><li>• FEV<sub>1</sub> = 60–80% predicted</li><li>• FEV<sub>1</sub>/FVC = 75–80%</li></ul> | <ul style="list-style-type: none"><li>• FEV<sub>1</sub> &lt;60% predicted</li><li>• FEV<sub>1</sub>/FVC &lt;75%</li></ul> |
| Risk                   | Exacerbations requiring oral systemic corticosteroids                                   | 0–1/year (see note)                                                                                                                                                                                                                                                                                               | ≥2 in 1 year (see note)                    |                                                                                                                             |                                                                                                                           |
|                        |                                                                                         |  Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.  |                                                                                                                             |                                                                                                                             |                                                                                                                           |
|                        |                                                                                         | Relative annual risk of exacerbations may be related to FEV <sub>1</sub>                                                                                                                                                                                                                                          |                                                                                                                             |                                                                                                                             |                                                                                                                           |

**Fig. 2.** Classification of asthma severity in children aged 5 to 11 years. EIB, exercise-induced bronchospasm; FEV<sub>1</sub>, forced expiratory volume in second; FVC, forced vital capacity; ICU, intensive care unit. Level of severity is determined by both impairment and risk. Assess impairment domain by patient’s/caregiver’s recall of the previous 2–4 weeks and spirometry. Assign severity to the most severe category in which any feature occurs. At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma. (From National Asthma Education and Prevention Program. Expert Panel report 3 (EPR3): guidelines for the diagnosis and management of asthma. Bethesda (MD): National Heart, Lung and Blood Institute; 2007. (NIH publication no 08-4051). Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>.)

from intermittent to persistent, then, the frequency of symptoms greater than 2 days a week determines the patient’s classification within the persistent categories.

For pediatric patients already on controller treatment, the lowest level of treatment that is needed to keep them in control determines their classification status.

Although initial diagnosis is crucial, after diagnosis, the focus of care must shift to long-term control and therapeutic responsiveness.

The goals are the same for every patient with asthma, despite varying baseline severity, and are as follows:

Periodic assessment is recommended every 1 to 6 months to assess if therapeutic goals are being met and to make modifications if needed.

Clinicians should encourage the patient or patient's family to keep a daily diary or fill out a periodic self-assessment form as a way of self-monitoring.

In children younger than 4 years, the clinician is encouraged, by the Expert Panel, to refer the patient to a specialist in asthma care, if after 3 to 6 months, the patient does not meet asthma therapy goals or requires step 3 or higher in children (Figs. 3 and 4) younger than 4 years.

### Major goals of asthma therapy

#### 1. Reduce impairment

- Prevent chronic and recurrent symptoms, such as coughing or breathlessness
- Require infrequent use (<2 days a week) of inhaled short-acting  $\beta$ -agonist
- Maintain near normal pulmonary function
- Maintain normal activity levels, including exercise and school attendance
- Meet patients' and families' expectations of asthma care

#### 2. Reduce risk

- Prevent recurrent exacerbations and minimize need for ED visits and hospitalizations
- Prevent reduced lung growth in children
- Provide optimal pharmacologic therapy with minimal or no adverse effects

### Component 2: education for partnership in asthma care

Education in self-management of asthma is crucial to provide patients and their families with the necessary skills to achieve asthma control and improve long-term outcomes.

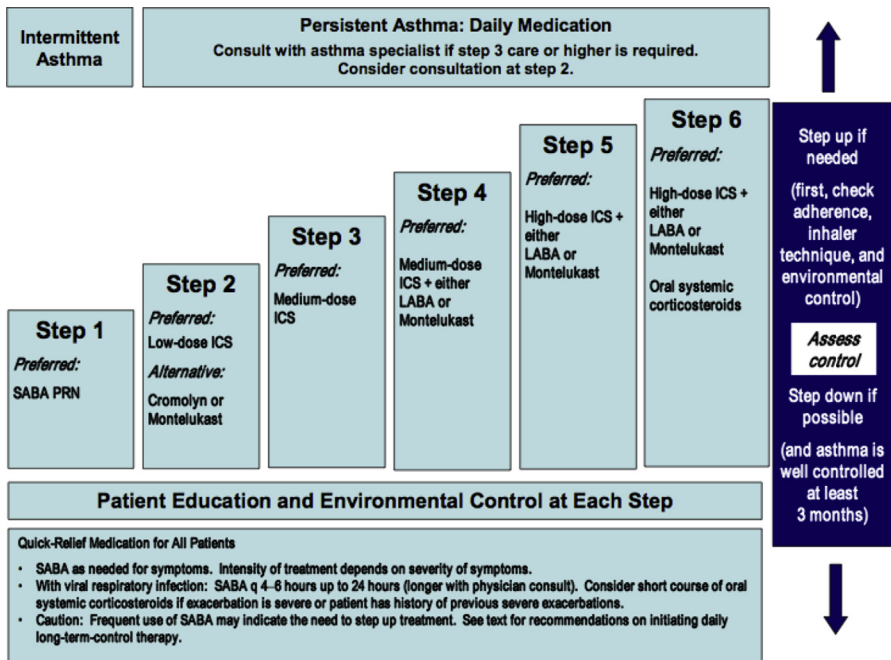


**Fig. 3.** The stepwise approach in children aged 0 to 4 years. (From National Asthma Education and Prevention Program. Expert Panel report 3 (EPR3): guidelines for the diagnosis and management of asthma. Bethesda (MD): National Heart, Lung and Blood Institute; 2007. (NIH publication no 08-4051). Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>.)

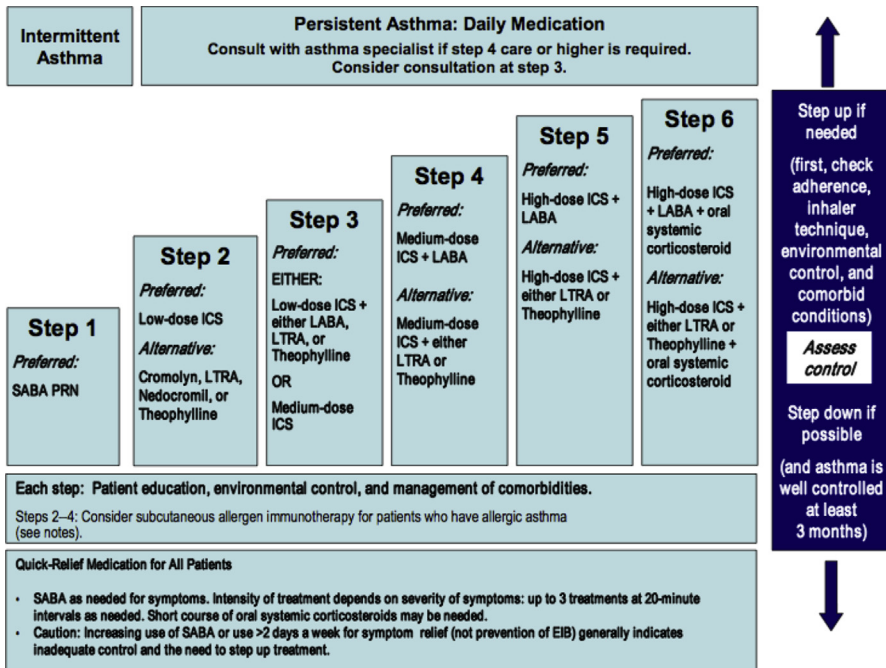


**Fig. 4.** The stepwise approach in children aged 5 to 11 years. ICS, inhaled corticosteroids; LABA, long-acting  $\beta$ -agonists; PRN, as needed; SABA, short-acting  $\beta$ -agonists. (From National Asthma Education and Prevention Program. Expert Panel report 3 (EPR3): guidelines for the diagnosis and management of asthma. Bethesda (MD): National Heart, Lung and Blood Institute; 2007. (NIH publication no 08-4051). Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>.)

- This education should begin when a diagnosis of asthma is first made and continue at each subsequent visit.
- To facilitate this goal, the Expert Panel<sup>6</sup> recommends that clinicians provide all patients with a written asthma action plan (**Fig. 5**).
- The plan should include daily management strategies and tips for recognizing exacerbations.

Key components of the written asthma action plan should include:

- Which medicines to take daily, including their specific names
- Ways to control environmental factors that exacerbate the patient's asthma
- Explicit ways to recognize and handle worsening symptoms and the medications to take in response
- Conditions for which the patient should seek emergent medical care, and the telephone numbers for the physician and ED

### **Component 3: control of environmental factors and comorbid conditions that affect asthma**

There is a strong relationship between asthma and allergy, especially indoor allergens. Patients experience increased asthma exacerbations and symptoms when exposed to allergens to which they are sensitive.<sup>6</sup>

In addition, studies show that sensitization to indoor allergens, such as animal dander, house-dust mite, and cockroaches, is an established risk for developing



asthma as a child. Outdoor pollen sensitization is less of a risk; however, ragweed and grass can be associated with seasonal asthma. It is crucial to eliminate, or significantly reduce, exposure to inhaled allergens.<sup>6</sup>

- The clinician can evaluate the role of allergens through obtaining a medical history of allergen exposure and skin testing or in vitro testing to determine sensitivity in the context of patient history.
- The first and most important step in controlling allergen-induced asthma is to reduce exposure in a multifaceted approach.
- A multistep process that includes all environments is most effective. Single steps are typically not effective. Precautions should be taken in the home, as well as other environments, like school or daycare.
- Families can contact the Asthma and Allergy Foundation of America toll-free hotline at 800-727-8462 or the Allergy and Asthma Network/Mothers of Asthmatics at 800-878-4403 for information about companies with products to help reduce allergen exposure.

All patients with asthma should avoid:

- Exposure to allergens to which the patient has documented sensitivities
- Exposure to environmental tobacco smoke and smoke from wood-burning stoves and fireplaces
- Outdoor exertion when air pollution levels are high
- Use of nonselective  $\beta$ -blockers
- Sulfite-containing foods and other foods to which they are sensitized
- Use of humidifiers and evaporative coolers in patient's home if there are known sensitivities to house-dust mites or mold
- Occupational exposures
- Dealing with household pets can be a difficult topics to address. If the patient is sensitive to the animal, the treatment of choice is to remove the animal from the home. However, if this is not an option, patients should keep the pet out of the bedroom and keep the door closed. Upholstered furniture and carpets should be removed, or pet access to those areas of the home should be limited.
- House-dust mites can be controlled by encasing the mattress and pillow in an impermeable cover or by weekly pillow washing. Sheets and blankets should be washed weekly in hot water, at a temperature greater than 130°F. Cockroach allergen can be reduced if patients and their families do not leave food and garbage exposed and focus on intensive cleaning of the home.
- Immunotherapy can be considered in patients showing clear evidence of symptoms after exposure to an antigen. Immunotherapy should be administered only in a physician's office, with trained personnel and available equipment to treat any life-threatening event, which, although rare, can occur.

#### **Component 4: pharmacologic management**

Asthma medications are categorized into long-term control medications used to achieve and maintain control of persistent asthma and quick-relief medications for acute symptoms and asthma exacerbations. Both categories of medications are listed in alphabetical order in [Tables 1](#) and [2](#).

The most comprehensive approach to managing asthma in patients of all ages is the stepwise approach, outlined in the Expert Panel.<sup>6</sup> The stepwise approach has been tailored for patients ages 0 to 4 years, 5 to 11 years, and those 12 years or older. The approach is intended to supplement but not replace the clinician's judgment and can be tailored to meet the patient's needs.

| Table 1<br>Long-term medications |                                                                                                                                                                           |                                                                                                                                                                |
|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Long-Term Medications            | Mechanism                                                                                                                                                                 | Indications                                                                                                                                                    |
| Corticosteroids                  | Block late-phase reaction to allergens, reduce airway hyperresponsiveness, and inhibit inflammatory cell activation                                                       | Inhaled corticosteroids (ICS) are the most potent and effective antiinflammatory medications available, used in severe persistent asthma                       |
| Cromolyn sodium and nedocromil   | Stabilizes mast cells and interferes with chloride channel function                                                                                                       | Alternative treatment of mild persistent asthma or prophylactic treatment of exercise                                                                          |
| Immunomodulators                 | Omalizumab (anti-IgE) is a monoclonal antibody that prohibits IgE from binding to receptors on basophils and mast cells                                                   | Adjunctive therapy for patients $\geq 12$ y old with allergies and severe persistent asthma, monitor patients after injection for anaphylaxis                  |
| Leukotriene modifiers            | Montelukast (patients $>1$ y) and zafirlukast (patients $>7$ y) are leukotriene receptor antagonists, zileuton is 5-lipoxygenase pathway inhibitor (patients $\geq 12$ y) | Alternative treatment option for mild persistent asthma, or as alternative adjunct to ICS when a LABA is not appropriate<br>Monitor liver function in zileuton |
| LABA                             | Salmeterol and formoterol bronchodilate for $\geq 12$ h                                                                                                                   | Used in combination with ICS for long-term control in moderate or severe persistent asthma in children $\geq 5$ y                                              |
| Methylxanthines                  | Sustained-released theophylline, mild to moderate bronchodilator                                                                                                          | Alternative, not preferred, adjunctive therapy with ICS<br>Monitor serum concentration                                                                         |

Abbreviations: ICS, inhaled corticosteroids, LABA, long-acting  $\beta$ -agonists.

- Pharmacologic management of childhood asthma is challenging, because children rarely stay in a single classification from season to season. This situation means that parental and patient education about their medications is an essential component.

| Table 2<br>Quick-relief medications |                                                                               |                                                                                            |
|-------------------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| Quick-Relief Medications            | Mechanism                                                                     | Indications                                                                                |
| Anticholinergics                    | Inhibit muscarinic cholinergic receptors and reduce vagal tone                | Alternative bronchodilator for patients who cannot tolerate a SABA                         |
| SABA                                | Albuterol, levalbuterol, and pirbuterol bronchodilate and relax smooth muscle | Therapy of choice for acute symptom relief and prevention of exercise-induced bronchospasm |
| Systemic corticosteroids            |                                                                               | Moderate and severe exacerbations, as adjunct to SABA to speed recovery                    |

Abbreviation: SABA, short-acting  $\beta$ -agonists.

- In addition, patient and parent education about use of devices can be a challenge, because children perceive being different (ie, needing medication) as not being socially accepted by their peers.
- Once a patient has been classified into a category, decisions concerning their directed therapy must be made in conjunction with parental and patient input. Therapy works only if there is buy-in by the patient or parent.
- First, consider a child who has intermittent asthma. This patient is best treated with a quick-acting inhaled  $\beta_2$ -selective adrenergic agonist, taken at the time that symptoms appear. The goal is to treat the intermittent symptoms, not prevent them.
- In addition, patient education concerning recognition of triggers of the symptoms is important to aid in avoidance of the use of medication.
- The medication of choice for most of the patients in this category or classification is albuterol sulfate via inhalation (other choices are levalbuterol, or if the child is  $\geq 12$  years of age, pirbuterol).
- In the United States, there are rarely indications for the use of oral quick-acting bronchodilators.
- Patient education is important to ensure that the medication is being delivered to the affected airways. In children, especially those younger than 4 years, a spacer with a mask is the most appropriate delivery method. Spacers should be encouraged for children of all ages if available.
- Close follow-up is necessary to monitor the patient's symptoms, assess for the need to adjust therapy, search for environmental triggers, and to continue patient education, especially over the first few months of therapy.
- If a child with apparent intermittent asthma has the need for systemic corticosteroids twice or more in a 6-month period, the child should be treated as a child with a persistent form of asthma.
- In young children (especially those  $<12$  months old), the use of a home nebulizer may be considered. Many families with older children who have abrupt exacerbations of their asthma are more comfortable with having a nebulizer as an additional or alternative means of providing rescue medication to their children.
- The child who is classified as having persistent asthma is at more risk for having symptoms that wax and wane, from the mild or moderate categories to the severe category during certain seasons.
- The initial additional medication for children in a category of persistent asthma is the addition of a controller medication. Much has been reported about the benefits of controller medications, especially inhaled corticosteroids.
- In the age of information and Internet availability, many patients' parents have some information and an opinion of the use of the benefits and risks of inhaled corticosteroids.

The use of a low-dose inhaled corticosteroid is recommended for initial therapy in children with apparent mild persistent asthma (budesonide is the only product approved for children  $<4$  years of age).

If there is parental resistance to the use of steroids as controller medication, especially in the mild persistent category, an alternative is the use of a leukotriene receptor antagonist (LTRA) (montelukast has been approved for use to treat rhinitis in children aged  $\geq 6$  months and is the most commonly used LTRA in children in the United States).

So, in children younger than 4 years, the use of budesonide is recommended, with the alternative being the use of montelukast in children older than 1 year (in

whom it has been approved for use to control asthma symptoms). If inhaled corticosteroids are used, we suggest rinsing of the oral cavity (or brushing of teeth) after each use.

The asthmatic child classified in the moderate persistent category should be treated with a medium daily dose of inhaled corticosteroids. Again, therapy should be closely monitored initially to assess control of symptoms. For children not controlled on medium doses of inhaled corticosteroids, an evaluation by an asthma specialist (pulmonologist or allergist) should be strongly considered by the primary care physician.

## SUMMARY

Asthma is a common chronic inflammatory disease of the airways. It affects at least 7 million children in the United States, with more than 150,000 annual pediatric hospital admissions and 185 pediatric deaths.<sup>1</sup> It is a complex disease, involving many different allergic, inflammatory, and environmental components. Patient and family education and a team-based approach are paramount for successful management of the disease. National guidelines have been put forth by the National Heart, Lung and Blood Institute, which provide a helpful framework in which to begin to manage patients and to navigate the many medication choices available. It is only through diligent attention to control of asthma symptoms that improved quality of life and prevention of long-term sequelae are possible for the pediatric asthma patient.

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