A 69-year-old African American woman with T2DM on insulin, HTN, and asthma presents to clinic for a routine health maintenance visit. She reports that she has been feeling well and has been taking her medicines as prescribed, though she occasionally forgets to take her “cholesterol pill” at night. Her blood glucose logbook indicates that her sugars typically run in the range of 76 - 160 mg/dL.

Regarding her asthma, she reports using her fluticasone inhaler twice daily as prescribed, though she still requires her rescue albuterol inhaler several times a day for adequate symptom relief. She is requesting a nebulizer machine because she does not feel that the inhaler works well enough. She denies recent illness, sick contacts, or allergy symptoms.

**PMH:**
- Asthma since childhood
- 1 intubation @ 20yo
- triggers: pollen, cigarette smoke, perfume
- HTN
- T2DM, on insulin
- Hypercholesterolemia

**Meds:**
- Chlorthalidone 25 mg daily
- Lisinopril 20 mg daily
- Metformin 500 mg BID
- Lantus 20 units SQ QHS
- Lispro 7 units SQ QAC
- Rosuvastatin 10 mg QHS
- Aspirin 81 mg daily
- Albuterol 90 mcg MDI inh PRN
- Fluticasone 250 mcg inh BID

**Soc Hx:**
- No tobacco
- No EtOH
- No illicit drugs

**ROS:**
(-) weight loss, (-) fevers or chills
(+) nocturnal asthma symptoms requiring rescue inhaler 2-3 times per week
(-) PND, orthopnea, LE edema, palpitations or chest pain

**Exam:**
- VS: T 37.4 HR 76 BP 128/80 RR 16 SpO₂ 99% (RA) BMI 31.8
- Gen: NAD
- Eyes: No conjunctival pallor, no scleral injection
- ENT: (+) edematous nasal mucosa, (+) cobblestoning of posterior pharynx
- CV: Normal S1S2, RRR, no M/R/G
- Resp: No increased WOB, lungs CTAB, no wheezing or rhonchi
- GI: Abdomen soft, NT/ND
- Feet: Microfilament sensation normal, no skin lesions

**Data:**
- MCV 81
- POC Glucose 114

*NOTE: This is not a real patient!
Given her ongoing symptoms, which of the following would be the MOST APPROPRIATE addition to her asthma regimen?

A. Albuterol nebulizer  
B. Ipratropium MDI with spacer  
C. Ipratropium nebulizer  
D. Salmeterol dry powder inhaler  
E. Montelukast PO  
F. Prednisone PO

You counsel her on the plan and schedule her return visit, but she is lost to follow-up. She returns 2 years later. Now, her symptoms suggest severe persistent asthma. Despite maximal medical therapy (see below) from an outside pulmonologist, she has had repeated exacerbations and hospitalizations over the past 6 months. She tells you that she typically improves after discharge, but after a week or two her asthma begins to worsen and she requires hospitalization again.

**Regimen:**
Albuterol MDI with spacer  
Fluticasone MDI with spacer  
Salmeterol dry powder inhaler  
Omalizumab SQ daily  
Montelukast PO daily  
Cetirizine PO daily  
Fluticasone NASAL spray BID

What would be the MOST APPROPRIATE addition to her maintenance asthma regimen at this time?

A. Prednisone 5 mg daily  
B. Tacrolimus 1 mg daily  
C. Clarithromycin 500 mg BID  
D. Theophylline 300 mg daily  
E. A and B  
F. A and C
Answers:

Given her ongoing symptoms, which of the following would be the MOST APPROPRIATE addition to her asthma regimen?

A. Albuterol nebulizer  
B. Ipratropium MDI with spacer  
C. Ipratropium nebulizer  
D. **Salmeterol dry powder inhaler**  
E. Montelukast PO  
F. Prednisone PO

You counsel her on the plan and schedule her return visit, but she is lost to follow-up. She returns 2 years later. Now, her symptoms suggest severe persistent asthma. Despite maximal medical therapy (see below) from an outside pulmonologist, she has had repeated exacerbations and hospitalizations over the past 6 months. She tells you that she typically improves after discharge, but after a week or two her asthma begins to worsen and she requires hospitalization again.

**Regimen:**
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Cetirizine PO daily  
Fluticasone NASAL spray BID

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B. Tacrolimus 1 mg daily  
C. Clarithromycin 500 mg BID  
D. Theophylline 300 mg daily  
E. A and B  
F. A and C

**Discussion Points:**
To answer the first question, you must first classify the severity of the patient’s asthma, then determine whether her asthma is controlled. Figure 1 lists the National Heart, Lung, and Blood Institute’s National Asthma Education and Prevention Program (NAEPP) Expert Panel Report 3 (EPR3): Guidelines for the Diagnosis and Management of Asthma (2007) classification system for asthma severity. Figure 2 lists EPR3’s classification of asthma control.
Figure 1. EPR3 Classification of Asthma Severity for Adults and Youths Age ≥ 12 Years.

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Classification of Asthma Severity</th>
<th>Intermittent</th>
<th>Mild</th>
<th>Persistent</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥12 years of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily</td>
<td>Daily</td>
<td>Throughout the day</td>
</tr>
<tr>
<td><strong>Fatigue and nighttime awakenings</strong></td>
<td>≤2x/month</td>
<td>3–4x/month</td>
<td>&gt;1x/week but not nightly</td>
<td>Often 7x/week</td>
<td></td>
</tr>
<tr>
<td><strong>Short-acting beta₂-agonist use for symptom control (not prevention of EIB)</strong></td>
<td>≤2 days/week but not daily, and not more than 1x on any day</td>
<td>Daily</td>
<td>Several times per day</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Interference with normal activity</strong></td>
<td>None</td>
<td>Minor limitation</td>
<td>Some limitation</td>
<td>Extremely limited</td>
<td></td>
</tr>
<tr>
<td><strong>Lung function</strong></td>
<td>• Normal FEV₁, between exacerbations</td>
<td>• FEV₁ &gt;80% predicted</td>
<td>• FEV₁ &gt;80% predicted</td>
<td>• FEV₁ &gt;60% but &lt;80% predicted</td>
<td>• FEV₁ &gt;60% but &lt;80% predicted</td>
</tr>
<tr>
<td></td>
<td>• FEV₁/FVC normal</td>
<td>• FEV₁/FVC normal</td>
<td>• FEV₁/FVC reduced 5%</td>
<td></td>
<td>• FEV₁/FVC reduced &gt;5%</td>
</tr>
</tbody>
</table>


Figure 2. EPR3 Classification of Asthma Control for Adults and Youths Age ≥ 12 Years.

<table>
<thead>
<tr>
<th>Components of Control</th>
<th>Classification of Asthma Control (≥12 years of age)</th>
<th>Well Controlled</th>
<th>Not Well Controlled</th>
<th>Very Poorly Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>≥4x/week</td>
<td></td>
</tr>
<tr>
<td><strong>Fatigue and nighttime awakenings</strong></td>
<td>≤2x/month</td>
<td>1–3x/week</td>
<td>Extremely limited</td>
<td></td>
</tr>
<tr>
<td><strong>Interference with normal activity</strong></td>
<td>None</td>
<td>Some limitation</td>
<td>Extremely limited</td>
<td></td>
</tr>
<tr>
<td><strong>Short-acting beta₂-agonist use for symptom control (not prevention of EIB)</strong></td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Several times per day</td>
<td></td>
</tr>
<tr>
<td><strong>FEV₁ or peak flow</strong></td>
<td>&gt;80% predicted/ personal best</td>
<td>60–80% predicted/ personal best</td>
<td>&lt;60% predicted/ personal best</td>
<td></td>
</tr>
<tr>
<td><strong>Validated questionnaires</strong></td>
<td>ATAQ ACQ ACT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0 ≤0.75* ≥20</td>
<td>1–2</td>
<td>3–4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.5</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>16–19</td>
<td>≤15</td>
<td></td>
</tr>
</tbody>
</table>


Thus, she has moderate persistent asthma that is uncontrolled. As she is on albuterol and inhaled steroids already, in addition to suggesting trigger avoidance and considering treatment for her probable allergic rhinitis, we should intensify therapy in stepwise fashion. Figure 3 lists EPR3’s stepwise algorithm for asthma treatment.
Figure 3. EPR3 Stepwise Approach for Managing Asthma in Adults and Youths Age ≥ 12 Years.

**Intermittent Asthma**

**Persistent Asthma: Daily Medication**
Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.

**Step 1**
Preferred: Low-dose ICS
Alternative: Cromolyn, LTRA, Nedocromil, or Theophylline

**Step 2**
Preferred: Low-dose ICS + LABA
Alternative: Medium-dose ICS + either LTRA, Theophylline, or Zileuton

**Step 3**
Preferred: Medium-dose ICS + LABA
Alternative: High-dose ICS + LABA + oral corticosteroid

**Step 4**
Preferred: Medium-dose ICS + LABA
Alternative: High-dose ICS + LABA + oral corticosteroid

**Step 5**
Preferred: High-dose ICS + LABA + oral corticosteroid
AND Consider Omalizumab for patients who have allergies

**Step 6**
Preferred: High-dose ICS + LABA + oral corticosteroid
AND Consider Omalizumab for patients who have allergies

---

**Quick-Relief Medication for All Patients**

- **SABA as needed for symptoms.** Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- **Use of SABA >2 days a week for symptom relief** (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

---

**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 beta-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta-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.

All patients with moderate persistent asthma are treated with maintenance inhaled corticosteroids to reduce airway inflammation and PRN bronchodilators to treat acute symptoms. As this patient’s symptoms are still not controlled, it would be most appropriate to add a long-acting beta agonist such as salmeterol or formoterol as our next step (Step 3).

Salmeterol is administered via a dry powder inhalation diskus (i.e., Serevent Diskus). Agents such as albuterol and ipratropium can be administered through HFA metered dose inhalers or as nebulized solutions. Studies have shown that meter-dosed inhalers with spacers are as effective or superior to nebulizers in cooperative, adult patients and are cost-effective and portable.

Also remember to set up an asthma action plan with your patients and counsel them on trigger avoidance. See sample patient handouts from the NAEPP report in the appendix.

In the second question, the patient now has severe persistent asthma and is likely steroid dependent. Early evidence suggests that macrolide antibiotics such as clarithromycin may improve asthma control in some patients with severe, refractory asthma on the basis of anti-inflammatory and antimicrobial effects, and some experts recommend a trial of therapy in refractory patients who describe asthma onset following a respiratory infection. There is currently insufficient evidence, however, to recommend macrolide therapy to most patients with severe asthma over proven therapies such as systemic corticosteroids. Among the other choices, tacrolimus has no role in asthma treatment, while theophylline is a consideration in moderate persistent asthma but not specifically recommended in severe persistent asthma.

References:

http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf


Appendix pages:

Doing Well

Take these long-term control medicines each day (include an anti-inflammatory).

<table>
<thead>
<tr>
<th>Medicine</th>
<th>How much to take</th>
<th>When to take it</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

And, if a peak flow meter is used,

Peak flow: more than  
(80 percent or more of my best peak flow)

My best peak flow is: 

Before exercise

2 or 4 puffs  
5 minutes before exercise

Asthma Is Getting Worse

- Or-

Peak flow: to  
(60 to 79 percent of my best peak flow)

Medical Alert!

- Or-

Peak flow: less than  
(50 percent of my best peak flow)

DANGER SIGNS

- Trouble walking and talking due to shortness of breath
- Lips or fingernails are blue

Take this medicine:

- 4 or 6 puffs of your quick-relief medicine AND
- Go to the hospital or call for an ambulance (phone)

See the reverse side for things you can do to avoid your asthma triggers.
How To Control Things That Make Your Asthma Worse

This guide suggests things you can do to avoid your asthma triggers. Put a check next to the triggers that you know make your asthma worse and ask your doctor to help you find out if you have other triggers as well. Then decide with your doctor what steps you will take.

### Allergens

- **Animal Dander**
  
  Some people are allergic to the flakes of skin or dried saliva from animals with fur or feathers.

  **The best thing to do:**
  
  - Keep furry or feathered pets out of your home.
  - If you can’t keep the pet outdoors, then:
    - Keep the pet out of your bedroom and other sleeping areas at all times, and keep the door closed.
    - Remove carpets and furniture covered with cloth from your home.
    - If that is not possible, keep the pet away from fabric-covered furniture and carpets.

- **Dust Mites**
  
  Many people with asthma are allergic to dust mites. Dust mites are tiny bugs that are found in every home—in mattresses, pillows, carpets, upholstered furniture, bedcovers, clothes, stuffed toys, and fabric or other fabric-covered items.

  **Things that can help:**
  
  - Encase your mattress in a special dust-proof cover.
  - Encase your pillow in a special dust-proof cover or wash the pillow each week in hot water. Water must be hotter than 130°F to kill the mites. Cold or warm water used with detergent and bleach can also be effective.
  - Wash the sheets and blankets on your bed each week in hot water.
  - Reduce indoor humidity to below 60 percent (ideally between 30—50 percent). Dehumidifiers or central air conditioners can do this.
  - Try not to sleep or lie on cloth-covered cushions.
  - 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 cooler water with detergent and bleach.

- **Cockroaches**
  
  Many people with asthma are allergic to the dried droppings and remains of cockroaches.

  **The best thing to do:**
  
  - 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.

### Indoor Mold

- Fix leaky faucets, pipes, or other sources of water that have mold around them.
- Clean moldy surfaces with a cleaner that has bleach in it.

### Pollen and Outdoor Mold

What to do during your allergy season (when pollen or mold spore counts are high):

- Try to keep your windows closed.
- Stay indoors with windows closed from late morning to 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.

### Irritants

- **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 or car.

- **Smoke, Strong Odors, and Sprays**
  
  - If possible, do not use a wood-burning stove, kerosene heater, or fireplace.
  - Try to stay away from strong odors and sprays, such as perfume, talcum powder, hair spray, and paints.

### Other things that bring on asthma symptoms in some people include:

- **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 double-layered or microfilter vacuum cleaner bag, or a vacuum cleaner with a HEPA filter.

- **Other Things That Can Make Asthma Worse**
  
  - Sulfites in foods and beverages: Do not drink beer or wine or eat dried fruit, processed potatoes, or shrimp 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 take. Include cold medicines, aspirin, vitamins and other supplements, and nonselective beta-blockers (including those in eye drops).

For More Information, go to: [www.nhlbi.nih.gov](http://www.nhlbi.nih.gov)

NIH Publication No. 07-5251

April 2007