Asthma Update: Clinical Aspects and Management

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Objectives

After completing this article, readers should be able to:

1. Discuss the treatment of children who have mild asthma.
2. Know that exercise–induced asthma often represents poorly controlled persistent asthma rather than mild intermittent asthma.
3. Discuss how to assess the severity of asthma and the progress of therapy.
4. Describe the most effective treatment for persistent asthma of any severity.
5. Know the most appropriate second-line therapeutic intervention for children who have moderate and severe asthma.

This is the second of a two-part article on asthma. Readers should consider both parts for a complete review.

Introduction

More than 26 million Americans have been diagnosed with asthma in their lifetime, with more than 9 million being younger than 18 years of age. Asthma deaths increased by 109% between 1979 and 1998, rising to 5,348 deaths in 1998 (American Lung Association, 2001). In light of these recent trends, the underdiagnosis and undertreatment of asthma is disturbing. In the first part of this update, we explored the epidemiology and pathophysiology of asthma. The second part examines diagnosis and management.

The National Asthma Education and Prevention Program (NAEPP), a committee of the National Heart, Lung, and Blood Institute (NHLBI), has convened three expert panels on the diagnosis and management of asthma. From these expert panels, two sets of guidelines were published in 1991 and in 1997. In November 2002, an Update on Selected Topics was published. It is anticipated that guidelines will be updated rather than rewritten for the foreseeable future to aid in the diagnosis and management of asthma using the latest in evidence-based medicine (see article on evidence-based medicine on page 358). The 1997 guidelines and the 2002 update can be found on the NHLBI Web site at www.nhlbi.nih.gov. Much of the information for this review is taken from these two documents and is supported by the primary literature reviewed in making the expert panel recommendations.

Definition of Severity

It may be difficult to recognize persistent asthma, especially in a child who seeks only episodic care, often from an emergency department (ED) or convenience clinic. However, even in those settings, a careful history will help to identify patients who have persistent asthma and require a different approach to care from those who have truly intermittent asthma. In general, the “Rule of Twos” should apply: anyone who has symptoms more than two times a week or more than two nights a month should be considered to have persistent asthma and managed as such (Fig. 1). The symptoms do not need to be dramatic; they may consist of only persistent cough, mild exercise intolerance, dyspnea

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Abbreviations

<table>
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<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>DPI</td>
<td>dry powder inhaler</td>
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<tr>
<td>ED</td>
<td>emergency department</td>
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<tr>
<td>FEV₁</td>
<td>forced expiratory volume in 1 second</td>
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<tr>
<td>MDI</td>
<td>metered dose inhaler</td>
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<td>NAEPP</td>
<td>National Asthma Education and Prevention Program</td>
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<td>NHLBI</td>
<td>National Heart, Lung, and Blood Institute</td>
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<tr>
<td>PF</td>
<td>peak flow</td>
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<tr>
<td>PFT</td>
<td>pulmonary function testing</td>
</tr>
<tr>
<td>URI</td>
<td>upper respiratory tract infection, usually viral</td>
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</table>
with little provocation, or night awakenings due to dyspnea or cough. Night awakenings may not be reported unless specific questions are asked. Among patients seeking episodic care for a more severe exacerbation, these subtle symptoms may be overlooked or underestimated, but it is these patients who represent the bulk of the underdiagnosed and undertreated population.

Even patients who have truly intermittent asthma may experience severe exacerbations that bring them to the ED or an unscheduled office visit. Young children whose asthma seems to be triggered only by viral upper respiratory infections (URIs) and who are symptom-free between URIs may be diagnosed appropriately and treated for mild intermittent asthma. However, a careful history is required to ascertain the lack of symptoms between infections.

The characteristics of mild, moderate, and severe asthma before intervention with medications are outlined in Table 1. Use of symptoms alone for diagnosis often can be misleading. Additional objective data from pulmonary function testing (PFT) or peak flow (PF) monitoring may aid in uncovering symptoms that are more severe than expected. Many patients complain only of exercise-related symptoms, but further questioning frequently elicits additional nonexercise-related symptoms. Exercise-induced asthma often is the harbinger of poorly controlled moderate asthma rather than a sign of mild intermittent asthma. Exercise-induced asthma manifests as cough, wheeze, or chest tightness after 5 to 6 minutes of moderate aerobic exercise that resolves after rest with or without bronchodilator intervention. Lung function testing during the symptomatic period usually demonstrates a decline in forced expiratory volume in 1 second (FEV₁) of 15% or more from the baseline value in a formal exercise test. However, many patients who are symptomatic only with exercise have a baseline FEV₁ of less than 80% predicted, automatically placing them in the category of moderate persistent severity.

Each patient has the potential for one or several trigger factors (Table 2). The role of clinicians is to help identify those triggers and control them as much as possible. Some may be obvious and part of the presenting complaint, but many may be more subtle and require careful questioning to identify.

### Young Children

Preschool-age children may present particular diagnostic dilemmas. The lack of objective data from PFT is limiting; reliable and reproducible PFT can be obtained in school-age children and older but not commonly in preschool or younger children. The clinician must rely on the history as reported by a secondary observer, the parent. On physical examination, the clinician might

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**Table 1. NAEPP Classification of Asthma Severity Before Treatment**

<table>
<thead>
<tr>
<th>AM symptoms</th>
<th>Intermittent</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2×/wk</td>
<td>&gt;2×/wk</td>
<td>Daily</td>
<td>Continual</td>
<td></td>
</tr>
<tr>
<td>&lt;1×/d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM symptoms</td>
<td>≤2×/mo</td>
<td>&gt;2×/mo</td>
<td>&gt;1×/wk</td>
<td>Frequent</td>
</tr>
<tr>
<td>FEV₁ or PEF% predicted</td>
<td>≥80</td>
<td>≥80</td>
<td>60 to 80</td>
<td>≤60</td>
</tr>
<tr>
<td>PEF Variability (%)</td>
<td>&lt;20</td>
<td>20 to 30</td>
<td>&gt;30</td>
<td>&gt;30</td>
</tr>
</tbody>
</table>

The presence of one of the features of severity is sufficient to place a patient in that category. FEV₁ = forced expiratory volume in 1 second; PEF = peak expiratory flow. Reprinted with permission from NIH/NHLBI Guideline Update. June 2002. NIH Publication No. 02-5075.
look for tachypnea, nasal flaring, or poor air exchange. In an acute episode, a young child may not be moving enough air to elicit a wheeze. As with older children, young patients may not be acutely symptomatic when examined and may not have abnormal physical findings on any given day. For the preschool-age child or those unable to perform PFTs, a chest radiograph may help to identify hyperinflation or increased peribronchial markings representative of airway inflammation. Also, a therapeutic trial of either oral or inhaled bronchodilators may help establish the diagnosis, but ongoing treatment with bronchodilators alone is not appropriate for a child who has persistent asthma. A child who requires bronchodilators more than once or twice a week (Rule of Twos) should be classified and treated as having persistent asthma.

**Asthma Management**

The mainstay of treatment is careful patient and family education regarding the pathophysiology of asthma, triggers, medications, and expectations. Regardless of severity, all patients need education. Pharmacotherapy is directed by the severity of asthma at the time of diagnosis and by the response to initial treatment. All levels of persistent asthma require daily anti-inflammatory treatment, and inhaled corticosteroids have been reaffirmed in the recent update of the asthma guidelines as the most effective treatment for persistent asthma of any severity. See Figures 2 and 3, respectively, for the recommended approach to maintenance asthma therapy in children 5 years and younger and children older than 5 years of age.

**Mild Intermittent and Mild Persistent Disease**

Patients who have mild intermittent asthma (symptoms <2 times weekly and night symptoms <2 times monthly) represent the only group for whom bronchodilators alone are the appropriate treatment. Mild persistent asthma at any age (normal baseline PFT findings but symptoms >2 times weekly and night symptoms >2 times monthly) is treated most appropriately with low-dose inhaled corticosteroids (Table 3). Appropriate inhaled steroids have been approved for use in children as young as 1 year of age; by extrapolation, these medications have been applied to those even younger. A leukotriene modifier can be used if inhaled therapy is not viable, but this is considered second-line rather than primary treatment, even in very young children. Montelukast is approved for use in those as young as age 2 years and has been used in younger patients, although there are no dosing guidelines for this group. Cromolyn and nedocromil may be alternative drugs for inhalation but are not the preferred treatment. They have an excellent safety profile, but their efficacy has been demonstrated to be significantly less than that of inhaled steroids in direct comparative studies of asthma management in older children. Theophylline continues to be listed as an alternative therapy for older children, but it is not preferred first-line treatment. See Table 4 for doses of long-term controller medications other than inhaled steroids. It is important to note that the dosing recommendations for both inhaled steroids and other medications divide child from adult at age 12 years whereas the stepwise approach guidelines (Figs. 3 and 4) differentiate between preschool-age children and older children/adults.

**Moderate Persistent Disease**

Moderate persistent asthma should be treated with low- to medium-dose inhaled steroids plus a long-acting bronchodilator. Alternatives include use of medium-dose inhaled steroids alone or selection of another drug such as a leukotriene modifier or theophylline with the inhaled steroids. Marketing of a combined inhaled steroid and long-acting bronchodilator product in multiple steroid strengths has simplified this area significantly for patient compliance. This dry powder inhaler (DPI) is appropriate for use in children as young as 4 to 5 years who can generate sufficient negative inspiratory force to activate the device adequately. The combined product is not approved for use in young children, but the two components are approved as stand-alone DPIs for use in children as young as 4 years. Metered dose inhaler (MDI) steroids and long-acting bronchodilators may be used more easily and effectively by preschool and early school-age children than the DPI when an appropriate spacer or holding device is added, although they are not approved specifically for use at that age. Substantial anecdotal and extrapolated experiential data promote the

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**Table 2. Asthma Triggers**

- Exercise
- Weather changes
- Cold air
- Allergens (eg, dust, mold, animal dander, pollen, cockroaches)
- Emotional expression (eg, anger, laughter, crying)
- Air pollution
- Environmental changes
- Tobacco smoke exposure
- Irritants
- Acid reflux
- Viral respiratory infections
benefits of long-acting bronchodilators in young children, but the MDI of salmeterol recently has been withdrawn from the market. For moderate persistent asthma, studies in older children and adults have demonstrated that the addition of a long-acting bronchodilator to low-dose inhaled steroid is more effective than doubling the dose of steroids and more effective than low-dose steroids plus a leukotriene modifier. It still may be necessary to increase the dose of inhaled steroids within the medium range even after adding a long-acting bronchodilator to control symptoms and normalize PFT results.

**Severe Persistent Disease**

Severe asthma is treated with high-dose inhaled steroids and long-acting bronchodilators. There is no evidence that leukotriene modifiers add benefit in this population, but they often are used in an effort to avoid the need for ongoing systemic steroids. Even at high doses (Table 3), inhaled steroids administered consistently over time provide less total systemic exposure than repeated courses of systemic steroids. For example, if a child who weighs 20 kg receives 2 mg/kg per day of oral prednisone, the systemic exposure is 200 mg with a single 5-day course. If this same preschool-age child takes two puffs of high-dose fluticasone twice daily (a total daily dose of 880 mcg), assuming 15% delivery (even with a spacer) and 100% compliance, the annual dose of systemic steroid exposure is only about 50 mg. Because compliance with chronic medication administration is approximately 50%, the annual dose would be lower.

**Growth**

There was concern in the mid-1990s about growth suppression with inhaled corticosteroids. Short-term studies with first-generation steroids (beclomethasone) and very sensitive assessments showing measurable decreases in linear growth aroused substantial alarm among the public and prescribing physicians. When longer-term studies (4 y versus 12 to 24 wk) were performed with second-generation steroids (fluticasone and budesonide), mild growth suppression was demonstrated in the first year of therapy, but it was overcome by the end of the 4-year study without any change in the steroid dose. In even longer studies, children reached predicted adult height despite ongoing use of inhaled steroids. Newer inhaled corticosteroids have first-pass metabolism in the liver that results in much less of a systemic effect. The potential effect can be decreased even further by using an appropriate spacer or holding device and rinsing the mouth.
after each drug dose. Nonetheless, close monitoring of linear growth is warranted in children receiving long-term inhaled steroids, particularly in high doses.

**Monitoring and Referral**

Interval monitoring, including PFT once or twice a year, is appropriate for all patients who have persistent asthma that requires daily anti-inflammatory treatment. The educational message should be reinforced and the intensity of therapy stepped down or up as appropriate. Newly diagnosed patients should be seen at least quarterly for the first year, then every 6 to 12 months, depending on their stability. Patients who have severe asthma should be seen more frequently. All patients who have severe asthma, those who have moderate asthma that is not responding to appropriate treatment, and children younger than 3 years of age who have moderate-to-severe asthma should be seen by an asthma specialist for initial evaluation and possible comanagement.

Use of a written plan, with intervention guidelines based either on symptoms or on PF values, is appropriate for all patients who have asthma. A PF meter is useful for patients who have moderate and severe asthma, but it is not likely to be used by those who have mild asthma. Review studies of written plans compared with verbal education alone are inconclusive, but the meta-analyses favor the benefits of written plans with or without PF guidelines. PF meters are particularly helpful for those who do not understand the severity of their symptoms. There can be a significant gap between perceived symptoms and the objective information obtained from PF or PFT. Patients who deny symptoms until they are in significant distress often are poor perceivers of severity, and this is the group that is least likely to be willing to comply with PF monitoring.

**Mild Acute Exacerbations**

Mild exacerbations, characterized by a decrease in PF to 50% to 80% of predicted, frequently can be managed by the addition of short-acting bronchodilators to maintenance preventive treatment. Early intervention based on prompt recognition of a change in status and adherence to a written plan has the best chance for a good resolution. Prompt communication with the clinician when the plan is not working also is important. Although controversial and not fully supported, the NAEPP guidelines in 1997 recommended doubling the dose of inhaled steroids for 7 to 10 days for PFTs in the yellow/caution zone.
or mild symptomatic exacerbations. For some patients who have a history of repeated severe exacerbations, it may be appropriate to maintain a supply of systemic steroids at home with instructions to initiate treatment early and call the clinician for further instructions. These patients should have a well-established relationship with the clinician and be following a written plan. These patients also are likely to have been evaluated by an asthma specialist. Even patients who have less severe asthma tend to underuse systemic steroids for fear of long-term adverse effects. Too many patients end up in the ED because of lack of early recognition and intervention, lack of knowledge of appropriate intervention steps (action plan), under-recognition of the severity of symptoms, and undertreatment with systemic steroids when increased bronchodilators and inhaled steroids are not effective.

Use of Antibiotics

Physicians tend to prescribe antibiotics for children who have a history of asthma and develop fever and a cough. The recent NAEPP update reviewed the literature regarding use of antibiotics in asthma exacerbations and found no evidence to support this practice. Clear manifestations of a bacterial infection should be present before beginning antibiotic therapy during an exacerbation of asthma. Viral infections are implicated much more commonly than are bacterial infections as triggers in children who have asthma.

Systemic steroids are more appropriate as secondary treatment following bronchodilators than are antibiotics. Steroids play a role in increasing adrenergic responsiveness, thus improving the benefit of the primary beta-agonist bronchodilator agents. Steroids also clearly improve PFT and oxygen saturation outcomes compared with use of bronchodilators alone in acutely ill children who have asthma. In general, there is no evidence that it is necessary to taper steroid doses in mild and moderate asthma exacerbations. A few patients who frequently need systemic steroids and who are receiving high doses of inhaled steroids will do better with a longer course of steroids, including tapering the dose over time, but this is the exception rather than the rule in primary care practice.

Moderate and Severe Acute Exacerbations

Severe airway obstruction that requires immediate attention and usually hospitalization may be manifested by severe retractions, inability to speak whole phrases, cyanosis, and decreased breath sounds with poor air exchange. Often, affected patients cannot even trigger a PF meter; a PF of less than 30% of predicted should be

### Table 3. Estimated Comparative Daily Dosages for Inhaled Corticosteroids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Medium Daily Dose</th>
<th>High Daily Dose</th>
<th>Adult Child*</th>
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<tbody>
<tr>
<td>Beclomethasone CFC 42 or 84 mcg/puff</td>
<td>84 to 336 mg/d</td>
<td>84 to 336 mg/d</td>
<td>168 to 504 mg/d</td>
</tr>
<tr>
<td>Beclomethasone HFA 40 or 80 mcg/puff</td>
<td>80 to 240 mg/d</td>
<td>80 to 240 mg/d</td>
<td>480 to 720 mg/d</td>
</tr>
<tr>
<td>Budesonide DPI 200 mcg/puff</td>
<td>200 to 400 mg/d</td>
<td>200 to 600 mg/d</td>
<td>400 to 800 mg/d</td>
</tr>
<tr>
<td>Flunisolide 250 mcg/puff</td>
<td>500 to 1,000 mg/d</td>
<td>500 to 1,000 mg/d</td>
<td>1,000 to 2,000 mg/d</td>
</tr>
<tr>
<td>Fluticasone MDI: 44, 110, or 220 mcg/puff</td>
<td>88 to 264 mg/d</td>
<td>88 to 264 mg/d</td>
<td>264 to 660 mg/d</td>
</tr>
<tr>
<td>Fluticasone DPI: 50, 100, or 250 mcg/puff</td>
<td>100 to 200 mg/d</td>
<td>100 to 200 mg/d</td>
<td>200 to 500 mg/d</td>
</tr>
<tr>
<td>Triamcinolone acetonide 100 mcg/puff</td>
<td>400 to 1,000 mg/d</td>
<td>400 to 1,000 mg/d</td>
<td>800 to 2,000 mg/d</td>
</tr>
</tbody>
</table>

*Children ≤ 12 years of age.

CFC = chlorinated fluorocarbon propellant, HFA = HFA-134a (1,1,1,2-tetrafluoroethane) propellant, MDI = metered dose inhaler, DPI = dry powder inhaler.
considered a sign of severe obstruction. Prompt and aggressive intervention is needed to prevent rapid decline to respiratory failure. Young children who have severe obstruction are likely to have tachypnea with or without retractions, poor air exchange, and irritability or somnolence.

Home and ED treatment of moderate and severe exacerbations include primarily short-acting bronchodilators and steroids. When adrenergic bronchodilators already are being overused acutely or chronically prior to seeking medical help, there is a risk of inducing adrenergic toxicity with additional bronchodilator use in the ED. Close monitoring of acutely ill patients receiving high doses of adrenergic agents for tremor, tachycardia, and hypokalemia is necessary to prevent toxicity. Controversy surrounds the role of inhaled anticholinergic agents as an adjunct to adrenergic therapy for exacerbations, with studies both supporting and denying the benefit of anticholinergics. They are not needed for all patients, but some may benefit from them. It may be appropriate for some patients who have demonstrated benefit from anticholinergics to have a supply at home for secondary intervention as part of a written plan. Doses of medications for use in exacerbations are found in Table 5.

Recently marketed levalbuterol (R-albuterol) has been proposed as superior to racemic albuterol, with a longer half-life and potential anti-inflammatory properties. Although there is a theoretical benefit to the use of R-albuterol, no hard data document its benefit in acute asthma over a racemic mixture of albuterol, and few data exist for its use in children. Levalbuterol probably is most appropriate for use in patients who have demonstrated tachycardia, tremor, and irritability from racemic albuterol. The cost is at least three to four times that of generic racemic albuterol for equipotent doses. More data in children may be forthcoming to support increased acceptance of levalbuterol as a primary bronchodilator for the treatment of asthma exacerbations.

There is no role for inhaled mucolytics and chest physical therapy as part of routine care of asthma exacerbations. Atelectasis due to mucus plugging is not uncommon but usually resolves with anti-inflammatory and
bronchodilator therapy. Atelectasis in asthma is not a sign of pneumonia and does not indicate the need for bronchoscopy in most patients.

The treatment of severe asthma requiring hospitalization is not addressed in this article. However, every time a child has an exacerbation severe enough to require hospitalization, the primary clinician should review the home situation and renew the search for triggers that may be contributing to the severity of the baseline state of asthma as well as to the exacerbation. Re-evaluation of baseline preventive therapy and consideration of the need to step up therapy is appropriate. A written asthma

<table>
<thead>
<tr>
<th>Table 5. Usual Dosages for Quick-relief Medications</th>
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<tbody>
<tr>
<td>Medication</td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td><strong>Short-acting Inhaled Beta-Agonists</strong></td>
</tr>
<tr>
<td>Albuterol MDI</td>
</tr>
<tr>
<td>Albuterol HFA</td>
</tr>
<tr>
<td>Piritrexol MDI</td>
</tr>
<tr>
<td>Albuterol Rotahaler DPI</td>
</tr>
<tr>
<td><strong>Albuterol</strong> Nebulizer solution</td>
</tr>
<tr>
<td>Bitotterol Nebulizer solution</td>
</tr>
<tr>
<td>Levalbuterol (R-albuterol) Nebulizer solution</td>
</tr>
<tr>
<td><strong>Anticholinergics</strong></td>
</tr>
<tr>
<td>Ipratropium MDI</td>
</tr>
<tr>
<td>Ipratropium with albuterol MDI</td>
</tr>
<tr>
<td><strong>Systemic Corticosteroids</strong></td>
</tr>
<tr>
<td>Methylprednisolone tablets</td>
</tr>
<tr>
<td>Prednisolone tablets</td>
</tr>
<tr>
<td>Prednisone tablets</td>
</tr>
</tbody>
</table>

*Child dose < 12 years of age
MDI=metered dose inhaler, DPI=dry powder inhaler
plan should be initiated or reviewed before hospital discharge.

**Conclusion**
The diagnosis and management of asthma has changed significantly over the more than 10 years since the first NAEPP Expert Panel Report. Better understanding of the epidemiology, pathophysiology, and inflammatory nature of the condition has led to better use of preventive therapy and adoption of inhaled corticosteroids as the primary treatment for all patients who have persistent asthma of any severity. Use of objective measures of lung function to judge severity has allowed practitioners to provide better maintenance approaches and more prompt intervention for exacerbations. The importance of patient education and participation in the treatment plan cannot be emphasized enough. If this can be translated to a decrease in hospitalization and in the mortality rate, we all will have succeeded in our mission as physicians and caregivers.

**Suggested Reading**
PIR Quiz
Quiz also available online at www.pedsinreview.org.

1. You are seeing a 7-year-old girl who has asthma for her health supervision visit. Her mother reports that the child has trouble breathing when she rides her bike, and she reports nighttime cough approximately three times per month. Her only medication is inhaled albuterol, which she takes only when she wheezes. Results of her physical examination are normal, and her peak flow is greater than 80% of the expected value. Which of the following best describes her asthma classification?
   A. Exercise-induced.
   B. Mild intermittent.
   C. Mild persistent.
   D. Moderate persistent.
   E. Severe persistent.

2. Which of the following statements about asthma management is true?
   A. A chest radiograph has very little benefit in helping to diagnose asthma in preschool-age children.
   B. Children who use inhaled steroids for more than 2 years have a decreased adult height compared with children who do not require steroids.
   C. Children whose asthma is triggered only by viral infections can be classified as having mild intermittent asthma.
   D. Only children who have moderate-to-severe persistent asthma have exacerbations severe enough to require hospitalization.
   E. The use of written plans has been proven to be beneficial only for patients who have moderate-to-severe asthma.

3. A 10-year-old girl who has moderate persistent asthma presents with continued nightly symptoms despite the addition of low-dose inhaled beclomethasone at her last visit a few weeks ago. On her physical examination, you note a prolonged expiratory phase, but no wheezing. Which of the following is most likely to improve her nightly symptoms?
   A. Adding inhaled cromolyn sodium to her current regimen.
   B. Adding inhaled salmeterol to her current regimen.
   C. Adding oral montelukast to her current regimen.
   D. Changing her from low-dose to high-dose beclomethasone.
   E. Prescribing a 5-day course of oral prednisone.

4. You are working in the emergency department when a 4-year-old girl who has mild intermittent asthma comes in with a 1-day history of a temperature to 101°F (38°C), a dry cough, and shortness of breath. Her mother reports no improvement with inhaled albuterol every 6 hours at home. On physical examination, she has normal oxygenation, a respiratory rate of 30 breaths/min, no retractions, bilateral wheezes, and slightly decreased breath sounds at the lung bases. Which of the following is the most appropriate management of this patient?
   A. Add a course of amoxicillin/clavulanate to cover for possible pneumonia.
   B. Add a course of oral prednisone for 5 days.
   C. Add inhaled low-dose budesonide for 5 days.
   D. Change from racemic albuterol to levalbuterol.
   E. Increase the frequency of albuterol and add chest physical therapy.