SECTION 2, DEFINITION, PATHOPHYSIOLOGY AND PATHOGENESIS OF ASTHMA, AND NATURAL HISTORY OF ASTHMA

KEY POINTS: DEFINITION, PATHOPHYSIOLOGY AND PATHOGENESIS OF ASTHMA, AND NATURAL HISTORY OF ASTHMA

- Asthma is a chronic inflammatory disorder of the airways. This feature of asthma has implications for the diagnosis, management, and potential prevention of the disease.

- The immunohistopathologic features of asthma include inflammatory cell infiltration:
  - Neutrophils (especially in sudden-onset, fatal asthma exacerbations; occupational asthma, and patients who smoke)
  - Eosinophils
  - Lymphocytes
  - Mast cell activation
  - Epithelial cell injury

- Airway inflammation contributes to airway hyperresponsiveness, airflow limitation, respiratory symptoms, and disease chronicity.

- In some patients, persistent changes in airway structure occur, including sub-basement fibrosis, mucus hypersecretion, injury to epithelial cells, smooth muscle hypertrophy, and angiogenesis.

- Gene-by-environment interactions are important to the expression of asthma.

- Atopy, the genetic predisposition for the development of an immunoglobulin E (IgE)-mediated response to common aeroallergens, is the strongest identifiable predisposing factor for developing asthma.
  - Viral respiratory infections are one of the most important causes of asthma exacerbation and may also contribute to the development of asthma.
**Box 2-1. Characteristics of Clinical Asthma**
- Symptoms
- Airway obstruction
- Inflammation
- Hyperresponsiveness

**Box 2-2. Features of Airway Remodeling**
- Inflammation
- Mucus hypersecretion
- Subepithelial fibrosis
- Airway smooth muscle hypertrophy
- Angiogenesis

---

**Figure 2-4. Host Factors and Environmental Exposures**

![Diagram showing the relationship between genetic factors, environmental factors, and persistent wheezing and asthma.](image)

- Genetic Factors
  - Cytokine response profiles

- Environment
  - Allergens
  - Pollution
  - Infections
  - Microbes
  - Stress

- Age

- Altered Innate and Adaptive Immune Responses

- Lower Airway Targeting

- LRI
  - RSV/PIV
  - Adenovirus
  - Chlamydia
  - Mycoplasma

**Persistent wheezing and asthma**

Key: LRI, lower respiratory illnesses; RSV, respiratory syncytial virus; PIV, parainfluenza virus
BOX 3–1. KEY INDICATORS FOR CONSIDERING A DIAGNOSIS OF ASTHMA

Consider a diagnosis of asthma and performing spirometry if any of these indicators is present.* These indicators are not diagnostic by themselves, but the presence of multiple key indicators increases the probability of a diagnosis of asthma. Spirometry is needed to establish a diagnosis of asthma.

- Wheezing—high-pitched whistling sounds when breathing out—especially in children. (Lack of wheezing and a normal chest examination do not exclude asthma.)

- History of any of the following:
  - Cough, worse particularly at night
  - Recurrent wheeze
  - Recurrent difficulty in breathing
  - Recurrent chest tightness

- Symptoms occur or worsen in the presence of:
  - Exercise
  - Viral infection
  - Animals with fur or hair
  - House-dust mites (in mattresses, pillows, upholstered furniture, carpets)
  - Mold
  - Smoke (tobacco, wood)
  - Pollen
  - Changes in weather
  - Strong emotional expression (laughing or crying hard)
  - Airborne chemicals or dusts
  - Menstrual cycles

- Symptoms occur or worsen at night, awakening the patient.

---

*Eczema, hay fever, or a family history of asthma or atopic diseases are often associated with asthma, but they are not key indicators.
FIGURE 3–2. SAMPLE QUESTIONS* FOR THE DIAGNOSIS AND INITIAL ASSESSMENT OF ASTHMA

A “yes” answer to any question suggests that an asthma diagnosis is likely.

In the past 12 months...

■ Have you had a sudden severe episode or recurrent episodes of coughing, wheezing (high-pitched whistling sounds when breathing out), chest tightness, or shortness of breath?

■ Have you had colds that “go to the chest” or take more than 10 days to get over?

■ Have you had coughing, wheezing, or shortness of breath during a particular season or time of the year?

■ Have you had coughing, wheezing, or shortness of breath in certain places or when exposed to certain things (e.g., animals, tobacco smoke, perfumes)?

■ Have you used any medications that help you breathe better? How often?

■ Are your symptoms relieved when the medications are used?

In the past 4 weeks, have you had coughing, wheezing, or shortness of breath...

■ At night that has awakened you?

■ Upon awakening?

■ After running, moderate exercise, or other physical activity?

*These questions are examples and do not represent a standardized assessment or diagnostic instrument. The validity and reliability of these questions have not been assessed.
**KEY POINTS: INITIAL ASSESSMENT OF ASTHMA**

- Once the diagnosis has been established, information obtained from the diagnostic evaluation, and additional information, if necessary, should be used to characterize the patient's asthma in order to guide decisions for therapy (EPR-2 1997):
  - Identify precipitating factors (e.g., exposure at home, work, daycare, or school to inhalant allergens, or irritants such as tobacco smoke, or viral respiratory infections) (Evidence A)
  - Identify comorbidities that may aggravate asthma (e.g., sinusitis, rhinitis, GERD) (Evidence B)
  - Classify asthma severity, using measures in both the impairment (Evidence B) and risk domains (Evidence C)

- Measures of pulmonary function, using spirometry, are recommended for assessing asthma severity. Low FEV₁ indicates current obstruction (impairment domain) and risk for future exacerbation (risk domain) (Evidence C). For children, FEV₁/FVC appears to be a more sensitive measure of severity in the impairment domain; FEV₁ is a useful measure of risk for exacerbations (Evidence C).

---

**KEY POINTS: PERIODIC ASSESSMENT OF ASTHMA CONTROL**

- The goals of therapy are to achieve asthma control by (Evidence A):
  - Reducing impairment:
    - Prevent chronic and troublesome symptoms (e.g., coughing or breathlessness in the daytime, at night, or after exertion)
    - Require infrequent use (≤2 days a week) of inhaled SABA for quick relief of symptoms
    - Maintain (near) “normal” pulmonary function
    - Maintain normal activity levels (including exercise and other physical activity and attendance at work or school)
    - Meet patients’ and families’ expectations of and satisfaction with asthma care
Reducing risk:

- Prevent recurrent exacerbations of asthma and minimize the need for ED visits or hospitalizations
- Prevent progressive loss of lung function; for children, prevent reduced lung growth
- Provide optimal pharmacotherapy with minimal or no adverse effects

Periodic assessments (at 1- to 6-month intervals) and ongoing monitoring of asthma control are recommended to determine if the goals of therapy are being met and if adjustments in therapy are needed (Evidence B, extrapolation from clinical trials; and Evidence C, observational studies). Measurements of the following are recommended:

- Signs and symptoms of asthma
- Pulmonary function
- Quality of life/functional status
- History of asthma exacerbations
- Pharmacotherapy (checking for adherence to therapy and potential side effects from medication)
- Patient–provider communication and patient satisfaction

Clinician assessment and patient self-assessment are the primary methods for monitoring asthma. Population-based assessment is used by health organizations, such as managed care organizations and disease management programs (EPR—2 1997).

The following frequencies for spirometry tests are recommended: (1) at the time of initial assessment (Evidence C), (2) after treatment is initiated and symptoms and PEF have stabilized, (3) during periods of progressive or prolonged loss of asthma control, and (4) at least every 1–2 years (Evidence D).

Use of minimally invasive markers ("biomarkers") to monitor asthma control and guide treatment decisions for therapy is of increasing interest. Some markers, such as spirometry measures, are currently and widely used in clinical care; others, such as sputum eosinophils and FeNO, may also be useful, but they require further evaluation in both children and adults before they can be recommended as clinical tools for routine asthma management (Evidence D).

Provide to all patients a written asthma action plan based on signs and symptoms and/or PEF; written action plans are particularly recommended for patients who have moderate or severe persistent asthma, a history of severe exacerbations, or poorly controlled asthma (Evidence B).

Whether peak flow monitoring, symptom monitoring (available data show similar benefits for each), or a combination of approaches is used, self-monitoring is important to the effective self-management of asthma (Evidence A).
Patients should be taught to recognize symptom patterns indicating inadequate asthma control and the need for additional therapy (Evidence A).

Consider peak flow monitoring for patients who have moderate or severe persistent asthma, patients who have a history of severe exacerbations (Evidence B), and patients who poorly perceive airflow obstruction and worsening asthma (Evidence D). Long-term daily peak flow monitoring can be helpful to (Evidence B):

- Detect early changes in asthma control that require adjustment in treatment.
- Evaluate responses to changes in treatment.
- Provide a quantitative measure of impairment.

**Figure 3-6. Sample Questions for Assessing and Monitoring Asthma Control**

**Monitoring Asthma Control**

**Ask the patient:**

- Has your asthma awakened you at night or early morning?

- Have you needed more quick-relief bronchodilator medication (inhaled short-acting beta₂-agonist) than usual?

- Have you needed any urgent medical care for your asthma, such as unscheduled visits to your doctor, an urgent care clinic, or the emergency department?

- Are you participating in your usual and desired activities?

- If you are measuring your peak flow, has it been below your personal best?

**Actions to consider:**

- Assess whether the medications are being taken as prescribed.

- Assess whether the medications are being inhaled with correct technique.

- Assess lung function with spirometry and compare to previous measurement.

- Adjust medications, as needed; either step up if control is inadequate or step down if control is maximized, to achieve the best control with the lowest dose of medication.

**FIGURE 3-7. COMPONENTS OF THE CLINICIAN’S FOLLOWUP ASSESSMENT: SAMPLE ROUTINE CLINICAL ASSESSMENT QUESTIONS**

<table>
<thead>
<tr>
<th>Monitoring Signs and Symptoms</th>
<th>Monitoring Pharmacotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>(Global assessment)</em> “Has your asthma been better or worse since your last visit?”</td>
<td><strong>Medications</strong></td>
</tr>
<tr>
<td>“Has your asthma worsened during specific seasons or events?”</td>
<td>“What medications are you taking?”</td>
</tr>
<tr>
<td><em>(Recent assessment)</em> “In the past 2 weeks, how many days have you:”</td>
<td>“How do you feel about taking medication?”</td>
</tr>
<tr>
<td>■ Had problems with coughing, wheezing, shortness of breath, or chest tightness during the day?”</td>
<td>“How often do you take each medication?”</td>
</tr>
<tr>
<td>■ Awakened at night from sleep because of coughing or other asthma symptoms?”</td>
<td>“How much do you take each time?”</td>
</tr>
<tr>
<td>■ Awakened in the morning with asthma symptoms that did not improve within 15 minutes of inhaling a short-acting beta-agonist?”</td>
<td>“Have you missed or stopped taking any regular doses of your medications for any reason?”</td>
</tr>
<tr>
<td>■ Had symptoms while exercising or playing?”</td>
<td>“Have you had trouble filling your prescriptions (e.g., for financial reasons, not on formulary)?”</td>
</tr>
<tr>
<td>■ Been unable to perform a usual activity, including exercise, because of asthma?”</td>
<td>“How many puffs of your inhaled short-acting beta-agonist (quick-relief medicine) do you use per day?”</td>
</tr>
<tr>
<td><strong>Monitoring Pulmonary Function</strong></td>
<td>“How many [name inhaled short-acting beta-agonist] inhalers (or pumps) have you been through in the past month?”</td>
</tr>
<tr>
<td><strong>Lung Function</strong></td>
<td>“Have you tried any other medicines or remedies?”</td>
</tr>
<tr>
<td>“What is the highest and lowest your peak flow has been since your last visit?”</td>
<td><strong>Side Effects</strong></td>
</tr>
<tr>
<td>“Has your peak flow dropped below ___ L/min (80 percent of personal best) since your last visit?”</td>
<td>“Has your asthma medicine caused you any problems?”</td>
</tr>
<tr>
<td>“What did you do when this occurred?”</td>
<td>■ Shakiness, nervousness, bad taste, sore throat, cough, upset stomach, hoarseness, skin changes (e.g., bruising)</td>
</tr>
<tr>
<td><strong>Peak Flow Monitoring Technique</strong></td>
<td><strong>Inhaler Technique</strong></td>
</tr>
<tr>
<td>“Please show me how you measure your peak flow.”</td>
<td>“Please show me how you use your inhaler.”</td>
</tr>
<tr>
<td>“When do you usually measure your peak flow?”</td>
<td><strong>Monitoring Patient–Provider Communication and Patient Satisfaction</strong></td>
</tr>
<tr>
<td><strong>Monitoring Quality of Life/Functional Status</strong></td>
<td>“What questions have you had about your asthma daily self-management plan and action plan?”</td>
</tr>
<tr>
<td>“Since your last visit, how many days has your asthma caused you to:”</td>
<td>“What problems have you had following your daily self-management plan? Your action plan?”</td>
</tr>
<tr>
<td>■ Miss work or school?”</td>
<td>“How do you feel about making your own decisions about therapy?”</td>
</tr>
<tr>
<td>■ Reduce your activities?”</td>
<td>“Has anything prevented you from getting the treatment you need for your asthma from me or anyone else?”</td>
</tr>
<tr>
<td>■ (For caregivers) Change your activity because of your child’s asthma?”</td>
<td>“Have the costs of your asthma treatment interfered with your ability to get asthma care?”</td>
</tr>
<tr>
<td>“Since your last visit, have you had any unscheduled or emergency department visits or hospital stays?”</td>
<td>“How satisfied are you with your asthma care?”</td>
</tr>
<tr>
<td><strong>Monitoring Exacerbation History</strong></td>
<td>“How can we improve your asthma care?”</td>
</tr>
<tr>
<td>“Since your last visit, have you had any episodes/times when your asthma symptoms were a lot worse than usual?”</td>
<td>“Let’s review some important information:”</td>
</tr>
<tr>
<td>If yes, “What do you think caused the symptoms to get worse?”</td>
<td>■ When should you increase your medications? Which medication(s)?”</td>
</tr>
<tr>
<td>If yes, “What did you do to control the symptoms?”</td>
<td>■ When should you call me [your doctor or nurse practitioner]? Do you know the after-hours phone number?”</td>
</tr>
<tr>
<td>“Have there been any changes in your home or work environment (e.g., new smokers or pets)”</td>
<td>■ If you can’t reach me, what emergency department would you go to?”</td>
</tr>
</tbody>
</table>

*These questions are examples and do not represent a standardized assessment instrument. The validity and reliability of these questions have not been assessed.*
FIGURE 3–8. VALIDATED INSTRUMENTS FOR ASSESSMENT AND MONITORING OF ASTHMA

- Asthma Control Questionnaire (Juniper et al. 1998b)
- Asthma Therapy Assessment Questionnaire (Vollmer et al. 1999) (See below.)
- Asthma Control Test (Nathan et al. 2004) (See below.)
- Asthma Control score (Boulet et al. 2002)

**ASTHMA THERAPY ASSESSMENT QUESTIONNAIRE (ATAQ)**

1. In the past 4 weeks did you miss any work, school, or normal daily activities because of your asthma? (1 point for YES)

2. In the past 4 weeks, did you wake up at night because of your asthma? (1 point for YES)

3. Do you believe your asthma was well controlled in the past 4 weeks? (1 point for NO)

4. Do you use an inhaler for quick relief from asthma symptoms? If yes, what is the highest number of puffs in 1 day you took of this inhaler? (1 point for more than 12)

Total points = 0–4, with more points indicating more control problems

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**ASTHMA CONTROL TEST™**

This survey was designed to help you describe your asthma and how your asthma affects how you feel and what you are able to do. To complete it, please mark an "X" in the box that best describes your answer.

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work or at home?
   - All of the time
   - Most of the time
   - Some of the time
   - A little of the time
   - None of the time

2. During the past 4 weeks, how often have you had shortness of breath?
   - More than once a day
   - Once a day
   - 2 to 3 times a week
   - Once or twice a week
   - Not at all

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?
   - Never
   - Once a week
   - 2 to 3 times a week
   - More than 3 times a week

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as Albuterol, Fenoterol, Ipratropium, or Primatene Mist)?
   - 3 or more times per day
   - 1 or 2 times per day
   - 2 or 3 times per week
   - Once a week or less
   - Not at all

5. How would you rate your asthma control during the past 4 weeks?
   - Completely controlled
   - Mostly controlled
   - Somewhat controlled
   - Not controlled
   - Not controlled at all


**CAUTION:** The sample questionnaires in figure 3–8 assess only the impairment domain of asthma control and NOT the risk domain. Measure of risk, such as exacerbations, urgent care, hospitalizations, and declines in lung function, are important elements of assessing the level of asthma control.
FIGURE 3-12. KEY EDUCATIONAL MESSAGES: TEACH AND REINFORCE AT EVERY OPPORTUNITY

Basic Facts About Asthma

- The contrast between airways of a person who has and a person who does not have asthma; the role of inflammation
- What happens to the airways in an asthma attack

Roles of Medications: Understanding the Difference Between:

- Long-term-control medications: prevent symptoms, often by reducing inflammation. Must be taken daily. Do not expect them to give quick relief.
- Quick-relief medications: short-acting beta2-agonists relax muscles around the airway and provide prompt relief of symptoms. Do not expect them to provide long-term asthma control. Using quick-relief medication on a daily basis indicates the need for starting or increasing long-term control medications.

Patient Skills

- Taking medications correctly
  - Inhaler technique (demonstrate to patient and have the patient return the demonstration)
  - Use of devices, such as prescribed valved holding chamber (VHC), spacer, nebulizer
- Identifying and avoiding environmental exposures that worsen the patient's asthma; e.g., allergens, irritants, tobacco smoke
- Self-monitoring to:
  - Assess level of asthma control
  - Monitor symptoms and, if prescribed, peak flow
  - Recognize early signs and symptoms of worsening asthma
- Using written asthma action plan to know when and how to:
  - Take daily actions to control asthma
  - Adjust medication in response to signs of worsening asthma
  - Seek medical care as appropriate
**FIGURE 3-10a. SAMPLE ASTHMA ACTION PLAN**

**My Asthma Action Plan**

<table>
<thead>
<tr>
<th>Long-Term-Control Medicines</th>
<th>How Much To Take</th>
<th>How Often</th>
<th>Other Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quick-Relief Medicines</th>
<th>How Much To Take</th>
<th>How Often</th>
<th>Other Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

### Special instructions when I feel **good**, **not good**, and **awful**.

**I feel good.**

*My peak flow is in the GREEN zone.*

- Take my long-term-control medicines (above) every day.
- Before exercise, take ___ puffs of ___.
- Avoid things that make my asthma worse.

**PREVENT** asthma symptoms everyday:

- Take my long-term-control asthma medicines every day.
- Before exercise, take ___ puffs of ___.
- Avoid things that make my asthma worse.

**I do not feel good.**

*My peak flow is in the YELLOW zone.*

My symptoms may include one or more of the following:
- Wheezing
- Tight chest
- Cough
- Shortness of breath
- Walking up at night with asthma symptoms
- Decreased ability to do usual activities

**CAUTION.** I should continue taking my long-term-control asthma medicines every day AND:

- Take ___.
- Increase ___.
- Add ___.
- Call ___.

If I still do not feel good, or my peak flow is not back in the Green Zone within 1 hour, then I should:

- Increase ___.
- Add ___.
- Call ___.

**I feel awful.**

*My peak flow is in the RED zone.*

Warning signs may include one or more of the following:
- It's getting harder and harder to breathe
- Unable to sleep or do usual activities because of trouble breathing

**MEDICAL ALERT! Get help!**

- Take ___ until I get help immediately.
- Take ___.
- Call ___.

**Danger! Get help immediately!**

Call 9-1-1 if you have trouble walking or talking due to shortness of breath or lips or fingernails are gray or blue.

<table>
<thead>
<tr>
<th>Assessment Questions</th>
<th>Information</th>
<th>Skills</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Focus on:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>■ Expectations of visit</td>
<td>■ What is asthma? Asthma is a chronic lung disease. The airways are very sensitive. They become inflamed and narrow; breathing becomes difficult.</td>
<td></td>
</tr>
<tr>
<td>■ Asthma control</td>
<td>■ The definition of asthma control: few daytime symptoms, no nighttime awakenings due to asthma, able to engage in normal activities, normal lung function.</td>
<td></td>
</tr>
<tr>
<td>■ Patients’ goals of treatment</td>
<td>■ Asthma treatments: two types of medicines are needed:</td>
<td></td>
</tr>
<tr>
<td>■ Medications</td>
<td>■ Long-term control: medications that prevent symptoms, often by reducing inflammation.</td>
<td></td>
</tr>
<tr>
<td>■ Quality of life</td>
<td>■ Quick relief: short-acting bronchodilator relaxes muscles around airways.</td>
<td></td>
</tr>
<tr>
<td>“What worries you most about your asthma?”</td>
<td>■ Bring all medications to every appointment.</td>
<td></td>
</tr>
<tr>
<td>“What do you want to accomplish at this visit?”</td>
<td>■ When to seek medical advice. Provide appropriate telephone number.</td>
<td></td>
</tr>
<tr>
<td>“What do you want to be able to do that you can’t do now because of your asthma?”</td>
<td>■ Teach or review and demonstrate:</td>
<td></td>
</tr>
<tr>
<td>“What do you expect from treatment?”</td>
<td>■ Inhaler (see figure 3–14) and spacer or valve holding chamber (VHC) use. Check performance.</td>
<td></td>
</tr>
<tr>
<td>“What medicines have you tried?”</td>
<td>■ Self-monitoring skills that are tied to a written action plan:</td>
<td></td>
</tr>
<tr>
<td>“What other questions do you have for me today?”</td>
<td>■ Recognize intensity and frequency of asthma symptoms.</td>
<td></td>
</tr>
<tr>
<td>“Are there things in your environment that make your asthma worse?”</td>
<td>■ Review the signs of deterioration and the need to reevaluate therapy:</td>
<td></td>
</tr>
</tbody>
</table>

**Recommendations for Initial Visit**

**Focus on:**

■ Expectations of visit
■ Asthma control
■ Patients’ goals of treatment
■ Medications
■ Quality of life

**Teach in simple language:**

■ What is asthma? Asthma is a chronic lung disease. The airways are very sensitive. They become inflamed and narrow; breathing becomes difficult.
■ The definition of asthma control: few daytime symptoms, no nighttime awakenings due to asthma, able to engage in normal activities, normal lung function.
■ Asthma treatments: two types of medicines are needed:
   ■ Long-term control: medications that prevent symptoms, often by reducing inflammation.
   ■ Quick relief: short-acting bronchodilator relaxes muscles around airways.
■ Bring all medications to every appointment.
■ When to seek medical advice. Provide appropriate telephone number.

**Teach or review and demonstrate:**

■ Inhaler (see figure 3–14) and spacer or valve holding chamber (VHC) use. Check performance.
■ Self-monitoring skills that are tied to a written action plan:
   ■ Recognize intensity and frequency of asthma symptoms.
   ■ Review the signs of deterioration and the need to reevaluate therapy:
     ■ Waking at night or early morning with asthma
     ■ Increased medication use
     ■ Decreased activity tolerance

**Recommendations for First Followup Visit (2 to 4 weeks or sooner as needed)**

**Focus on:**

■ Expectations of visit
■ Asthma control
■ Patients’ goals of treatment
■ Medications
■ Patient treatment preferences
■ Quality of life

Ask relevant questions from previous visit and also ask:

■ “What medications are you taking?”
■ “How and when are you taking them?”
■ “What problems have you had using your medications?”
■ “Please show me how you use your inhaled medications.”

**Teach in simple language:**

■ Use of two types of medications.
■ Remind patient to bring all medications and the peak flow meter, if using, to every appointment for review.
■ Self-assessment of asthma control using symptoms and/or peak flow as a guide.

**Teach or review and demonstrate:**

■ Use of written asthma action plan. Review and adjust as needed.
■ Peak flow monitoring if indicated (See figure 3–11.).
■ Correct inhaler and spacer or VHC technique.
### FIGURE 3-13. DELIVERY OF ASTHMA EDUCATION BY CLINICIANS DURING PATIENT CARE VISITS (CONTINUED)

<table>
<thead>
<tr>
<th>Assessment Questions</th>
<th>Information</th>
<th>Skills</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Focus on:</strong></td>
<td><strong>Teach in simple language:</strong></td>
<td><strong>Teach or review and demonstrate:</strong></td>
</tr>
<tr>
<td>▪ Expectations of visit</td>
<td>▪ Self-assessment of asthma control, using symptoms and/or peak flow as a guide.</td>
<td>▪ Inhaler/spacer or VHC technique.</td>
</tr>
<tr>
<td>▪ Asthma control</td>
<td>▪ Relevant environmental control/avoidance strategies (See figure 3–15.):</td>
<td>▪ Peak flow monitoring technique.</td>
</tr>
<tr>
<td>▪ Patients’ goals of treatment</td>
<td>▪ — How to identify home, work, or school exposures that can cause or worsen asthma</td>
<td>▪ Use of written asthma action plan. Review and adjust as needed.</td>
</tr>
<tr>
<td>▪ Medications</td>
<td>▪ — How to control house-dust mites, animal exposures if applicable</td>
<td>▪ Confirm that patient knows what to do if asthma gets worse.</td>
</tr>
<tr>
<td>▪ Quality of life</td>
<td>▪ — How to avoid cigarette smoke (active and passive)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Review all medications.</td>
<td></td>
</tr>
</tbody>
</table>

**Ask relevant questions from previous visits and also ask:**

- “Have you noticed anything in your home, work, or school that makes your asthma worse?”
- “Describe for me how you know when to call your doctor or go to the hospital for asthma care.”
- “What questions do you have about the asthma action plan? “Can we make it easier?”
- “Are your medications causing you any problems?”
- “Have you noticed anything in your environment that makes your asthma worse?”
- “Have you missed any of your medications?”

**Recommendations for All Subsequent Visits**

<table>
<thead>
<tr>
<th>Focus on:</th>
<th>Teach in simple language:</th>
<th>Teach or review and demonstrate:</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Expectations of visit</td>
<td>▪ Review and reinforce all:</td>
<td>▪ Inhaler/spacer or VHC technique.</td>
</tr>
<tr>
<td>▪ Asthma control</td>
<td>▪ — Educational messages</td>
<td>▪ Peak flow monitoring technique, if appropriate.</td>
</tr>
<tr>
<td>▪ Patients’ goals of treatment</td>
<td>▪ — Environmental control strategies at home, work, or school</td>
<td>▪ Use of written asthma action plan. Review and adjust as needed.</td>
</tr>
<tr>
<td>▪ Medications</td>
<td>▪ — Medications</td>
<td>▪ Confirm that patient knows what to do if asthma gets worse.</td>
</tr>
<tr>
<td>▪ Quality of life</td>
<td>▪ — Self-assessment of asthma control, using symptoms and/or peak flow as a guide</td>
<td></td>
</tr>
<tr>
<td>Ask relevant questions from previous visits and also ask:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“How have you tried to control things that make your asthma worse?”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Please show me how you use your inhaled medication.”</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Sources:** Adapted from Guevara et al. 2003; Janson et al. 2003; Powell and Gibson 2003; Wilson et al. 1993.
FIGURE 3–14. HOW TO USE YOUR METERED-DOSE INHALER

HOW TO USE YOUR METERED-DOSE INHALER

Using an inhaler seems simple, but most patients do not use it the right way. When you use your inhaler the wrong way, less medicine gets to your lungs.

For the next few days, read these steps aloud as you do them or ask someone to read them to you. Ask your doctor or nurse to check how well you are using your inhaler.

Use your inhaler in one of the three ways pictured below. A or B are best, but C can be used if you have trouble with A and B. Your doctor may give you other types of inhalers.

Steps for Using Your Inhaler

<table>
<thead>
<tr>
<th>Getting ready</th>
<th>1. Take off the cap and shake the inhaler.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2. Breathe out all the way.</td>
</tr>
<tr>
<td></td>
<td>3. Hold your inhaler the way your doctor said (A, B, or C below).</td>
</tr>
<tr>
<td>Breathe in slowly</td>
<td>4. As you start breathing in slowly through your mouth, press down on the inhaler one time. (If you use a holding chamber, first press down on the inhaler. Within 5 seconds, begin to breathe in slowly.)</td>
</tr>
<tr>
<td>Hold your breath</td>
<td>5. Keep breathing in slowly, as deeply as you can.</td>
</tr>
<tr>
<td></td>
<td>6. Hold your breath as you count to 10 slowly, if you can.</td>
</tr>
<tr>
<td></td>
<td>7. For inhaled quick-relief medicine (beta-agonists), wait about 15–30 seconds between puffs. There is no need to wait between puffs for other medicines.</td>
</tr>
</tbody>
</table>

A. Hold inhaler 1 to 2 inches in front of your mouth (about the width of two fingers).

B. Use a spacer/holding chamber. These come in many shapes and can be useful to any patient.

C. Put the inhaler in your mouth. Do not use for steroids.

Clean your inhaler as needed, and know when to replace your inhaler. For instructions, read the package insert or talk to your doctor, other health care provider, or pharmacist.
**Figure 3-15. How to Control Things That Make Your Asthma Worse**

You can help prevent asthma episodes by staying away from things that make your asthma worse. This guide suggests many ways to help you do this.

You need to find out what makes your asthma worse. Some things that make asthma worse for some people are not a problem for others. You do not need to do all of the things listed in this guide.

Look at the things listed in dark print below. Put a check next to the ones that you know make your asthma worse, particularly if you are allergic to the things. Then, decide with your doctor what steps you will take. Start with the things in your bedroom that bother your asthma. Try something simple first.

### Tobacco Smoke
- If you smoke, ask your doctor for ways to help you quit. Ask family members to quit smoking, too.
- Do not allow smoking in your home, car, or around you.
- Be sure no one smells at a child’s daycare center or school.

### Dust Mites
Many people who have asthma are allergic to dust mites. Dust mites are like tiny “bugs” you cannot see that live in cloth or carpet.

**Things that will help the most:**

- Encase your mattress in a special dust mite-proof cover.*
- Encase your pillow in a special dust mite-proof cover* or wash the pillow each week in hot water. Water must be hotter than 130 °F to kill the mites. Cooler water used with detergent and bleach can also be effective.
- Wash the sheets and blankets on your bed each week in hot water.

**Other things that can help:**

- Reduce indoor humidity to or below 60 percent; ideally 30–50 percent. Dehumidifiers or central air conditioners can do this.
- Try not to sleep or lie on cloth-covered cushions or furniture.
- Remove carpets from your bedroom and those laid on concrete, if you can.
- Keep stuffed toys out of the bed, or wash the toys weekly in hot water or in cooler water with detergent and bleach. Placing toys weekly in a dryer or freezer may help. Prolonged exposure to dry heat or freezing can kill mites but does not remove allergen.

---

*To find out where to get products mentioned in this guide, call:

- **Asthma and Allergy Foundation of America** (900–727–8462)
- **Allergy and Asthma Network/Mothers of Asthmatics, Inc.** (800–878–4403)
- **American Academy of Allergy, Asthma, and Immunology** (800–822–2762)
- **National Jewish Medical and Research Center** (Lung Line) (800–222–5864)
- **American College of Allergy, Asthma, and Immunology** (800–842–7777)
Animal Dander

Some people are allergic to the flakes of skin or dried saliva from animals.
The best thing to do:
- Keep animals with fur or hair out of your home.

If you can’t keep the pet outdoors, then:
- Keep the pet out of your bedroom, and keep the bedroom door closed.
- Remove carpets and furniture covered with cloth from your home. If that is not possible, keep the pet out of the rooms where these are.

Cockroach

Many people with asthma are allergic to the dried droppings and remains of cockroaches.
- Keep all food out of your bedroom.
- Keep food and garbage in closed containers (never leave food out).
- Use poison baits, powders, gels, or paste (for example, boric acid). You can also use traps.
- If a spray is used to kill roaches, stay out of the room until the odor goes away.

Vacuum Cleaning

- Try to get someone else to vacuum for you once or twice a week, if you can. Stay out of rooms while they are being vacuumed and for a short while afterward.
- If you vacuum, use a dust mask (from a hardware store), a central cleaner with the collecting bag outside the home, or a vacuum cleaner with a HEPA filter or a double-layered bag.*

Indoor Mold

- Fix leaking faucets, pipes, or other sources of water.
- Clean moldy surfaces.
- Dehumidify basements if possible.

Pollen and Outdoor Mold

During your allergy season (when pollen or mold spore counts are high):
- Try to keep your windows closed.
- If possible, stay indoors with windows closed during the midday and afternoon, if you can. Pollen and some mold spore counts are highest at that time.
- Ask your doctor whether you need to take or increase anti-inflammatory medicine before your allergy season starts.

Smoke, Strong Odors, and Sprays

- If possible, do not use a wood-burning stove, kerosene heater, fireplace, unvented gas stove, or heater.
- Try to stay away from strong odors and sprays, such as perfume, talcum powder, hair spray, paints, new carpet, or particle board.

Exercise or Sports

- You should be able to be active without symptoms. See your doctor if you have asthma symptoms when you are active—such as when you exercise, do sports, play, or work hard.
- Ask your doctor about taking medicine before you exercise to prevent symptoms.
- Warm up for a period before you exercise.
- Check the air quality index and try not to work or play hard outside when the air pollution or pollen levels (if you are allergic to the pollen) are high.

Other Things That Can Make Asthma Worse

- Sulfites in foods: Do not drink beer or wine or eat shrimp, dried fruit, or processed potatoes if they cause asthma symptoms.
- Cold air: Cover your nose and mouth with a scarf on cold or windy days.
- Other medicines: Tell your doctor about all the medicines you may take. Include cold medicines, aspirin, and even eye drops.
<table>
<thead>
<tr>
<th><strong>Inhalant Allergens</strong></th>
<th><strong>Workplace Exposures</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the patient have symptoms year round? (If yes, ask the following questions. If no, see next set of questions.)</td>
<td>Does the patient cough or wheeze during the week, but not on weekends when away from work?</td>
</tr>
<tr>
<td>- Does the patient keep pets indoors? What type?</td>
<td>- Do the patient’s eyes and nasal passages get irritated soon after arriving at work?</td>
</tr>
<tr>
<td>- Does the patient have moisture or dampness in any room of his or her home (e.g., basement)? (Suggests house-dust mites, molds.)</td>
<td>- Do coworkers have similar symptoms?</td>
</tr>
<tr>
<td>- Does the patient have mold visible in any part of his or her home? (Suggests molds.)</td>
<td>- What substances are used in the patient’s worksite? (Assess for sensitizers.)</td>
</tr>
<tr>
<td>- Has the patient seen cockroaches or rodents in his or her home in the past month? (Suggests significant cockroach exposure.)</td>
<td></td>
</tr>
<tr>
<td>- Assume exposure to house-dust mites unless patient lives in a semiarid region. However, if a patient living in a semiarid region uses a swamp cooler, exposure to house-dust mites must still be assumed.</td>
<td></td>
</tr>
<tr>
<td><strong>Do symptoms get worse at certain times of the year? (If yes, ask when symptoms occur.)</strong></td>
<td></td>
</tr>
<tr>
<td>- Early spring? (trees)</td>
<td>Does the patient have heartburn?</td>
</tr>
<tr>
<td>- Late spring? (grass)</td>
<td>Does food sometimes come up into the patient’s throat?</td>
</tr>
<tr>
<td>- Late summer to autumn? (weeds)</td>
<td>Has the patient had coughing, wheezing, or shortness of breath at night in the past 4 weeks?</td>
</tr>
<tr>
<td>- Summer and fall? (Alternaria, Cladosporium, mites)</td>
<td>Does the infant vomit, followed by cough, or have wheezy cough at night? Are symptoms worse after feeding?</td>
</tr>
<tr>
<td>- Cold months in temperate climates? (animal dander)</td>
<td></td>
</tr>
<tr>
<td><strong>Tobacco Smoke</strong></td>
<td><strong>Sulfite Sensitivity</strong></td>
</tr>
<tr>
<td>- Does the patient smoke?</td>
<td>Does the patient have wheezing, coughing, or shortness of breath after eating shrimp, dried fruit, or processed potatoes or after drinking beer or wine?</td>
</tr>
<tr>
<td>- Does anyone smoke at home or work?</td>
<td><strong>Medication Sensitivities and Contraindications</strong></td>
</tr>
<tr>
<td>- Does anyone smoke at the child’s daycare?</td>
<td>- What medications does the patient use now (prescription and nonprescription)?</td>
</tr>
<tr>
<td><strong>Indoor/Outdoor Pollutants and Irritants</strong></td>
<td>- Does the patient use eyedrops? What type?</td>
</tr>
<tr>
<td>- Is a wood-burning stove or fireplace used in the patient’s home?</td>
<td>- Does the patient use any medications that contain beta-blockers?</td>
</tr>
<tr>
<td>- Are there unvented stoves or heaters in the patient’s home?</td>
<td>- Does the patient ever take aspirin or other nonsteroidal anti-inflammatory drugs?</td>
</tr>
<tr>
<td>- Does the patient have contact with other smells or fumes from perfumes, cleaning agents, or sprays?</td>
<td>- Has the patient ever had symptoms of asthma after taking any of these medications?</td>
</tr>
<tr>
<td>- Have there been recent renovations or painting in the home?</td>
<td></td>
</tr>
</tbody>
</table>

*These questions are examples and do not represent a standardized assessment or diagnostic instrument. The validity and reliability of these questions have not been assessed.*
Classifying severity for patients who are not currently taking long-term control medications.

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Classification of Asthma Severity (Youths ≥12 years of age and adults)</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intermittent</td>
<td>Mid</td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤2 days/week</td>
<td>&gt; 2 days/week but not daily</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≥2x/month</td>
<td>3–4x/month</td>
</tr>
<tr>
<td>Short-acting beta-agonist use for symptom control (not prevention of EIB)</td>
<td>≤2 days/week</td>
<td>&gt; 2 days/week but not &gt; 1x/day</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Minor limitation</td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV&lt;sub&gt;1&lt;/sub&gt; between exacerbations</td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; &gt; 80% predicted</td>
</tr>
<tr>
<td>Normal FEV&lt;sub&gt;1&lt;/sub&gt;, FVC</td>
<td>80–88%</td>
<td>80–75%</td>
</tr>
<tr>
<td>Risk</td>
<td>Exacerbations requiring oral systemic corticosteroids</td>
<td>6–1/year (see note)</td>
</tr>
</tbody>
</table>

Level of severity is determined by assessment of both impairment and risk. Assess impairment domain by patient’s/caregiver’s recall of previous 2–4 weeks and spirometry. Assign severity to the most severe category in which any feature occurs.

At present, there are inadequate data to correspond frequencies of exacerbations with different levels of asthma severity. In general, more frequent and intense exacerbations (e.g., requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate greater underlying disease severity. For treatment purposes, patients who had ≥2 exacerbations requiring oral systemic corticosteroids in the past year may be considered the same as patients who have persistent asthma, even in the absence of impairment levels consistent with persistent asthma.

Classifying severity in patients after asthma becomes well controlled, by lowest level of treatment required to maintain control.*

<table>
<thead>
<tr>
<th>Lowest level of treatment required to maintain control (See figure 4–5 for treatment steps.)</th>
<th>Classification of Asthma Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent</td>
<td>Persistent</td>
</tr>
<tr>
<td>Step 1</td>
<td>Mild</td>
</tr>
<tr>
<td>Step 2</td>
<td>Step 3 or 4</td>
</tr>
</tbody>
</table>

Key: EIB, exercise-induced bronchospasm; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; ICU, intensive care unit

*Notes:

For population-based evaluations, clinical research, or characterization of a patient’s overall asthma severity after control is achieved. For clinical management, the focus is on monitoring the level of control (See figure 3–5c.), not the level of severity, once treatment is established.

See figure 3–5c for definition of asthma control.
KEY POINTS: SAFETY OF INHALED SHORT-ACTING 
BETA₂-AGONISTS

- SABAs are the most effective medication for relieving acute bronchospasm (Evidence A).
- Increasing use of SABA treatment or using SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control of asthma and the need for initiating or intensifying anti-inflammatory therapy (Evidence C).
- Regularly scheduled, daily, chronic use of SABA is not recommended (Evidence A).

KEY POINTS: SAFETY OF INHALED LONG-ACTING 
BETA₂-AGONISTS

- The addition of LABA (salmeterol or formoterol) to the treatment of patients whose asthma is not well controlled on low- or medium-dose ICS improves lung function, decreases symptoms, and reduces exacerbations and use of SABA for quick relief in most patients (EPR—Update 2002; Greenstone et al. 2005; Masoli et al. 2005).
- A large clinical trial comparing daily treatment with salmeterol or placebo added to usual asthma therapy (Nelson et al. 2006) resulted in an increased risk of asthma-related deaths in patients treated with salmeterol (13 deaths out of 13,176 patients treated for 28 weeks with salmeterol versus 3 deaths out of 13,179 patients with placebo). In addition, increased numbers of severe asthma exacerbations were noted in the pivotal trials submitted to the FDA for formoterol approval, particularly in the higher dose formoterol arms of the trials (Mann et al. 2003). Thus the FDA determined that a Black Box warning was warranted on all preparations containing a LABA.
- The Expert Panel recommends that the established, beneficial effects of LABA for the great majority of patients whose asthma is not well controlled with ICS alone should be weighed against the increased risk for severe exacerbations, although uncommon, associated with the daily use of LABAs.
- Therefore, the Expert Panel has modified its previous recommendation (EPR—Update 2002) and has now concluded that, for patients who have asthma not sufficiently controlled with ICS alone, the option to increase the ICS dose should be given equal weight to the option of the addition of a LABA to ICS.
- Daily use of LABA generally should not exceed 100 mcg salmeterol or 24 mcg formoterol.
- It is not currently recommended that LABA be used for treatment of acute symptoms or exacerbations.
- LABAs are not to be used as monotherapy for long-term control. Patients should be instructed not to stop ICS therapy while taking salmeterol or formoterol even though their symptoms may significantly improve.
## FIGURE 3-22. LONG-TERM CONTROL MEDICATIONS

<table>
<thead>
<tr>
<th>Name/Products</th>
<th>Indications/Mechanisms</th>
<th>Potential Adverse Effects</th>
<th>Therapeutic Issues</th>
</tr>
</thead>
</table>
| **Corticosteroids** (Glucocorticoids) | **Indications**  
- Long-term prevention of symptoms; suppression, control, and reversal of inflammation.  
- Reduce need for oral corticosteroid. | **Cough, dysphonia, oral thrush (candidiasis).**  
- In high doses (see figures 4-4b and 4-8a), systemic effects may occur, although studies are not conclusive, and clinical significance of these effects has not been established (e.g., adrenal suppression, osteoporosis, skin thinning, and easy bruising) (Barros and Pedersen 1993; Kamada et al. 1996). In low-to-medium doses, suppression of growth velocity has been observed in children, but this effect may be transient, and the clinical significance has not been established (CAMP 2000; Guilbert et al. 2006). | **Spacer/holding chamber devices with nonbreath-activated MDIs and mouth washing after inhalation decrease local side effects.**  
**Preparations are not absolutely interchangeable on a mcg or per puff basis (see figures 4-4b and 4-8b for estimated clinical comparability). New delivery devices may provide greater delivery to airways; this change may affect dose.**  
**The risks of uncontrolled asthma should be weighed against the limited risks of ICS therapy. The potential but small risk of adverse events is well balanced by their efficacy. (See text.)**  
**“Adjustable dose” approach to treatment may enable reduction in cumulative dose of ICS treatment over time without sacrificing maintenance of asthma control.**  
**Dexamethasone is not included as an ICS for long-term control because it is highly absorbed and has long-term suppressive side effects.**  
**Use at lowest effective dose. For long-term use, alternate-day a.m. dosing produces the least toxicity. If daily doses are required, one study shows improved efficacy with no increase in adrenal suppression when administered at 3 p.m. rather than in the morning (Bean et al. 1992).** |
| **Inhaled (ICS):**  
- Becomethasone dipropionate  
- Budesonide  
- Flunisolide  
- Fluticasone propionate  
- Mometasone furoate  
- Triamcinolone acetonide | **Mechanisms**  
- Anti-inflammatory. Block late reaction to allergen and reduce airway hyperresponsiveness. Inhibit cytokine production, adhesion protein activation, and inflammatory cell migration and activation.  
- Reverse beta-2-receptor downregulation. Inhibit microvascular leakage. | | |
| **Systemic:**  
- Methylprednisolone  
- Prednisolone  
- Prednisone | **Indications**  
- For short-term (3–10 days) “burst” to gain prompt control of inadequately controlled persistent asthma.  
- For long-term prevention of symptoms in severe persistent asthma: suppression, control, and reversal of inflammation. | **Short-term use: reversible abnormalities in glucose metabolism, increased appetite, fluid retention, weight gain, mood alteration, hypertension, peptic ulcer, and rarely septic necrosis.**  
**Long-term use: adrenal axis suppression, growth suppression, dermal thinning, hypertension, diabetes, Cushing’s syndrome, cataracts, muscle weakness, and—in rare instances—impaired immune function.**  
**Consideration should be given to coexisting conditions that could be worsened by systemic corticosteroids, such as herpes virus infections, varicella, tuberculosis, hypertension, peptic ulcer, diabetes mellitus, osteoporosis, and Strongyloides.** | |
## Figure 3-22. Long-Term Control Medications (Continued)

<table>
<thead>
<tr>
<th>Name/Products (Listed Alphabetically)</th>
<th>Indications/Mechanisms</th>
<th>Potential Adverse Effects</th>
<th>Therapeutic Issues (Not All Inclusive)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cromolyn Sodium and Nedocromil</strong></td>
<td><em>Indications</em>&lt;br&gt;Long-term prevention of symptoms in mild persistent asthma; may modify inflammation.&lt;br&gt;Preventive treatment prior to exposure to exercise or known allergen.&lt;br&gt;<em>Mechanisms</em>&lt;br&gt;Anti-inflammatory. Blocks early and late reaction to allergen. Interferes with chloride channel function. Stabilizes mast cell membranes and inhibits activation and release of mediators from eosinophils and epithelial cells.&lt;br&gt;Inhibits acute response to exercise, cold dry air, and SO₂.</td>
<td>Cough and irritation.&lt;br&gt;15–20 percent of patients complain of an unpleasant taste from nedocromil.</td>
<td>Therapeutic response to cromolyn and nedocromil often occurs within 2 weeks, but a 4- to 6-week trial may be needed to determine maximum benefit.&lt;br&gt;Dose of cromolyn by MDI (1 mg/actuator) may be inadequate to affect airway hyperresponsiveness. Nebulizer delivery (20 mg/ampule) may be preferred for some patients.&lt;br&gt;Safety is the primary advantage of these agents.</td>
</tr>
<tr>
<td><strong>Immunomodulators</strong>&lt;br&gt;Omalizumab (Anti-IgE)&lt;br&gt;For subcutaneous use</td>
<td><em>Indications</em>&lt;br&gt;Long-term control and prevention of symptoms in adults (≥12 years old) who have moderate or severe persistent allergic asthma inadequately controlled with ICS.&lt;br&gt;<em>Mechanisms</em>&lt;br&gt;Binds to circulating IgE, preventing it from binding to the high-affinity (FceRI) receptors on basophils and mast cells.&lt;br&gt;Decreases mast cell mediator release from allergen exposure.&lt;br&gt;Decreases the number of FcεR1s in basophils and submucosal cells.</td>
<td>Pain and bruising of injection sites has been reported in 5–20 percent of patients.&lt;br&gt;Anaphylaxis has been reported in 0.2 percent of treated patients.&lt;br&gt;Malignant neoplasms were reported in 0.5 percent of patients compared to 0.2 percent receiving placebo; relationship to drug is unclear.</td>
<td>Monitor patients following injection. Be prepared and equipped to identify and treat anaphylaxis that may occur.&lt;br&gt;The dose is administered either every 2 or 4 weeks and is dependent on the patient's body weight and IgE level before therapy.&lt;br&gt;A maximum of 150 mg can be administered in one injection.&lt;br&gt;Needs to be stored under refrigeration at 2–8 °C.&lt;br&gt;Whether patients will develop significant antibody titers to the drug with long-term administration is unknown.</td>
</tr>
</tbody>
</table>
## Figure 3-22. Long-Term Control Medications (continued)

<table>
<thead>
<tr>
<th>Name/Products (Listed Alphabetically)</th>
<th>Indications/Mechanisms</th>
<th>Potential Adverse Effects</th>
<th>Therapeutic Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukotriene Receptor Antagonists (LTRAs)</td>
<td><strong>Mechanisms</strong>&lt;br&gt;Leukotriene receptor antagonist; selective competitive inhibitor of CysLT1 receptor.</td>
<td></td>
<td>May attenuate EiB in some patients, but less effective than ICS therapy (Vidal et al. 2001). Do not use LTRA + LABA as a substitute for ICS + LABA.</td>
</tr>
<tr>
<td>Montelukast tablets and granules</td>
<td><strong>Indications</strong>&lt;br&gt;Long-term control and prevention of symptoms in mild persistent asthma for patients ≥1 year of age. May also be used with ICS as combination therapy in moderate persistent asthma.</td>
<td>No specific adverse effects have been identified. Rare cases of Churg-Strauss have occurred, but the association is unclear.</td>
<td>A flat dose-response curve, without further benefit, if dose is increased above those recommended.</td>
</tr>
<tr>
<td>Zafirlukast tablets</td>
<td>Long-term control and prevention of symptoms in mild persistent asthma for patients ≥7 years of age. May also be used with ICS as combination therapy in moderate persistent asthma.</td>
<td>Postmarketing surveillance has reported cases of reversible hepatotoxicity and, rarely, irreversible hepatic failure resulting in death and liver transplantation.</td>
<td>Administration with meals decreases bioavailability; take at least 1 hour before or 2 hours after meals. Zafirlukast is a microsomal P450 enzyme inhibitor that can inhibit the metabolism of warfarin. INRs should be monitored during coadministration. Patients should be warned to discontinue use if they experience signs and symptoms of liver dysfunction (right upper quadrant pain, pruritus, lethargy, jaundice, nausea), and patients’ ALTs should be monitored.</td>
</tr>
<tr>
<td>5-Lipoxygenase Inhibitor</td>
<td><strong>Mechanisms</strong>&lt;br&gt;Inhibits the production of leukotrienes from arachidonic acid, both LTE4 and the cysteinyl leukotrienes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zileuton tablets</td>
<td><strong>Indications</strong>&lt;br&gt;Long-term control and prevention of symptoms in mild persistent asthma for patients ≥12 years of age. May be used with ICS as combination therapy in moderate persistent asthma in patients ≥12 years of age.</td>
<td>Elevation of liver enzymes has been reported. Limited case reports of reversible hepatitis and hyperbilirubinemia.</td>
<td>Zileuton is microsomal P450 enzyme inhibitor that can inhibit the metabolism of warfarin and theophylline. Doses of these drugs should be monitored accordingly. Monitor hepatic enzymes (ALT).</td>
</tr>
<tr>
<td>Name/Products</td>
<td>Indications/Mechanisms</td>
<td>Potential Adverse Effects</td>
<td>Therapeutic Issues</td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------</td>
<td>--------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Short-Acting Beta₂-Agonists (SABA)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Inhaled SABA:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol</td>
<td>Relief of acute symptoms; quick-relief medication.</td>
<td>Tachycardia, skeletal muscle tremor, hypokalemia, increased lactic acid, headache, hyperglycemia. Inhaled route, in general, causes fewer systemic adverse effects. Patients with pre-existing cardiovascular disease, especially the elderly, may have adverse cardiovascular reactions with inhaled therapy.</td>
<td>Drugs of choice for acute bronchospasm. Inhaled route has faster onset, fewer adverse effects, and is more effective than systemic routes. The less beta₂-selective agents (isoproterenol, metaproterenol, isoetharine, and epinephrine) are not recommended due to their potential for excessive cardiac stimulation, especially in high doses. Oral systemic beta₂-agonists are not recommended.</td>
</tr>
<tr>
<td>Levosalbuterol</td>
<td>Preventive treatment for EIB prior to exercise.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pirbuterol</td>
<td>Bronchodilation. Binds to the beta₂-adrenergic receptor, producing smooth muscle relaxation following adenylate cyclase activation and increase in cyclic AMP producing functional antagonism of bronchoconstriction.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For patients who have intermittent asthma, regularly scheduled daily use either harms nor benefits asthma control (Drazen et al. 1996). Regularly scheduled daily use is not recommended.

Regular use >2 days/week for symptom control (not prevention of EIB), increasing use, or lack of expected effect indicates inadequate asthma control.

For patients frequently using SABA, anti-inflammatory medication should be initiated or intensified.

Levalbuterol at one-half the mcg dose produces clinically comparable bronchodilation and systemic side effects as racemic albuterol.
<table>
<thead>
<tr>
<th>Name/Products</th>
<th>Indications/Mechanisms</th>
<th>Potential Adverse Effects</th>
<th>Therapeutic Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticholinergics</strong></td>
<td>■ Relief of acute bronchospasm (See Therapeutic Issues column).</td>
<td>▪ Drying of mouth and respiratory secretions, increased wheezing in some individuals, blurred vision if sprayed in eyes. If used in the ED, produces less cardiac stimulation than SABAs.</td>
<td>▪ Reverses only cholinergically mediated bronchospasm; does not modify reaction to antigen. Does not block EIB.</td>
</tr>
<tr>
<td>Ipratropium bromide</td>
<td>■ Bronchodilation. Competitive inhibition of muscarinic cholinergic receptors.</td>
<td></td>
<td>▪ Multiple doses of ipratropium in the ED provide additive effects to SABA.</td>
</tr>
<tr>
<td></td>
<td>▪ Reduces intrinsic vagal tone of the airways. May block reflex bronchoconstriction secondary to irritants or to reflux esophagitis.</td>
<td></td>
<td>▪ May be alternative for patients who do not tolerate SABA.</td>
</tr>
<tr>
<td></td>
<td>▪ May decrease mucous gland secretion.</td>
<td></td>
<td>▪ Treatment of choice for bronchospasm due to beta-blocker medication.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>▪ Has not proven to be efficacious as long-term control therapy for asthma.</td>
</tr>
<tr>
<td><strong>Corticosteroids</strong></td>
<td>■ For moderate or severe exacerbations to prevent progression of exacerbation, reverse inflammation, speed recovery, and reduce rate of relapse</td>
<td>▪ Short-term use: reversible abnormalities in glucose metabolism, increased appetite, fluid retention, weight gain, facial flushing, mood alteration, hypertension, peptic ulcer, and rarely aseptic necrosis.</td>
<td>▪ Short-term therapy should continue until patient’s symptoms resolve. This usually requires 3–10 days but may require longer.</td>
</tr>
<tr>
<td>Systemic:</td>
<td></td>
<td></td>
<td>— Action may begin within an hour.</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td></td>
<td></td>
<td>▪ There is no evidence that tapering the dose following improvement is useful in preventing a relapse in asthma exacerbations.</td>
</tr>
<tr>
<td>Prednisolone</td>
<td></td>
<td></td>
<td>▪ Other systemic corticosteroids such as hydrocortisone and dexamethasone given in equipotent daily doses are likely to be as effective as prednisolone.</td>
</tr>
<tr>
<td>Prednisone</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key: ED, emergency department; EIB, exercise-induced bronchospasm
**Key:** Alphabetical order is used when more than one treatment option is listed within either preferred or alternative therapy. EIB, exercise-induced bronchospasm; ICS, inhaled corticosteroid; LABA, long-acting inhaled beta₂-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta₂-agonist

**Notes:**
- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- If alternative treatment is used and response is inadequate, discontinue it and use the preferred treatment before stepping up.
- Zileuton is a less desirable alternative due to limited studies as adjunctive therapy and the need to monitor liver function. Theophylline requires monitoring of serum concentration levels.
- In step 6, before oral systemic corticosteroids are introduced, a trial of high-dose ICS + LABA + either LTRA, theophylline, or zileuton may be considered, although this approach has not been studied in clinical trials.
- Step 1, 2, and 3 preferred therapies are based on Evidence A; step 3 alternative therapy is based on Evidence A for LTRA, Evidence B for theophylline, and Evidence D for zileuton. Step 4 preferred therapy is based on Evidence B and alternative therapy is based on Evidence B for LTRA and theophylline and Evidence D for zileuton. Step 5 preferred therapy is based on Evidence B. Step 6 preferred therapy is based on (EPR—2 1997) and Evidence B for omalizumab.
- Immunotherapy for steps 2–4 is based on Evidence B for house-dust mites, animal danders, and pollens; evidence is weak or lacking for molds and cockroaches. Evidence is strongest for immunotherapy with single allergens. The role of allergy in asthma is greater in children than in adults.
- Clinicians who administer immunotherapy or omalizumab should be prepared and equipped to identify and treat anaphylaxis that may occur.
<table>
<thead>
<tr>
<th><strong>FIGURE 5–2a.  RISK FACTORS FOR DEATH FROM ASTHMA</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asthma history</strong></td>
</tr>
<tr>
<td>Previous severe exacerbation (e.g., intubation or ICU admission for asthma)</td>
</tr>
<tr>
<td>Two or more hospitalizations for asthma in the past year</td>
</tr>
<tr>
<td>Three or more ED visits for asthma in the past year</td>
</tr>
<tr>
<td>Hospitalization or ED visit for asthma in the past month</td>
</tr>
<tr>
<td>Using &gt;2 canisters of SABA per month</td>
</tr>
<tr>
<td>Difficulty perceiving asthma symptoms or severity of exacerbations</td>
</tr>
<tr>
<td>Other risk factors: lack of a written asthma action plan, sensitivity to <em>Alternaria</em></td>
</tr>
<tr>
<td><strong>Social history</strong></td>
</tr>
<tr>
<td>Low socioeconomic status or inner-city residence</td>
</tr>
<tr>
<td>Illicit drug use</td>
</tr>
<tr>
<td>Major psychosocial problems</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>Other chronic lung disease</td>
</tr>
<tr>
<td>Chronic psychiatric disease</td>
</tr>
<tr>
<td><strong>Key</strong>: ED, emergency department; ICU, intensive care unit; SABA, short-acting beta2-agonist</td>
</tr>
<tr>
<td><strong>Sources</strong>: Abramson et al. 2001; Greenberger et al. 1993; Hardie et al. 2002; Kallenbach et al. 1993; Kikuchi et al. 1994; O’Hollaren et al. 1991; Rodrigo and Rodrigo 1993; Strunk and Mrazek 1986; Suissa et al. 1994</td>
</tr>
</tbody>
</table>
Assess Severity
- Patients at high risk for a fatal attack (see figure 5-2a) require immediate medical attention after initial treatment.
- Symptoms and signs suggestive of a more serious exacerbation such as marked breathlessness, inability to speak more than short phrases, use of accessory muscles, or drowsiness (see figure 5-3) should result in initial treatment while immediately consulting with a clinician.
- Less severe signs and symptoms can be treated initially with assessment of response to therapy and further steps as listed below.
- If available, measure PEF—values of 50–75% predicted or personal best indicate the need for quick-relief mediation. Depending on the response to treatment, contact with a clinician may also be indicated. Values below 50% indicate the need for immediate medical care.

Initial Treatment
- Inhaled SABA: up to two treatments 20 minutes apart of 2–8 puffs by metered-dose inhaler (MDI) or nebulizer treatments.
- Note: Medication delivery is highly variable. Children and individuals who have exacerbations of lesser severity may need fewer puffs than suggested above.

Good Response
- No wheezing or dyspnea (assess tachypnea in young children).
- PEF ≥80% predicted or personal best.
- Contact clinician for followup instructions and further management.
- May continue inhaled SABA every 3–4 hours for 24–48 hours.
- Consider short course of oral systemic corticosteroids.

Incomplete Response
- Persistent wheezing and dyspnea (tachypnea).
- PEF 50–79% predicted or personal best.
- Add oral systemic corticosteroid.
- Continue inhaled SABA.
- Contact clinician urgently (this day) for further instruction.

Poor Response
- Marked wheezing and dyspnea.
- PEF <50% predicted or personal best.
- Add oral systemic corticosteroid.
- Repeat inhaled SABA immediately.
- If distress is severe and nonresponsive to initial treatment:
  —Call your doctor AND
  —PROCEED TO ED;
  —Consider calling 9-1-1 (ambulance transport).
- To ED.

Key: ED, emergency department; MDI, metered-dose inhaler; PEF, peak expiratory flow; SABA, short-acting beta2-agonist (quick-relief inhaler)
**FIGURE 5–6. MANAGEMENT OF ASTHMA EXACERBATIONS: EMERGENCY DEPARTMENT AND HOSPITAL-BASED CARE**

**Initial Assessment (see figures 5–1, 5–3)**
Brief history, physical examination (auscultation, use of accessory muscles, heart rate, respiratory rate), PEF or FEV₁, oxygen saturation, and other tests as indicated.

- **FEV₁ or PEF ≥40% (Mid-to-Moderate)**
  - Oxygen to achieve SaO₂ ≥90%
  - Inhaled SABA by nebulizer or MDI with valved holding chamber, up to 3 doses in first hour
  - Oral systemic corticosteroids if no immediate response or if patient recently took oral systemic corticosteroids

- **FEV₁ or PEF <40% (Severe)**
  - Oxygen to achieve SaO₂ ≥90%
  - High-dose inhaled SABA plus ipratropium by nebulizer or MDI plus valved holding chamber, every 20 minutes or continuously for 1 hour
  - Oral systemic corticosteroids

- **Impending or Actual Respiratory Arrest**
  - Intubation and mechanical ventilation with 100% oxygen
  - Nebulized SABA and ipratropium
  - Intravenous corticosteroids
  - Consider adjunct therapies

**Repeat Assessment**
Symptoms, physical examination, PEF, O₂ saturation, other tests as needed

**Moderate Exacerbation**
FEV₁ or PEF 40–60% predicted/personal best
Physical exam: moderate symptoms
- Inhaled SABA every 60 minutes
- Oral systemic corticosteroid
- Continue treatment 1–3 hours, provided there is improvement; make admission decision in <4 hours

**Severe Exacerbation**
FEV₁ or PEF <40% predicted/personal best
Physical exam: severe symptoms at rest, accessory muscle use, chest retraction
History: high-risk patient
No improvement after initial treatment
- Oxygen
- Nebulized SABA + ipratropium, hourly or continuous
- Oral systemic corticosteroids
- Consider adjunct therapies

**Admit to Hospital Intensive Care (see box below)**

**Good Response**
- FEV₁ or PEF ≥70%
- Response sustained 60 minutes after last treatment
- No distress
- Physical exam: normal

**Incomplete Response**
- FEV₁ or PEF 40–60%
- Mid-to-moderate symptoms

**Poor Response**
- FEV₁ or PEF <40%
- PCO₂ ≥52 mm Hg
- Physical exam: symptoms severe, drowsiness, confusion

**Individualized decision re: hospitalization (see text)**

**Discharge Home**
- Continue treatment with inhaled SABA.
- Continue course of oral systemic corticosteroid.
- Consider initiation of an ICS.
- Patient education:
  - Review medications, including inhaler technique.
  - Review/Initiate action plan.
  - Recommend close medical followup.

**Admit to Hospital Ward**
- Oxygen
- Inhaled SABA
- Systemic (oral or intravenous) corticosteroid
- Consider adjunct therapies
- Monitor vital signs, FEV₁, or PEF, SaO₂

**Admit to Hospital Intensive Care**
- Oxygen
- Inhaled SABA hourly or continuously
- Intravenous corticosteroid
- Consider adjunct therapies
- Possible intubation and mechanical ventilation

**Discharge Home**
- Continue treatment with inhaled SABAs.
- Continue on ICS; For those not on long-term control therapy, consider initiation of an ICS.
- Patient education (e.g., review medications, including inhaler technique and, whenever possible, environmental control measures, review/initiate action plan; recommend close medical followup).
- Before discharge, schedule followup appointment with primary care provider and/or asthma specialist in 1–4 weeks.

**Key**
- FEV₁, forced expiratory volume in 1 second; ICS, inhaled corticosteroid; MDI, metered dose inhaler; PCO₂, partial pressure carbon dioxide; PEF, peak expiratory flow; SABA, short-acting beta₂-agonist; SaO₂, oxygen saturation
## Figure 5-8. Checklist For Hospital Discharge of Patients Who Have Asthma

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Dose/Timing</th>
<th>Education/Advice</th>
<th>M.D./R.N. Initials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled medications (e.g., MDI with valved holding chamber [VHC or spacer]; nebulizer)</td>
<td>Select agent dose, and frequency (e.g., albuterol)</td>
<td>Teach purpose&lt;br&gt;Teach and check technique&lt;br&gt;For MDIs, emphasize the importance of VHC or spacer</td>
<td></td>
</tr>
<tr>
<td>SABA</td>
<td>2–6 puffs every 3–4 hours as needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Medium dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral medications</td>
<td>Select agent dose, and frequency (e.g., prednisone 50 mg qd for 5 days)</td>
<td>Teach purpose&lt;br&gt;Teach side effects</td>
<td></td>
</tr>
<tr>
<td>Peak flow meter</td>
<td>For selected patients: measure a.m. and p.m. PEF, and record best of three tries each time</td>
<td>Teach purpose&lt;br&gt;Teach technique&lt;br&gt;Distribute peak flow diary</td>
<td></td>
</tr>
<tr>
<td>Followup visit</td>
<td>Make appointment for followup care with primary clinician or asthma specialist</td>
<td>Advise patient (or caregiver) of date, time, and location of appointment, ideally within 7 days of hospital discharge</td>
<td></td>
</tr>
<tr>
<td>Action plan</td>
<td>Before or at discharge</td>
<td>Instruct patient (or caregiver) on simple plan for actions to be taken when symptoms, signs, or PEF values suggest airflow obstruction</td>
<td></td>
</tr>
</tbody>
</table>

Key: MDI, metered-dose inhaler; PEF, peak expiratory flow; SABA, short-acting beta-agonist.