46 ASTHMA IN THE PRESCHOOL-AGE CHILD

Miles Weinberger, MD, and Mutasim Abu-Hasan, MD

ASTHMA IN THE PRESCHOOL-AGE CHILD

What Is Asthma?

What is asthma? This question is of particular importance in evaluating respiratory disease in the young child where euphemisms for asthma have been common, including *reactive airway disease (RAD), wheezy bronchitis, obstructive bronchitis, recurrent bronchiolitis,* and so on. Sometimes describing or defining asthma is like the parable of the blind men describing the elephant who felt it was like a tree, a snake, or a rope depending on whether they were feeling a leg, the trunk, or the tail. Like the blind men examining only one part of the elephant, asthma is sufficiently diverse in its presentation that its perception depends on the experience of the observer. Some have suggested that, like love it cannot be defined, but it is recognizable when confronted.[1]

The complexity and challenge of defining asthma has been discussed extensively by Sears.[2] In examining the 12 definitions and references in his review, a common theme to all is the presence of airway disease that varies over time either spontaneously or as a result of treatment. A committee of the American Thoracic Society agreed upon the definition that "Asthma is a disease characterized by an increased responsiveness of the trachea and bronchi to various stimuli and manifested by a widespread narrowing of the airways that changes in severity either spontaneously or as a result of therapy."[3] This definition was expanded by a subsequent committee of the American Thoracic Society to include "The major symptoms of asthma are paroxysms of dyspnea, wheezing and cough, which may vary from mild and almost undetectable to severe and unremitting…"[4] This definition and others, most notably that of Simon Godfrey, added to the definition that the airflow obstruction and clinical symptoms are largely or completely reversed by treatment with bronchodilators or corticosteroids.[5]

Inflammation was introduced into the definition by Hargreave[6] and subsequently incorporated into the National Asthma Education Program Expert Panel Reports from the U.S. National Institutes of Health.[7,8] However, a definition based on inflammation is not helpful in differential diagnosis or early disease identification because noninvasive measures of inflammation are neither readily available nor well validated. This is especially true for young children, where even the ability to make physiologic measurements is limited. For a definition of a disease to be useful, it should provide a basis for making the diagnosis. While airway inflammation is certainly a component of asthma, the value of including this as a major component of the definition has also been challenged by McFadden and Gilbert, who commented, "Airway inflammation and hyperresponsiveness…are not unique to this illness. The usefulness of these characteristics in defining asthma is unclear."[9] This issue is discussed further by Brusasco and colleagues, who argued that the airway narrowing in asthma is not necessarily related to airway inflammation.[10] Asthma has thus proved to be challenging to define because of the diversity in its clinical presentation, the variability of its clinical course, and the absence of a specific diagnostic test.

The ability to define asthma is essential for both the study of the disease and for diagnosis. The reported prevalence of asthma varies greatly depending on how asthma is defined for the purpose of diagnosis in epidemiologic studies.[11,12] Similarly, attempts to study the genetics of asthma have struggled with the definition.[13–15] The challenge of defining asthma becomes greatest in the very young child. While there is an absence of internationally accepted criteria for the definition of asthma in early childhood, birth cohort studies have nonetheless been attempted using various criteria to define asthma or potential asthma.[16] Martinez has emphasized the heterogeneity of asthma and the identification of specific phenotypes based on patterns of natural history and presence of early allergic sensitization.[17] Others have further categorized asthma by clinical phenotype in both children and adults.[18–20] This recognition of different, yet often overlapping clinical patterns of disease certainly complicates epidemiologic and natural history studies. Nonetheless, it is essential to appreciate and identify these differing clinical patterns that share primarily the end-organ responsiveness that we identify as asthma. Treatment decisions and family counseling regarding the expected outcome often relate to the early phenotype in the preschool-age child.

THE EPIDEMIOLOGY OF EARLY CHILDHOOD ASTHMA

When Does Asthma Start?

While asthma can begin at almost any age, it most commonly begins in infancy with a viral respiratory infection that causes the lower airway inflammatory disease with consequent wheezing and coughing that is commonly known in the United States as bronchiolitis. The most common cause of this initial wheezing episode is respiratory syncytial virus (RSV). Rhinovirus, although less commonly the cause of the initial episode, may be even more likely associated with subsequent recurrent wheezing.[21] Other viruses that cause similar acute respiratory symptoms include human metapneumovirus, coronavirus, and

others.[22] As many as 3% of infants in the United States are hospitalized annually because of lower respiratory illness from these infections.[23] While it is premature to call the first episode of such symptoms *asthma*, this initial viral respiratory infection–induced lower airway obstruction in infancy is often the harbinger of more to come, consistent with a diagnosis of asthma. In fact, when the onset of symptoms consistent with asthma was examined in an epidemiologic study of the population in the vicinity of Rochester, Minnesota, by investigators at the Mayo Clinic, the majority of those with asthma had their onset during the first year of life (Fig. 46-1).[24]

Thus, when a healthy baby becomes infected with RSV (or rhinovirus), as virtually all of them eventually do, most get only the symptoms of a common cold with coryza. A substantial minority experience bronchiolitis, the most common cause of hospitalization during the first year of life. Of those who experience bronchiolitis, approximately 25% to 50% subsequently have symptoms of an intermittent pattern of asthma manifested by recurrent wheezing in association with subsequent viral respiratory infections.[25,26] While clinical experience and natural history studies suggest that remission is common later in childhood, some continue to have recurrent or chronic symptoms consistent with a diagnosis of asthma throughout childhood, and some recur or continue into adult life[27] (Fig. 46-2).[28]

Who Gets Asthma?

An asthma phenotype is present in approximately 25% of the offspring of a parent with asthma.[29] Further evidence for a genetic influence on the asthma phenotype is seen in twin studies, where there is a higher concordance in monozygotic twins compared to dizygotic twins, even though both twins share the same environment.[30,31] But even in identical twins, the concordance is not much over 50%. Both genetics and environment therefore appear to contribute to asthma.

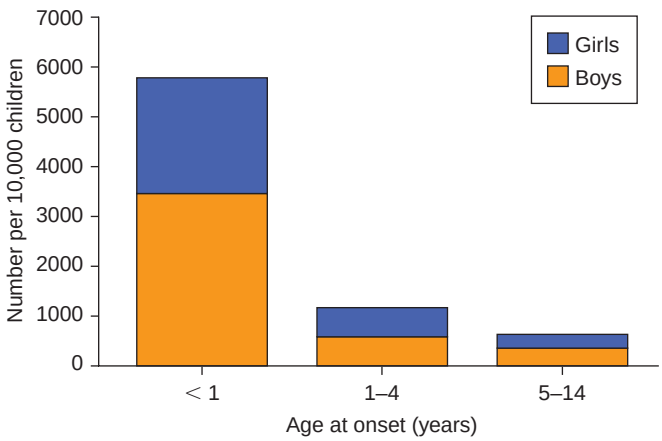

FIGURE 46-1. Annual age- and sex-adjusted incidence of asthma onset in a population-based epidemiologic study in Rochester, Minnesota. (From Yunginger JW, Reed CE, O'Connell EJ, et al. A community-based study of the epidemiology of asthma. Incidence rates, 1964-1983. *Am Rev Respir Dis.* 1992;146:888-894.)

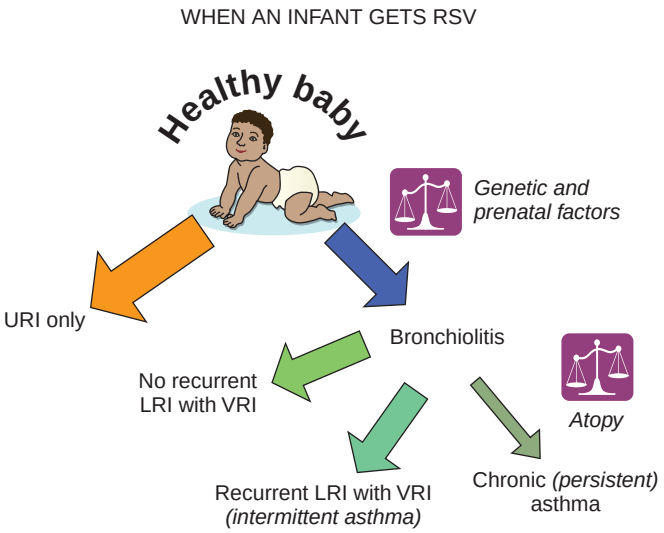

FIGURE 46-2. Clinical consequences of initial infection following respiratory syncytial virus in infancy. *URI,* Upper respiratory illness; *LRI,* lower respiratory illness; *VRI,* viral respiratory infection. (Reproduced with permission from Weinberger M. Clinical patterns and natural history of asthma. *J Pediatr.* 2003;142:S15-S20.)

The genetics are complex. Airway hyperresponsiveness and IgE-mediated sensitivity to inhalant allergens appear to be independent characteristics.[32] Airway reactivity or hyperresponsiveness is considered a hallmark of asthma.[33] Persistence of asthma beyond the preschool years has been found to be associated with increased airway responsiveness in early life.[34] However, airway hyperresponsiveness is not diagnostic of asthma. Airway hyperresponsiveness to a cholinergic stimulus is found with increased frequency in nonasthmatic parents of children with asthma at a frequency that suggests that such responsiveness is transmitted as an autosomal dominant trait, which is a necessary but not sufficient biologic variable to cause clinical asthma.[35,36]

Total IgE production appears to have strong genetic determination based on the observations of very high concordance in monozygotic twins and lesser concordance in dizygotic twins, both of whom should have similar environmental exposures.[37] However, less well studied is the genetics of antigen-specific IgE. Other genetic variables that can affect the phenotypic manifestations of atopic sensitization include the affinity of IgE receptors on target cells, the interaction of IgE with receptors, IgE-induced release of mediators, and end-organ responsiveness. Despite their clinical usefulness as an aid in the assessment of diseases affected by atopic sensitization, neither the size of allergy skin tests nor the titer of antigen-specific IgE can reliably predict disease or severity.

Although inhalant sensitivity tends to develop later than ingestant sensitivity in early childhood, Wilson and colleagues found sensitivity to cockroach in 29%, dust mite in 10%, cat in 10%, and *Alternaria* in 4% of 49 asthmatic infants younger than 1 year of age.[38] Arshad and Hyde examined the development of atopy in a prospective study of 1167 infants.[39] They found that dust mite–positive skin tests were more prevalent in formula-fed infants. While positive skin tests to animal danders were more prevalent among infants exposed to the respective

animals, they did not find that exposure to animal dander influenced the prevalence of clinical disorders. However, in a case control study of 193 children with asthma 1 to 4 years of age, Lindfors and coworkers found that high-dose exposure to cat or dog resulted in increased risk of asthma, with indoor dampness and exposure to environmental tobacco smoke having apparent synergistic effects.[40] In a subsequent report, they described a dose-response relationship between cat exposure and sensitization to cat but not to dog.[41] Sears and colleagues found a relationship between children born in winter and sensitization to cats and house dust mites.[42] In a prospective longitudinal study in Tucson, Sherrill and coworkers found an association between sensitization before 8 years of age as determined by skin testing and symptoms of asthma, whereas those who developed positive skin tests only after 8 years of age did not differ in frequency of asthmatic symptoms from those never sensitized.[43] While Nelson and colleagues found an association of many positive skin tests among 1041 school-age children with "mild to moderate" asthma, these investigators found that only dog, cat, and *Alternaria* mold correlated independently with increased lower airway hyperresponsiveness measured by methacholine challenge, although there was no correlation with decreased pulmonary function.[44] Although this latter study did not involve preschool-age children, it indicates that some inhalant allergens are more asthmagenic than others. In an English birth cohort study, Cullinan and coworkers found no linear relationship between early allergen exposure, sensitization, and asthma.[45]

Thus, developing asthma is a function of genetic and environmental variables, not all of which are known. While those with a viral respiratory infection–induced intermittent pattern appear to have a familial predisposition, the genetics of that pattern are not well studied. Both airway hyperresponsiveness and IgE-mediated sensitivity to inhalant allergens in infancy appear to be predictors of the eventual development of persistent symptoms.

THE PATHOPHYSIOLOGY OF EARLY CHILDHOOD ASTHMA

There are only limited studies of the pathophysiology of asthma in preschool-age children. Such studies are obviously hindered by the ethical dilemma of subjecting nonconsenting and vulnerable children to intrusive pathologic and physiologic assessment procedures.[46] Autopsy and bronchial biopsy data are rare in infants and young children because of the rare occurrence of death in this age group and the evident difficulty of obtaining endobronchial biopsies in children.[47–49] One study examined mucosal biopsies in a small number of highly selected children 1 to 3 years of age with severe, recurrent wheeze, most of whom were atopic. They observed in those children increased thickness of reticular basement membrane and increased eosinophil density consistent with the characteristic pathologic features of asthma in adults and older children.[50] In contrast, another highly selected group of much younger infants referred for severe wheeze at a median age of 12 months had no evidence of airway inflammation or structural change on bronchial biopsy,[51] which implies that these changes develop between 1 and 3 years of age.

Because of the paucity of data, there has been a tendency to discuss the pathophysiology of asthma as if it were a homogeneous entity across age groups. However, concepts and models of asthma derived from adult studies may not be applicable to common phenotypes of asthma in the young child.[52] This is particularly evident for the non-atopic intermittent viral respiratory infection–induced asthma that predominates in infants and children. This seems to be distinct from the chronic atopic asthma found more commonly in older children and adults.[18,28,53] Bronchoalveolar lavage studies, for instance, show no evidence of airway inflammation in children with a history of intermittent non-atopic asthma during their symptom-free periods,[54] while airway inflammation seems to persist in patients with atopic asthma, even when they are asymptomatic.[55,56] Symptomatic preschool-age non-atopic asthmatic children have predominantly noneosinophilic airway inflammation compared to the eosinophilic airway inflammation characteristic of atopic children with asthma, which suggests different inflammatory mechanisms between these asthma phenotypes.[57–62]

RSV bronchiolitis has been associated with an increased incidence of subsequent episodes of wheezing and asthma.[63–65] Studies in twins investigated whether RSV bronchiolitis alters airway reactivity and creates recurrent wheezing and asthma or whether it is just a marker of infants who are genetically predisposed to respond to RSV and other common viral respiration infections with lower airway inflammation and bronchospasm.[66,67] Evidence from these studies supports the latter hypothesis. Recent investigations have provided evidence that the predisposition relates to a defect in innate immunity that permits common respiratory viruses to propagate in the lower airway. The result is profuse inflammatory response of the airways, resulting in narrowing and obstruction to air flow rather than just causing upper respiratory inflammation with coryza (as occurs in nonasthmatics).[68–71] For the preschool asthmatic, this is of particular importance because of their high frequency of viral respiratory infections.

While there are many strongly held opinions and anecdotal reports for gastroesophageal reflux causing wheezing and cough, evidence supporting this hypothesis is largely absent.[72–74] Similarly, arguments for sinusitis and postnasal drainage as a cause of cough are not based on sound data.[75,76] A systematic approach permits the identification of the causes of wheeze and cough, which, when recurrent, will most frequently be a manifestation of asthma.[77]

THE NATURAL HISTORY OF EARLY CHILDHOOD ASTHMA

Viral respiratory infections are a major cause of asthma exacerbations at all ages[78–81] and appear to be the major risk factor for the large increase in hospital admissions for asthma that occurs in the fall months.[82] Preschool-age children have a particularly high frequency of viral respiratory infections, with most getting 3 to 8 infections per year and

10% to 15% getting 12 or more per year.[83] This is a likely explanation for the frequency of asthma hospitalization in the preschool age group exceeding that of older children and adults. The smaller airways in the young child are also more easily obstructed by inflammation associated with a viral respiratory infection, which is a likely contributing factor to increased hospitalization. The hospitalization rate for asthma among U.S. children 1 to 4 years of age has been approximately 1 in 200 compared with 1 in 500 among children 5 to 14 years of age, and 1 in 1000 for individuals 15 to 24 years of age (Fig. 46-3).[84]

While most preschool-age children with asthma remit or greatly improve by school age, those with evidence for atopy (i.e., the predisposition to make IgE antibody to major inhalants) are most likely to continue having a substantial frequency of asthmatic symptoms (Fig. 46-4).[85] The long-term clinical course of asthma in young children has been examined in a prospective study with repeated evaluations for up to 35 years.[86] In 1963, all children entering the first grade in Melbourne, Australia, had a medical examination that included a short questionnaire and interview. As part of the questionnaire, parents were asked if their child had experienced episodes of wheezing or asthma during their preschool years and whether it had been associated with a viral respiratory infection. Based on this survey, an overall community prevalence for asthma symptoms in childhood was estimated to be about 20%, a rate similar to that described more recently in the United States.[87–89]

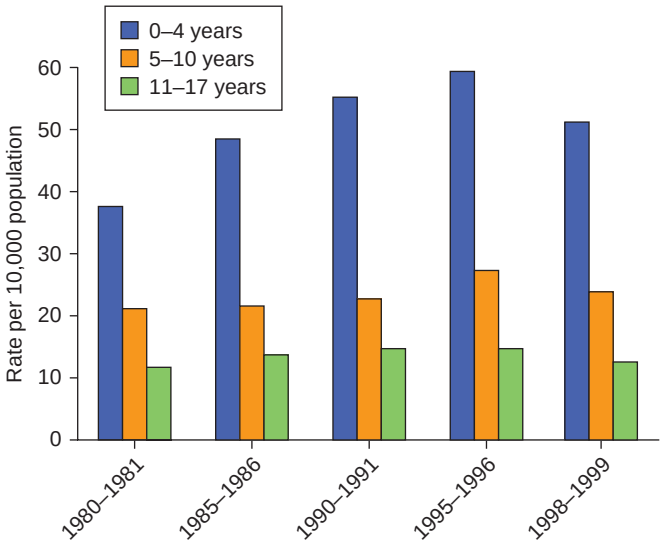

FIGURE 46-3. Hospital discharge rates for asthma as the first-listed diagnosis, by age group and year—United States, 1980-1999. Data from the National Center for Health Statistics, Center for Disease Control. (Adapted from Akinbami LJ, Schoendorf KC. Trends in childhood asthma: prevalence health care utilization, and mortality. *Pediatrics*. 2002;110:315-322.)

A stratified sample was then randomly selected the following year from the approximately 30,000 7-year-old children previously surveyed. This sample included 105 second graders who had never wheezed to serve as controls, 75 with less than 5 episodes of wheezing with viral respiratory infections, 104 with 5 or more episodes of wheezing with viral respiratory infections, and 113 with recurrent wheezing not limited to association with viral respiratory infections. Three years later, the investigators entered 83 children from the same population who had severe chronic asthma since before 3 years of age. These children, then 10 years of age, had persistent symptoms at the time of entry with a barrel chest deformity and/or forced expiratory volume in 1 second (FEV_1) that was ≤50% of the forced vital capacity (FVC). All of the groups of children were reevaluated at ages 14, 21, 28, 35, and 42 years of age.[90–93]

When the subjects were examined at 42 years of age, a correlation between the nature of the symptoms in childhood and the subsequent outcome was apparent (Fig. 46-5). Over 50% of those with asthma symptoms limited to an association with viral respiratory infection prior to 7 years of age were asymptomatic at 42 years of age. A substantial number were still having episodic asthma,

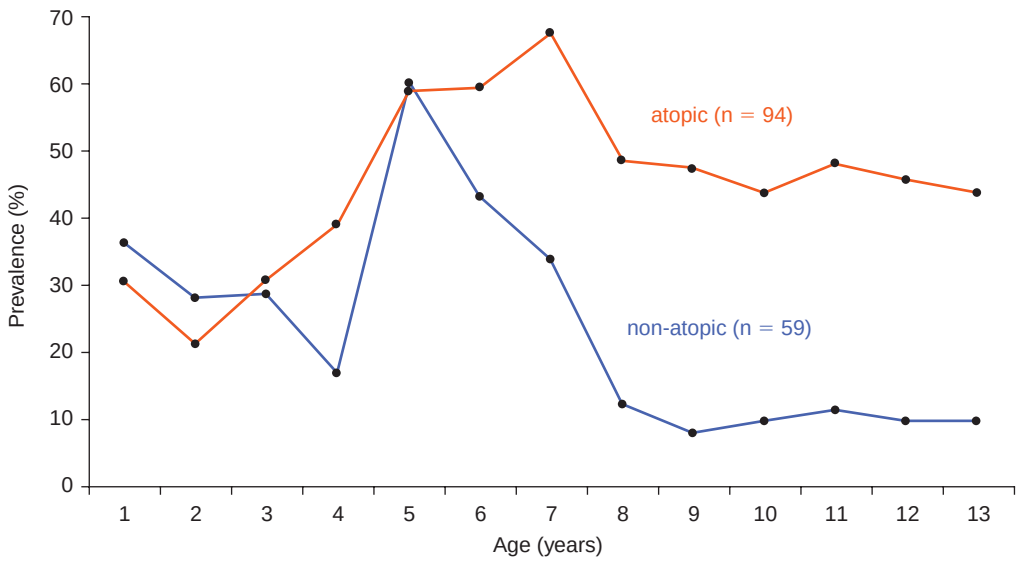

FIGURE 46-4. Prevalence of symptoms by age in atopic and non-atopic asthma. (Reproduced with permission from Illi S, von Mutius E, Lau S, et al. Perennial allergy sensitization early in life and chronic asthma in children: a birth cohort study. *Lancet* 2006;368:763-770.)

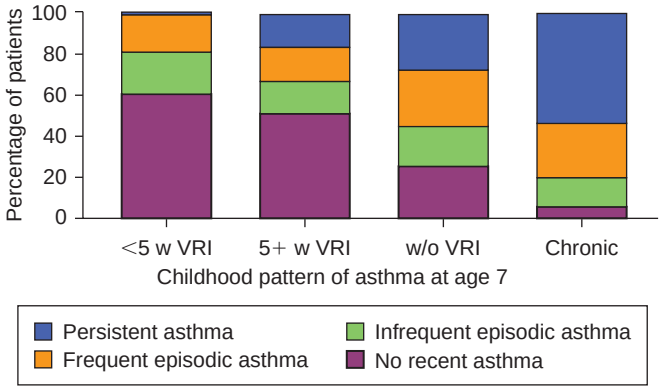

FIGURE 46-5. Clinical expression of childhood asthma at age 42 years among a stratified random sample from a population of 30,000 children surveyed at entry to first grade, about 20% of whom had symptoms consistent with asthma. The sample included 105 second graders who never wheezed, 75 with less than 5 episodes of wheezing with viral respiratory infections (<5 w VRI), 104 with 5 or more episodes of wheezing with viral respiratory infections (5+ w VRI), 113 with recurrent wheezing not associated with viral respiratory infections (w/o VRI), and 83 from the same population who had severe chronic asthma (chronic). (Adapted from Phelan PD, Robertson CF, Olinsky A. The Melbourne asthma study: 1965-1999. *J Allergy Clin Immunol*. 2002;109:189-194.)

and a few had developed persistent asthma. Nevertheless, the frequency of all patterns of active asthma at 42 years of age was greater among those in whom wheezing without viral respiratory infection had been reported in childhood. About 50% of those with chronic asthma as children continued to have persistent symptoms at 42 years of age with only 11% reporting no recent asthma. Repeated measurements of FEV_1 to 42 years of age did not differ significantly from controls among the two groups of children who had only wheezing with viral respiratory infection. Those with chronic asthma generally had significant decrements in FEV_1 that persisted but were not progressive (Fig. 46-6).

It is notable that the subjects in this 35-year study who began with asthma in their preschool years had, for the most part, little in the way of what today would be considered optimal treatment. The initial identification of these patients occurred prior to the introduction of inhaled corticosteroids, cromolyn, or even optimal use of oral theophylline. The investigators did not intervene in the patients' care, limiting their involvement to the interval assessments and recommendations communicated only to the subjects' physicians. However, the authors commented that the recommendations were rarely followed. This longitudinal study therefore provides unique data regarding the natural history of asthma, beginning in the preschool years.

DIAGNOSIS AND ASSESSMENT

Clinical Presentation

The typical symptoms of asthma include cough, expiratory wheezing, and dyspnea. Wheezing, the classical finding associated with asthma, is defined as musical, continuous sounds that originate from oscillations in narrowed airways. However, parental reporting of wheezing is confounded by their conceptual understanding of the term.[94] In a survey of parents whose infants had noisy breathing, 59% initially used *wheeze* to describe the respiratory noise their infant made. However, after being shown video clips

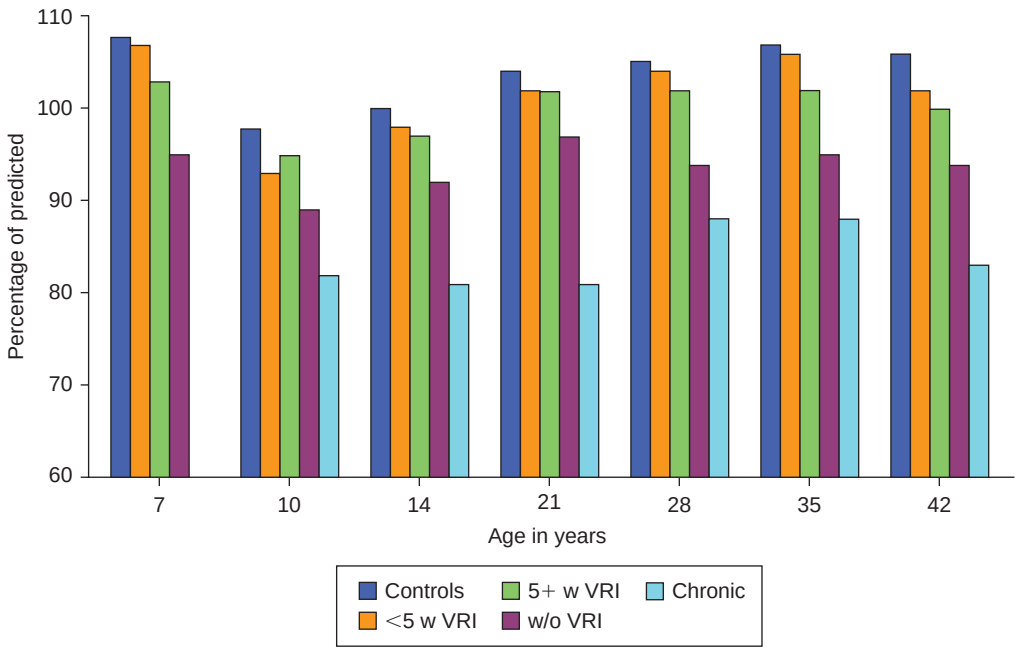

FIGURE 46-6. Forced expiratory volume in 1 second (FEV_1 expressed as percent of predicted) for children over time by classification of childhood asthma at the time of recruitment. The categories of asthma at the time of entry into the study included those with <5 wheezing episodes with viral respiratory infections (<5 w VRI), those with >5 episodes with VRI (5+ w VRI), those with episodic wheezing without VRI (w/o VRI), and those with severe persistent asthma (chronic), and controls from the same cohort. (Adapted from Phelan PD, Robertson CF, Olinsky A. The Melbourne asthma study: 1965-1999. *J Allergy Clin Immunol*. 2002;109:189-194.)

illustrating wheezing and an upper airway *rattle* (*ruttle* is the British term), only 36% still described the respiratory sound of their infant as *wheezing*, whereas the use of the word *ruttle* doubled.[95] In another report using video clips, 30% of parents labeled other sounds as wheeze, while 30% used other words to describe wheezing.[96] Confusion regarding terminology for respiratory sounds is also seen among health care professionals.[97] This illustrates the importance of reliable physician observation of the respiratory sounds to distinguish polyphonic expiratory wheezing from other respiratory sounds. This confusion should be borne in mind when interpreting epidemiologic studies of the prevalence of "wheeze."

Troublesome cough is a characteristic of asthma,[98] and in our experience cough is as frequent a symptom as wheezing. In one report, where children with chronic cough as the only symptom were followed for 3 years, 75% were subsequently diagnosed with classic asthma as the cause of the cough.[99] Shortness of breath and recurrent dyspnea, especially with exertion, are other typical symptoms of asthma, but they are rarely present alone in the absence of wheezing or cough. However, isolated cough, especially of recent onset, should not be too readily diagnosed as asthma.

During an acute severe exacerbation of asthma, labored breathing with intercostal and suprasternal and substernal retractions may be present. Physical findings commonly include polyphonic expiratory wheezing as a manifestation of diffusely narrowed small airways. Coarse crackles can be present from mucous in the larger airways. Hypoxemia from ventilation-perfusion mismatching is common early in the course of acute asthma with a somewhat decreased PCO_2 resulting from the increased hypoxic ventilatory drive. A rising PCO_2 is an indication of impending respiratory failure. At other times, physical signs of asthma may be absent. This may mean that the asthma is quiescent at the time, but symptoms present hours before or a nightly cough may still be occurring in the absence of any physical signs when seen by the physician.

Chest radiographs of infants and young children with asthma often show varying patterns of opacification. Common observations include areas of atelectasis from mucous plugging of the airways. Peribronchial thickening by inflammation may appear as "rings" and "tram tracks" when airways are cut on cross-section or linearly, respectively. These radiologic abnormalities and the presence of coarse crackles on auscultation are a likely explanation for the frequent diagnoses of pneumonia made in infants and young children with asthma.[100,101] Obtaining chest films in nonfebrile wheezing children therefore results in no useful clinical information and has the adverse effect of encouraging inappropriate use of antibiotics.[102] In our own survey of school-age children with unequivocal asthma referred to our clinic, 30% had prior diagnoses of pneumonia associated with symptoms identical to those subsequently associated with diagnoses of asthma.[103]

Therefore, in the preschool-age child who is not symptomatic at the time seen, the diagnosis is dependent on a careful history of previous symptoms consistent with the definition of asthma. Specifically, children with recurrent lower airway symptoms manifested by wheezing, cough, or labored breathing should be considered to potentially have asthma. A family history of asthma or recurrent lower respiratory disease in early childhood is supportive evidence. Confirmation of the diagnosis requires a convincing history of completely symptom-free periods either spontaneously or as a result of treatment. If encountered when symptomatic, a complete response to an inhaled bronchodilator is strong supportive evidence. However, commonly a short course of relatively high-dose systemic corticosteroid is needed to reverse the inflammation contributing to the airway obstruction. This is a particularly efficient and safe method to test the reversibility of the airway disease. Persistence of symptoms not responsive to such a diagnostic trial of systemic corticosteroid requires consideration of alternative diagnoses.

Wheezing and Cough: When Is It Asthma, and When Is It Not?

Asthma is often underdiagnosed[11] because recurrent lower respiratory symptoms are attributed to bronchitis or pneumonia. Since acute exacerbations of asthma are associated with airway inflammation that causes similar symptoms, signs, and radiologic changes to an acute viral or *Mycoplasma pneumoniae* infectious process, misdiagnosis is understandable if the episode is observed in isolation. However, true pneumonia is uncommon in wheezing children, especially if they are afebrile.[103] Moreover, recurrence with repeated viral respiratory infections distinguishes the hyperresponsive airway of asthma from the normal airway, where similar lower respiratory symptoms occur only rarely. Asthma is also overdiagnosed when symptoms characteristic of but not confined to asthma (e.g., wheeze, cough, and dyspnea) are too readily attributed to asthma, even when other characteristics of asthma are not present (see Table 46-1).[104–106]

TABLE 46-1 DIAGNOSES TO CONSIDER WHEN COUGH, WHEEZE, OR LABORED BREATHING IN THE PRESCHOOL-AGE CHILD IS NOT CONSISTENT WITH ASTHMA

Aspiration syndromes
Bronchomalacia
Bronchopulmonary dysplasia
Protracted bacterial bronchitis (see Chapter 26)
Compression of the airway from aberrant great vessels (e.g., vascular ring)
Cystic fibrosis
Foreign body in the airway
Foreign body in the esophagus (compressing the airway)
Primary ciliary dyskinesia
Pertussis
Tracheal polyps
Tracheomalacia
Vocal cord dysfunction

The Clinical Patterns of Asthma

Three rather distinct clinical patterns of asthma can be seen in childhood: intermittent, chronic, and seasonal allergic. By far the most common, particularly in the preschool child, is an intermittent pattern in which symptoms occur exclusively following the viruses that cause the common cold; these children are completely free from symptoms during the intercurrent periods. Although it is an intermittent pattern, the symptoms may range from mild to severe. They are, in fact, the major contributors to the high hospitalization rate in this age group (see Fig. 46-3).[84] Because children in this age group have a particularly high frequency of acquiring viral respiratory infections (especially if they are in daycare or have older siblings in school), it can be difficult during peak times of seasonal viral respiratory illnesses to distinguish this pattern from the less common chronic pattern of asthma. Moreover, children with persistent symptoms from chronic asthma also experience exacerbations from viral respiratory infections, and this compounds the diagnostic difficulty. At this age, an absence of specific IgE to major inhalant allergens is generally predictive of a viral respiratory infection–induced pattern.[86,107] When the pattern is unclear during the peak of the viral respiratory disease season, the marked decrease in the frequency of acute exacerbations during summer months when viral respiratory illness is less common can eventually make it more apparent that the pattern is indeed intermittent from viral respiratory infections.[82]

The chronic pattern of asthma is associated with persistent symptoms. While exacerbations may occur with viral respiratory illnesses as is seen in the more common intermittent pattern, these children have daily or near daily symptoms of asthma, even between such exacerbations. Such children most commonly, though not always, have evidence for specific IgE to inhalant allergens. Demonstration of the chronic pattern of asthma may require close clinical monitoring following complete clearing of symptoms with a short course of systemic corticosteroids to determine if symptoms return spontaneously soon after discontinuation of the systemic corticosteroids. If the patient remains well until an apparent viral respiratory illness, then this is consistent with an intermittent pattern of asthma.

Less common in this age group but nonetheless important to recognize are children with a seasonal allergic pattern. Diagnosis of this pattern requires demonstration of specific IgE to seasonal inhalant allergens associated with asthma in patients whose symptoms occur with exposure to those seasonal inhalant allergens. These allergens vary geographically and therefore require some knowledge of the aerobiology of the region where the child lives. Examples of major allergens that contribute to seasonal allergic asthma are grass pollen, which peaks in May and June in the California and Pacific Northwest valley areas,[108] and *Alternaria* in the Midwest farm country, which is variably present throughout the growing season but peaks when the farmers are stirring up decaying vegetation during harvest time.[109]

Evaluation of the Preschool Child with Asthma

A detailed history is the major tool for evaluating asthma, and this is particularly true for the preschool child. Recurring lower respiratory symptoms consisting of cough, labored breathing, and expiratory wheezing are consistent with a diagnosis of asthma. Since the major event preceding these symptoms is commonly that of a viral respiratory infection, sometimes with an initial fever at the onset of the illness, diagnoses of bronchitis or pneumonia might have been made previously for these symptoms. It therefore becomes essential in the history to query the specific symptoms that have occurred rather than to accept prior diagnoses of bronchitis or pneumonia uncritically. The history is essential for both diagnosing asthma and identifying the clinical pattern. When the history is unclear or the duration of symptoms has been brief, a prospective history can be useful by utilizing parent-maintained diaries of symptoms and responses to bronchodilators and corticosteroids.

The physical examination in the preschool child with asthma may be normal at the time seen since an intermittent pattern is common at this age. If symptomatic at the time of examination, physical findings may include varying degrees of respiratory distress with retractions, tachypnea, and use of accessory muscles of respiration. Even if such findings are present, a diagnosis of asthma can only be made if there have been recurrences of lower respiratory tract symptoms. In infancy, only a first episode should be called *bronchiolitis*. While such an initial presentation identifies a child at risk for having recurrences consistent with a diagnosis of asthma, it is the pattern of recurrences that characterizes asthma.

A chest radiograph is not generally helpful but may be useful if the diagnosis of asthma is questionable and other diagnoses need to be considered. Pulse oximetry provides a useful screen for oxygenation. Low oxygen saturation justifies blood gases to determine if the PCO_2 is low or elevated, which identifies whether the desaturation is a manifestation of ventilation-perfusion mismatching or a sign of respiratory failure that requires prompt admission to an intensive care unit capable of providing assisted ventilation. Pulmonary function testing, which is so valuable in the evaluation of asthma, is not readily obtainable in the preschool-age child. However, carefully and patiently instructed older preschoolers have the potential to perform spirometry, and the effort can lead to useful information.[110]

Confirmation of the asthma diagnosis sometimes requires a therapeutic trial. When a child is seen with expiratory wheezing and increased work of breathing and he or she has an impressive response to a bronchodilator, this is obviously supportive of the diagnosis. But with viral respiratory infection–induced symptoms where the inflammatory component of airway obstruction with mucous secretion and mucosal edema predominates, bronchodilator responses may be equivocal. For children with troublesome and persisting symptoms, a therapeutic trial of systemic corticosteroids becomes an effective means for assessment. Persistence of respiratory

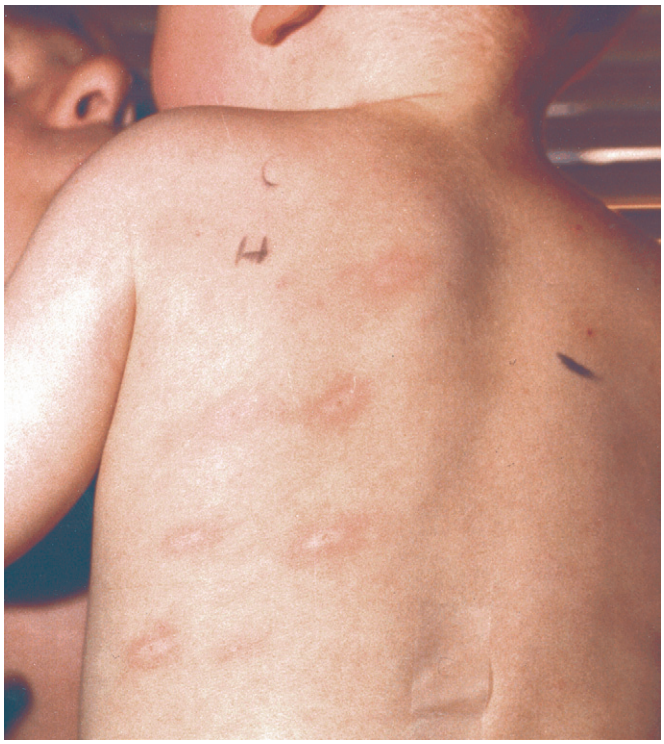

FIGURE 46-7. This 11-month-old infant was hospitalized at 9 months of age with severe acute asthma preceded by rhinoconjunctivitis during the peak of the grass pollen season in a northern California valley area. The typical wheal and flare of the multiple related species of grass pollen native to that area are seen on the left side of the infant's back. They are much larger than the histamine control *(H)* with no reactivity to the diluent control *(C)*. Skin tests on the right side of the back to other common inhalant allergens were all negative. While immunotherapy using injections of allergenic extracts is rarely indicated at this age, this infant illustrates a striking exception where benefit could reasonably be expected.

symptoms, despite a high dose of oral or parenteral corticosteroids, warrants reconsideration of the diagnosis and further evaluation.

Allergy skin testing is a quick and useful means of assessing the potential role for specific IgE to inhalant allergens in a child with asthma (Fig. 46-7). There is a common belief that allergy skin testing is not useful in this age group. However, there is extensive documentation of positive skin prick tests in the preschool-age child and even in infancy.[38–43] The presence of allergen-specific IgE to inhalant allergens can identify the occasional young child with asthma who has an allergic component to his or her disease. Intradermal tests provide greater sensitivity than prick testing, though with less specificity for correlations with clinical symptoms for most allergens. Clinical correlation for an intradermal test has been reported to be better than prick testing for Alternaria,[111] a major outdoor mold, and it is our clinical impression that the greater sensitivity of intradermal testing provides clinical relevance for other molds, epidermals, and dust mites. Even when results do not correlate with symptoms, in a child with the common pattern of viral respiratory infection–induced asthma at the time initially evaluated, the presence or absence of allergen-specific IgE to inhalant allergens provides prognostic information regarding a greater risk for developing persistent symptoms.[112,113]

From the history, physical findings, response to treatment, and allergy skin testing, the diagnosis can be confirmed, the pattern of asthma identified, and the likelihood of decreasing versus persistent symptoms can be determined.[114] When the evaluation raises doubts about the diagnosis of asthma, alternative diagnoses should be considered and appropriate diagnostic tests undertaken (see Table 46-1).

Recognizing an Exacerbation of Asthma

Asthma is typically characterized by a fluctuating course. While many increases in symptoms readily respond to administration of a bronchodilator, the most severe episodes, commonly referred to as *exacerbations,* require more vigorous treatment, and often lead to hospitalization. Since early treatment may prevent the need for emergency visits and hospitalization, recognition of an impending exacerbation is an important part of evaluation. Since wheezing is commonly associated with labored respiration, a yearlong study examined the antecedent symptoms and signs that precede wheezing in children with a pattern of intermittent exacerbations. The most reliable indicator of subsequent wheezing was troublesome cough.[115] Examining specifically the clinical characteristics of an asthma exacerbation, defined as requiring an oral corticosteroid, in children 2 to 5 years of age, the combination of increased daytime cough, daytime wheeze, and nighttime requirement for use of bronchodilators preceded the need for oral corticosteroids by 1 day.[116]

Treatment

There have been many therapeutic options available for asthma.[117] Epinephrine by injection was introduced for treatment of asthma in the early twentieth century. Ephedrine, an oral agent with epinephrine-like properties, was isolated from the ancient Chinese herb, Ma Huang, in the 1920s. Subsequent evolution of pharmaceutical development led to inhalational adrenergic bronchodilators with progressively more β_2-specific agonist activity and longer duration of action. Theophylline had been used as a bronchodilator for the relief of acute asthmatic symptoms since the 1930s, initially in patients unresponsive to injected epinephrine,[118] and subsequently as an oral agent in fixed dose combination with ephedrine.[119] The most important use for theophylline eventually became maintenance therapy for controlling the symptoms of chronic asthma.[120] Studies of the pharmacodynamic and pharmacokinetic characteristics of theophylline, the development of reliably absorbed slow-release formulations, and the availability of rapid, specific serum assays improved both the efficacy and safety of this drug. Identification of anti-inflammatory effects for theophylline increased interest in this medication.[121] However, inhaled corticosteroids have largely replaced its use.

Corticosteroids were introduced for treatment of asthma in the 1950s, initially for systemic use and in the 1970s as inhalational agents. Cromolyn, a mast cell stabilizer, also became available in the 1970s. Leukotriene modifiers are the newest class of medications available

for the treatment of asthma. Other agents described in the medical literature as having a role for asthma treatment are anticholinergic bronchodilators, magnesium sulfate, and nedocromil. Injections of allergenic extracts have been used for many years as treatment for inhalant allergen–induced rhinoconjunctivitis and asthma. An anti-IgE monoclonal antibody, omalizumab, is available as another means of treating allergic asthma. Since there is little data for use of omalizumab in the preschool asthmatic, it should rarely be considered for use in this age group, and even then only by an experienced specialist. Environmental manipulation has long been a nonpharmaceutical approach to treatment. The availability of so-called "alternative therapy" and folk remedies further confound choices for both physician and patient.

Consideration of strategies for treatment selection provides a more focused selection of therapeutic options. Essentially, treatment can be divided into *intervention,* which are the measures used to stop acute symptoms of asthma, and maintenance medication, which are the measures used to prevent asthma symptoms.

Intervention Measures

Virtually all children with asthma will need occasional intervention for acute symptoms. Bronchodilators and systemic corticosteroids are the major medications used for acute symptoms of asthma. A β_2-adrenergic bronchodilator, such as albuterol (salbutamol), provides rapid airway smooth muscle relaxation. However, viral respiratory infection–induced exacerbations commonly result in progression of symptoms leading to an exacerbation that could result in requirement for unscheduled urgent medical care and hospitalization. A typical pattern of such a viral respiratory infection–induced exacerbation is initial rhinorrhea, followed within a day or so by troublesome cough, with another day resulting in respiratory distress manifested by labored breathing, chest retractions, and wheezing. Examining the most reliable signs of an impending major exacerbation, coughing was found to be the most predictive.[115,116] Bronchodilators provide quick relief from the bronchospastic component of the airway obstruction of asthma but have no effect on the progression of the process that results from inflammation. Identification of progression by increasingly troublesome cough permits consideration for early use of a systemic corticosteroid. It is important to consider that much viral respiratory–induced wheezing in young children runs a brief, benign, and self-limited course. However, for those with a history of prolonged symptoms or for those with a pattern of urgent care requirements or hospitalization, early use of adequate doses of corticosteroids provides substantial clinical benefit.[122]

Acute symptoms generally can be relieved by an inhaled β_2 agonist. Infants, toddlers, and preschool-age children can receive this bronchodilator effectively from a metered-dose inhaler (MDI) delivered through a valved holding chamber (Fig. 46-8). Efficacy generally matches or exceeds that from a nebulizer with more rapid delivery and convenience for home care.[123–125] The addition of aerosolized ipratropium to albuterol, while not routinely of added benefit, does have a clinically important additive effect for those with more severe acute airway obstruction.[126] Theophylline, magnesium, and intravenous β_2 agonists are additional agents of potential clinical value when severe airway obstruction is not rapidly relieved by an inhaled β_2 agonist even with ipratropium.

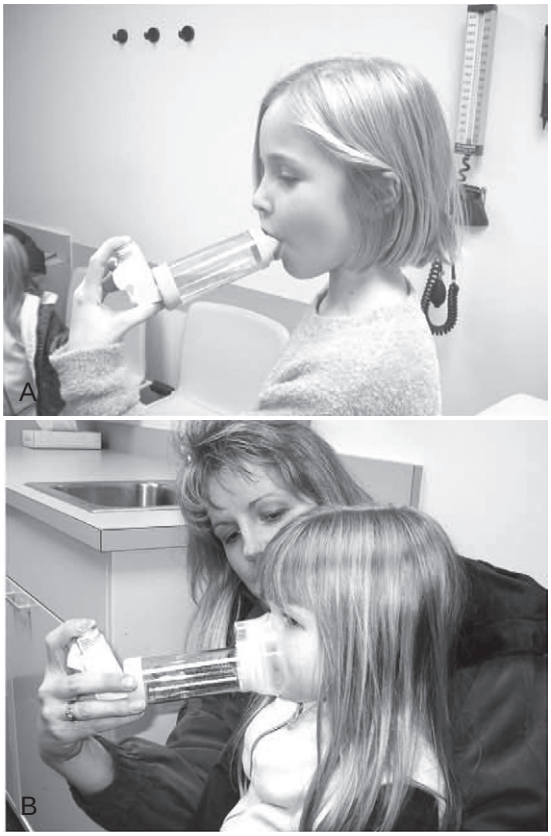

FIGURE 46-8. Demonstration of inhaled medication from a metered-dose inhaler (MDI) with a valved holding chamber in a preschool-age child **(A)** and with a facemask in a toddler **(B).** The MDI injects aerosol into the chamber with one-way valves that permits inhalation of the medication from the chamber while exhalation is into the ambient air. Three to six actuations of albuterol (90 mcg/actuation) in this manner with at least three to four breaths after each actuation to evacuate the chamber provides bronchodilator effectiveness equivalent to 2.5 mg of albuterol by open nebulizer with greater convenience and lower cost.

Systemic corticosteroids are potent anti-inflammatory agents for asthma and have long been recognized as effective for treating acute exacerbations. However, the tradition for many years was to use them only when it was apparent that more conservative measures had failed. Several studies over the past 15 years have demonstrated that earlier aggressive use of systemic corticosteroids in children with an acute exacerbation of asthma decreases the likelihood of requiring urgent medical care and hospitalization.[127] While there is concern that the high frequency of viral respiratory infection–induced asthma in the preschool-age child will, at least for periods of time, result in an excessive frequency of oral corticosteroid use, the risks of this effective strategy appears minimal.[128]

Storr and colleagues examined the effect of oral prednisolone in children who were hospitalized with acute asthma.[129] In a randomized double-blind placebo-controlled trial, 67 children received prednisolone and 73 received placebo shortly after admission. Mean age of the

children was 5 years. Those younger than 5 years of age received 30 mg of prednisolone, and those 5 years of age or older received 60 mg. At a 5-hour decision time, about 20% of those who received prednisolone could be discharged compared with only about 2% of those who received placebo. Among those not discharged at 5 hours, more rapid improvement and earlier discharge occurred in the prednisolone-treated patients than in those in who received placebo.

Tal and coworkers examined the value of systemic corticosteroids in children ranging from 0.5 to 5 years of age seen in an emergency room for acute asthma.[130] Using 4 mg/kg of IM methylprednisolone, or normal saline, in a double-blind placebo-controlled trial, the decision to admit to hospital at 3 hours after medication administration was reduced from over 40% of the 35 children given placebo to about 20% of the 39 given the methylprednisolone.

Scarfone and colleagues examined the effect of oral prednisone in children with a mean age of 5 years seen in an emergency room.[131] In a randomized double-blind trial, 36 received 2 mg/kg of prednisone and 39 received placebo. No differences were seen in a mock decision to admit at 2 hours, but at 4 hours, about 50% of the placebo-treated children were admitted, compared with only about 30% of the prednisone-treated children. The differences were substantially larger for a subgroup judged most sick in which over 70% of the placebo-treated children were admitted, compared to less than half that number for the prednisone-treated children.

These studies suggest that an adequate dosage of systemic corticosteroids administered early in the course of an asthma exacerbation has the potential to prevent the need for unscheduled medical care or hospitalization.[122] Some studies examining the early use of systemic corticosteroids in primary care, and in children with relatively mild symptoms admitted to the hospital, have demonstrated that many preschool-age children have sufficiently rapid improvement during exacerbations that the addition of a systemic corticosteroid may be superfluous.[77,78] An additional confounding factor in the decision for early use of a systemic corticosteroid during an acute exacerbation of asthma is the lack of information regarding optimal dosage in pediatrics. However, a study in adults with acute asthma in an intensive care unit demonstrated progressive benefit from 15-, 40-, and 125-mg doses.[134] Thus, higher doses are likely to provide more benefit than lower doses, but we have only empirical experience by which to make optimal dosage selection.[135]

The response to systemic corticosteroids for bronchiolitis has been controversial.[136,137] In an attempt to reconcile conflicting data regarding corticosteroids for bronchiolitis, a review of existing studies suggested that high doses early in the course *may* have the potential to favorably influence the clinical course.[138] However, this still remains speculative.

The use of inhaled corticosteroids for acute symptoms of asthma has been examined in the emergency department and at the onset of exacerbations at home. Such attempts have been only marginally successful with (at best) some amelioration of symptoms at very high doses.[139] Only one study, in which fluticasone 1500 mcg/day was initiated at the onset of a respiratory tract infection and continued for 10 days, was associated with a decrease in oral corticosteroid use, but there was no significant decrease in hospitalization, acute care visits, or albuterol use.[140] The authors expressed concern regarding the adverse effects on growth resulting from prolonged courses of high-dose fluticasone and did not recommend the strategy studied.

Maintenance Therapy

Maintenance medication, sometimes called *controller therapy,* has evolved considerably over the years. These are medications used to prevent daily or frequently recurring symptoms. Cromolyn sodium, nedocromil, theophylline, montelukast, and the various inhaled corticosteroids have been the major maintenance medications. In general, only cromolyn and nedocromil generally have become of historical interest. They are weakly potent, require frequent administration, and if an aerosol medication is to be given, low doses of inhaled corticosteroids are more effective and equally safe. Theophylline, while more effective than cromolyn and nedocromil, has a narrow therapeutic index and is still less effective than a low-dose inhaled corticosteroid.[120]

Montelukast appears to be no more effective than cromolyn or nedocromil but has the convenience factor of being a once-daily oral medication that is very safe, although there has been a recent warning about behavioral side effects added to the U.S. package insert because of postmarketing case reports. However, extensive analysis of available data from clinical trials in 8827 subjects who received montelukast and 4724 who received placebo found no difference in behavior-related adverse experiences.[141,142] Montelukast is less effective than an inhaled corticosteroid.[143] While there has been some suggestion that montelukast decreases viral respiratory infection–induced wheezing in children 2 to 5 years of age,[144] the high frequency of atopy in this study makes it likely that the small decrease in symptoms was simply a consequence of the modest effect previously documented for montelukast in young children with mild persistent asthma.[145] Another study in children 2 to 14 years of age showed modest reductions when used episodically for intermittent asthma,[146] but again a high frequency of atopy confounded the interpretation that the effect was on viral respiratory infection–induced asthma rather than just influencing a worsening of the allergic component of asthma. Montelukast was also examined to see if the increase in troublesome symptoms during fall in children 2 to 14 years of age could be attenuated with seasonal use of montelukast. Beneficial effect was limited to boys 2 to 5 years of age and girls 10 to 14 years of age.[147] Montelukast has also been examined for its effect to prevent the recurring respiratory symptoms following bronchiolitis and was found ineffective for this purpose.[148,149]

Inhaled corticosteroids have become the maintenance medication with the greatest degree of efficacy. In preschool-age children with persistent asthma, these agents

can be effectively delivered either by MDI via a valved holding chamber or by nebulizer, with a decrease in asthmatic symptoms.[150–152] Although there is evidence for dose-related systemic effects,[153] conventional low doses have a well-established safety record.[154,155] A minimal degree of hypothalamic-pituitary axis suppression and a small degree of transient growth suppression is detectable at modest doses, but neither clinically detectable adverse effects nor sustained effect on growth are apparent except at higher doses.[156] A newer inhaled corticosteroid appears not to have dose-related systemic effects.[157]

Limitation of Maintenance Medication

There is considerable emphasis currently on maintenance medication, with inhaled corticosteroids demonstrably and unequivocally the most effective medication for eliminating the daily symptoms and signs of chronic (persistent) asthma. However, convincing data have demonstrated that these agents, at least in conventional doses, do not prevent exacerbations of asthma from viral respiratory infections.[158–160] There are no currently available therapeutic measure that can, as safe maintenance therapy, prevent viral respiratory infection–induced asthma.[161] Since viral respiratory infections are the major contributors to acute care requirements for asthma,[78–82] especially in young children who have a high frequency of these common cold viruses,[83] providing effective intervention measures for the family to treat viral respiratory infection–induced asthma is critically important in current efforts to stem the endemic tide of asthma morbidity.

Environmental Aspects of Treatment

Environmental factors that influence the course of asthma in young children include both irritant and immunologic (i.e., allergic) stimuli. By far the most important and well-documented factor that worsens asthma and increases the risk of emergency care requirements and hospitalizations is environmental tobacco smoke.[162–164] The greatest effect appears to be in younger children, although many asthmatic children readily relate an increase in symptoms from even casual exposure to cigarette smoke. While parents may state that they do not smoke around the child, such partial measures appear to have little effect in decreasing exposure in the young child. In a cross-sectional survey, only banning smoking from the home was found to be associated with reduction in urinary cotinine levels in infants.[165] Particulate-producing indoor fires such as wood-burning stoves and fireplaces are potential offenders. Strong odors such as perfume, incense, and other airway irritants such as burning leaves can also act as environmental triggers for asthma.[166] Leaf burning, with its release of toxic and irritating smoke, can cause considerable problems in communities that continue to permit the practice in populated areas.[167]

Questions have been raised about other environmental substances and their role in asthma. Natural gas from range-top burners or nonventilated room heaters releases substances that at least have the potential to be airway irritants and have been associated with some increase in the frequency of respiratory illness in children.[168] Areas of controversy relate to low levels of naturally occurring chemicals. Formaldehyde has been a topic of concern. While formaldehyde and many other chemicals have potentially toxic effects on the airway at high concentrations (as may occur during occupational exposure),[169] it is not apparent that normal household exposure to trace amounts of formaldehyde that leach from some manufactured products actually causesproblems.[170,171] Because asthma is commonly triggered by multiple factors, with common cold viruses causing some of the most severe symptoms in children and accounting for the majority of emergency room visits and hospitalizations, the mere presence of low levels of chemical substances (e.g., formaldehyde) does not necessarily imply an etiologic role.

House-dust mites have been identified as a major factor in increasing symptoms in known asthmatic children living in humid areas such as the southeast United States. They are probably a less significant problem in dry climates or cold northern climates, where central heating results in very low humidity during winter. Airborne particles from cockroaches have been identified as an environmental factor triggering asthma in northeastern inner-city areas.[172] Indoor molds can be a major trigger for asthma, depending upon the indoor environment. Indoor molds thrive in high-humidity situations and particularly when there is water seepage (e.g., in basements or bathrooms).[40] Outdoor molds that grow on decaying vegetation are a major seasonal allergic trigger for asthma in many parts of the country, particularly in the U.S. farm belt.[109] Animal danders can be triggers for asthma in sensitized children.[41]

Environmental manipulation as treatment of asthma in young children therefore requires identification of the major offenders. Tobacco smoke and other indoor lung irritants should obviously be avoided. Traditional environmental control measures for allergens require documentation that the child has specific IgE to those factors. Creating homeless dogs and cats, or compulsive cleaning, for a nonallergic child with predominantly viral respiratory infection–induced asthma is unlikely to provide clinical benefit. When specific IgE to a household inhalant is found, measures to decrease exposure should be undertaken if the history supports those inhalants as risk factors for worsening the disease. There are no rigid guidelines for making these decisions, which require a clinical judgment that is complicated by the multiple factors that can worsen asthma. Placing dustproof casings on the mattress and pillow, the major sources of exposure to dust mites, is a prudent measure for those with large positive skin tests to dust mites, as is using a vacuum cleaner with a HEPA filter. These and other dust mite measures have the potential to be effective for selected patients.[174,175] Reducing humidity in the home to below 60% has the potential to decrease indoor molds and thereby potentially decrease symptoms for those demonstrated to be clinically sensitive to these common aeroallergens.

Immunotherapy (Allergy Shots) for Environmental Aeroallergens

There has long been controversy regarding the potential for clinical benefit from administration of allergenic extracts, either as subcutaneous immunotherapy (SCIT) or the more recently considered sublingual immunotherapy (SLIT).[176] The issue is not whether or not injections of some allergenic extracts can reduce symptoms of inhalant allergy; this evidence is well supported with controlled clinical trials.[108] The problem relates to the complexity of asthma, the multiple factors that contribute to symptoms (not all of which are allergic), and the limitations of evidence from controlled clinical trials. The major precipitants for asthma in young children are viral respiratory infections, for which there is little reason to expect benefit from immunotherapy with allergenic extracts, even among those with some positive allergy skin tests. When aeroallergens are judged to contribute to the asthma of a young child, some of the most potent asthmagenic aeroallergens such as the molds have little evidence for the efficacy of immunotherapy.[177] Thus, while the clinical indications for administration of allergenic extracts are extremely limited for asthma, especially for preschool-age children, there will be occasional exceptions where it should be considered (see Fig. 46-7).

Family Education

Many families who have young children with asthma lack knowledge of their disease[178,179] and fail to recognize and respond appropriately to symptoms and signs that precede severe attacks.[180,181] The recognition that patient self-management skills needed to be upgraded led to the development of several self-management programs.[182] Most cover similar topics: discrimination of symptoms, explanations of how different medications work and when to use them, recognition of situations that require emergency care, discussions of asthma triggers and how to avoid them, and the importance of effective communication between the patient or family and health care workers.[183] These programs are based on social and behavioral theories that suggest education can improve understanding of asthma and thereby provide motivation to take an active part in one's own asthma management.[184] Social learning theory suggests that cognitive factors, memory or retention, motivation, and self-efficacy are crucial links between initial training and subsequent performance of the desired tasks in asthma self-management programs.[185] However, the results of these programs have often been equivocal at best.[186,187]

Since asthma is a heterogeneous disease with various clinical patterns, generic family education has limited value. Once the diagnosis is made and the asthma in the individual child is characterized regarding clinical pattern and precipitating factors, the information should be shared with the family. Because the most common pattern of asthma in young children is a viral respiratory infection–induced pattern, an explanation of this mechanism and the frequency of viral respiratory infections in the preschool-age group prepares the family for anticipated events. Whether or not maintenance medication is used for an element of persistent symptoms unrelated to viral respiratory infections, an explanation that exacerbations are likely to occur with colds prepares the family for the need to utilize intervention measures at these times. Further, explaining the limitation of bronchodilators with regard to the inflammatory component of airway disease in asthma prepares the family for the need to recognize bronchodilator subresponsiveness as a sign of progressive airway inflammation and the need to intervene with an oral corticosteroid. These principles should be outlined in a very simple written action plan (Table 46-2).

TABLE 46-2 PATIENT INSTRUCTION INTERVENTION ACTION PLAN FOR ACUTE SYMPTOMS OF ASTHMA

Asthma symptoms include cough, wheeze, and labored breathing.
Symptoms are particularly likely to begin or increase with a viral respiratory infection (common cold).
Increasing cough is often the first sign of asthma triggered by a viral respiratory infection and can be used to identify when an oral corticosteroid may be indicated to prevent progression to wheezing and labored breathing.[115,116]
When you observe asthma symptoms in your child, do the following:
First: use an inhaled bronchodilator.
If symptoms stop completely: Repeat inhaled bronchodilator when necessary.
If symptoms are not completely relieved: Repeat inhaled bronchodilator.
If symptoms still are not completely relieved or if a third dose for acute symptoms is needed within 8 hours or if more than four doses in 24 hours: a short course of oral corticosteroids may be needed; call for advice if you have questions, or give the first dose and then call so that frequency of courses and response can be monitored.

SUMMARY

The controversies and confusion regarding defining asthma are greater in the preschool-age child than later in childhood. This is caused, at least in part, by the varying clinical patterns of asthma, with the predominance of viral respiratory infection–induced asthma in the early years. While the persistent pattern of asthma in later childhood typically has its origins in the early years, spontaneous improvement with age is common for the intermittent viral respiratory infection–induced pattern. The genetics of asthma in young children is complex, with components of both airway hyperresponsiveness and atopic allergy for those who eventually develop persistent asthma. However, even the intermittent viral respiratory infection–induced pattern appears to have a familial tendency, although this has been less well studied. The inflammatory component of asthma is different for asthma associated exclusively with viral respiratory infections from that seen in the allergic model of asthma. The natural history of asthma in the preschool years has been well studied. While more than half of those with the common viral respiratory infection–induced pattern will remit, most with severe chronic asthma will continue into adult life. Despite the benign course of the intermittent pattern in the early

age group has the greatest frequency of hospitalizations because of the frequency of viral respiratory infections in this age group. Maintenance therapy, even with inhaled corticosteroids, does not prevent viral respiratory infection–induced exacerbations in these patients. Early intervention with a short course of relatively high-dose oral corticosteroids is essential to minimize the need for urgent care and hospitalization for acute severe exacerbations from viral respiratory infections. Inhaled corticosteroids are the most effective agents for maintenance in those with persistent asthma, and they can be effective when given by nebulizer or more conveniently by MDI with a valved holding chamber for infants and young children. Allergic evaluation may provide information for therapeutic environmental elimination measures in this age group, however it is primarily of prognostic value, with the absence of specific IgE to common inhalant allergens predictive of less likelihood for persistent symptoms later in childhood.

Suggested Reading

Busse WW, Lemanske Jr RF, Gern JE. Role of viral respiratory infections in asthma and asthma exacerbations. *Lancet*. 2010;376:826–834.

Phelan PD, Robertson CF, Olinsky A. The Melbourne asthma study: 1965-1999. *J Allergy Clin Immunol*. 2002;109:189–194.

Weinberger M. Pediatric asthma and related allergic and non-allergic diseases: patient-oriented evidence based essentials that matter. *Pediatric Health*. 2008;2:631–650.

Weinberger M, Abu-Hasan M. Pseudo-asthma: when cough, wheezing, and dyspnea are not asthma. *Pediatrics*. 2007;120:855–864.

Weinberger M, Solé D. The natural history of childhood asthma. In: Pawankar R, Holgate S, Rosenwasser L, eds. *Allergy Frontiers: Therapy & Prevention*. Vol. 5. Springer; 2010:511–530.

References

The complete reference list is available online at www.expertconsult.com