Learning Objectives

1. Classify patients, assess control, and select and monitor appropriate acute and preventive treatments for pediatric and adult patients with asthma and for adult patients with chronic obstructive pulmonary disease, depending on patient-specific factors.
2. Assess, classify, and select appropriate acute and chronic pharmacotherapy (including nonpharmacologic therapy), and monitor, reassess, and adjust therapy in patients with gout.
3. Determine appropriate immunizations for an adult given his or her age and medical conditions and apply cautions, contraindications, and drug interactions with immunizations to adult patients.

Self-Assessment Questions

Answers and explanations to these questions can be found at the end of this chapter.

1. A 20-year-old woman is admitted to the hospital for an asthma exacerbation. She states that she has been using her boyfriend’s albuterol inhaler on a regular basis for the past 2 years. During the past few months, she has been using the inhaler throughout the day on a daily basis and sometimes at night. Which best classifies her asthma severity?
   A. Mild intermittent.
   B. Mild persistent.
   C. Moderate persistent.
   D. Severe persistent.

2. Which is the best maintenance therapy for her asthma?
   A. Fluticasone low dose.
   B. Montelukast.
   C. Fluticasone medium dose plus salmeterol.
   D. Theophylline.

3. Which type of measurement best classifies the number of times a short-acting β₂-agonist (SABA) is used in 1 month?
   A. Nominal.
   B. Ordinal.
   C. Interval.
   D. Ratio.

4. You are designing a study in which you will compare the percentage of patients with an asthma-related hospitalization receiving fluticasone/salmeterol with those receiving fluticasone alone. Which statistical test is best for analyzing this comparison?
   A. Analysis of variance (ANOVA).
   B. Chi-square.
   C. Mann-Whitney U test.
   D. Student unpaired t test.

5. A 22-year-old woman with asthma is taking an albuterol metered dose inhaler (MDI) 2 puffs as needed and fluticasone (Flovent) 110 mcg/puff MDI 2 puffs twice daily. She received the influenza vaccine during last year’s influenza season, and her last tetanus vaccine (tetanus, diphtheria, and pertussis [Tdap]) was at age 17; there is no documentation of her having received a pneumococcal vaccine. Which is the best vaccine for her to receive at her next family medicine clinic appointment scheduled in July?
   A. Influenza.
   B. Pneumococcal.
   C. Td (tetanus and diphtheria).
   D. Herpes zoster.

6. A 60-year-old man with chronic obstructive pulmonary disease (COPD) has been using albuterol HFA 2 puffs four times per day as needed. His symptoms have worsened during the past year, and now he has persistent symptoms and shortness of breath, even while walking around his one-level house. His Modified Medical Research Council (mMRC) score is 2. His spirometry shows a forced expiratory volume in 1 second (FEV₁) of 70% of predicted and an FEV₁/forced vital capacity (FEV₁/FVC) of 60% of predicted. He has had no previous COPD exacerbations. Which medication is best to initiate?
   A. Fluticasone.
   B. Tiotropium.
   C. Fluticasone/salmeterol combination inhaler.
   D. Omalizumab.
7. A patient with severe polyarticular gout and three tophi, uric acid 12.3 mg/dL, and stage 4 chronic kidney disease (CKD) (glomerular filtration rate [GFR] 25 mL/minute/1.73 m²) requires urate-lowering therapy (ULT). Which is the most appropriate drug and starting dose?
A. Probenecid 500 mg twice daily.
B. Probenecid 250 mg twice daily.
C. Allopurinol 100 mg once daily.
D. Allopurinol 50 mg once daily.
I. ASTHMA

Guidelines:


A. Definition: Asthma is a chronic inflammatory disorder of the airways causing recurrent episodes of wheezing, breathlessness, cough, and chest tightness, particularly at night or early in the morning. During episodes, there is variable airway obstruction, often reversible spontaneously or with treatment. There is also increased bronchial hyperresponsiveness to a variety of stimuli.

B. Diagnosis
   1. Episodic symptoms of airflow obstruction are present.
   2. Airway obstruction is reversible (FEV₁ improves by 12% or more after short-acting β₂-agonists [SABAs]).
   3. Alternative diagnoses are excluded. Asthma versus COPD:
      a. Cough is usually nonproductive with asthma and productive with COPD.
      b. FEV₁ is reversible with asthma but is irreversible with COPD.
      c. Cough is worse at night and early in the morning with asthma; occurs throughout the day with COPD.
      d. Asthma is often related to allergies and environmental triggers; patients with COPD have a common history of smoking or exposure to other irritants.
      e. Asthma can be reversible; lung damage from COPD is irreversible.
   4. Asthma-COPD overlap syndrome (ACOS)
      a. Persistent airflow limitation with features of both asthma and COPD.
      b. If three or more features favor asthma, use diagnosis/treatment for asthma.
      c. If three or more features favor COPD, use diagnosis/treatment for COPD.
      d. If a similar number of features exist for both asthma and COPD, consider a diagnosis of ACOS (Table 1).
   5. Exercise-induced bronchospasm
      a. Presents with cough, shortness of breath, chest pain or tightness, wheezing, or endurance problems during exercise.
      b. Diagnosis is made by an exercise challenge in which a 15% decrease in FEV₁, or peak expiratory flow occurs before and after exercise, measured at 5-minute intervals for 20–30 minutes.
### Table 1. Syndromatic Diagnosis in Adults: Asthma vs. COPD vs. ACOS

<table>
<thead>
<tr>
<th>Feature</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>☐ Before age 20 years</td>
<td>☐ After age 40 years</td>
</tr>
<tr>
<td>Pattern of symptoms</td>
<td>☐ Variation in symptoms over minutes, hours, or days</td>
<td>☐ Persistence of symptoms despite treatment</td>
</tr>
<tr>
<td></td>
<td>☐ Worse during the night or early morning</td>
<td>☐ Good and bad days but always daily symptoms and exertional dyspnea</td>
</tr>
<tr>
<td></td>
<td>☐ Triggered by exercise, emotions, dust, or exposure to allergens</td>
<td>☐ Chronic cough and sputum precede onset of dyspnea, unrelated to triggers</td>
</tr>
<tr>
<td>Lung function</td>
<td>☐ Record of variable airflow limitation (spirometry or peak flow), showing reversibility</td>
<td>☐ Record of persistent airflow limitation (postbronchodilator FEV₁/FVC &lt;0.7)</td>
</tr>
<tr>
<td>Lung function between symptoms</td>
<td>☐ Normal</td>
<td>☐ Abnormal</td>
</tr>
<tr>
<td>Past history or family history</td>
<td>☐ Previous diagnosis of asthma</td>
<td>☐ Previous diagnosis of COPD, chronic bronchitis, or emphysema</td>
</tr>
<tr>
<td></td>
<td>☐ Family history of asthma and other allergic conditions (allergic rhinitis or eczema)</td>
<td>☐ Heavy exposure to a risk factor: tobacco smoke, biomass fuels</td>
</tr>
<tr>
<td>Time course</td>
<td>☐ No worsening of symptoms over time; symptoms vary either seasonally or from year to year</td>
<td>☐ Symptoms slowly worsen over time (progressive course over years)</td>
</tr>
<tr>
<td></td>
<td>☐ May improve spontaneously or have an immediate response to bronchodilators or ICS over weeks</td>
<td>☐ Rapid-acting bronchodilator provides only limited relief</td>
</tr>
<tr>
<td>Chest radiograph</td>
<td>☐ Normal</td>
<td>☐ Severe hyperinflation</td>
</tr>
</tbody>
</table>

**Syndromatic Diagnosis Instructions:**

1. Check each box in both columns that pertains to the patient.
2. Count the number of check boxes in each column.
3. If three or more boxes are checked for either asthma or COPD, that diagnosis is suggested.
4. If similar number of boxes are checked in each column, consider a diagnosis of ACOS.

COPD = chronic obstructive pulmonary disease; ACOS = asthma COPD overlap syndrome; ICS = inhaled corticosteroids; FEV₁/FVC = forced expiratory volume in 1 second/forced vital capacity.

Table 2. Interpreting Spirometry

<table>
<thead>
<tr>
<th>Component</th>
<th>What It Measures</th>
<th>Normal Values</th>
</tr>
</thead>
</table>
| FEV₁      | Volume of air exhaled forcefully in the first second of maximal expiration | Normal is ≥80%  
In asthma, reversibility is shown by an increase in FEV₁ of ≥12% after SABA |
| FVC       | The maximum volume of air that can be exhaled after full inspiration | Reported in liters and percentage predicted  
Normal adults can empty 80% of air in <6 seconds |
| FEV₁/FVC  | Differentiates between obstructive and restrictive disease | Normal: Within 5% of predicted range, which varies with age; usually 75%–80% in adults  
Decreased in obstructive disease (asthma, COPD) (<70%)  
Normal or high in restrictive disease (pulmonary fibrosis) |

COPD = chronic obstructive pulmonary disease; FEV₁/FVC = forced expiratory volume in 1 second/forced vital capacity; SABA = short-acting β-agonist.
### C. Classification of Asthma Severity and Control

**Table 3. Classification of Asthma Severity in Adults and Children**

<table>
<thead>
<tr>
<th>Components</th>
<th>Age Group (years)</th>
<th>Intermittent</th>
<th>Mild Persistent</th>
<th>Moderate Persistent</th>
<th>Severe Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of symptoms</td>
<td>All ages</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Daily</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>Nighttime awakening</td>
<td>≥12</td>
<td>≤2 times/month</td>
<td>3 or 4 times/month</td>
<td>More than once weekly but not nightly</td>
<td>Often 7 times/week</td>
</tr>
<tr>
<td></td>
<td>5–11</td>
<td>0</td>
<td>1 or 2 times/month</td>
<td>3 or 4 times/month</td>
<td>More than once weekly</td>
</tr>
<tr>
<td></td>
<td>0–4</td>
<td>0</td>
<td>1 or 2 times/month</td>
<td>3 or 4 times/month</td>
<td>More than once weekly</td>
</tr>
<tr>
<td>SABA; used for symptom control</td>
<td>All ages</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily</td>
<td>Daily</td>
<td>Several times a day</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>All ages</td>
<td>None</td>
<td>Minor limitation</td>
<td>Some limitations</td>
<td>Extremely limited</td>
</tr>
<tr>
<td>FEV₁/FVC&lt;sup&gt;b&lt;/sup&gt;</td>
<td>≥12</td>
<td>Normal</td>
<td>Normal</td>
<td>Reduced 5%</td>
<td>Reduced &gt;5%</td>
</tr>
<tr>
<td></td>
<td>5–11</td>
<td>&gt;85%</td>
<td>&gt;80%</td>
<td>75%–80%</td>
<td>&lt;75%</td>
</tr>
<tr>
<td></td>
<td>0–4</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ (% of normal)</td>
<td>≥12</td>
<td>&gt;80% (normal)</td>
<td>&gt;80% (normal)</td>
<td>&gt;60% to &lt;80%</td>
<td>&lt;60%</td>
</tr>
<tr>
<td></td>
<td>5–11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0–4</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exacerbations requiring oral steroids</td>
<td>≥12</td>
<td>0 or 1/year</td>
<td>≥2/year</td>
<td>≥2/year</td>
<td>≥2/year</td>
</tr>
<tr>
<td></td>
<td>5–11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0–4</td>
<td>0 or 1/year</td>
<td>≥2 in 6 months or ≥4 wheezing episodes per year&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recommended step for initiating treatment (see Table 5)</td>
<td>≥12</td>
<td>Step 1</td>
<td>Step 2</td>
<td>Step 3&lt;sup&gt;d&lt;/sup&gt; and consider short course of oral steroids</td>
<td>Step 4 or 5 and consider short course of oral steroids</td>
</tr>
<tr>
<td></td>
<td>5–11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0–4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>The patient is classified according to the sign or symptom that is in the most severe category.

<sup>b</sup>Normal FEV₁/FVC: 8–19 years old, 85%; 20–39 years old, 80%; 40–59 years old, 75%; 60–80 years old, 70%.

<sup>c</sup>Episodes lasting >1 day and risk factors for persistent asthma.

<sup>d</sup>For ages 5–11, initial step 3 therapy should be medium-dose ICS.

FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity; ICS = inhaled corticosteroid; N/A = not applicable; SABA = short-acting β-agonist.

### Table 4. Assessing Asthma Control in Adults and Children

<table>
<thead>
<tr>
<th>Component</th>
<th>Age Group (years)</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></td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>5–11</td>
<td></td>
<td>≤2 days/week but not &gt;1 time each day</td>
<td>&gt;2 days/week or &gt;1 time/day on any day</td>
<td></td>
</tr>
<tr>
<td>0–4</td>
<td></td>
<td>≥1 time/day each day</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nighttime awakenings</strong></td>
<td></td>
<td>≤2 times/month</td>
<td>1–3 times/week</td>
<td>≥4 times/week</td>
</tr>
<tr>
<td>5–11</td>
<td></td>
<td>≤1 time/month</td>
<td>≥2 times/month</td>
<td>≥2 times/week</td>
</tr>
<tr>
<td>0–4</td>
<td></td>
<td>&gt;1 time/month</td>
<td>&gt;1 time/month</td>
<td>&gt;1 time/month</td>
</tr>
<tr>
<td><strong>Interference with normal activity</strong></td>
<td>All ages</td>
<td>None</td>
<td>Some limitations</td>
<td>Extremely limited</td>
</tr>
<tr>
<td><strong>SABA use for symptom control</strong></td>
<td>All ages</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Several times a day</td>
</tr>
<tr>
<td><strong>FEV₁ or peak flow</strong></td>
<td></td>
<td>&gt;80% of predicted/personal best</td>
<td>60%–80% of predicted/personal best</td>
<td>&lt;60% of predicted/personal best</td>
</tr>
<tr>
<td>5–11</td>
<td></td>
<td>≥12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–4</td>
<td></td>
<td>5–11</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Questionnaires</strong></td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>ATAQ</td>
<td>≥12</td>
<td>0</td>
<td>1 or 2</td>
<td>3 or 4</td>
</tr>
<tr>
<td>(N/A if &lt;12)</td>
<td>≤0.75</td>
<td>≥1.5</td>
<td>N/A</td>
<td>16–19</td>
</tr>
<tr>
<td>ACQ</td>
<td>≥12</td>
<td>0</td>
<td>1 or 2</td>
<td>3 or 4</td>
</tr>
<tr>
<td>ACT</td>
<td>N/A</td>
<td>0 or 1/year</td>
<td>≥2/year</td>
<td>≥2/year</td>
</tr>
<tr>
<td>Exacerbations requiring oral steroids</td>
<td>≥12</td>
<td>2 or 3 times/year</td>
<td>&gt;3 times/year</td>
<td></td>
</tr>
<tr>
<td>5–11</td>
<td></td>
<td>0 or 1/year</td>
<td>≥2/year</td>
<td></td>
</tr>
<tr>
<td>0–4</td>
<td></td>
<td>0 or 1/year</td>
<td>≥2/year</td>
<td></td>
</tr>
<tr>
<td><strong>Recommended action for treatment</strong></td>
<td>All ages</td>
<td>Maintain current step; regular follow-up every 1–6 months; consider step-down if well controlled ≥3 months</td>
<td>Step-up one step; reevaluate in 2–6 weeks</td>
<td>Consider short course of oral steroids Step-up one or two steps; reevaluate in 2 weeks</td>
</tr>
</tbody>
</table>

*Does not include β₂-agonist used to prevent exercise-induced asthma.


### D. Treatment Goals

1. Minimal or no chronic symptoms day or night
2. Minimal or no exacerbations
3. No limitations on activities; no school or work missed
4. Maintain (near) normal pulmonary function.
5. Minimal use of SABAs
6. Minimal or no adverse effects from medications

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E. Treatment Guidelines

**Table 5. Pharmacologic Treatment of Asthma**

<table>
<thead>
<tr>
<th>Step</th>
<th>Age Group (years)</th>
<th>Long-term Control</th>
<th>Quick Relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>All ages</td>
<td>No controller needed</td>
<td>Use SABA PRN</td>
</tr>
<tr>
<td>2</td>
<td>≥12</td>
<td>Preferred: Low-dose ICS</td>
<td>SABA &gt;2 times/week (excluding preexercise doses) indicates inadequate control and need to step up treatment</td>
</tr>
<tr>
<td></td>
<td>5–11</td>
<td>Alternatives: LTM, theophylline, or cromolyn&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0–4</td>
<td>Preferred: Low-dose ICS Alternatives: Montelukast or cromolyn&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>≥12</td>
<td>Preferred: Low-dose ICS plus LABA OR medium-dose ICS alone Alternative: Low-dose ICS plus LTM or theophylline</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5–11</td>
<td>Preferred: Low-dose ICS plus LABA, LTM, or theophylline OR medium-dose ICS alone (medium-dose ICS preferred as initial therapy)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0–4</td>
<td>Medium-dose ICS</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>≥12</td>
<td>Preferred: Medium-dose ICS plus LABA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5–11</td>
<td>Alternative: Medium-dose ICS plus LTM or theophylline</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0–4</td>
<td>Preferred: Medium-dose ICS plus LABA or montelukast Alternative: Medium-dose ICS plus other LTM or theophylline</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>≥12</td>
<td>High-dose ICS plus LABA AND consider omalizumab for patients with allergic asthma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5–11</td>
<td>Preferred: High-dose ICS plus LABA Alternative: High-dose ICS plus LTM or theophylline</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0–4</td>
<td>High-dose ICS plus LABA or montelukast</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>≥12</td>
<td>High-dose ICS plus LABA plus systemic corticosteroids AND consider omalizumab for patients with allergic asthma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5–11</td>
<td>Preferred: High-dose ICS plus LABA plus systemic corticosteroids Alternative: High-dose ICS plus LTM or theophylline plus systemic corticosteroids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0–4</td>
<td>High-dose ICS plus LABA or montelukast plus systemic corticosteroids</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Cromolyn and nedocromil are included in the National Asthma Education and Prevention Program guidelines. Cromolyn and nedocromil inhalers have been discontinued by the manufacturer; only generic cromolyn nebulization solution is still available.

ICS = inhaled corticosteroid; LABA = long-acting β<sub>2</sub>-agonist; LTM = leukotriene modifier; PRN = as needed; SABA = short-acting β<sub>2</sub>-agonist.

F. Pharmacologic Therapy for Asthma

Table 6. Pharmacologic Agents Used for Asthma and COPD

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Dose</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Corticosteroid inhalers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beclomethasone MDI 40 mcg/puff</td>
<td>QVAR (HFA)</td>
<td>See ICS dosing table</td>
<td><strong>Inhaled:</strong> Oral candidiasis Hoarseness May slow bone growth in children but similar adult height</td>
<td></td>
</tr>
<tr>
<td></td>
<td>80 mcg/puff</td>
<td></td>
<td>ICSs are first line for persistent asthma</td>
<td></td>
</tr>
<tr>
<td>Beclomethasone MDI 44 mcg/puff</td>
<td>Flovent HFA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>110 mcg/puff</td>
<td>Flovent Diskus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>220 mcg/puff</td>
<td>Arnuity Ellipta</td>
<td>1 inhalation once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone MDI 50 mcg/puff</td>
<td>Flovent HFA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 mcg/puff</td>
<td>Flovent Diskus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>250 mcg/puff</td>
<td>Arnuity Ellipta</td>
<td>1 inhalation once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone furoate (inhalation powder) 100 mcg/puff</td>
<td>Flovent HFA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200 mcg/puff</td>
<td>Flovent Diskus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arnuity Ellipta</td>
<td>1 inhalation once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone DPI 220 mcg/puff</td>
<td>Asmanex Twixhaler</td>
<td>Can be used once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide DPI 90 mcg/dose 180 mcg/dose 0.25-, 0.5-, and 1-mg/2-mL nebs</td>
<td>Pulmicort Flexhaler and Respules</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciclesonide MDI 80 mcg/puff 160 mcg/puff</td>
<td>Alvesco (HFA)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anticholinergics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium MDI 17 mcg/puff</td>
<td>Atrovent HFA</td>
<td>2–4 puffs TID–QID (up to 12 puffs/24 hours)</td>
<td>Headache Flushed skin Blurred vision Tachycardia Palpitations</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Used mainly for COPD and for acute asthma exacerbations requiring emergency treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Duration: 2–8 hours Also available as a solution for nebulization</td>
<td></td>
</tr>
<tr>
<td>Tiotropium DPI 18 mcg</td>
<td>Spiriva</td>
<td>Inhale 1 capsule/day 2 puffs once daily</td>
<td>Used for COPD; not currently standard of care for asthma Long acting; not for rapid relief Duration: &gt;24 hours</td>
<td></td>
</tr>
<tr>
<td>Tiotropium mist 2.5mcg</td>
<td>Spiriva Respimat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acidininium bromide DPI 400 mcg per puff</td>
<td>Tudorza Pressair</td>
<td>1 puff BID</td>
<td>Long-acting anticholinergic for COPD Dry powder inhaler with counter; does not involve putting capsules into inhaler at each dose</td>
<td></td>
</tr>
</tbody>
</table>

| **β2-Agonists (short acting): SABA** | | | | |
| Albuterol MDI 90 mcg/puff | Proventil HFA | 2 puffs every 4–6 hours PRN | Tremor Tachycardia Hypokalemia Hypomagnesemia Hyperglycemia Tachyphylaxis |
| | Ventolin HFA | | Used for acute bronchospasm; regular use indicates poor control Also available as solution for nebulization Duration of effect (MDI): 3–4 hours (up to 6) |
| | ProAir HFA | | |
| Levalbuterol MDI 45 mcg/puff | Xopenex HFA | 2 puffs every 4–6 hours PRN | R-enantiomer of albuterol Also available as a solution for nebulization Duration (MDI): 3–4 hours (up to 6) |
### Table 6. Pharmacologic Agents Used for Asthma and COPD (continued)

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Dose</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β&lt;sub&gt;2&lt;/sub&gt;-Agonists (long acting): LABA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol DPI 50 mcg/puff</td>
<td>Serevent Diskus</td>
<td>Inhale 1 blister/puff BID</td>
<td>Tremor, Tachycardia, Electrolyte effects (rare)</td>
<td>Not for acute symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Should not be used as monotherapy for asthma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Duration: 8–12 hours</td>
</tr>
<tr>
<td>Formoterol DPI 12-mcg capsule</td>
<td>Foradil Aerolizer</td>
<td>Inhale 1 capsule BID</td>
<td></td>
<td>Onset of action 1–3 minutes but should not be used as acute therapy</td>
</tr>
<tr>
<td>Formoterol 20-mcg/2-mL nebs</td>
<td>Perforomist</td>
<td>20-mcg BID nebs</td>
<td></td>
<td>Should not be used as monotherapy for asthma</td>
</tr>
<tr>
<td>Arformoterol 15-mcg/2-mL nebs</td>
<td>Brovana</td>
<td>15-mcg BID nebs</td>
<td></td>
<td>Duration of MDI: 8–12 hours</td>
</tr>
<tr>
<td>Indacaterol inhalation powder 75-mcg</td>
<td>Arcapta Neohaler</td>
<td>Inhale 1 capsule once daily</td>
<td></td>
<td>Formoterol Aerolizer is indicated to prevent exercise-induced bronchospasm; should be used at least 15 minutes before exercise Arformoterol is the R,R-isomer of racemic formoterol</td>
</tr>
<tr>
<td>Indacaterol is only indicated for COPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Duration of action: 24 hours</td>
</tr>
<tr>
<td><strong>Combination inhalers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol/ipratropium MDI 100/20 mcg</td>
<td>Combivent Respimat</td>
<td>1 puff QID (Respimat)</td>
<td>Maximum dose 6 puffs/day</td>
<td>Used primarily for COPD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Combivent MDI is no longer available</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Combination solution for nebulization is also available as DuoNeb or generic</td>
</tr>
<tr>
<td>Fluticasone/salmeterol DPI 100/50,</td>
<td>Advair Diskus</td>
<td>1 puff BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>250/50, 500/50 mcg/puff</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone/salmeterol MDI 45/21,</td>
<td>Advair HFA</td>
<td>2 puffs BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>115/21, 230/21 mcg/puff</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide/formoterol MDI 80/4.5,</td>
<td>Symbicort (HFA)</td>
<td>2 puffs BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>160/4.5 mcg/puff</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone/formoterol MDI 100/5,</td>
<td>Dulera (HFA)</td>
<td>2 puffs BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>200/5 mcg/puff</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone furoate/vilanterol</td>
<td>Breo Ellipta (double-foil blister strips of powder)</td>
<td>1 inhalation once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>inhalation powder 100/25 mcg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 6. Pharmacologic Agents Used for Asthma and COPD (continued)

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Dose</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methylxanthine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Theophylline</td>
<td>Theo-Dur</td>
<td>Adults: 300 mg/day</td>
<td>At high levels: Nausea</td>
<td>Achieve concentrations of 5–15 mcg/mL</td>
</tr>
<tr>
<td></td>
<td>Uniphyl</td>
<td>divided according to formulation</td>
<td>Vomiting</td>
<td>Beneficial for night symptoms</td>
</tr>
<tr>
<td></td>
<td>Theo-24</td>
<td>Adjust according to concentration</td>
<td>CNS stimulation</td>
<td>Not for acute relief</td>
</tr>
<tr>
<td></td>
<td>Theochron</td>
<td>Usual dose 400–600 mg/day</td>
<td>Headache</td>
<td>Duration: variable, up to 24 hours</td>
</tr>
<tr>
<td></td>
<td>Elixophyllin</td>
<td><strong>Children:</strong> Start at 10 mg/kg/day</td>
<td>Tachycardia, SVT</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adjust according to concentration</td>
<td>Hematremasis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Smokers may need higher doses at more frequent intervals</td>
<td>Hyperglycemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hypokalemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>At therapeutic levels: Insomnia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>GI upset</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Difficult urination in some children</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Difficult urination in BPH</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Duration: variable, up to 24 hours</td>
<td></td>
</tr>
<tr>
<td><em><em>Leukotriene modifiers (note: FDA Caution</em>)</em>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zafirlukast</td>
<td>Accolate</td>
<td>10–20 mg BID</td>
<td>Hepatotoxicity (zileuton and zafirlukast only)</td>
<td>Drug interactions: Warfarin, erythromycin, theophylline</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Zileuton: monitor LFTs (baseline, every month × 3 months, every 2–3 months for remainder of first year)</td>
<td>FDA approved for children ≥5 years old</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Zafirlukast: monitor symptoms, regular LFT monitoring not required; could be considered</td>
<td>Bioavailability decreases with food; take 1 hour before or 2 hours after meals</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Headache</td>
<td>Also indicated in exercise-induced bronchospasm and seasonal and perennial allergic rhinitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>GI upset</td>
<td>Drug interactions: Phenobarbital</td>
</tr>
<tr>
<td>Montelukast</td>
<td>Singulair</td>
<td>Dose in the evening Adults and children ≥15 years: 10 mg/day</td>
<td>Drug interactions: Warfarin and theophylline</td>
<td>FDA approved for use in children ≥1 year old; used in children 6 months and older</td>
</tr>
<tr>
<td>Oral 10-mg tablet</td>
<td></td>
<td>Children 6 to &lt;15 years: 5 mg/day</td>
<td>Churg-Strauss syndrome associated with tapering doses of steroids</td>
<td>Churg-Strauss syndrome associated with tapering doses of steroids</td>
</tr>
<tr>
<td>Chewable 4- and 5-mg tablets</td>
<td></td>
<td>Children 1 to &lt;6 years: 4 mg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral granules</td>
<td></td>
<td></td>
<td>*FDA Caution: Risk of neuropsychiatric events (behavior and mood changes: aggression, agitation, anxiousness, dream abnormalities, hallucinations, depression, insomnia, irritability, restlessness, suicidal thinking and behavior, tremor)</td>
<td>Only for those ≥12 years old</td>
</tr>
<tr>
<td>Zileuton</td>
<td>Zyflo CR</td>
<td>1200 mg BID</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 6. Pharmacologic Agents Used for Asthma and COPD (continued)

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Dose</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Omalizumab    | Xolair| 150–375 mg SC every 2–4 weeks Dose and frequency based on baseline IgE and weight in kilograms Do not inject >150 mg per injection site | Injection site reactions  
  - Urticaria  
  - Thrombocytopenia (transient)  
  - Anaphylaxis (rare)  
  - Malignancy | September 2014: New FDA Drug Safety Communication. Slightly increased risk of cardiovascular and cerebrovascular serious adverse events, including MI, unstable angina, TIA, PE/DVT, pulmonary HTN; no increased risk of stroke or CV death  
Used in severe persistent allergy-related asthma  
Use in ≥12 years  
Half-life: 26 days  
Second-line therapy  
Expensive |

BPH = benign prostatic hyperplasia; BID = twice daily; CNS = central nervous system; COPD = chronic obstructive pulmonary disease; CR = controlled release; CV = cardiovascular; DOC = drug of choice; DPI = dry powder inhaler; DVT = deep vein thrombosis; FDA = US Food and Drug Administration; GERD = gastroesophageal reflux disease; GI = gastrointestinal; HFA = hydrofluoroalkane; HTN = hypertension; ICS = inhaled corticosteroid; IgE = immunoglobulin E; LABA = long-acting β₂-agonist; LFT = liver function test; MDI = metered dose inhaler; MI, myocardial infarction; MOA = mechanism of action; nebs = nebulizers; OTC = over the counter; PE = pulmonary embolism; PRN = as needed; QID = four times daily; SC = subcutaneously; SVT = supraventricular tachycardia; TIA = transient ischemic attack; TID = three times daily.
### Table 7. Inhaled Corticosteroid Daily Dosing in Children and Adults

<table>
<thead>
<tr>
<th>Inhaled Corticosteroids</th>
<th>Low Dose (mcg/day) Steps 2 and 3</th>
<th>Medium Dose (mcg/day) Steps 3 and 4</th>
<th>High Dose (mcg/day) Steps 5 and 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age group (years)</strong></td>
<td>0–4</td>
<td>5–11</td>
<td>≥12</td>
</tr>
<tr>
<td><strong>Budesonide</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmicort DPI 90, 180</td>
<td>N/A</td>
<td>180–400</td>
<td>180–600</td>
</tr>
<tr>
<td><strong>Fluticasone</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flovent DPI 50, 100, 250</td>
<td>N/A</td>
<td>88–176</td>
<td>100–200</td>
</tr>
<tr>
<td>Arinity Ellipta 100, 200*</td>
<td></td>
<td>100–200</td>
<td>100–300</td>
</tr>
<tr>
<td><strong>Beclomethasone</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QVAR HFA 40, 80</td>
<td>N/A</td>
<td>80–160</td>
<td>80–240</td>
</tr>
<tr>
<td><strong>Mometasone</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asmanex DPI 110, 220 (delivers 100 and 200 mcg/puff)*</td>
<td>110 (age 4 only)</td>
<td>110</td>
<td>200</td>
</tr>
<tr>
<td><strong>Ciclesonide</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alvesco HFA 80, 160</td>
<td>N/A</td>
<td>N/A</td>
<td>160</td>
</tr>
<tr>
<td><strong>Budesonide suspension for nebulization</strong></td>
<td>0.25–0.5 mg</td>
<td>0.5 mg</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*Once daily.

The guidelines state the delivered dose of mometasone, not the actual dose; indicated in ages 4–11 after guidelines were published; doses are estimated from package insert.

*Ciclesonide was not available when the National Asthma Education and Prevention Program guidelines were published. The dose ranges are estimated from the package insert.

DPI = dry powder inhaler; HFA = hydrofluoroalkane; N/A = not applicable.

Patient Cases

1. A 23-year-old woman has been coughing and wheezing about twice weekly, and she wakes up at night about three times per month. She has never received a diagnosis of asthma, and she has not been to a doctor “in years.” She uses her boyfriend’s albuterol inhaler, but he recently ran out of refills, so she is seeking care. Her activities are not limited by her symptoms. Spirometry is done today, and her FEV₁ is 82% of predicted. From the current NAEPP guidelines, which is the best classification of her asthma?
   A. Intermittent.
   B. Mild persistent.
   C. Moderate persistent.
   D. Severe persistent.

2. Which medication is best to recommend for her, in addition to albuterol metered dose inhaler (MDI) 1 or 2 puffs every 4–6 hours as needed?
   A. No additional therapy needed.
   B. Montelukast 10 mg/day.
   C. Mometasone dry powder inhaler (DPI) 220 mcg/puff 1 puff daily.
   D. Budesonide/formoterol 80/4.5 mcg per puff 2 puffs twice daily.

3. At first, her symptoms were well controlled on your recommended therapy. However, when winter arrived, she started having symptoms and using her albuterol about 3 or 4 days per week during the day. Which is the preferred treatment change?
   A. No change in therapy is needed.
   B. Switch to budesonide/formoterol MDI 160/4.5 mcg per puff 2 puffs twice daily.
   C. Add montelukast orally 10 mg daily.
   D. Increase mometasone DPI to 220 mcg/puff 2 puffs daily.

4. An 8-year-old boy has been having daytime asthma symptoms once or twice weekly and is awakened twice weekly at night with coughing. In addition to albuterol MDI 1 or 2 puffs every 4–6 hours as needed, which is the best initial therapy for him?
   A. Fluticasone 44 mcg/puff 1 puff twice daily.
   B. Montelukast 10 mg/day.
   C. Fluticasone/salmeterol 100/50 mcg per puff 1 puff twice daily.
   D. Fluticasone 110 mcg/puff 1 puff twice daily.

G. Pharmacologic Treatment of ACOS
   1. Start treatment according to an asthma diagnosis.
   2. Inhaled corticosteroid (ICS) and long-acting β₂-agonist (LABA) combination therapy should be used.
   3. Do not use LABA monotherapy if there are features of asthma.
   4. Do not use ICS monotherapy if there are features of COPD.
H. Long-Acting $\beta_2$-Agonists (LABAs): According to a U.S. Food and Drug Administration (FDA) safety announcement, issued because of safety concerns with LABAs:
1. Use of a LABA alone without a long-term asthma control drug such as an ICS is contraindicated.
2. LABAs should not be used in patients whose asthma is adequately controlled on low- or medium-dose ICSs.
3. LABAs should be used only as additional therapy for patients who are currently taking but not adequately controlled on a long-term asthma control agent (e.g., an ICS).
4. Once asthma control is achieved and maintained, patients should be assessed at regular intervals and stepped down (e.g., discontinue the LABA), if possible, and the patients should continue to be treated with a long-term asthma control agent (e.g., an ICS).
5. Pediatric and adolescent patients who require a LABA and an ICS should use a combination product to ensure adherence to both medications.

I. Exercise-Induced Bronchospasm: Prevention and Treatment of Symptoms
1. Long-term control therapy, if otherwise appropriate (initiate or step-up)
2. Pretreatment with a SABA before exercise
3. Leukotriene modifiers (LTMs) can attenuate symptoms in 50% of patients.

J. Monitoring
1. Peak flow monitoring
   a. Symptom-based and peak flow–based monitoring have similar benefits; either is appropriate for most patients. Symptom-based monitoring is more convenient.
   b. May consider daily home peak flow monitoring for moderate to severe persistent asthma if patient has history of severe exacerbations or has poor perception of worsening of asthma symptoms.
   c. Personal best peak expiratory flow rate (PEFR), not predicted PEFR, should be determined if using peak flow–based asthma action plan.
      i. Personal best PEFR is the highest number attained after daily monitoring for 2 weeks twice daily when asthma is under good control.
      ii. Predicted PEFR is based on population norms using sex, height, and age.
2. Spirometry (only used if 5 years or older)
   a. At initial assessment
   b. After treatment is started and symptoms are stabilized
   c. If prolonged or progressive loss of asthma control
   d. At least every 2 years or more often depending on response to therapy

K. Asthma Action Plan: Usually symptom based (equal benefits of symptom-based or peak flow–based monitoring); home treatment of an asthma exacerbation
### Table 8. Asthma Action Plan

<table>
<thead>
<tr>
<th>Zone</th>
<th>Signs and Symptoms</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Green | Doing well; no or minimal symptoms of coughing, wheezing, or dyspnea | Take long-term asthma control agent only (if one is prescribed)  
Use 2 puffs of SABA 5–15 minutes before exercise if exercise-induced asthma and before known triggers |
| | PEFR 80%–100% of personal best | |
| Yellow | Getting worse; increased frequency of symptoms (e.g., coughing, wheezing, or dyspnea) | Use SABA: 2–4 puffs by MDI (up to 6 puffs if needed) or 1 nebulizer treatment; may repeat in 20 minutes if needed; reassess 1 hour after initial treatment  
If complete response at 1 hour, contact clinician for follow-up instructions and consider OCS burst<sup>a</sup>  
If incomplete response in 1 hour (still some coughing, wheezing, or dyspnea), repeat SABA and add OCS burst; contact clinician that day for further instructions  
If poor response in 1 hour (e.g., marked coughing, wheezing, or dyspnea), repeat SABA immediately; add OCS burst; contact clinician immediately; proceed to the ED if the distress is severe and unresponsive to treatment; consider calling 911  
May continue to use SABA every 3–4 hours regularly for 24–48 hours |
| | PEFR 50%–79% of personal best | |
| Red | Medical alert (e.g., marked coughing, wheezing, or dyspnea); inability to speak more than short phrases; use of accessory respiratory muscles; drowsiness | Begin treatment and consult clinician immediately  
Use SABA: 2–6 puffs by MDI (higher dose of 4–6 puffs usually recommended) or 1 nebulizer treatment; repeat every 20 minutes up to 3 times; add OCS burst  
If incomplete or poor response, repeat SABA immediately; proceed to the ED or call 911 if distress is severe and unresponsive to treatment  
Call 911 or go to the ED immediately if lips or fingernails are blue or gray or if there is trouble walking or talking because of shortness of breath  
Continue using SABA every 3–4 hours regularly for 24–48 hours |
| | PEFR <50% of personal best | |

<sup>a</sup>OCS burst: prednisone (or equivalent) 40–60 mg/day for 5–10 days (adults) or 1–2 mg/kg/day (maximum 60 mg/day) for 3–10 days (children).  
ED = emergency department; MDI = metered dose inhaler; OCS = oral corticosteroid; PEFR = peak expiratory flow rate; SABA = short-acting beta agonist.

After initial treatment, immediate medical attention is required if patient is at high risk of a fatal attack. Risk factors: Asthma-related (history of severe attack [previous intubation or intensive care unit admission for asthma], 2 or more asthma hospitalizations for asthma in past year, 3 or more ED visits for asthma in past year, hospitalization or ED visit for asthma in past month, using more than 2 canisters of SABA a month, difficulty perceiving asthma symptoms), social (low socioeconomic status or inner-city residence, illicit drug use, major psychosocial problems), and comorbidities (cardiovascular disease, other chronic lung disease, chronic psychiatric disease).
L. Managing Exacerbations: Initial—Emergency Department (ED) or Hospital

Table 9. Classifying Severity of Asthma Exacerbations in the Urgent or Emergency Care Setting

<table>
<thead>
<tr>
<th>Symptoms and Signs</th>
<th>Initial PEF or FEV₁</th>
<th>Clinical Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Dyspnea only with activity</td>
<td>≥70% of predicted or personal best</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Usually cared for at home</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prompt relief with an inhaled SABA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Possible short course of OCS</td>
</tr>
<tr>
<td>Moderate</td>
<td>Dyspnea interferes with or limits usual activity</td>
<td>40%–69% of predicted or personal best</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Usually requires office or ED visit</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relief from frequently inhaled SABAs and OCS; some symptoms last for 1–2 days after treatment is begun</td>
</tr>
<tr>
<td>Severe</td>
<td>Dyspnea at rest; interferes with conversation</td>
<td>&lt;40% of predicted or personal best</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Usually requires ED visit and likely hospitalization</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Partial relief from frequent inhaled SABA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral systemic corticosteroids; some symptoms last for ≥3 days after treatment is begun</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adjunctive therapies are helpful</td>
</tr>
<tr>
<td>Life threatening</td>
<td>Too dyspneic to speak; perspiring</td>
<td>&lt;25% of predicted or personal best</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Requires ED or hospitalization, possible ICU</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Little or no relief from frequent inhaled SABAs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IV corticosteroids</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adjunctive therapies are helpful</td>
</tr>
</tbody>
</table>

aFor all ages.
bLung function measures (PEF or FEV₁) may be useful for children ≥5 years old but may not be attainable in children during an exacerbation.

ED = emergency department; FEV₁ = forced expiratory volume in 1 second; ICU = intensive care unit; IV = intravenous; OCS = oral corticosteroid; PEF = peak expiratory flow; SABA = short-acting β₂-agonist.


1. Mild to moderate exacerbation (FEV₁ of 40% or more)
   a. Oxygen to achieve oxygen saturation (Sao₂) of 90% or more
   b. An inhaled SABA (MDI with valved holding chamber or nebulizer) up to three doses in the first hour
      i. Adult dose: Albuterol MDI 4–8 puffs every 20 minutes for up to 4 hours, then every 1–4 hours as needed or by nebulizer 2.5–5 mg every 20 minutes for three doses, then 2.5–10 mg every 1–4 hours as needed
      ii. Pediatric dose (12 years or younger): Albuterol MDI 4–8 puffs every 20 minutes for three doses, then every 1–4 hours as needed; use holding chamber (add mask if younger than 4 years) or by nebulizer 0.15 mg/kg (minimal dose 2.5 mg) every 20 minutes for three doses, then 0.15–0.3 mg/kg up to 10 mg every 1–4 hours as needed
   c. Oral corticosteroid (OCS) if no response immediately or if patient recently took an OCS
2. Severe exacerbation (FEV \(_1\) less than 40%)
   a. Oxygen to achieve \(\text{Sa}_2\) of 90% or more
   b. High-dose inhaled SABA plus ipratropium by MDI plus valved holding chamber or nebulizer every 20 minutes or continuously for 1 hour
   c. Oral corticosteroids
      i. Adult dose: Prednisone 40–80 mg/day in one or two divided doses until peak expiratory flow reaches 70% of predicted
      ii. Pediatric dose (12 years or younger): 1–2 mg/kg in two divided doses (maximum 60 mg/day) until peak expiratory flow reaches 70% of predicted
   d. Consider adjunctive therapies (intravenous magnesium or heliox) if still unresponsive.
3. Impending or actual respiratory arrest
   a. Intubation and mechanical ventilation with oxygen 100%
   b. Nebulized SABA plus ipratropium
   c. Intravenous corticosteroids
   d. Consider adjunctive therapies (intravenous magnesium or heliox) if patient is still unresponsive to therapy.
   e. Admit to intensive care.

M. Managing Exacerbations: ED or Hospital After Repeat Assessment
1. Moderate exacerbation (FEV \(_1\) 40%–69%)
   a. Inhaled SABA every 60 minutes
   b. Oral corticosteroid
   c. Continue treatment for 1–3 hours if improving.
2. Severe exacerbation (FEV \(_1\) less than 40%); no improvement after initial treatment
   a. Oxygen
   b. Nebulized SABA plus ipratropium; hourly or continuous
   c. Consider adjunctive therapies.
3. If good response to above treatment and maintained for at least 60 minutes
   a. Continue inhaled SABA.
   b. Continue OCS course.
   c. Consider initiating an ICS (if not already taking one).
   d. Discharge home.
4. If incomplete response (FEV \(_1\) 40%–69%), admit to hospital ward.
5. If poor response (FEV \(_1\) less than 40%), admit to intensive care.

<table>
<thead>
<tr>
<th>Patient Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. A 25-year-old man presents to the ED with shortness of breath at rest. He is having trouble with conversation. He used 4 puffs of albuterol MDI at home with no resolution of symptoms. His FEV (_1) is checked, and it is 38% of predicted. Which is the best initial therapy for him in the ED, in addition to oxygen?</td>
</tr>
<tr>
<td>A. Oxygen alone is sufficient.</td>
</tr>
<tr>
<td>B. Give inhaled albuterol MDI 8 puffs every 20 minutes for 1 hour.</td>
</tr>
<tr>
<td>C. Give inhaled albuterol plus ipratropium by nebulizer every 20 minutes for 1 hour plus intravenous corticosteroids.</td>
</tr>
<tr>
<td>D. Give inhaled albuterol plus ipratropium by nebulizer every 20 minutes for 1 hour plus an OCS.</td>
</tr>
</tbody>
</table>
N. Vaccines: Adults with asthma (19–64 years of age) should receive
   1. The 23-valent pneumococcal polysaccharide vaccine (PPSV23; Pneumovax) once, then follow U.S. Centers for Disease Control and Prevention (CDC) recommendations for pneumococcal vaccination at age 65 and older
   2. Influenza vaccine every fall or winter

O. Asthma in Pregnancy
   1. Asthma may worsen, improve, or stay the same during pregnancy.
   2. Asthma may increase the risk of perinatal mortality, hyperemesis, vaginal hemorrhage, preeclampsia, complicated labor, neonatal mortality, prematurity, and low-birth-weight infants, especially if uncontrolled. Risks are small and are not shown in all studies.
   3. Medications
      a. Preferred controller: Budesonide ICS (only category B ICS); however, if well controlled on other ICS before pregnancy, it may be continued.
      b. Preferred rescue: Albuterol
      c. LABAs are category C; less clinical experience. Use during pregnancy is reasonable if necessary for asthma control. Salmeterol is preferred LABA.
      d. LTMs have limited data; most data are with montelukast (category B), and the data for montelukast are reassuring. Considered an alternative therapy.
      e. Prednisone is category C; potential adverse effects in pregnancy are cleft palate, preeclampsia, gestational diabetes, low birth weight, and prematurity. However, few studies were of patients with asthma, and women might have been exposed to longer-term prednisone use. Prednisone should be used, if necessary, for acute exacerbations in pregnancy.

II. CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Guidelines:

A. Definition: COPD is a syndrome of chronic limitation in expiratory airflow encompassing emphysema and chronic bronchitis. Airflow obstruction may be accompanied by airway hyperresponsiveness and may be not be fully reversible.
   1. Chronic bronchitis consists of persistent cough plus sputum production for most days of 3 months in at least 2 consecutive years.
   2. Emphysema is abnormal permanent enlargement of the airspaces distal to the terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis.
B. Diagnosis and Assessment

1. The diagnosis of COPD is based on a history of exposure to risk factors and the presence of airflow limitation that is not fully reversible, with or without the presence of symptoms.
   a. Symptoms: Dyspnea (described by patients as “increased effort to breathe,” “heaviness,” “air hunger,” or “gasping”), poor exercise tolerance, chronic cough, sputum production, wheezing
   b. GOLD guidelines: Perform spirometry and consider COPD if a patient is older than 40 years and has any of the following:
      i. Dyspnea that is progressive (worsens over time), persistent (present every day), and worse with exercise or on exertion
      ii. Chronic cough that is present intermittently or every day; often present throughout the day; seldom only nocturnal. May be nonproductive
      iii. Chronic sputum production in any pattern
      iv. History of exposure to risk factors, especially tobacco smoke (most common risk factor), occupational dusts and chemicals, and smoke from home cooking and heating fuels
   c. American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society (ACP/ACCP/ATS/ERS) guidelines: The single best predictor of airflow obstruction is the presence of all three of the following:
      i. Smoking history of more than 55 pack-years
      ii. Wheezing on auscultation
      iii. Patient self-reported wheezing

2. For the diagnosis and assessment of COPD, spirometry is the gold standard.
   a. Spirometry showing an FEV/FVC less than 70% of predicted is the hallmark of COPD. Bronchodilator reversibility testing is no longer recommended.
   b. Measurement of arterial blood gas tension should be considered for all patients with FEV₁ less than 50% of predicted or clinical signs suggestive of respiratory failure or right heart failure.

3. Validated symptom scales or questionnaires
   a. Modified Medical Research Council (mMRC) breathlessness scale for assessing severity of breathlessness (Bestall et al. 1999)
   b. COPD Assessment Test (CAT) measures health status impairment in COPD (www.catestonline.org).

C. Factors Determining Severity of COPD

1. Severity of symptoms
2. Severity of airflow limitation (FEV₁)
3. Frequency of exacerbations
4. Presence of comorbidities that may restrict activity (e.g., heart failure, heart disease, musculoskeletal disorders)

D. Therapy Goals

1. Relieve symptoms.
2. Reduce the frequency and severity of exacerbations.
3. Improve exercise tolerance.
4. Improve health status.
5. Minimize adverse effects from treatment.

E. Management of Stable COPD

1. Description of levels of evidence or grades of recommendations
Table 10. Grades for Strength of Recommendations for COPD Guidelines

<table>
<thead>
<tr>
<th></th>
<th>GOLD Guidelines</th>
<th>ACP/ACC/ATS/ERS Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomized clinical trials</td>
<td>Strong (S): Benefits clearly outweigh risks and burden, or risks and burden clearly outweigh benefits</td>
</tr>
<tr>
<td></td>
<td>Rich body of data</td>
<td>Weak (W): Benefits finely balanced with risks and burden</td>
</tr>
<tr>
<td></td>
<td>Randomized clinical trials</td>
<td>Quality of evidence High (H)</td>
</tr>
<tr>
<td></td>
<td>Limited body of data</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nonrandomized trials</td>
<td>Moderate (M)</td>
</tr>
<tr>
<td></td>
<td>Observational studies</td>
<td>Low (L)</td>
</tr>
<tr>
<td></td>
<td>Panel judgment consensus</td>
<td></td>
</tr>
</tbody>
</table>

2. Existing medications for COPD have not been shown to modify the long-term decline in lung function, the hallmark of this disease (level of evidence A). Therefore, pharmacotherapy for COPD is used to decrease symptoms, complications, or both.

3. Smoking cessation is a critical component of COPD management.

4. Bronchodilator medications are central to the symptomatic management of COPD (level of evidence A).
   a. They are given on an as-needed basis or on a regular basis to prevent or reduce symptoms.
   b. The principal bronchodilator treatments are \( \beta_2 \)-agonists, anticholinergics, or a combination of these drugs. Theophylline is also a bronchodilator but is not recommended unless other long-term bronchodilators are unavailable or unaffordable.
   c. Inhaled therapy is preferred.
   d. The choice between a LABA, anticholinergic, theophylline, and combination therapy depends on availability and individual response in symptom relief and adverse effects.
   e. Regular treatment with a long-acting (LA) bronchodilator is more effective and convenient than regular treatment with SABAs (level of evidence A).
   f. Combining bronchodilators from different pharmacologic classes may improve efficacy with the same or fewer adverse effects compared with increasing the dose of a single bronchodilator (level of evidence A).
   g. Adding tiotropium to a LABA-ICS combination (triple therapy) improves lung function and health-related quality of life and reduces the number of exacerbations (level of evidence B). Retrospective data show decreased mortality, fewer hospital admissions, and fewer OCS bursts. All bronchodilators improve symptoms and exercise capacity.
   i. Treatment with an LA anticholinergic delays first exacerbation, reduces the overall number of COPD exacerbations and related hospitalizations, improves symptoms and health status (level of evidence A), and improves the effectiveness of pulmonary rehabilitation (level of evidence B). LA anticholinergics have no effect on the rate of decline of lung function. Initial studies with tiotropium showed elevated cardiovascular risk, but newer strong evidence shows no increase in risk. Anticholinergics may not significantly improve FEV\(_1\).
ii. LABAs improve health status, quality of life, and FEV, and decrease COPD exacerbation rate (level of evidence A). LABAs have no effect on mortality and rate of decline of lung function. Salmeterol reduces hospitalization rate (level of evidence B). Indacaterol significantly improves breathlessness, health status, and exacerbation rate (level of evidence B). Indacaterol is a LABA with a significantly greater bronchodilator effect than formoterol and salmeterol and a bronchodilator effect similar to that of tiotropium (level of evidence A). LABAs do not have the same potential safety concerns as with use in asthma.

iii. LA anticholinergic versus LABAs:
   (a) POET-COPD study: Tiotropium is more effective than salmeterol as initial LA bronchodilator therapy in moderate to very severe COPD regarding time to first exacerbation and annual number of exacerbations. (Vogelmeier et al. 2011)
   (b) Cochrane review concluded that tiotropium is more effective than LABAs in preventing COPD exacerbations and COPD-related hospitalization but not in overall hospitalization or mortality. Symptom and lung function improvement were similar. However, there are only a few studies. Fewer serious adverse events and withdrawals from studies occurred with tiotropium versus LABAs (Chong et al. 2012).

5. ICSs in stable COPD
   a. ICSs improve symptoms, lung function, and quality of life and decrease the frequency of exacerbations in patients with FEV, less than 60% of predicted; they do not modify the progressive decline in FEV, or decrease mortality (level of evidence A).
   b. The dose response with ICS in COPD is unknown (in contrast to asthma treatment). Moderate to high doses have been used in COPD clinical trials.
   c. An ICS combined with a LABA is more effective than the individual components (level of evidence A). An ICS/LABA combination reduces the rate of decline of FEV, and reduces the exacerbation rate; the reduction in mortality compared with placebo fell just short of statistical significance (relative risk reduction 17.5%; absolute risk reduction 2.6%; adjusted p=0.052) (Calverley et al. 2007). A subsequent meta-analysis showed that ICS/LABA might reduce mortality (number needed to treat was 36) (level of evidence B) (Nannini et al. 2007).
   d. ICS use is associated with an increased incidence of pneumonia in COPD (Singh et al. 2009; Ernst et al. 2007).
   e. Long-term monotherapy with ICSs is not recommended; they are less effective than ICS/LABA combination.
   f. Long-term treatment with ICSs should not be used outside their indications because of the risk of pneumonia and possible increased risk of fractures after long-term exposure.
   g. Chronic treatment with OCSs should be avoided because of an unfavorable benefit-risk ratio (level of evidence A).

6. Patient assessment and selection of therapy
   a. GOLD guidelines combine symptoms (based on symptom scores), airflow limitation (based on postbronchodilator FEV,), and frequency of exacerbations to determine patient risk group and recommended treatment.
   b. ACP/ACCP/ATS/ERS guidelines simplify treatment even further on the basis of FEV, in patients with COPD with symptoms. They do not provide detailed treatment guidelines.
### Table 11. GOLD Guidelines: Assessment of COPD Severity and Risk

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Characteristic</th>
<th>Spirometric GOLD Classification*</th>
<th>Exacerbations per Yeara</th>
<th>Symptom Scoreb</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low risk</td>
<td>Fewer symptoms</td>
<td>GOLD 1: Mild (FEV₁ ≥80% of predicted) or GOLD 2: Moderate (50% ≤ FEV₁ &lt;80% of predicted)</td>
<td>≤1 and no hospitalization</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Low risk</td>
<td>More symptoms</td>
<td>GOLD 1: Mild (FEV₁ ≥80% of predicted) or GOLD 2: Moderate (50% ≤ FEV₁ &lt;80% of predicted)</td>
<td>≤1 and no hospitalization</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>High risk</td>
<td>Fewer symptoms</td>
<td>GOLD 3: Severe (30% ≤ FEV₁ &lt; 50% of predicted) or GOLD 4: Very severe (FEV₁ &lt;30% of predicted)</td>
<td>≥2 or ≥1 with hospitalization</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>High risk</td>
<td>More symptoms</td>
<td>GOLD 3: Severe (30% ≤ FEV₁ &lt; 50% of predicted) or GOLD 4: Very severe (FEV₁ &lt;30% of predicted)</td>
<td>≥2 or ≥1 with hospitalization</td>
</tr>
</tbody>
</table>

*Postbronchodilator FEV₁ should be used. To determine the risk of exacerbation, either the spirometric GOLD classification or the number of exacerbations per year can be used. If they are both used and the patient would fall into two different categories, always assign patient to the category with the highest risk and symptoms.

*aCAT score is preferred, but any can be used.

CAT = COPD Assessment Test (validated questionnaire); COPD = chronic obstructive pulmonary disease; FEV₁ = forced expiratory volume in 1 second; GOLD = Global Initiative for Chronic Obstructive Lung Disease; mMRC = Modified Medical Research Council breathlessness scale (validated questionnaire).

Table 12. GOLD Guidelines: Pharmacotherapy for Stable COPD

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Recommended First Choice</th>
<th>Alternative Choice</th>
<th>Other Possible Treatments$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SA anticholinergic PRN or SABA PRN</td>
<td>LA anticholinergic or LABA or SABA + SA anticholinergic</td>
<td>Theophylline$^b$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>LA anticholinergic or LABA</td>
<td>LA anticholinergic + LABA</td>
<td>SABA and/or SA anticholinergic Theophylline$^b$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LA anticholinergic</td>
<td>LA anticholinergic + LABA or LA anticholinergic + PDE-4 inhibitor$^c$ or LABA + PDE-4 inhibitor$^c$</td>
<td>SABA and/or SA anticholinergic Theophylline$^b$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA and/or LA anticholinergic</td>
<td>ICS + LABA + LA anticholinergic or ICS + LABA + PDE-4 inhibitor$^c$ or LA anticholinergic + LABA or LA anticholinergic + PDE-4 inhibitor$^c$</td>
<td>SABA and/or SA anticholinergic Theophylline$^b$</td>
</tr>
</tbody>
</table>

Note: All medication choices are listed in alphabetical order and are not necessarily in order of preference.

$^a$Medications in third column (other possible treatments) can be used alone or in combination with first- and alternative-choice columns.

$^b$Theophylline is not recommended unless other long-term bronchodilators are unavailable or unaffordable.

$^c$If patient has chronic bronchitis.

COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; ICS = inhaled corticosteroid; LA = long-acting; LABA = long-acting $\beta_2$-agonist; PDE-4 = phosphodiesterase type-4; PRN = as needed; SA = short-acting; SABA = short-acting $\beta_2$-agonist.

Table 13. ACP/ACCP/ATS/ERS Guidelines: Treatment Recommendations for Stable COPD

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>For patients with respiratory symptoms and FEV₁ between 60% and 80% of predicted, treatment with LA inhaled bronchodilators is suggested.</td>
<td>W</td>
<td>L</td>
</tr>
<tr>
<td>For patients with respiratory symptoms and FEV₁ &lt;60% of predicted, treatment with LA inhaled bronchodilators is recommended.</td>
<td>S</td>
<td>M</td>
</tr>
<tr>
<td>Monotherapy using either LA inhaled anticholinergics or LABAs is recommended for symptomatic patients with FEV₁ &lt;60% of predicted. The choice of specific monotherapy should be based on patient preference, cost, and adverse effect profile.</td>
<td>S</td>
<td>M</td>
</tr>
<tr>
<td>Combination inhaled therapies (LA inhaled anticholinergics, LABAs, or ICS) may be used for symptomatic patients with FEV₁ &lt;60% of predicted.</td>
<td>W</td>
<td>M</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease; FEV₁ = forced expiratory volume in 1 second; ICS = inhaled corticosteroid; LA = long-acting; LABA = long-acting β-agonist.


7. Other pharmacologic treatments
   a. Phosphodiesterase-4 inhibitor: Roflumilast (Daliresp)
      i. Indication: As a daily treatment to reduce the risk of COPD exacerbations in patients with severe COPD (FEV₁, less than 50% of predicted) associated with chronic bronchitis and a history of frequent exacerbations. In these patients, studies show a reduction in exacerbations and a reduction in the composite end point of moderate exacerbations treated with oral or systemic corticosteroids or severe exacerbations requiring hospitalization or causing death (level of evidence B). These effects also occur when roflumilast is added to LA bronchodilators (level of evidence B). No trials have assessed the effects of roflumilast on COPD exacerbations when added to an ICS-LA bronchodilator combination. No comparison of adding roflumilast versus ICS to LA bronchodilators is available (currently being studied).
      ii. Mechanism: Reduces inflammation through inhibition of the breakdown of intracellular cyclic adenosine monophosphate; no direct bronchodilator activity.
      iii. Dose: 500 mcg orally once daily
      iv. Contraindications: Moderate to severe liver impairment; use in nursing mothers
      v. Precautions: Weight loss (monitor); psychiatric events including suicidality (monitor; weigh risk-benefit ratio in patients with preexisting psychiatric illness). Twenty percent of patients studied had weight loss of 5%-10% of body weight compared with 7% with placebo; average weight loss was 2 kg.
      vi. Adverse reactions: Diarrhea, weight loss or decreased appetite, nausea, headache, back pain, influenza, insomnia, and dizziness
      vii. Drug interactions: Use with strong cytochrome P450 (CYP) enzyme inducers is not recommended (e.g., rifampin, phenobarbital, carbamazepine, phenytoin); use with CYP3A4 inhibitors or dual inhibitors of CYP3A4 and CYP1A2 (e.g., erythromycin, ketoconazole, fluvoxamine) increases roflumilast exposure and adverse effects (risk-benefit ratio must be weighed).
   b. Smoking cessation therapy (essential for all patient groups A–D)
   c. Influenza vaccine annually (essential for all patient groups A–D)
d. The 23-valent pneumococcal polysaccharide vaccine (PPSV23; Pneumovax) once before age 65, then follow CDC recommendations for pneumococcal vaccination at age 65 and older.

e. α1-Antitrypsin augmentation therapy (level of evidence C)
   i. For young patients with severe hereditary α1-antitrypsin deficiency and established emphysema, but an expensive treatment
   ii. Patients with α1-antitrypsin deficiency usually are white, usually develop COPD at a young age (younger than 45 years), and have a strong family history. It may be worthwhile to screen such patients.

Patient Cases

6. A 62-year-old man was recently diagnosed with COPD. Spirometry shows he has an FEV1/FVC 60%, prebronchodilator FEV1 70% of predicted, and postbronchodilator FEV1 72% of predicted. His symptoms are very bothersome. He reports walking more slowly than others because of shortness of breath and having to stop to catch his breath every so often when walking on level ground (mMRC grade 2). He had one exacerbation in the past year. Which is the most appropriate patient group classification for him, according to the GOLD guidelines?
   A. Patient group A.
   B. Patient group B.
   C. Patient group C.
   D. Patient group D.

7. In addition to albuterol HFA 2 puffs every 4–6 hours as needed, which pharmacotherapy option is most appropriate to initiate?
   A. No additional therapy needed.
   B. Formoterol: Inhale contents of 1 capsule twice daily.
   C. Salmeterol/fluticasone 50/500 1 puff twice daily.
   D. Salmeterol/fluticasone 50/500 1 puff twice daily plus roflumilast 500 mcg orally once daily.

8. A 52-year-old woman with COPD reports a gradual worsening in shortness of breath during the past few years. Spirometry shows FEV1/FVC 55% and FEV1 63% of predicted. Her CAT score is 10. She has not had a COPD exacerbation or received systemic corticosteroids in the past 2 years. Her current COPD medications are tiotropium inhaler once daily and albuterol HFA as needed. According to the GOLD guidelines, which is the most appropriate course of action?
   A. Add salmeterol 1 puff twice daily.
   B. Add long-term azithromycin 250 mg once daily.
   C. Add fluticasone 110 mcg 2 puffs twice daily.
   D. Discontinue tiotropium and initiate salmeterol/fluticasone 250/50 1 puff twice daily.
8. Nonpharmacologic therapy
   a. Home oxygen therapy
      i. Recommended in patients who have a PaO₂ of 55 mm Hg or less (or 55–60 mm Hg if pulmonary hypertension, peripheral edema, or polycythemia [level of evidence D]) or SaO₂ of 88% or less, with or without hypercapnia, confirmed twice during a 3-week period (level of evidence B)
      ii. Long-term (more than 15 hours/day) use in patients with chronic respiratory failure improves survival.
   b. Pulmonary rehabilitation (essential for patient groups B–D; level of evidence A)
      i. Includes exercise training, nutrition counseling, and education
      ii. Recommended for stage II–IV COPD. Patients should be referred when they have moderate (stage II) COPD; not wait until it is more severe.
      iii. Improves many outcomes in COPD, including quality of life and survival.

9. Newer data in COPD
   a. Chronic azithromycin for prevention of COPD exacerbations (Albert et al. 2011)
      i. Compared with placebo, daily azithromycin significantly lengthened time to first exacerbation, decreased rate of exacerbations, and improved quality of life in patients with COPD at increased risk of exacerbations, at the expense of risk of hearing decrements and increasing macrolide-resistant organism colonization.
      ii. Number needed to treat to prevent one acute exacerbation of COPD is 2.86; number needed to harm for hearing decrements is 20.
      iii. The GOLD guidelines state that the role of treatment with daily antibiotics is unclear and that treatment is currently not recommended because of an unfavorable balance between benefits and adverse effects.
   b. β-Blockers
      i. Observational data suggest that long-term treatment with β-blockers reduces risk of exacerbations and improves survival, even in patients without overt cardiovascular disease (Rutten et al. 2010).
      ii. More than half of the patients studied had cardiovascular risk factors or coronary artery disease. Mostly cardioselective β-blockers were used.
      iii. It is too early to recommend β-blockers for the treatment of COPD, but β-blockers should not be withheld in patients with COPD who also have heart disease, chronic heart failure, or other cardiovascular conditions in which β-blockers are beneficial (Salpeter 2002, update 2005, reviewed 2008)
      iv. Mechanism for benefit in COPD is unknown, but β-blockers can upregulate β₂-receptors in the lungs, which may improve the effectiveness of inhaled β-agonists.

F. Management of Acute Exacerbations of Chronic COPD
   1. A COPD exacerbation is an acute worsening of a patient’s baseline respiratory symptoms (e.g., dyspnea, cough, and/or an increase in quantity or purulence of sputum) that is worse than normal day-to-day variation and results in a change in medication. Diagnosis is based purely on clinical presentation.
   2. Common precipitating factors include infection of tracheobronchial tree and viral upper respiratory tract infections (most common) and air pollution. However, the cause of one-third of exacerbations cannot be determined.
   3. Spirometry is not accurate during an exacerbation and is not recommended.
   4. Pulse oximetry can be used to determine the need for supplemental oxygen, which should be given in severe exacerbations. In exacerbations requiring hospitalization, an arterial blood gas measurement should be performed.
5. Inhaled bronchodilators (inhaled SABAs with or without short-acting anticholinergics) are the preferred treatment of COPD exacerbations (level of evidence C).
   a. Usual doses of albuterol are 2.5 mg via nebulizer every 1–4 hours as needed or 4–8 puffs by MDI with holding chamber every 1–4 hours as needed.
   b. Short-acting anticholinergics (ipratropium) are generally added for acute exacerbation.
6. Systemic corticosteroids are effective, and they shorten recovery time, improve FEV₁, and improve hypoxemia (level of evidence A). They also lower the risk of treatment failure, early relapse rate, and length of hospital stay. Systemic corticosteroids should be used in most exacerbations. OCS dose for outpatient treatment: 40 mg of oral prednisone once daily for 5 days is recommended in the GOLD guidelines (level of evidence B), but insufficient data are available to provide strong conclusions about the optimal duration.
   a. Higher daily doses or oral prednisone/prednisolone may be used (e.g., 50–60 mg daily).
   b. A recent study showed that in patients with a COPD exacerbation presenting to the hospital, a shorter course of systemic corticosteroids (5 days) was noninferior to a longer (14 days) course with respect to re-exacerbation within 6 months (Leuppi et al. 2013).
7. Antibiotic treatment should be initiated for exacerbations if the criteria below are met. The most common pathogens in COPD exacerbations: *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. In patients with GOLD 3 and 4 severity, *Pseudomonas aeruginosa* infection becomes an important pathogen.
   a. The three cardinal symptoms in COPD exacerbations are increased dyspnea, increased sputum volume, and increased sputum purulence.
      i. Antibiotics should be given if all three cardinal symptoms are present (level of evidence B).
      ii. Antibiotics should be given if two of the three cardinal symptoms are present and if increased sputum purulence is one of the symptoms (level of evidence C).
      iii. Antibiotics should be given to patients with a severe exacerbation requiring mechanical ventilation (level of evidence B).
   b. Recommended duration of antibiotic treatment is usually 5–10 days (level of evidence D).
   c. Recommended antibiotics
      i. Optimal antibiotic therapy has not been determined but should be based on local resistance patterns.
      ii. If recent (less than 3 months) antibiotics, use alternative class.
      iii. Usual initial antibiotics for uncomplicated COPD include azithromycin, clarithromycin, doxycycline, trimethoprim/sulfamethoxazole, and amoxicillin, with or without clavulanate.
      iv. In complicated COPD with risk factors: Amoxicillin/clavulanate, levofloxacin, moxifloxacin.
         Risk factors: Comorbid diseases, severe COPD (FEV₁ less than 50% of predicted), more than 3 exacerbations/year, antibiotic use in past 3 months
      v. If at risk of *Pseudomonas* infection: High-dose levofloxacin (750 mg) or ciprofloxacin; obtain sputum culture. Risk factors: Four or more courses of antibiotics in past year, recent hospitalization (past 90 days), isolation of *Pseudomonas* during past hospitalization, severe COPD (FEV₁ less than 50% of predicted)
      vi. If exacerbation does not respond to initial antibiotic, sputum culture and sensitivity should be performed.
G. Vaccinations: All patients with COPD should receive the influenza vaccine yearly and the polysaccharide pneumococcal vaccine once before age 65; then a one-time revaccination 5 years or more after the first vaccination.
**Patient Case**

9. A 64-year-old woman with COPD in GOLD patient group A presents for a clinic visit. In the past few days, she has had a worsening in shortness of breath and a productive cough with more “cloudy” and more copious sputum than usual. Pulse oximetry is 95% on room air. She has a nebulizer at home. In addition to regular use of albuterol plus ipratropium by nebulizer every 1–4 hours, which is the best course of action?

A. No additional therapy is necessary.
B. Add oral prednisone 40 mg once daily for 5 days
C. Add trimethoprim/sulfamethoxazole double-strength 1 tablet twice daily for 7 days.
D. Add oral prednisone 40 mg once daily for 5 days and trimethoprim/sulfamethoxazole double strength 1 tablet twice daily for 7 days.

**III. GOUT**

**Guidelines:**


A. Definition: A spectrum of clinic and pathologic features caused by hyperuricemia (serum urate level more than 6.8 mg/dL), resulting in tissue deposition of monosodium urate monohydrate crystals in the extracellular fluid of joints and other sites. Most common rheumatic disease of adults; prevalence estimated at 3.9% of adults (around 8.3 million people)

B. Diagnosis
1. Typically presents as acute episodic arthritis.
2. Can also present as chronic arthritis of one or more joints.
3. Tophi may be present: Detected by physical examination or imaging and pathology.
4. Renal manifestations include urolithiasis.
5. Features of acute gouty attack
   a. Severe pain, redness, swelling; maximum severity in 12–24 hours; may continue for a few days to several weeks.
   b. Most often occurs in the lower extremities and in a single joint.
      i. Most common joint: First metatarsophalangeal joint (podagra) or knee
      ii. May occur in many other joints, including upper extremity.
      iii. May be polyarticular at first presentation (less than 20% of cases).
6. Ideally, definitive diagnosis should be made by visualization of monosodium urate crystals by polarized compensated light microscopy in fluid aspirated from the affected joint during an acute gouty attack.
   a. For diagnosis of gout, monosodium urate crystals are negatively birefringent (needle-shaped or rods).
   b. In pseudogout, crystals are calcium pyrophosphate dihydrate and are weakly positively birefringent (rods or rhomboidal).
c. Diagnosis by joint aspiration is difficult because patients are in severe pain and often refuse joint aspiration during an acute attack. In this case, a provisional diagnosis may be made according to clinical data.

7. If diagnosis by joint aspiration is not possible, a tentative diagnosis may be made by a combination of presentation or clinical picture and elevated uric acid. Use of hyperuricemia as one of the criteria for diagnosing gout may be difficult during an initial acute attack because serum uric acid may be low during flares. Best time to check uric acid is 2 weeks after a flare.

C. Predisposing Factors (Singh et al. 2011)
1. Dietary: High meat and seafood consumption, fatty foods, dietary overindulgence, high intake of beer and spirits in men (not wine), sugar-sweetened soft drinks, high-fructose foods
2. Drugs: Xanthine oxidase inhibitors (XOIs) and uricosuric agents (with initial therapy), thiazides and loop diuretics, niacin, calcineurin inhibitors, low-dose aspirin (325 mg/day or less)
3. Medical conditions and other factors: Obesity, diabetes, hypertension, dyslipidemia, renal insufficiency, early menopause, trauma, surgery, starvation, dehydration

D. Classification
1. Three stages of gout:
   a. Acute gouty arthritis
   b. Intercritical gout
   c. Chronic recurrent gout
2. Severities of chronic tophaceous gouty arthropathy (CTGA)
   a. Mild: One joint, stable disease
   b. Moderate: Two to four joints, stable disease
   c. Severe
      i. Chronic CTGA of more than four joints OR
      ii. One or more unstable, complicated, severe articular tophi
3. Size of joints
   a. Large joints (e.g., knee, ankle, wrist, elbow, hip, shoulder)
   b. Medium joints (e.g., wrist, ankle, elbow)
   c. Small joints (e.g., interphalangeal)

E. Treatment Goals
1. Serum urate target: Minimum is less than 6 mg/dL.
2. Serum urate target of less than 5 mg/dL may be needed to improve gout signs and symptoms. Consider goal of less than 5 mg/dL if tophi present.
3. Decrease frequency of acute gouty attacks.
F. Nonpharmacologic Therapy

Table 14. Nonpharmacologic Therapy for Gout

<table>
<thead>
<tr>
<th>Lifestyle and General Health</th>
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<tbody>
<tr>
<td>Weight loss if obese</td>
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<tr>
<td>Healthy overall diet</td>
</tr>
<tr>
<td>Exercise</td>
</tr>
<tr>
<td>Smoking cessation</td>
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<tr>
<td>Proper hydration</td>
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</tbody>
</table>

| Organ meats high in purine (e.g., liver, kidney, sweetbreads) | Serving sizes of: Beef, lamb, pork Seafood with high purine content (e.g., sardines, shellfish) | Low-fat or nonfat dairy products |
| High-fructose corn syrup–sweetened sodas, other beverages, foods | Servings of naturally sweet fruit juices Table sugar, sweetened beverages, desserts | Vegetables |
| Alcohol overuse (>2 per day for men and >1 per day for women) in all patients with gout | Alcohol (particularly beer but also wine and spirits) in all patients with gout |
| Any alcohol use in gout during times of frequent gouty attacks or advanced gout under poor control |


G. Pharmacologic Treatment of Hyperuricemia

1. Consider discontinuing nonessential medications that cause hyperuricemia.
2. Indications for urate-lowering therapy (ULT):
   a. Tophi by clinical examination or imaging study
   b. Two or more acute gouty attacks per year
   c. CKD stage 2 or worse
   d. Past urolithiasis
3. ULT can be initiated during an acute gouty attack as long as concomitant anti-inflammatory therapy is given.
4. First-line ULT:
   a. XOI: Allopurinol or febuxostat
   b. Can switch to alternative XOI if patient is intolerant of or refractory to first XOI.
5. Alternative first-line ULT (uricosuric): Probenecid (if at least one XOI is contraindicated or not tolerated). History of urolithiasis and CrCl less than 50 mL/minute contraindicates first-line use of probenecid.
6. Initiate anti-inflammatory prophylaxis for acute gout concomitantly with or just before ULT in all patients.
   a. Early increase in acute gouty attacks during initiation of ULT
      i. May be caused by rapid decrease in urate concentrations, resulting in remodeling of articular urate crystal deposits
      ii. Often leads to nonadherence to ULT; patient education is critical.
   b. Oral low-dose colchicine is first-line option.
   c. Other first-line option is low-dose nonsteroidal anti-inflammatory drugs (NSAIDs) (lower evidence grade than colchicine). Add concomitant proton pump inhibitor or other agent for suppression of peptic ulcer disease when indicated.
   d. OCS is an alternative for anti-inflammatory gouty attack prophylaxis (level of evidence C).
      i. If colchicine and NSAIDs are contraindicated, not tolerated, or ineffective
      ii. Because of risks associated with prolonged use of OCSs, the risk-benefit ratio of this strategy should be considered and reevaluated with continued ULT therapy because the risk of acute gout decreases in time.
   e. Anti-inflammatory prophylaxis of acute gout should continue for the greater of:
      i. 6 months (level of evidence A)
      ii. 3 months after achieving target serum urate level if no tophi (level of evidence B)
      iii. 6 months after achieving target serum urate level if tophi were previously present but are now resolved (level of evidence C)
      iv. However, continue anti-inflammatory prophylaxis if any clinical evidence of gout disease activity is present (tophi, recent acute gouty attacks, chronic gouty arthritis).

7. Monitor serum urate every 2–5 weeks. After goal is achieved, continue monitoring every 6 months. If serum urate goals are not achieved:
   a. Titrate single-agent XOI to maximum appropriate dose.
   b. Next, add uricosuric to XOI (probenecid, losartan, or fenofibrate). Probenecid is first-line uricosuric; losartan and fenofibrate are off-label but recommended second-line uricosurics.
   c. If goal serum urate still not achieved, add pegloticase only if severe gout disease burden and patient is refractory to or intolerant of other ULT options. Pegloticase is not recommended for first-line therapy in any case.

8. Indefinite duration of ULT is recommended.

9. Allopurinol hypersensitivity syndrome (AHS)
   a. Risk of severe morbidity and hospitalization
   b. Mortality rate of 20%–25% in AHS
   c. Manifestations of AHS: Stevens-Johnson syndrome, toxic epidermal necrolysis, clinical constellation of symptoms: eosinophilia, rash, vasculitis, major end-organ disease
   d. Highest risk is during the first few months of therapy.
   e. Risk factors: Concomitant thiazide diuretics, renal impairment, people of Han Chinese or Thai descent (irrespective of renal function), people of Korean descent with stage 3 or worse CKD. Consider testing for HLA-B*5801 in these ethnic groups (if positive, higher risk of AHS).

H. Treatment of Acute Gout
1. Assess severity of gouty attack (Table 15) and select treatment according to severity.
2. Initiate pharmacologic treatment within 24 hours of onset of acute gouty attack. Colchicine is appropriate only if initiated within 36 hours of attack onset.
3. Continue established ULT without interruption during acute gouty attack (do not discontinue ULT).
Table 15. Severity, Duration, and Extent of Acute Gouty Attacks

<table>
<thead>
<tr>
<th>Severity</th>
<th>Duration Since Onset</th>
<th>Extent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>≤4</td>
<td>One or a few small joints</td>
</tr>
<tr>
<td>Moderate</td>
<td>5–6</td>
<td>One or two large joints</td>
</tr>
<tr>
<td>Severe</td>
<td>≥7</td>
<td>Polyarticular</td>
</tr>
</tbody>
</table>

(a) For mild to moderate pain affecting one or a few small joints or one or two large joints, use monotherapy.

(b) For severe pain or polyarticular attack, or if multiple large joints are affected, use initial combination therapy.

i. Monotherapy: NSAID or OCSs or colchicine (level of evidence A for all choices), supplemented with topical ice (adjunctive therapy) as needed
   (a) No preference for one choice over another; select treatment according to gout flare presentation, comorbidities, previous response, and patient preference.
      (1) Consider intra-articular corticosteroids if one or two large joints; use OCSs for all other presentations; may consider single-dose intramuscular triamcinolone followed by an OCS.
      (2) Concomitant use of colchicine with P-glycoprotein (Pgp) inhibitors or strong CYP3A4 inhibitors is contraindicated in renal or hepatic impairment (fatal toxicity has occurred).
      (3) Colchicine dose should be reduced if normal renal or hepatic function and concomitant use of Pgp inhibitors or moderate to strong CYP3A4 inhibitors.
      (4) If the patient has received acute gout treatment with colchicine in the past 2 weeks, use alternative therapy.
      (5) Colchicine should not be used to treat gouty attacks in patients with renal or hepatic impairment who are taking prophylactic colchicine, according to labeling.
   (b) Celecoxib is an option in certain patients with contraindications or intolerance to NSAIDs; risk-benefit ratio unclear.
   (c) Adrenocorticotropic hormone 20–40 international units subcutaneously is an option if patient is taking nothing by mouth.

ii. Initial combination therapy: Can use full doses of both agents or, when appropriate, full dose of one agent and prophylactic dose of another agent
   (a) Colchicine plus an NSAID
   (b) OCSs plus colchicine
(c) Intra-articular steroids with all other modalities
(d) Combination of an NSAID and systemic corticosteroids has synergistic GI toxicity.

iii. Continue acute treatment until the gouty attack has resolved.

4. If inadequate response to initial treatment of acute gouty attack:
   a. Inadequate response defined as either less than 20% improvement in pain score in 24 hours or less than 50% improvement in 24 hours or more after starting drug therapy for acute attack.
   b. If inadequate response, switch to a different monotherapy (level of evidence C) or add a second agent (level of evidence C).
   c. Biologic agents that inhibit interleukin-1 (anakinra and canakinumab) are considered investigational for the treatment of acute gout but can be considered when gout flares are frequent and resistant to all other therapies.

5. Educate patients and provide a prescription so that patients can initiate treatment for acute gouty attacks on their own.

### Table 16. Medication Dosing for Gout

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
</table>
| **Colchicine** (Colcrys) | 1.2 mg; then 0.6 mg 1 hour later; then 0.6 mg once or twice daily until attack resolves  
CrCl 30–80 mL/minute: Monitor for adverse effects; dose adjustment not necessary  
CrCl <30 mL/minute: Dose adjustment not necessary but may be considered; do not repeat course of treatment more than every 2 weeks  
Dialysis: 0.6-mg single dose; do not repeat course of treatment more than every 2 weeks  
Severe hepatic impairment: Dose reduction not required but may be considered; do not repeat course of treatment more frequently than every 2 weeks | Concomitant use of colchicine with Pgp inhibitors or strong CYP3A4 inhibitors is contraindicated in renal or hepatic impairment (fatal toxicity has occurred)  
Colchicine dose should be reduced if renal and hepatic function is normal and if used concomitantly with Pgp inhibitors or moderate to strong CYP3A4 inhibitors |
| **NSAIDs**            | Naproxen: 750 mg initially, followed by 250 mg every 8 hours  
Naproxen ER: 1000–1500 mg once daily, followed by 1000 mg once daily  
Indomethacin: 50 mg 3 times daily until pain tolerable, then reduce dose until attack resolves  
Sulindac: 200 mg twice daily  
Use at anti-inflammatory/analgesic doses of other NSAIDs, same as for treatment of acute pain or inflammation | Only FDA-approved NSAIDs are naproxen, indomethacin, and sulindac; however, other NSAIDs may be as effective  
Continue full dose until attack completely resolves  
Can taper dose if comorbidities or renal or hepatic impairment is present |
| **Celecoxib** (Celebrex) | 800 mg once, followed by 400 mg on day 1, then 400 mg twice daily for 1 week | Only in certain patients when NSAIDs are contraindicated or not tolerated |
### Table 16. Medication Dosing for Gout (continued)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute Gouty Attack Treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>OCSs for all cases of gout (level of evidence B)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prednisone 0.5 mg/kg per day for 5–10 days (level of evidence A) OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prednisone 0.5 mg/kg per day for 2–5 days, then taper for 7–10 days, then discontinue (level of evidence C) OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Methylprednisolone dose pack (level of evidence C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Option for 1 or 2 large joints: Intra-articular corticosteroids (level of evidence B)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dose based on the size of the joint (e.g., triamcinolone 40 mg for large joint, 30 mg for medium joint, 10 mg for small joint or equivalent)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IM triamcinolone followed by OCS (level of evidence C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 mg IM, followed by OCS (dosed as above)</td>
<td></td>
</tr>
<tr>
<td><strong>Urate-Lowering Therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allopurinol (Zyloprim)(a)</td>
<td>Starting dose: 100 mg daily (50 mg daily in stage 4 CKD)</td>
<td>XOI</td>
</tr>
<tr>
<td></td>
<td>Gradually titrate dose every 2–5 weeks to appropriate maximum dose (800 mg daily with normal renal function) or until goal urate level reached</td>
<td>Low starting dose reduces early gout flares and risk of hypersensitivity syndrome</td>
</tr>
<tr>
<td></td>
<td>Maintenance dose can be higher than 300 mg daily, even in CKD, as long as patient is educated and regular monitoring occurs for hypersensitivity, rash, pruritus, elevated hepatic enzymes, and eosinophilia</td>
<td>Consider keeping dose lower in CKD and not increasing to maximum dose; data with dosing &gt;300 mg/day in CKD are limited</td>
</tr>
<tr>
<td>Febuxostat (Uloric)(a)</td>
<td>Starting dose: 40 mg once daily</td>
<td>XOI</td>
</tr>
<tr>
<td></td>
<td>May increase dose to 80 mg once daily if goal serum urate not reached</td>
<td>More expensive than allopurinol; no generic available</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt;30 mL/minute: Use caution; insufficient data</td>
<td></td>
</tr>
<tr>
<td>Probenecid (generic only)(a)</td>
<td>Starting dose: 250 mg twice daily</td>
<td>XOI</td>
</tr>
<tr>
<td></td>
<td>May increase weekly in 500-mg/day increments to maximum dose of 1 g twice daily if needed</td>
<td>Uricosuric; first-line</td>
</tr>
<tr>
<td></td>
<td>Avoid if CrCl &lt; 30 mL/minute</td>
<td></td>
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</tbody>
</table>

### Notes
- OCS: Oral Corticosteroids
- XOI: Xanthine Oxypurine Inhibitor
- CRCl: Creatinine Clearance
- NSAID: Nonsteroidal Anti-Inflammatory Drug
- Uricosuric: Increases uric acid excretion

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**Table 16. Medication Dosing for Gout (continued)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urate-Lowering Therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Losartan</td>
<td>Dose according to other indications and as tolerated</td>
<td>Uricosuric; second-line</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Off-label use</td>
</tr>
<tr>
<td>Fenofibrate</td>
<td>Dose according to other indications and as tolerated</td>
<td>Uricosuric; second line</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Off-label use</td>
</tr>
<tr>
<td>Pegloticase (Krystexxa)*</td>
<td>8 mg intravenously every 2 weeks</td>
<td>Use only if severe gout disease burden and refractory to or intolerant of other ULT options</td>
</tr>
<tr>
<td></td>
<td>No dosage adjustment for CKD</td>
<td>All other antihyperuricemic agents must be discontinued before initiating pegloticase; do not administer concomitantly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Premedicate with antihistamines and corticosteroids</td>
</tr>
<tr>
<td><strong>Gouty Attack Prophylaxis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colchicine (Colcrys)</td>
<td>0.6 mg once or twice daily</td>
<td>First-line</td>
</tr>
<tr>
<td></td>
<td>CrCl 30–80 mL/minute: Monitor for adverse effects; dose adjustment not required</td>
<td>Concomitant use of colchicine with Pgp inhibitors or strong CYP3A4 inhibitors is contraindicated in renal or hepatic impairment (fatal toxicity has occurred)</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt;30 mL/minute: Initial dose 0.3 mg/day; use caution and monitor if dose titrated further</td>
<td>Colchicine dose should be reduced if renal and hepatic function is normal and if used concomitantly with Pgp inhibitors or moderate to strong CYP3A4 inhibitors</td>
</tr>
<tr>
<td></td>
<td>Dialysis: 0.3 mg twice weekly; monitor for adverse effects</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Severe hepatic impairment: Dose reduction not required necessary but may be considered; do not repeat course of treatment more often than every 2 weeks</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Lower doses than used for acute attacks (e.g., naproxen 250 mg twice daily, indomethacin 25 mg twice daily)</td>
<td>Alternative first-line; less strong evidence than with colchicine</td>
</tr>
<tr>
<td>OCSs</td>
<td>Prednisone or prednisolone ≤10 mg daily</td>
<td>Alternative</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Only if colchicine and NSAIDs are both contraindicated, ineffective, or not tolerated</td>
</tr>
</tbody>
</table>

*Always initiate concomitant prophylactic therapy.

ACR = American College of Rheumatology; CKD = chronic kidney disease; CrCl = creatinine clearance; CYP = cytochrome P450; ER = extended release; FDA = U.S. Food and Drug Administration; IM = intramuscular(ly); NSAID = nonsteroidal anti-inflammatory drug; OCS = oral corticosteroid; Pgp = P-glycoprotein; PUD = peptic ulcer disease; ULT = urate-lowering therapy; XOI = xanthine oxidase inhibitor.
### Patient Cases

10. A 60-year-old man presents with his third gouty attack in the past year. His last attack was 10 days ago, for which he took colchicine with good response. His pain is in his left knee and in the third and fourth proximal interphalangeal joints on his left hand. The pain started about 10 hours ago. He rates his pain as 6/10. He has COPD and dyslipidemia, his renal function is normal, and his weight is 80 kg. His uric acid level from 1 month ago is 10 mg/day. He has no tophi. His only medications are inhaled tiotropium, albuterol, and simvastatin. Which is most appropriate for treatment of this acute gouty attack?
   A. Naproxen 750 mg, then 250 mg every 8 hours.
   B. Colchicine 1.2 mg, then 0.6 mg in 1 hour, then 0.6 mg every 12 hours.
   C. Intra-articular triamcinolone injection of all affected joints.
   D. Prednisone 40 mg daily plus naproxen 750 mg, then 250 mg every 8 hours.

11. Which is most appropriate regarding ULT in this patient?
   A. Probenecid should be started, but treatment should be delayed until after the acute attack is resolved.
   B. Probenecid should be started and can be initiated during the acute attack.
   C. Allopurinol should be started, but treatment should be delayed after the acute attack has resolved.
   D. Allopurinol should be started and can be initiated during the acute attack.

12. Which regimen for anti-inflammatory prophylaxis with ULT therapy is most appropriate in this patient, once the acute attack has resolved?
   A. Colchicine 0.6 mg once daily.
   B. Prednisone 10 mg daily.
   C. Colchicine 0.6 mg once daily plus naproxen 250 mg twice daily.
   D. Pegloticase 8 mg intravenously every 2 weeks.

13. What is the initial goal uric acid level and duration of anti-inflammatory prophylaxis in this patient?
   A. Goal <6 mg/dL; continue for a total of 6 months.
   B. Goal <6 mg/dL; continue for 3 months after achieving goal serum urate for at least 6 months total.
   C. Goal <5 mg/dL; continue for a total of 6 months.
   D. Goal <5 mg/dL; continue for 3 months after achieving goal serum urate for at least 6 months total.
IV. ADULT IMMUNIZATIONS

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>AGE GROUP</th>
<th>IMMUNO-COMPROMISING CONDITIONS</th>
<th>HIV INFECTION CD4+ T-LYMPHOCYTE COUNT</th>
<th>INFECTIOUS DISEASES</th>
<th>CHRONIC DISEASES</th>
<th>ANEMIA</th>
<th>CHRONIC LIVER DIS</th>
<th>DIABETES</th>
<th>HEALTHCARE PERSONNEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>19-21 years</td>
<td>&lt;200 cells/μL</td>
<td>≥200 cells/μL</td>
<td>Persons with HIV/AIDS</td>
<td>Headache</td>
<td>Anti-HIV infection</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Tetanus, diphtheria, pertussis (Tdap)</td>
<td>22-26 years</td>
<td>3 doses</td>
<td>3 doses</td>
<td>3 doses through age 26 yrs</td>
<td>3 doses through age 26 yrs</td>
<td>3 doses through age 21 yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella</td>
<td>27-49 years</td>
<td>Contraindicated</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMR)</td>
<td>50-59 years</td>
<td>Contraindicated</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal 13-valent conjugate (PCV13)</td>
<td>≥ 65 years</td>
<td>Contraindicated</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSV23)</td>
<td>1 dose annually</td>
<td>Contraindicated</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>1 dose IIV annually</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1 dose IIV annually</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenza type b (Hib)</td>
<td>1 dose IIV annually</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Covered by the Vaccine Injury Compensation Program

Report all clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System (VAERS). Reporting forms and instructions on filing a VAERS report are available at www.vaers.hhs.gov or by telephone, 800-822-7967. Information on how to file a Vaccine Injury Compensation Program claim is available at www.hrsa.gov/vaccinecompensation or by telephone, 800-338-2382. To file a claim for vaccine injury, contact the U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington, D.C. 20000; telephone, 202-357-6400.

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

Figure 1. Recommended adult immunization schedule, by vaccine and age group. United States, 2015.


Figure 2. Vaccines that might be indicated for adults, based on medical and other indications. United States, 2015.

*The above recommendations must be read together with the footnotes on the following pages of this schedule.

Footnotes—Recommended Immunization Schedule for Adults Aged 19 Years or Older: United States, 2015

1. Additional information
   • Additional guidance for the use of the vaccines described in this supplement is available at www.cdc.gov/vaccines/hcp/acip-recs/index.html.
   • Information on vaccination recommendations when vaccination status is unknown and other general immunization information can be found in the General Recommendations on Immunization at www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm.
   • Information on travel vaccine requirements and recommendations (e.g., for hepatitis A and B, meningococcal, and other vaccines) is available at wwwnc.cdc.gov/travel/destinations/list.
   • Additional information and resources regarding vaccination of pregnant women can be found at www.cdc.gov/vaccines/adults/rec-vac/pregnant.html.

2. Influenza vaccination
   • Annual vaccination against influenza is recommended for all persons aged 6 months and older.
   • Persons aged 6 months or older, including pregnant women and persons with hives-only allergy to eggs can receive the inactivated influenza vaccine (IIV). An age-appropriate IV formulation should be used.
   • Adults aged 18 years or older can receive the recombinant influenza vaccine (RIV) (Flucelvax) or IIV.
   • Health care personnel who receive RIV should avoid providing care for severely immunocompromised persons who require care in a protected environment should receive IV or RIV; health care personnel who receive LAIV should avoid providing care for severely immunocompromised persons for 7 days after vaccination.
   • The intramuscularly or intradermally administered IIV are options for adults aged 18 years or older.
   • Adults aged 65 years or older can receive the standard-dose IV or the high-dose IV (Fluzone High-Dose).
   • A list of currently available influenza vaccines can be found at www.cdc.gov/flu/protect/vaccine/vaccines.htm.

3. Tetanus, diphtheria, and acellular pertussis (Td/Tdap) vaccination
   • Administer 1 dose of Tdap vaccine to pregnant women during each pregnancy (preferably during 27 to 36 weeks’ gestation regardless of interval since prior Td or Tdap vaccination).
   • Persons aged 11 to 12 years or who have not received Tdap vaccine or for whom vaccine status is unknown should receive a dose of Tdap followed by tetanus and diphtheria toxoids (Td) booster doses every 10 years thereafter. Tdap can be administered regardless of interval since the most recent tetanus or diphtheria-toxoid containing vaccine.
   • Adults with an unknown or incomplete history of completing a 3-dose primary vaccination series with 10 containing vaccines should begin or complete a primary vaccination series including a Tdap dose.
   • For unvaccinated adults, administer the first 2 doses at least 4 weeks apart and the third dose 6 to 12 months after the second.
   • For incompletely vaccinated (i.e., less than 3 doses) adults, administer remaining doses.
   • Refer to the ACIP statement for recommendations for administering Td/Tdap as prophylaxis in wound management (see footnote 1).

4. Varicella vaccination
   • All adults without evidence of immunity to varicella (as defined below) should receive 2 doses of single-antigen varicella vaccine or a second dose if they have received only 1 dose.
   • Vaccination should be emphasized for those who have close contact with persons at high risk for severe disease (e.g., health care personnel and family contacts of persons with immunocompromising conditions) or are at high risk for exposure or transmission (e.g., teachers; child care employees; residents of long-term care institutions; college students; military personnel; adolescents and adults living in households with children; nonpregnant women of childbearing age; and international travelers).
   • Pregnant women should be assessed for evidence of varicella immunity. Women who do not have evidence of immunity should receive the first dose of varicella vaccine upon completion or termination of pregnancy and before discharge from the health care facility. The second dose should be administered 4 to 8 weeks after the first dose.
   • Evidence of immunity to varicella in adults includes any of the following:
     - documentation of 2 doses of varicella vaccine at least 4 weeks apart;
     - U.S.-born before 1980, except health care personnel and pregnant women who are working in a health care facility, or
     - laboratory evidence of immunity or laboratory confirmation of disease.
   • For persons vaccinated before 1979 with either killed mumps vaccine or mumps vaccine of unknown type who are at high risk for mumps infection (e.g., persons who are working in a health care facility) should be considered for revaccination with 2 doses of MMR vaccine.

5. Human papillomavirus (HPV) vaccination
   • Two vaccines are licensed for use in females, bivalent HPV vaccine (HPV2) and quadrivalent HPV vaccine (HPV4), and one HPV vaccine for use in males (HPV4).
   • For females, either HPV4 or HPV2 is recommended in a 3-dose series for routine vaccination at age 11 or 12 years and for those aged 13 through 26 years, if not previously vaccinated.
   • For males, HPV4 is recommended in a 3-dose series for routine vaccination at age 11 or 12 years and for those aged 13 through 21 years, if not previously vaccinated. Males aged 22 through 26 years may be vaccinated.
   • HPV4 is recommended for men who have sex with men through age 26 years for those who did not get any or all doses when they were younger.
   • A complete series for either HPV4 or HPV2 consists of 3 doses. The second dose should be administered 4 to 8 weeks (minimum interval of 4 weeks) after the first dose; the third dose should be administered 24 weeks after the first dose and 16 weeks after the second dose (minimum interval of at least 12 weeks).
   • HPV vaccines are not recommended for use in pregnant women. However, pregnancy testing is not needed before vaccination. If a woman is found to be pregnant after initiating the vaccination series, no intervention is needed; the remainder of the 3-dose series should be delayed until completion or termination of pregnancy.

6. Zoster vaccination
   • A single dose of zoster vaccine is recommended for adults aged 60 years or older regardless of whether they report a prior episode of herpes zoster.
   • Additional information and resources regarding vaccination of pregnant women can be found at www.cdc.gov/vaccines/adults/rec-vac/pregnant.html.

7. Measles, mumps, rubella (MMR) vaccination
   • Adults born before 1957 are generally considered immune to measles and mumps. All adults born in 1957 or later should have documentation of 1 or more doses of MMR vaccine unless they have a medical contraindication to the vaccine or laboratory evidence of immunity to any of the three diseases. Documentation of provider-diagnosed disease is not considered acceptable evidence of immunity for measles, mumps, or rubella.
   • Measles component:
     - A routine second dose of MMR vaccine, administered a minimum of 28 days after the first dose, is recommended for adults who:
       — are students in postsecondary educational institutions,
       — work in a health care facility, or
       — travel internationally.
   • Mumps component:
     - A routine second dose of MMR vaccine, administered a minimum of 28 days after the first dose, is recommended for adults who:
       — are students in postsecondary educational institutions,
       — work in a health care facility, or
       — plan to travel internationally.
   • Rubella component:
     - For women of childbearing age, regardless of birth year, rubella immunity should be determined. If there is no evidence of immunity, women who are not pregnant should be vaccinated. Pregnant women who do not have evidence of immunity should receive MMR vaccine upon completion or termination of pregnancy and before discharge from the health care facility.

8. Pneumococcal (13-valent pneumococcal conjugate vaccine [PCV13] and 23-valent pneumococcal polysaccharide vaccine [PPSV23]) vaccination
   • General information:
     — When indicated, only a single dose of PCV13 is recommended for adults.
     — No additional dose of PPSV23 is indicated for adults vaccinated with U.S.-licensed PPSV23 at or after age 65 years.
     — When both PCV13 and PPSV23 are indicated, PCV13 should be administered first; PCV13 and PPSV23 should not be administered during the same visit.
     — When indicated, PCV13 and PPSV23 should be administered to adults whose pneumococcal vaccination history is incomplete or unknown.
   • Adults aged 65 years or older who
     — have not received PCV13 or PPSV23: Administer PCV13 followed by PPSV23 in 6 to 12 months.
     — have not received PCV13 but have received a dose of PPSV23 at age 65 years or older: Administer PPSV23 at least 1 year after the dose of PPSV23 received at age 65 years or older.
8. Pneumococcal vaccination (continued)

- Have received PCV13 but not PCV23 before age 65: Administer PCV13 at least 1 year after the most recent dose of PCV23 to adults who have not received PCV23, administer a dose of PCV23 to adults who have received PCV23 at least 6 months after PCV13, or as soon as possible if this time window has passed, and at least 5 years after the most recent dose of PCV23.
- Have received PCV13 but not PCV23 before age 65: Administer PCV23 to adults who have received PCV13 at least 6 months after PCV13, or as soon as possible if this time window has passed, and at least 5 years after the most recent dose of PCV23.
- Have received PCV13 and 1 or more doses of PCV23 before age 65: Administer PCV23 to adults who have received PCV13 at least 6 months after PCV13, or as soon as possible if this time window has passed, and at least 5 years after the most recent dose of PCV23.
- Have received PCV13 but not PCV23 before age 65: Administer PCV23 to adults who have received PCV13 at least 6 months after PCV13, or as soon as possible if this time window has passed, and at least 5 years after the most recent dose of PCV23.
- Have received PCV13 but not PCV23: Administer a second dose of PCV23 to adults who have received PCV13 at least 5 years after the first dose of PCV23.
- Have not received PCV13 or PCV23: Administer PCV13 followed by PCV23 at least 8 weeks after PCV13; administer a second dose of PCV23 at least 5 years after the first dose of PCV23.
- Have not received PCV13 but have received 1 dose of PCV23: Administer PCV13 at least 1 year after the most recent dose of PCV23.
- Have not received PCV13 but not PCV23: Administer PCV23 at least 8 weeks after PCV13, administer a second dose of PCV23 at least 5 years after the first dose of PCV23.
- Have not received PCV13 but have received 2 doses of PCV23: Administer PCV13 at least 1 year after the most recent dose of PCV23.
- Have not received PCV13 but not PCV23: Administer PCV23 at least 8 weeks after PCV13, administer a second dose of PCV23 at least 5 years after the first dose of PCV23.
- Adults aged 19 through 64 years with immunocompromising conditions or anatomical or functional asplenia (defined below) who
  - Have not received PCV13 or PCV23: Administer PCV13 followed by PCV23 at least 8 weeks after PCV13; administer a second dose of PCV23 at least 5 years after the first dose of PCV23.
  - Adults aged 19 through 64 years with chronic heart disease (including congenital heart failure and cardiomyopathies, excluding hypertension), chronic lung disease (including chronic obstructive lung disease, emphysema, and asthma), chronic liver disease (including cirrhosis), alcoholism, or diabetes mellitus: Administer PCV23.
  - Adults aged 19 through 64 years who smoke cigarettes or reside in nursing home or long-term care facilities: Administer PCV23.
  - Routine pneumococcal vaccination is not recommended for American Indian/Alaska Native adults, because they live in areas with increased risk for invasive pneumococcal disease.
  - Immunocompromising conditions that are indications for pneumococcal vaccination are: Congenital or acquired immunity deficiencies (including B- or T-lymphocyte deficiency, complement deficiencies, and phagocytic disorders excluding chronic granulomatous disease), HIV infection, chronic renal failure, leukemia, lymphoma, Hodgkin disease, generalized malignancy, multiple myeloma, solid organ transplant, and iatrogenic immunosuppression (including long-term systemic corticosteroids and radiation therapy). Adults with any of the above conditions should receive 1 dose of 40 mcg/mL (Recombivax HB) administered on days 0, 7, and 21 to 30 followed by a booster dose at month 12.

9. Meningococcal vaccination

- Adults aged 2 to 55 years with quaternary meningococcal conjugate vaccine (MenACWY [Menactra, Menveo]) at least 2 months apart to adults of all ages with functional asplenia or persistent complement component deficiencies. HIV infection is not an indication for routine vaccination with MenACWY. If an HIV-infected person of any age is vaccinated, 2 doses of MenACWY should be administered at least 2 months apart.
- Administer single dose of meningococcal vaccine to microbiologists routinely exposed to isolates of Neisseria meningitidis, military recruits, persons at risk during an outbreak attributable to a vaccine serogroup, and persons who travel to or live in countries in which meningococcal disease is endemic or epidemic.
- First-year college students up through age 21 years who are living in residence halls should be vaccinated if they have not received a dose on or after their 16th birthday.

- MenACWY is preferred for adults with any of the preceding indications who are aged 55 years or younger as well as for adults aged 56 years or older who a) were vaccinated previously with MenACWY and are recommended for revaccination, or b) for whom multiple doses are anticipated. Meningococcal polysaccharide vaccine (MPSV4 [Menomune]) is preferred for adults aged 56 years or older who have not received MenACWY previously and who require a single dose only (e.g., travelers).
- Revaccination with MenACWY every 5 years is recommended for adults previously vaccinated with MenACWY or MPSV4 who remain at increased risk for infection (e.g., adults with MenACWY but not MPSV4 or MPSV4 but not MenACWY who have been treated for immunodeficiency or other factors that increase meningococcal disease risk).

10. Hepatitis A Vaccination

- Vaccinate any person seeking protection from hepatitis A virus (HAV) infection and persons with any of the following indications:
  - men who have sex with men and persons who use injection or noninjection illicit drugs;
  - persons working with HAV-infected primates or with HAV in a research laboratory setting;
  - persons with chronic liver disease and persons who receive clotting factor concentrates;
  - persons traveling to or working in countries that have high or intermediate endemicity of hepatitis A;
  - unvaccinated persons who anticipate close personal contact (e.g., household or regular babysitting) with an international adoptee during the first 60 days after arrival in the United States from a country with high or intermediate endemicity of hepatitis A;
- The first dose of the 2-dose hepatitis A vaccine series should be administered as soon as adoption is planned, ideally 2 or more weeks before the arrival of the adoptee.

- Single-antigen vaccine formulations should be administered in a 2-dose schedule at either 0 and 6 months, 0 and 12 months, or 0 and 18 months.
- If the combined hepatitis A and hepatitis B vaccine (Twinrix) is used, administer 3 doses at 0, 1, and 6 months, respectively, of a 4-dose schedule may be used, administered on days 0, 7, and 21 to 30 followed by a booster dose at month 12.

11. Hepatitis B vaccination

- Vaccinate persons with any of the following indications and any person seeking protection from hepatitis B virus (HBV) infection:
  - sexually active persons who are not in a long-term, monogamous relationship (e.g., persons with more than 1 sex partner during the previous 6 months); persons seeking evaluation or treatment for a sexually transmitted disease (STD); current or recent injection drug users; and men who have sex with men;
  - health-care personnel and public safety workers who are potentially exposed to blood or other infectious body fluids;
  - persons with diabetes who are younger than age 60 years as soon as feasible after diagnosis, persons with diabetes who are age 60 years or older at the discretion of the treating clinician based on the likelihood of acquiring HBV infection, including the risk posed by an increased need for assisted blood glucose monitoring;
  - all adults in the following settings: STD treatment facilities, HIV testing and treatment facilities, providing drug abuse treatment and prevention services, health care settings targeting services to injection drug users or men who have sex with men, correctional facilities, end-stage renal disease programs and facilities for chronic hemodialysis patients, and institutions and nonresidential day care facilities for persons with developmental disabilities.
- Administer missing doses to complete a 3-dose series of hepatitis B vaccine to those persons not vaccinated or not completely vaccinated. The second dose should be administered 1 month after the first dose; the third dose should be given at least 2 months after the second dose (and at least 4 months after the first dose). If the combined hepatitis A and hepatitis B vaccine (Twinrix) is used, give 3 doses at 0-, 1-, and 6-months, alternatively, a 4-dose schedule should be used, administered on days 0, 7, and 21 to 30 followed by a booster dose at month 12 may be used.
- Adults patients receiving hemodialysis or with other immunocompromising conditions should receive 1 dose of 40 mcg/mL (Recombivax HB) administered on a 3-dose schedule at 0, 1, and 6 months or 2 doses of 20 mcg/mL (Engerix-B) administered simultaneously on a 4-dose schedule at 0, 1, 2, and 6 months.

12. Haemophilus influenzae type b (Hib) vaccination

- One dose of Hib vaccine should be administered to persons who have anatomical or functional asplenia or sickle cell disease or are undergoing elective splenectomy if they have not previously received Hib vaccine. Hib vaccine 14 or more days before splenectomy is suggested.
- Recipients of a hematopoietic stem cell transplant (HSCT) should be vaccinated with a 3-dose regimen 6 to 12 months after a successful transplant, regardless of vaccination history; at least 4 weeks should separate doses.
- Hib vaccine is not recommended for adults with HIV infection since their risk for Hib infection is low.

13. Immunocompromising conditions

- Inactivated vaccines generally are acceptable (e.g., pneumococcal, meningococcal, and inactivated influenza vaccine) and live vaccines generally are avoided in persons with immune deficiencies or immunocompromising conditions. Information on specific conditions is available at www.cdc.gov/vaccines/hcp/acip-recs/index.html.

**Table 17. Contraindications and Precautions to Commonly Used Vaccines in Adults: United States, 2015**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Contraindications</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza, inactivated (IV)²</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after previous dose of any influenza vaccine, or to a vaccine component, including egg protein</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td>Influenza, recombinant (RIV)</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after previous dose of RIV or to a vaccine component. RIV does not contain any egg protein¹</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td>Influenza, live attenuated (LAIV)²</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine, or to a previous dose of any influenza vaccine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• In addition, ACIP recommends that LAIV not be used in the following populations:</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td></td>
<td>— pregnant women</td>
<td>History of Guillain-Barre Syndrome within 6 weeks of previous influenza vaccination</td>
</tr>
<tr>
<td></td>
<td>— immunosuppressed adults</td>
<td>History of Guillain-Barre Syndrome within 6 weeks of previous influenza vaccination</td>
</tr>
<tr>
<td></td>
<td>— adults with egg allergy of any severity</td>
<td>Asthma in persons aged 5 years and older</td>
</tr>
<tr>
<td></td>
<td>— adults who have taken influenza antiviral medications (amantadine, rimantadine, oseltamivir, or zanamivir) within the previous 48 hours</td>
<td>Other chronic medical conditions, other chronic lung diseases, chronic cardiovascular disease (including isolated hypertension), diabetics, chronic renal or hepatic disease, hematologic disease, neurologic disease, and metabolic disorders</td>
</tr>
<tr>
<td>Tetanus, diphtheria, pertussis (Tdap); tetanus, diphtheria (Td)</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td></td>
<td>• For pertussis-containing vaccines: encephalopathy (e.g., coma, decreased level of consciousness, or prolonged seizures) not attributable to another identifiable cause within 7 days of administration of a previous dose of Tdap, diphtheria and tetanus toxoids and pertussis (TTP) vaccine</td>
<td>Guillain-Barre Syndrome within 6 weeks after a previous dose of tetanus toxoid-containing vaccine</td>
</tr>
<tr>
<td></td>
<td>• Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, or long-term immunosuppressive therapy, or patients with human immunodeficiency virus (HIV) infection who are severely immunocompromised)</td>
<td>History of Arthus-type hypersensitivity reactions after a previous dose of tetanus or diphtheria toxoid-containing vaccine</td>
</tr>
<tr>
<td></td>
<td>• Pregnancy</td>
<td>For pertussis-containing vaccines: progressive or unstable neurologic disorder, uncontrolled seizures, or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized</td>
</tr>
<tr>
<td>Varicella</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.</td>
<td>Recent (within 11 months) receipt of antibody-containing blood product (specific interval depends on product)⁶</td>
</tr>
<tr>
<td></td>
<td>• Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, or long-term immunosuppressive therapy, or patients with human immunodeficiency virus (HIV) infection who are severely immunocompromised)</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td></td>
<td>• Pregnancy</td>
<td>Receipt of specific antivirals (i.e., acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination; avoidance of these antiviral drugs for 14 days after vaccination</td>
</tr>
<tr>
<td>Human papillomavirus (HPV)⁴</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td></td>
<td>• Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, or long-term immunosuppressive therapy, or patients with human immunodeficiency virus (HIV) infection who are severely immunocompromised)</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>Zoster</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) or to a vaccine component.</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td></td>
<td>• Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, or long-term immunosuppressive therapy, or patients with HIV infection who are severely immunocompromised)</td>
<td>Receipt of specific antivirals (i.e., acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination; avoidance of these antiviral drugs for 14 days after vaccination</td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMR)⁴</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td></td>
<td>• Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, or long-term immunosuppressive therapy, or patients with HIV infection who are severely immunocompromised)</td>
<td>Recent (within 11 months) receipt of antibody-containing blood product (specific interval depends on product)⁶</td>
</tr>
<tr>
<td></td>
<td>• Pregnancy</td>
<td>History of thrombocytopenia or thrombocytopenic purpura</td>
</tr>
<tr>
<td></td>
<td>• Need for tuberculin skin testing¹</td>
<td>Need for tuberculin skin testing¹</td>
</tr>
<tr>
<td>Pneumococcal conjugate (PCV)³</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSV23)</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td>Meningococcal, conjugate (MenACWY); meningococcal polysaccharide (MPSV4)</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
<tr>
<td>Haemophilus influenza Type b (Hi)</td>
<td>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.</td>
<td>Moderate or severe acute illness with or without fever</td>
</tr>
</tbody>
</table>

1. Vaccine package inserts and the full ACIP recommendations for these vaccines should be consulted for additional information on vaccine-related contraindications and precautions and for more information on vaccine reactants. Events or conditions listed as precautions should be reviewed carefully. Benefits of and risks for administering a specific vaccine to a person under these circumstances should be considered. If the risk from the vaccine is believed to outweigh the benefit, the vaccine should not be administered. If the benefit of vaccination is believed to outweigh the risk, the vaccine should be administered. A contraindication is a condition in a recipient that increases the chance of a serious adverse reaction. Therefore, a vaccine should not be administered when a contraindication is present.

2. For more information on use of influenza vaccines among persons with egg allergies and a complete list of conditions that CDC considers to be reasons to avoid receiving LAIV, see CDC. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP) — United States, 2014–15 Influenza Season. MMWR 2014;63(32):891–97.

3. LAIV, MMR, varicella, or zoster vaccines can be administered on the same day. If not administered on the same day, live vaccines should be separated by at least 28 days.

4. Immunosuppressive steroid dose is considered to be ≥2 weeks of daily receipt of 20 mg of prednisone or the equivalent. Vaccination should be deferred for at least 1 month after discontinuation of such therapy. Providers should consult ACIP recommendations for complete information on the use of specific live vaccines among persons on immune-suppressing medications or with immune suppression because of other reasons.


6. Measles vaccination might suppress tuberculin reactivity temporarily. Measles-containing vaccine may be administered on the same day as tuberculin skin testing. If testing cannot be performed until after the day of MMR vaccination, the test should be postponed for at least 4 weeks after the vaccination. If an urgent need exists to skin test, do so with the understanding that reactivity might be reduced by the vaccine.


† Regarding latex allergy, consult the package insert for any vaccine administered.
A. Major Changes in the 2015 Adult Immunization Schedule from the 2014 Schedule  
1. Pneumococcal vaccination  
   a. PCV13 (Prevnar) should now be used for adult pneumococcal vaccination in people age 65 years and older, in addition to PPSV23 (Pneumovax).  
   b. In pneumococcal vaccine-naive patients 65 years or older: PCV13 at age 65 years or older, followed by PPSV23 6–12 months later.  
   c. In patients who previously received PPSV23 at age 65 years or older: Vaccinate with PCV13 1 year or more after PPSV23.  
   d. In patients who previously received PPSV23 before age 65 years who are now aged 65 years or older: Vaccinate with PCV13 1 year or more after receipt of PPSV23 and revaccinate with PPSV23 6–12 months after PCV13, as long as 5 or more years has passed since the previous PPSV23.  
2. Influenza vaccination  
   a. All adults aged 18 and older can receive recombinant hemagglutinin influenza vaccine, trivalent (RIV3) [previously was adults aged 18 – 49]  
   b. There are changes to the contraindications and precautions section for LAIV  
      i. Influenza antiviral use within the last 48 hours is now a contraindication (was previously a precaution)  
      ii. Asthma and chronic lung diseases; cardiovascular, renal and hepatic diseases; and diabetes and other conditions are now precautions (were previously contraindications)  
B. Newer Issues with Influenza Vaccine  
1. Trivalent inactivated influenza vaccine (TIV) is now called inactivated influenza vaccine, trivalent (IIV3) (all egg-based); several brands available, including one that is high-dose.  
2. Quadrivalent IIV vaccines (IIV4) are available (all egg-based); several brands available.  
3. A trivalent cell culture–based IIV3 is available (not egg-based) (ccIIV3) (Flucelvax), indicated for age 18 and older.  
   – Egg amount is very low but is not considered egg-free.  
4. A recombinant hemagglutinin influenza vaccine, trivalent (RIV3) (FluBlok) is available, indicated for age 18 and older.  
   – Eggs not used in development; is completely egg-free.  
5. LAIV is still available as a nasal spray and is now quadrivalent, indicated for healthy, nonpregnant patients age 2–49 years.  
   a. LAIV should not be used in:  
      i. Patients aged less than 2 or more than 49 years  
      ii. Children aged 2–17 years who are receiving aspirin or aspirin-containing products  
      iii. Pregnant women  
      iv. Immunocompromised patients  
      v. Patients with an egg allergy or with history of a severe allergic reaction to the vaccine  
      vi. Children aged 2–4 years who have asthma or who have had a wheezing episode in the past 12 months  
         – Use with caution in patients of any age who have asthma, because they are at greater risk of wheezing after receipt of LAIV.  
      vii. Patients who have taken influenza antiviral medications in past 48 hours  
      viii. Patients who care for immunocompromised people should not receive LAIV or should avoid contact for 7 days after receiving the vaccine.  
6. Egg allergy  
   a. If a patient has experienced only hives after eating eggs or egg-containing foods, he or she should receive influenza vaccine, either IIV3, IIV4, ccIIV3, or RIV3. Avoid LAIV.
i. If IIV3, IIV4, or ccIIV3 is used, the health care provider administering the vaccine should be familiar with manifestations of egg allergy.

ii. The vaccine recipient should be observed for at least 30 minutes after each vaccine dose.

iii. If RIV3 is used, no special precautions are necessary.

b. If a patient has experienced a severe reaction to eggs, such as angioedema, respiratory distress, lightheadedness, or recurrent emesis, or required epinephrine or emergency treatment, he or she may receive RIV3 (if age 18–49 years).

i. If RIV3 is not available or the recipient is outside the age range, any of the IIVs can be used but should be administered by a physician with experience in recognition and management of severe allergic conditions.

ii. The vaccine recipient should be observed for at least 30 minutes after each vaccine dose.

c. Some people who report egg allergies may not actually be allergic to eggs. Those who are able to eat lightly cooked egg (e.g., scrambled egg) without a reaction are not likely to be allergic and can receive any influenza vaccine.

C. Current Issues with Herpes Zoster Vaccine (HZV): The HZV package insert states not to give HZV and PPSV concurrently but to separate them by at least 4 weeks because of decreased immunologic response to HZV. Their conclusion is based on a Merck-sponsored, unpublished study. The ACIP states that the clinical relevance of this recommendation is unknown, and a subsequent study showed no compromise in HZV efficacy. The Advisory Committee on Immunization Practices/Centers for Disease Control and Prevention (ACIP/CDC), which reviewed the data, continues to recommend that HZV and PPSV be administered at the same visit if the person is eligible for both vaccines.
**Patient Cases**

14. A 71-year-old woman with COPD is taking tiotropium (Spiriva) inhaled 1 capsule/day. She received the influenza vaccine last October, her last tetanus and diphtheria (Td) vaccine was at age 65, and her PPSV23 was given at age 60. She has not previously received the zoster vaccine, but she had an episode of severe zoster infection 5 years ago. Which is the most appropriate choice of vaccines that should be given at her October internal medicine clinic appointment?
   
   A. Only the influenza vaccine should be given.
   
   B. Influenza and PPSV23 vaccines should be given.
   
   C. Influenza, PPSV23, and zoster vaccines should be given.
   
   D. Influenza, PPSV23, zoster, and tetanus, diphtheria, and pertussis [Tdap] vaccines should be given.

15. A 20-year-old woman who is going away to college presents for a physical examination in July. She will be living in the dormitory. She smokes 1/2 pack/day but has no other medical conditions. She is up to date with all of her routine childhood vaccines, but she has not received any vaccines in the past 11 years. She is not sexually active. Which is the most appropriate choice for vaccines that should be given today?
   
   A. Td and human papillomavirus (HPV) vaccines.
   
   B. Tdap, quadrivalent meningococcal conjugate vaccine (MenACWY), and HPV vaccines.
   
   C. MenACWY, PPSV23, and Td vaccines.
   
   D. MenACWY, PPSV23, Tdap, and HPV vaccines.

16. A 21 year-old man with type 1 diabetes presents for an influenza vaccine. He has an egg allergy. After further questioning, you find out that when he has eaten scrambled eggs, he has experienced hives. Which is the most appropriate regarding influenza vaccination in this patient?
   
   A. Either IIV3, IIV4, ccIIV3, RIV3, or LAIV can be used; observe patient for 30 minutes.
   
   B. Either IIV3, IIV4, ccIIV3, or RIV3 can be used; observe patient for 30 minutes.
   
   C. Only RIV3 should be used; observe patient for 30 minutes.
   
   D. He should not receive any type of influenza vaccine.
REFERENCES

Asthma


Chronic Obstructive Pulmonary Disease


**Gout**


**Immunizations**


ANSWERS AND EXPLANATIONS TO PATIENT CASES

1. **Answer: B**
   Her symptom frequency of twice weekly, her FEV₁ of more than 80% of predicted (normal), and the lack of interference with activity are consistent with intermittent asthma. However, her night awakenings for asthma symptoms occur three times per month, which is consistent with mild persistent asthma. In addition, mild persistent asthma still has normal spirometry. The specific level of persistent asthma is based on the most severe category met, so even though only one of her signs and symptoms falls under mild persistent and the rest under intermittent, she would be categorized as mild persistent.

2. **Answer: C**
   Because she has mild persistent asthma, step 2 is recommended for initial treatment. In addition to an inhaled SABA as needed, she would need to use a low-dose ICS (preferred treatment); mometasone 220 mcg once daily is a low-dose ICS. Montelukast is an alternative therapy (not first line) for step 2. Budesonide/formoterol, in the dose listed, is a low-dose ICS plus a LABA, which is a step 3 therapy.

3. **Answer: D**
   Her asthma is not well controlled because the frequency of her daytime symptoms and albuterol use is greater than 2 days/week. Recommended action for treatment is to step up to step 3: a low-dose ICS plus a LABA or a medium-dose ICS alone. The budesonide/formoterol MDI is incorrect because it is a medium-dose ICS plus a LABA (a step 4 treatment). Adding montelukast to low-dose ICS is an alternative therapy.

4. **Answer: D**
   This patient has moderate persistent asthma because of his nighttime symptoms twice weekly and requires step 3 therapy. A medium-dose ICS alone is preferred as initial therapy in this age group (5–11 years). Fluticasone 44 mcg 1 puff twice daily is a low-dose ICS for this age group. Montelukast is not recommended as monotherapy for moderate persistent asthma in this age group; montelukast is recommended only in combination with a low-dose ICS. Fluticasone/salmeterol 100/50 twice daily is a medium-dose ICS plus a LABA, which is step 4 in this age group.

5. **Answer: D**
   Because he is experiencing shortness of breath at rest, has trouble with conversation, and has an FEV₁ less than 40%, his asthma exacerbation is classified as severe. For severe asthma exacerbations in the ED setting, the recommended treatment is oxygen to achieve an $\text{SaO}_2$ of 90% or greater, high-dose inhaled SABA plus ipratropium by either nebulizer or MDI with valved holding chamber every 20 minutes for 1 hour or continuously, and OCSs.

6. **Answer: B**
   He is in GOLD guidelines patient group B because his postbronchodilator FEV₁ is between 50% and 80%, he has had 1 or no exacerbations in the past year, and his mMRC score is 2 or more. If the CAT were being used, the score would be 10 or greater.

7. **Answer: B**
   According to the GOLD guidelines, the recommended treatment for patient group B is regular treatment with an LA bronchodilator (either a LABA or LA anticholinergic), in addition to an SA bronchodilator as needed. Inhaled corticosteroids are recommended only in groups C and D. Roflumilast is recommended only if FEV₁ is less than 50% of predicted with chronic bronchitis and the patient has a history of frequent exacerbations.

8. **Answer: A**
   This patient is in GOLD risk group B, according to spirometry and CAT score, and is on the first-choice therapy. Because her control is worsening, she should go to the second-choice therapy, for which combined LA bronchodilators can be used. Inhaled corticosteroids are recommended only in risk groups C and D. Although a recent study showed benefits with chronic azithromycin, the guidelines do not recommend regular treatment with long-term antibiotics. In addition, the study showing the benefits of azithromycin included only patients at a higher risk of exacerbations (on continuous oxygen therapy or using systemic corticosteroids, plus a history of exacerbation requiring an ED visit or hospitalization). She does not meet these criteria.
9. **Answer: D**
According to the latest GOLD guidelines, OCSs are indicated in most exacerbations. The recommended dose is oral prednisone 40 mg daily for 5 days. Antibiotic treatment is also indicated because the patient has all three cardinal symptoms of airway infection: increased sputum purulence, increased sputum volume, and increased dyspnea. Trimethoprim/sulfamethoxazole is one of the recommended antibiotics.

10. **Answer: A**
NSAIDs (in anti-inflammatory or acute pain doses), colchicine, or corticosteroids are all appropriate for first-line therapy for acute gout. However, colchicine would not be recommended for this patient because he took acute colchicine doses in the past 2 weeks. Intra-articular corticosteroids are recommended only if only one or two large joints are affected. This patient is having an acute gouty attack of moderate severity. Combination therapy is recommended for initial therapy only if the patient has a severe attack. Oral prednisone alone would also be appropriate; however, this was not a choice.

11. **Answer: D**
Urate-lowering therapy is indicated in this patient because he has had two or more attacks in the past year. Allopurinol and febuxostat (XOIs) are first-line ULTs; probenecid is an alternative first-line ULT only if XOIs are contraindicated or not tolerated. Urate-lowering therapy can be initiated during an acute gouty attack, according to the American College of Rheumatology guidelines, as long as anti-inflammatory prophylaxis is instituted.

12. **Answer: A**
Oral corticosteroids are associated with significant risks in long-term therapy; they should not be used for anti-inflammatory prophylaxis unless both colchicine and NSAIDs are contraindicated, not tolerated, or ineffective. Combination therapy is not recommended for anti-inflammatory prophylaxis. Pegloticase is ULT, not anti-inflammatory prophylaxis.

13. **Answer: B**
If no tophi are present, the initial goal serum urate is <6 mg/dL; if gouty signs and symptoms are still present, then a secondary goal urate is <5 mg/dL. Anti-inflammatory prophylaxis if no tophi are present should continue for 3 months after goal serum urate is achieved, as long as the total duration is at least 6 months.

14. **Answer: D**
The CDC recommends that the influenza vaccine be given every year in every person 6 months and older. People 65 years and older should have a one-time pneumococcal (PPSV23) revaccination if they were vaccinated 5 or more years previously and were younger than 65 years at the time of primary vaccination. Zoster vaccination is recommended in all adults 60 years and older, regardless of previous zoster infection. The Tdap vaccine is recommended in all people, now including those 65 years and older.

15. **Answer: D**
First-year college students up to age 21 who live in dormitories, if not previously vaccinated on or after age 16, should receive the meningococcal vaccine (MenACWY; Menactra, Menevo). The PPSV23 is recommended for smokers 19–64 years of age, and this patient is a smoker. The Td vaccine should be given every 10 years. In adults younger than 65, a one-time dose of Tdap should be given, regardless of the time interval since the most recent tetanus vaccination. The HPV vaccine is for girls and women 11–26 years of age. Ideally, it should be given before the start of sexual activity, but it should still be administered to sexually active girls and women.

16. **Answer: B**
In people with an egg allergy who have only hives, either IIV3, IIV4, ccIIV3, or RIV3 can be used; LAIV should be avoided. The vaccine should be administered by a health professional with knowledge of the manifestations of egg allergy, and the patient should be observed for 30 minutes after administration.
ANSWERS AND EXPLANATIONS TO SELF-ASSESSMENT QUESTIONS

1. **Answer: D**
That she uses her inhaler throughout the day, every day, and sometimes at night indicates she has daily symptoms. “Severe persistent” means that frequency of symptoms is throughout the day, nighttime symptoms are often 7 times/week, a SABA several times a day, normal activity is extremely limited, FEV₁ is less than 60% of predicted, FEV₁/FVC is reduced more than 5%.

2. **Answer: C**
“Severe persistent” initial treatment is step 4 or 5. Step 4 preferred: inhaled steroid (medium dose) plus a LABA. Alternative: inhaled steroid (medium dose) plus either an LTM or sustained-release theophylline or zileuton. Step 5 preferred: inhaled steroid (high dose) plus a LABA.

3. **Answer: D**
Ratio data are ranked in a specific order with a consistent level of magnitude difference between units, with an absolute zero.

4. **Answer: B**
The percentage of patients receiving fluticasone/salmeterol who have an asthma-related hospitalization will be compared with the percentage of patients receiving fluticasone who have an asthma-related hospitalization. We assume that these two groups are normally distributed. These data are considered nominal. Chi-square test is appropriate to analyze nominal or categoric data. Analysis of variance is appropriate when there are more than two treatment groups. The Student unpaired t-test is used for continuous data that are normally distributed. The Mann-Whitney U test is appropriate when continuous data are not normally distributed.

5. **Answer: B**
Pneumococcal vaccine is recommended in persons 19–64 years of age with asthma. This patient falls into this category. Influenza vaccine is recommended in persons with chronic cardiovascular or pulmonary diseases such as asthma. However, usually, the influenza vaccine is given in the fall or early winter to offer protection when the risk of infection is highest. The tetanus booster (Td) is recommended every 10 years, and it has not been 10 years since this patient’s last Td, which was given as Tdap. The HZV (Zostavax) is recommended at 60 years and older by the CDC; however, it is indicated at 50 years and older in the manufacturer’s package insert.

6. **Answer: B**
This patient is in GOLD patient group B. A single LA bronchodilator is first choice for medication treatment. Tiotropium (Spiriva) is an LA bronchodilator (anticholinergic) that would be appropriate to initiate in this patient. A LABA would also be appropriate, but it was not one of the choices. Omalizumab is recommended for asthma, not COPD. An ICS is recommended only in patient group C or D and should never be used as monotherapy in COPD.

7. **Answer: D**
The starting allopurinol dose is 50 mg/day in stage 4 (GFR 15–29 mL/minute/1.73 m²) or worse CKD; the dose should be gradually titrated every 2–5 weeks. Probenecid is not recommended as first-line ULT if CrCl is less than 50 mL/minute.