Asthma for Primary Care: Assessment, Control, and Long-Term Management

Learning Objectives
After participating in this educational activity, participants should be better able to:

1. Choose the optimal asthma therapy on underlying pathophysiology for both atopic and non-atopic asthma

2. Assess asthma severity, control, and response to treatment within the domains of impairment and risk

3. Aggressively manage more difficult to treat asthmatics
Introduction

Despite the introduction of multiple medications and an increased understanding of asthma pathophysiology, asthma continues to be a growing burden. Its prevalence increased from 7.3% in 2001 to 8.4% in 2010, with a higher prevalence among children than adults.[1] Yet, health care visits for asthma declined in primary care offices, while emergency department visits and hospitalization rates were stable.[1] In children, asthma is the most common cause of school absences, and those with persistent asthma and frequent absenteeism perform lower on standardized tests.[2] Adult work life is also affected by asthma accounting for a total loss of $5.1 billion in the US economy.[2]

Although the death rate has fallen, it still hovers around 3,400/year in 2010.[3]

Key indicators that assist in the diagnosis of asthma include:
- Difficulty breathing
- Chest tightness and/or cough
- Recurrent wheezing
- Shortness of breath

These symptoms may occur or get worse at night or in the presence of triggers such as dust mites, pollen, weather changes, mold, smoke, viral infections, eczema, menses, and strong emotions.

Physical examination may also assist in the diagnosis. Findings that are non-specific can include a prolonged expiratory phase, wheezing during normal respiration, increased nasal secretions, and mucosal swelling in the nares. Eczema, atopic dermatitis and nasal polyps may also be present.

Pre-Test Question
1. The control of atopic and non-atopic asthma involves treating the inflammatory process in both forms of this disease.
   a. True
   b. False

Asthma is inflammation of the airways characterized by airway narrowing that may be episodic, and may resolve spontaneously or with treatment. It is obstructive in nature and contributing factors include chronic inflammation, which if not treated aggressively, may lead to airway remodeling and airway hyperresponsiveness to stimuli, which in non-asthmatics elicit minimal or no bronchodilation response.

Asthmatic inflammation is a complex process producing edema of the airways and mucous plug formation, which produces hyperresponsiveness and airway remodeling. Airflow limitation is the end result.
Asthma presents more often in children than in adults with the major risk factor being atopy, which is the genetic predisposition to immunoglobulin e (IgE) mediated response to environmental stimuli. A family allergic history is thought to play a role in adult onset asthma.

The mechanism of non-atopic or non-allergic asthma is unclear, but there is a similar inflammatory process as in atopic asthma. Long standing, untreated inflammation contributes to rigidity of the airways and poorer than expected pulmonary function improvement, despite treatment. Early anti-inflammatory treatment may thus slow or halt airway remodeling. In fact, untreated asthma may contribute to the future development of chronic obstructive pulmonary disease (COPD), chronic bronchitis, and emphysema.[4]

The treatment of asthma should thus have an impact on IgE dependent mast cell degranulation of mediators such as prostaglandins, leukotrienes, histamine, and tryptase. Anti-inflammatory medications are therefore the treatment of choice.

Pre-Test Question
2. Current guidelines for the assessment of asthma severity at the initial visit include:
   a. Spirometry measuring forced expiratory volume in one second/forced vital capacity (FeV1/FVC)
   b. Symptoms including nighttime awakenings
   c. Frequency of short-acting bronchodilator use
   d. Interference with normal activity
   e. All of the above

Pre-Test Question
3. Assessment of asthma control at a follow-up visit includes:
   a. Symptoms less than 2X/week
   b. Nighttime awakenings less than 2X/month
   c. No interference with normal activity
   d. Short-acting beta agonist (SABA) use less than 2 days a week
   e. FeV1 greater than 80% of predicted
   f. Score greater than 20 on the asthma control test
   g. a, b, d
   h. All of the above

The Expert Panel Report 3 (EPR-3) on asthma care has identified that primary care physicians consider severity of asthma the most important factor in the monitoring and treatment of this disease, when determination of control and responsiveness to medication is also important in the evaluation of impairment and risk to the patient.[5] In fact, because the focus in the past has been on severity as defined by spirometry only, as many as 58% of adults and 46% of children with asthma visiting a primary care physician for any reason had uncontrolled asthma.[6]

Assessment and monitoring of asthma are closely linked to severity, control, and responsiveness, as defined in (Table 1).[5]
Table 1. Assessment and Monitoring of Asthma.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Control</th>
<th>Responsiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>The intrinsic intensity of the disease process, which is most easily measured in a patient not receiving long-term control medication.</td>
<td>The degrees to which the consequences of asthma symptoms, functional impairments, and risk of untoward events are minimized.</td>
<td>The ease that therapy achieves control. The goals of therapy are also met.</td>
</tr>
</tbody>
</table>

Table 2. The Goals of Asthma Therapy are to Reduce Impairment and risk.[5]

<table>
<thead>
<tr>
<th>Reduce Impairment</th>
<th>Reduce Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Prevent chronic symptoms everyday</td>
<td>- Prevent exacerbations and reduce the need for emergency department visits and hospitalizations</td>
</tr>
<tr>
<td>- SABA use is ≤ 2 days/week</td>
<td>- Prevent progressive loss of lung function</td>
</tr>
<tr>
<td>- Maintain near-normal pulmonary function</td>
<td>- Provide the most optimal pharmacotherapy that is safe and has minimal or no adverse effects</td>
</tr>
<tr>
<td>- Maintain normal activity levels</td>
<td></td>
</tr>
<tr>
<td>- Meet patients and families' expectation of and satisfaction with care</td>
<td></td>
</tr>
</tbody>
</table>

CASE STUDY

Barbara
Barbara is a 24-year-old female with a new patient visit to your practice in July who has been diagnosed with asthma since the age of 10. She is a non-smoker and has a history of seasonal allergic rhinitis, which she states is mild and whose symptoms occur primarily in the spring and fall.

Current Medications
- Albuterol MDI prn
- Loratadine 10 mg po prn (rarely uses)

Subjective Complaints
She reports asthma symptoms 5 or more days/week; awakens at night 5 or 6 times a month with symptoms that require her Albuterol. Exercising often precipitates symptoms for which she takes Albuterol as well. She notes that colds “linger” and often move “directly to my chest”. On careful questioning, patient admits inhaler use of at least 5 days/week.

Physical Examination
Completely negative except for slightly boggy turbinates.

Investigation
Pulmonary function test: FeV₁ 78% of predicted, FeV₁ / FVC 75%
She has not had an exacerbation requiring corticosteroids in the past year.
Before deciding treatment, the practitioner must assign severity by assessing impairment based on the patient’s/caregiver’s recall of the previous 2-4 weeks, and spirometry results. The assessment will include symptoms, nighttime awakenings, SABA use for symptom control, interference with activity, and lung function as measured by the FeV$_1$ and the FeV$_1$/FVC. Assessing the risk of the patient, ie, the number of exacerbations requiring systemic corticosteroids is also noted.

The assessment of severity is directed to the MOST SEVERE CATEGORY in which any feature occurs. These categories are Intermittent, Mild Persistent, Moderate Persistent, and Severe Persistent.

With reference to (Table 3), Barbara would fit the Moderate Persistent category and her treatment should be based on the stepwise control for managing long-term asthma.

Table 3. Asthma Care Quick Reference [7]

<table>
<thead>
<tr>
<th>Components of Sev.</th>
<th>Intermittent</th>
<th>Mild</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages 0-4 years</td>
<td>Ages 5-11 years</td>
<td>Ages 12+ years</td>
<td>Ages 0-4 years</td>
</tr>
<tr>
<td>Symptoms</td>
<td>0 days/week</td>
<td>0 days/week</td>
<td>0 days/week</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Use of SABA for symptom control</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Interference with activity</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV, between exacerbations</td>
<td>Normal FEV, between exacerbations</td>
<td>Normal FEV, between exacerbations</td>
</tr>
<tr>
<td>FEV$_1$/FVC</td>
<td>80%</td>
<td>80%</td>
<td>80%</td>
</tr>
<tr>
<td>Asthma exacerbations requiring oral systemic corticosteroids</td>
<td>0/year</td>
<td>≤2/year</td>
<td>≤2/year</td>
</tr>
</tbody>
</table>

The assessment, if a report is made, does not replace the differential medical judgment needed to treat individual patients.

*4 Administration: 88% aerosol or sustained inhaler; 88% aerosol or sustained inhaler, volume in 1 month; 88% aerosol or sustained inhaler, volume in 1 month; 88% aerosol or sustained inhaler, volume in 1 month; 88% aerosol or sustained inhaler, volume in 1 month.

4 High for FEV, if age: 0-4 years, 10th; 5-11 years, 25th; 12-17 years, 25th; 18-34 years, 25th; 35-49 years, 25th; 50-64 years, 25th; 65-74 years, 25th; 75+ years, 25th.

5 Data are insufficient to link the frequency of exacerbations with different levels of asthma severity. Generally, more frequent and severe exacerbations (eg, requiring urgent care, hospitalization, or intensive care admission, and oral corticosteroids in the first 24 h) indicate greater disease severity. The frequency of exacerbations may be correlated to few persistent asthmatics, even in the absence of persistent wheezing or asthma. In persistent asthma.
### Table 4. Asthma Care Quick Reference [7]

#### STEPSWISE APPROACH FOR MANAGING ASTHMA LONG TERM

The stepwise approach tailors the selection of medication to the level of asthma severity (see page 5) or asthma control (see page 6). The stepwise approach is meant to help, not replace, the clinical decision-making needed to meet individual patient needs.

<table>
<thead>
<tr>
<th>STEP I</th>
<th>STEP II</th>
<th>STEP III</th>
<th>STEP IV</th>
<th>STEP V</th>
<th>STEP VI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Persistent Asthma</strong></td>
<td><strong>Intensified Asthma</strong></td>
<td><strong>Preferred Treatment 1</strong></td>
<td><strong>Preferred Treatment 2</strong></td>
<td><strong>Preferred Treatment 3</strong></td>
<td><strong>Preferred Treatment 4</strong></td>
</tr>
<tr>
<td>Consult with asthma specialist if step 1 or higher is required. Consider consultation at step 2.</td>
<td>Consult with asthma specialist if step 1 or higher is required. Consider consultation at step 2.</td>
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<td>Consult with asthma specialist if step 1 or higher is required. Consider consultation at step 2.</td>
</tr>
<tr>
<td><strong>Step-up if needed</strong></td>
<td><strong>Step-down if possible</strong></td>
<td><strong>Step-up if needed</strong></td>
<td><strong>Step-down if possible</strong></td>
<td><strong>Step-up if needed</strong></td>
<td><strong>Step-down if possible</strong></td>
</tr>
<tr>
<td>(and asthma well controlled for at least 3 months)</td>
<td>(and asthma well controlled for at least 3 months)</td>
<td>(and asthma well controlled for at least 3 months)</td>
<td>(and asthma well controlled for at least 3 months)</td>
<td>(and asthma well controlled for at least 3 months)</td>
<td>(and asthma well controlled for at least 3 months)</td>
</tr>
</tbody>
</table>

**Preferred Treatment 1:**

- SABA	extsuperscript{*} as needed
- low-dose ICS	extsuperscript{*}
- medium-dose ICS
- medium-dose ICS + LABA
- medium-dose ICS + LABA or montelukast
- high-dose ICS + LABA
- high-dose ICS + LABA or montelukast
- high-dose ICS + LABA or montelukast + oral corticosteroids

**Alternative Treatment 1:**

- cromolyn or montelukast

**Preferred Treatment 2:**

- SABA	extsuperscript{*} as needed
- low-dose ICS
- low-dose ICS + LABA
- low-dose ICS + LABA or thymopentin	extsuperscript{#}
- medium-dose ICS
- medium-dose ICS + LABA
- medium-dose ICS + LABA or thymopentin	extsuperscript{#}
- high-dose ICS + LABA
- high-dose ICS + LABA or thymopentin	extsuperscript{#}
- high-dose ICS + LABA or thymopentin	extsuperscript{#} + oral corticosteroids

**Alternative Treatment 2:**

- cromolyn, LTRA	extsuperscript{#} or thymopentin

**Preferred Treatment 3:**

- SABA	extsuperscript{*} as needed
- low-dose ICS
- low-dose ICS + LABA
- low-dose ICS + LABA or thymopentin	extsuperscript{#}
- medium-dose ICS
- medium-dose ICS + LABA
- medium-dose ICS + LABA or thymopentin	extsuperscript{#}
- high-dose ICS + LABA
- high-dose ICS + LABA or thymopentin	extsuperscript{#}
- high-dose ICS + LABA + oral corticosteroids

**Alternative Treatment 3:**

- cromolyn, LTRA	extsuperscript{#} or thymopentin

**Preferred Treatment 4:**

- SABA	extsuperscript{*} as needed
- low-dose ICS
- low-dose ICS + LABA
- low-dose ICS + LABA or thymopentin	extsuperscript{#}
- medium-dose ICS
- medium-dose ICS + LABA
- medium-dose ICS + LABA or thymopentin	extsuperscript{#}
- high-dose ICS + LABA
- high-dose ICS + LABA or thymopentin	extsuperscript{#}
- high-dose ICS + LABA + oral corticosteroids

**Alternative Treatment 4:**

- cromolyn, LTRA	extsuperscript{#} or thymopentin

**Quick-Relief Medication**

- SABA	extsuperscript{*} as needed. The intensity of treatment depends on severity of symptoms: up to 3 treatments every 20 minutes as needed. Short course of oral systemic corticosteroids may be needed.
- LABA	extsuperscript{*}
- cromolyn, LTRA	extsuperscript{#} or thymopentin

**Quick-Relief Medication for patients who have persistent, allergic asthma:**

- SABA	extsuperscript{*}
- LABA	extsuperscript{*}
- LABA	extsuperscript{*} + oral corticosteroids

**Quick-Relief Medication for patients who have persistent, allergic asthma:**

- SABA	extsuperscript{*}
- LABA	extsuperscript{*}
- LABA	extsuperscript{*} + oral corticosteroids

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\textsuperscript{*} Asthmdicin: SABA, inhaled albuterol bronchodilator; ICS, inhaled corticosteroid; LABA, inhaled long-acting beta	extsubscript{2}, agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta	extsubscript{2} agonist.

\textsuperscript{#} Treatment options are listed in alphabetical order; if more than one.

\textsuperscript{#} If alternative treatment is used and response is inadequate, discontinues and unscheduled treatment before step up.

\textsuperscript{#} Thymopentin is a less desirable alternative because of the need for medication concentration levels.

\textsuperscript{#} Based on evidence for dual use, oral corticosteroids and polyclonal evidence in adults and long-term therapy for adults with chronic asthma.

\textsuperscript{#} These medications are prescribed in increasing doses as needed and as tolerated.

\textsuperscript{#} Inhalers may also be used for long-term therapy (e.g., in some cases, inhaled corticosteroids).
With reference to (Table 4), we see that Barbara’s persistent asthma should be treated by either a low-dose inhaled corticosteroid/long-acting beta agonist (ICS/LABA) or a medium dose ICS. Alternative treatments could also be used, but if the response is inadequate, they should be discontinued and the preferred treatment used before stepping up.

Here, a medium dose ICS was chosen. The EPR-3 guidelines state for symptomatic patients being treated with rescue medication, ICSs should be considered first. The ICS/LABA combination should be used when asthma is not adequately controlled with an ICS, or when disease severity clearly warrants treatment with that combination. The visit should also include instruction in the use of the controller inhaler (ICS) and the SABA for relief. Barbara should be encouraged to bring her inhalers on the return visit for assessment. Many physicians use an Asthma Action Plan (available on the EPR-3 website), but multiple studies have shown that compliance and persistence with written Asthma Action Plans is suboptimal. Her allergic rhinitis seems minimal so a decision on allergy testing was deferred.

Barbara’s return visit was due 4 weeks later. She brought in her inhalers and her technique was acceptable. Compliance was assessed and also reported as excellent.

<table>
<thead>
<tr>
<th>Barbara Reports</th>
<th>Results</th>
<th>Controlled</th>
<th>Not Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>3X weekly</td>
<td>√</td>
<td>X</td>
</tr>
<tr>
<td>SABA use</td>
<td>3X weekly</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>4 times/month</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>Some limitation</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>FeV₁</td>
<td>80%</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>FeV₁/FVC</td>
<td>78%</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Asthma Control Test score</td>
<td>15</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Asthma exacerbations requiring corticosteroids</td>
<td>0</td>
<td>√</td>
<td>X</td>
</tr>
</tbody>
</table>

The Asthma Control Test™ (ACT™) [http://www.qualitmetric.com/demos/TP_Launch.aspx?SID=52461](http://www.qualitmetric.com/demos/TP_Launch.aspx?SID=52461) is a five-question survey used to measure asthma control in individuals 12 years of age and older.

Table 5 was used in making the next treatment decision.
Table 5. Asthma Care Quick Reference[7]

FOLLOW-UP VISITS: ASSESSING ASTHMA CONTROL AND ADJUSTING THERAPY

Level of control (Columns 2-4) is based on the most severe component of impairment (symptoms and functional limitations) or risk (exacerbations). Assess impairment by patients’ or caregivers’ recall of events listed in Column 1 during the previous 2-4 weeks and by spirometry and/or peak flow measures. Symptom assessment for longer periods should reflect a global assessment, such as inquiring whether the patient’s asthma is better or worse since the last visit. Assess risk by recall of exacerbations during the previous year and since the last visit. Recommendations for adjusting therapy based on level of control are presented in the last row.

Barbara clearly fits the not well-controlled category. Her risk is there may be, if the situation continues, a progressive loss of lung function, although at the present this is not the case. Her treatment then should move up one step and the preferred recommendation in (Table 4) would be a medium dose ICS/LABA. Her SABA was continued for symptom relief and a return visit was scheduled in one month.
Pre-Test Question
4. In moderate persistent asthma, when there are daily symptoms with some limitation of normal activity and FeV₁ between 60-80% of predicted and negative testing for aeroallergens, a humanized monoclonal antibody that binds free IgE is approved by the FDA for treatment.
   a. True
   b. False

Barbara returns for a follow up visit a month later in September. She reports daily symptoms and daily use of a relief inhaler. Her use of Loratadine for allergic rhinitis symptoms has increased to 3 times weekly. She reports some difficulty during exercise, but an improvement over her initial visit. Her FeV₁ is at 76% of predicted. Nighttime awakenings were 5 in the past month. Her Asthma Control Test scored 13.

Physical examination revealed mildly boggy turbinates. Her chest was clear. Her inhaler technique is acceptable. She has lost her Action Asthma Plan. She has not had an exacerbation requiring oral corticosteroids. Her practitioner orders a serum IgE and allergy testing and requests a follow up visit within two weeks. She is to continue her current treatment.

Her return visit reveals positive testing for aeroallergens and a serum IgE of 185 iu/ml. This result is above normal.

In determining Barbara’s treatment plan by referring to (Table 5), we see that her asthma is still not well controlled, but does not fit into the very poorly controlled category. She has tested positive for aeroallergens and has a positive IgE, but her FeV₁ does not fit the severe category, and therefore, humanized monoclonal antibody therapy would be two steps up.

Barbara’s controller was therefore increased to a medium dose ICS/LABA combination and a return visit was scheduled. She was reminded of adhering to an Asthma Action Plan, but admits that she would not likely be compliant with same as it is “troublesome”. She was offered a specialist consultation, but declined. She also declined an inhaled nasal steroid (INS) to treat her allergic rhinitis.

Return visit one month later revealed she was taking her ICS/LABA controller as instructed with rescue medication now reduced to once weekly. Her symptoms reduced to the once weekly category as well. She reports her allergic rhinitis symptoms have resolved with no use of her Loratadine. There was one nighttime awakening and her FeV₁ was 80% of predicted. An Asthma Control Test done at this visit was scored at 20. Barbara was advised to continue her current regimen with a reassessment booked in three months with an aim to reducing her controller dosage if possible.
This case demonstrates a patient who progressed from being diagnosed with Moderate Persistent asthma at the initial visit, which was treated according to the EPR-3 guidelines, did not achieve control. On her return visit she therefore fit the not-well controlled category and her controller therapy was changed. She was adherent to all aspects of her now recommended care, except for not following her Asthma Action Plan, not an unusual occurrence. Her next visit showed deterioration in her FeV1 with increased symptoms and rescue inhaler use. Despite a positive serum IgE and positive allergy testing, she did not fit the category requiring the use of a monoclonal antibody medication to bind free IgE. By guidelines, her controller dose was increased and her last visit showed improvement of symptoms, decreased rescue inhaler use, and improved FeV1.

The lessons from this case are that practitioners, by being familiar with the EPR-3 guidelines, can make decisions with their patients that improve the quality of their lives, reduce risk of airway remodeling, impact the risk of exacerbations, and keep the overall costs of therapy reasonable.

**Pre-Test Question**
5. Inhaled corticosteroid treatment in asthma carries the same risk as an anabolic steroid.
   a. True
   b. False

In conclusion, one must also address questions that patients may have regarding their treatment choices, given the highly charged controversies that have arisen regarding ICS and LABA therapy.

**Regarding Corticosteroids [7]**
- ICSs are the most effective medicine for the long-term control of persistent asthma.
- Potential risks of ICSs are well-balanced by their benefits.
- ICSs may slow a child’s growth rate slightly, but is not progressive and must be balanced with the well-known fact that poorly controlled asthma can slow a child’s growth.
- ICSs are generally safe for pregnant women.
- ICSs are not the same as anabolic steroids used illegally to increase sports performance.

**Regarding LABAs [7]**
- The addition of a LABA for the treatment of patients who require more than a low dose ICS improves lung function, decreases symptoms, exacerbations, and use of SABA for quick relief to a greater extent than doubling the dose of the ICS.
- LABAs should not be used as monotherapy for long-term control or to treat acute symptoms or exacerbations.
- Severe exacerbations, although uncommon, may be associated with daily LABA therapy.
- A large clinical trial found slightly more deaths taking Salmeterol as a single inhaler in addition to usual therapy (13 out of 13,176), compared to a placebo plus usual asthma therapy (3 out of 13,179). [8] Trials for Formoterol in a single inhaler at higher doses in
addition to usual therapy, found more severe exacerbations compared to those taking a placebo added to usual therapy. Therefore there is a boxed warning on all drugs containing a LABA.[9]

References


