

in the clinic

Chronic Obstructive Pulmonary Disease

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Chronic obstructive pulmonary disease (COPD) is a common cause of morbidity and mortality worldwide. Unlike the sharp reduction in death from heart disease, there has been an almost 100% increase in age-adjusted mortality between 1970 and 2002 due to COPD. It is currently the fourth leading cause of mortality and is projected to continue increasing for the foreseeable future. In 2000, the number of deaths in women was equal to that in men (1).

Screening

What is COPD, and which patient populations are at risk?

COPD is a treatable and preventable, but incurable, disease characterized by progressive airflow obstruction associated with an abnormal inflammatory response of the lungs to noxious particles or gases (2–4). Patients with COPD may meet the spirometry criteria for the diagnosis but remain asymptomatic. On the other hand, they may present with a variety of respiratory symptoms, including those of chronic bronchitis, or signs of emphysema on physical examination or imaging studies.

Patients younger than 35 years rarely get COPD, because susceptible individuals develop COPD only after inhalational exposure of sufficient intensity and duration to causative agents. It is estimated that about 80% to 90% of COPD is due to tobacco smoke (whether from smoking or exposure to “second-hand” smoke). The prevalence of COPD among cigarette smokers depends on the number of pack-years, the age of the patient, and the genetic predisposition. A risk of 15% for clinically significant COPD among cigarette smokers is commonly quoted, but this may be an underestimate (5).

Between 10% and 20% of COPD is caused by occupational or other exposure to chemical vapors, irritants, and fumes. More information is needed to determine the role of other possible inhaled irritants, such as those found in outdoor air pollution.

Although genetic factors remain largely unknown, the most clearly documented genetic risk for the development of COPD is serum α_1 -antitrypsin deficiency.

Should clinicians screen asymptomatic patients for COPD?

There are no clear-cut data to support screening of asymptomatic patients for COPD with spirometry. Therefore, the United States Preventive Services Task Force recommends against screening for COPD in the general population (6). On the other hand, epidemiologic evidence suggests that one half of the current population with COPD has not been identified (7), and patients who smoke or have other risk factors may have COPD despite being asymptomatic.

A potential benefit of early detection is that it is an opportunity to further encourage patients to stop smoking. However, data on the effectiveness of COPD screening in motivating smoking cessation conflict (8). Screening may detect patients who consider themselves to be asymptomatic but in fact have adapted their lifestyle to accommodate a reduced level of activity. However, there are also few data to support this as a rationale for screening asymptomatic patients (9).

Other professional organizations recommend a case-finding approach in patients who present with risk factors or possible symptoms. For example, the updated 2007 guidelines from the Global Initiative for Chronic Obstructive Lung Disease suggest that

1. Global Initiative for Chronic Obstructive Lung Disease. Accessed at www.goldcopd.org on 17 January 2008.
2. American Thoracic Society. COPD Guidelines. Accessed at www.thoracic.org/copd on 17 January 2008.
3. Department of Veterans Affairs and Department of Defense. COPD Guidelines. Accessed at www.oqpp.med.va.gov/cpg/COPD/COPD_base.htm on 17 January 2008.
4. National Institute of Clinical Excellence. Management of chronic obstructive pulmonary disease in adults in primary and secondary care. Accessed at www.nice.org.uk/nice/media/pdf/CG012_niceguideline.pdf on 17 January 2008.
5. Rennard SI, Vestbo J. COPD: the dangerous underestimate of 15%. *Lancet*. 2006; 367:1216-9. [PMID: 16631861]
6. U.S. Preventive Services Task Force. Screening for Chronic Obstructive Pulmonary Disease Using Spirometry: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med*. 2008. In press.
7. Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet*. 2007;370:765-73. [PMID: 17765526]

clinicians doing spirometry look for COPD in patients with symptoms, such as chronic cough and sputum or shortness of breath (1). The American Thoracic Society/

European Respiratory Society recommends spirometry in people exposed to tobacco smoke and those with a family history of COPD (2).

Screening... The major risk factors for COPD are inhalational exposure to tobacco smoke, including second-hand smoke, and occupational or other exposure to dusts, chemical vapors, irritants, and fumes. α_1 -Antitrypsin deficiency is the most clearly documented genetic risk factor that clinicians should consider, especially when patients develop COPD before age 50 years. Screening for COPD in the asymptomatic general population is not recommended. Some professional organizations recommend spirometry in specific patient groups as a case-finding measure and to encourage patients to stop smoking.

CLINICAL BOTTOM LINE

Diagnosis

When should clinicians consider a diagnosis of COPD?

Patients with COPD exhibit a broad spectrum of clinical findings, which are more specific than sensitive. When present, symptoms include cough, sputum production, dyspnea, and decreased exercise tolerance. Examination may reveal evidence of hyperinflation, such as hyperresonance and distant breath sounds. However, whereas chronic bronchitis (defined as at least 90 days of cough and sputum production for 2 consecutive years) and emphysema (a pathologic diagnosis suggested by hyperinflation on examination and imaging studies) are commonly associated with COPD, neither is required to make the diagnosis.

What is the role of pulmonary function testing in the diagnosis of COPD?

Spirometry is the essential component of pulmonary function testing required for diagnosis and classification of COPD. The spirometric criterion for the diagnosis of COPD is a postbronchodilator FEV_1/FVC ratio less than 0.70. The FEV_1 percentage predicted can be measured to classify COPD as mild (>80%), moderate (50%–80%),

severe (30%–50%), or very severe (<30%) (1–3).

The other components of pulmonary function testing, including lung volumes, diffusing capacity, and arterial blood gases and pulse oximetry, are not required for diagnosis. These tests may be helpful in further determining severity of COPD; suggesting the presence of emphysema; excluding other lung diseases, such as restrictive lung disease; and determining if a patient is a candidate for long-term oxygen therapy or if chronic hypercapnia is present. Moreover, the degree of reversibility of airflow limitation (for example, degree of improvement in FEV_1 after bronchodilator or other intervention) is not recommended for diagnosis, differential diagnosis with asthma, or prediction of response to long-term treatment with bronchodilators or glucocorticosteroids (1).

Spirometric data can also be used in calculating the BODE index (Table 1) (10), which stands for **B**ody mass index; **O**bstruction, as measured by FEV_1 ; **D**yspnea, as measured by the Modified Medical Research Council dyspnea questionnaire (11); and **E**xercise, as

- Wilt TJ, Niewoehner D, Kim C, et al. Use of spirometry for case finding, diagnosis, and management of chronic obstructive pulmonary disease (COPD). *Evid Rep Technol Assess (Summ)*. 2005;1-7. [PMID: 16238364]
- Wilt TJ, Niewoehner D, MacDonald R, et al. Management of stable chronic obstructive pulmonary disease: a systematic review for a clinical practice guideline. *Ann Intern Med*. 2007;147:639-53. [PMID: 17975187]
- Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med*. 2004;350:1005-12. [PMID: 14999112]
- Bestall JC, Paul EA, Garrod R, et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax*. 1999;54:581-6. [PMID: 10377201]

Table 1. The MMRC Dyspnea Severity Scale* for Calculation of the BODE Index

Severity	Score	Degree of Breathlessness Related to Activities
None	0	Not troubled with breathlessness except with strenuous exercise
Mild	1	Troubled by shortness of breath when hurrying or walking up a slight hill
Moderate	2	Walks slower than people of the same age due to breathlessness or has to stop for breath when walking at own pace on level ground
Severe	3	Stops for breath after walking approximately 100 meters or after a few minutes on level ground
Very severe	4	Too breathless to leave the house or breathless when dressing or undressing

Variable	Points on BODE Index [†]			
	0	1	2	3
FEV ₁ (percentage predicted)	≥65	50–64	36–49	≤35
Distance walked in 6 min, m	≥350	250–349	150–249	≤149
MMRC dyspnea scale score	0–1	2	3	4
Body mass index	>21	≤21		

* Adapted from Veterans' Affairs and Department of Defense guidelines (3). BODE = Body mass index, Obstruction, Dyspnea, and Exercise; COPD = chronic obstructive pulmonary disease; MMRC = Modified Medical Research Council.

† Points for each variable are summed with a possible range from 0 to 10. Higher numbers indicate worse prognosis. Adapted from (10).

determined by a 6-minute walk test. The BODE index is beneficial in estimating risk for hospitalization and determining prognosis and is recommended in evaluating patients for lung transplantation (12).

The BODE index was validated prospectively in 625 patients with COPD. The average FEV₁ percentage predicted varied from 39% to 47%. For each 1-point increase in the BODE index, there was a 1.34 increase in the hazard ratio for subsequent death from any cause and a 1.62 increase for death from respiratory failure (10).

What other laboratory tests should clinicians order when evaluating patients with COPD?

Apart from the specific pulmonary function tests described previously, no other tests are routinely recommended in diagnosing COPD, classifying its severity, or helping to determine prognosis. However, chest X-rays show flattened diaphragms and hyperlucency and computed tomography (CT) scanning shows destruction of pulmonary parenchyma (in patients with emphysema).

Clinicians should consider obtaining an α_1 -antitrypsin level in patients who have documented

COPD with onset as early as the fifth decade of life or in the absence of a recognized risk factor, such as smoking and occupational dust exposure. It should also be considered in patients with a family history of emphysema or α_1 -antitrypsin deficiency, bronchiectasis, liver disease, or panniculitis.

Exercise testing may also be useful in the differential diagnosis of patients with dyspnea when it is unclear whether symptoms are pulmonary or cardiac in origin.

What other disorders should clinicians consider in patients with suspected COPD?

Clinicians should consider any condition that produces airflow obstruction, such as asthma; bronchiectasis; cystic fibrosis; bronchiolitis; and upper airway obstruction due to tumors of the trachea, tracheal stenosis, tracheomalacia, and vocal cord dysfunction. Clinicians should also consider other conditions that cause dyspnea, such as interstitial lung disease. Patients with dyspnea and cardiac disease are a frequent challenge and often require specific cardiologic studies to determine the cause of their symptoms.

12. Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. International guidelines for the selection of lung transplant candidates: 2006 update—a consensus report from the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant*. 2006; 25:745-55. [PMID: 16818116]
13. Anthonisen NR, Connett JE, Kiley JP, et al. Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV₁. The Lung Health Study. *JAMA*. 1994;272:1497-505. [PMID: 7966841]

How should clinicians distinguish between patients with COPD and those with asthma?

Because spirometric obstruction, cough, wheeze, and dyspnea are common to both COPD and asthma, it is sometimes difficult to distinguish between the disorders. In general, patients with asthma develop symptoms at a younger

age, are less likely to be smokers, and experience symptoms intermittently and with more variability. Those with COPD tend to have onset of disease later in life; commonly have chronic productive cough; have more persistent dyspnea; and may have a less consistent response to drugs, such as inhaled corticosteroids.

Diagnosis... Clinicians should suspect COPD in patients with a smoking history or occupational exposure to inhaled irritants; those with chronic cough, sputum, or dyspnea; and those with a family history of respiratory disease. Confirm the diagnosis by spirometry with a FEV₁/FVC ratio of less than 0.70 measured after administration of a bronchodilator. Use clinical data to determine disease severity and to exclude other disorders. Consider ordering an α_1 -antitrypsin level test in patients who present with early-onset COPD or in those with a compatible family history.

CLINICAL BOTTOM LINE

What is the evidence that smoking cessation benefits patients even after COPD is present, and what smoking cessation interventions are most effective in patients with COPD?

Clinicians should urge all patients with COPD who smoke to quit and enroll in a smoking cessation program. There is excellent evidence that patients with COPD who stop smoking have a reduced rate of decline in pulmonary function (13).

In a multicenter, randomized, controlled trial (RCT) of an intensive smoking cessation program that included behavioral modification and nicotine gum versus placebo, middle-aged smokers in the intervention group had a smaller decline in FEV₁ of 34 mL/y than those in the placebo group, who declined 63 mL/y, over a 5-year period (13).

Smoking cessation therapies range from brief interventions in physicians' offices to more structured programs, which typically include 2 to 3 longer advice sessions and medications, such as nicotine preparations, bupropion, or varenicline. These programs are effective in up to 30% of patients at 1 year.

However, it is unclear that any particular medication is more effective than another in patients with COPD (14). For more information, see our issue on Smoking Cessation (15).

How should clinicians approach drug therapy in patients with COPD?

Inhaled medications—including β_2 -agonists, anticholinergics, and corticosteroids—form the cornerstone of pharmacotherapy for COPD and should be considered as part of an overall treatment strategy that includes smoking cessation, education, and pulmonary rehabilitation. None of these therapies significantly alter the course of the disease in reducing the rate of decline in pulmonary function or decreasing mortality. The goal of treatment should be symptom relief, particularly dyspnea; prevention of exacerbations; and improvement in respiratory health status.

Before therapy is initiated, it is important to assess pulmonary function and severity, including history of exacerbations, both through clinical assessment and use

Treatment

14. Wu P, Wilson K, Dimoulas P, et al. Effectiveness of smoking cessation therapies: a systematic review and meta-analysis. *BMC Public Health*. 2006;6:300. [PMID: 17156479]
15. Wilson JF. In the Clinic Smoking Cessation Toolkit. Accessed at www.annals.org/intheclinic/toolkit-smoking-cessation.html?itcab out on 17 January 2008.

16. Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2007;147:633-8. [PMID: 17975186]
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19. van Noord JA, Aumann JL, Janssens E, et al. Effects of tiotropium with and without formoterol on airflow obstruction and resting hyperinflation in patients with COPD. *Chest.* 2006;129:509-17. [PMID: 16537846]
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21. COMBIVENT Inhalation Aerosol Study Group. In chronic obstructive pulmonary disease, a combination of ipratropium and albuterol is more effective than either agent alone. An 85-day multicenter trial. COMBIVENT Inhalation Aerosol Study Group. *Chest.* 1994; 105:1411-9. [PMID: 8181328]

of validated instruments, such as the Modified Medical Research Council scale of dyspnea (Table 1), and to reassess periodically as the disease progresses. Symptoms do not necessarily correlate with the level of FEV₁, and dyspnea may respond to drug therapy at any level. However, most studies of the effectiveness of drug therapy with end points of health status and frequency of COPD exacerbations have been performed in symptomatic patients with an FEV₁ less than 60% predicted. In view of this, the American College of Physicians (ACP) recommends that long-acting bronchodilator and inhaled corticosteroid treatment for stable COPD be reserved for patients who have respiratory symptoms and FEV₁ less than 60% predicted (16).

How should clinicians use inhaled bronchodilators?

There are no data to recommend initial use of any particular bronchodilator over another, and the choice

should be based on patient preference, potential toxicity, and cost. Clinicians should begin with single bronchodilator therapy and step up to combination bronchodilator therapy if additional symptomatic relief is required. Inhaled corticosteroids are then added as needed, again usually when the FEV₁ is less than 60% (9). The Figure, which is from the American Thoracic Society/European Respiratory Society guidelines (2), outlines an approach to step therapy.

Clinicians should choose short-acting bronchodilators with durations of action of 3 to 6 hours in patients with mild COPD, patients who need treatment of intermittent symptoms, or those on regular medication regimens who need rescue treatment for breakthrough symptoms. These include β_2 -agonists or the anticholinergic agent ipratropium (Table 2). Ipratropium is also short-acting (albeit with slower onset of action) and can be used for rescue as monotherapy or

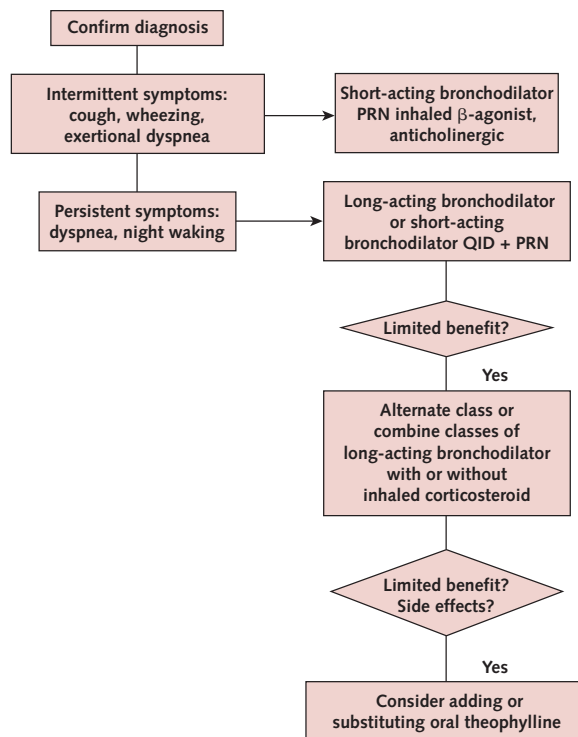


Figure. Step therapy for patients with COPD (from the ATS/ERS guidelines)

Table 2. Drug Treatment for COPD*

Agent	Dosage	Side Effects	Notes
<i>Bronchodilator agents</i>			
Inhaled short-acting β_2 -agonist: albuterol levalbuterol metaproterenol pirbuterol	2 inhalations as needed, up to 12 inhalations per day	Sympathomimetic symptoms, such as tremor and tachycardia	Generally used as needed
Inhaled short-acting anticholinergic: ipratropium	2 inhalations qid, increase as tolerated	Dry mouth, mydriasis on contact with eye	Use as maintenance therapy. Not to be used with tiotropium
Inhaled long-acting anticholinergic: tiotropium	18 μ g/d	Dry mouth, mydriasis on contact with eye	Use as maintenance therapy. Not to be used with ipratropium
Inhaled long-acting β_2 -agonist: salmeterol formoterol aformoterol	Salmeterol, 42 μ g bid by MDI and 50 μ g bid by DPI; formoterol, 12 μ g bid by DPI and 20 μ g by nebulized solution; aformoterol, 15 μ g bid by nebulized solution	Sympathomimetic symptoms, such as tremor and tachycardia	Use as maintenance therapy. Overdosage can be fatal. No change for exacerbations
Oral theophylline aminophylline: generic and brand name sustained and short acting	Aim for serum levels between 5 and 14 μ g/mL	Tachycardia, nausea, vomiting, disturbed pulmonary function, and sleep. Overdose can be fatal with seizures and arrhythmias	Use as maintenance therapy. Use intravenously in emergency departments. May also improve respiratory muscle function.
Oral β_2 -agonists: albuterol metaproterenol terbutaline	Albuterol, 4 mg bid; metaproterenol, 5 to 10 mg tid to qid; terbutaline, 2.5 to 5 mg tid	Sympathomimetic symptoms, such as tremor and tachycardia	Use as maintenance therapy. Rarely used because of side effects but may be beneficial to patients who cannot use inhalers.
<i>Anti-inflammatory agents</i>			
Inhaled corticosteroids: fluticasone budesonide triamcinolone	Fluticasone, 880 μ g/d; budesonide, 800 μ g/d; triamcinolone, 1200 μ g/d; all in divided doses.	Skin bruising, oral candidiasis, rarely adrenal suppression possibly glaucoma, decreased bone density, diabetes systemic hypertension, and cataracts	Can be used as maintenance therapy. In patients with a history of frequent exacerbations, high doses are best studied. Pulmonary function improved in in 10%–20% of patients, but symptoms and exacerbations reduced in a larger percentage. No effect on decline in pulmonary function. Not approved by the FDA for treatment of COPD.
Oral corticosteroids: prednisone prednisolone	Varying doses	Skin bruising, adrenal suppression, glaucoma, osteoporosis	Avoid use, if possible, in stable COPD. Pulmonary function improved in 10%–20% of patients. Reduce to lowest effective dose, including transition to inhaled corticosteroids, alternate day oral corticosteroids, or both. Intravenous or oral corticosteroids are standard therapy and are effective for acute exacerbations.
<i>Combination agents</i>			
Combined inhaled long-acting β_2 -agonist and inhaled corticosteroid: fluticasone salmeterol	Fluticasone, 250 μ g bid, and salmeterol, 50 μ g bid, single inhaler; combination of comparable doses of inhaled corticosteroids and long-acting β_2 -agonists in separate inhalers	See long-acting β_2 agonist and inhaled corticosteroid	The single inhaler combination is approved by the FDA for maintenance treatment of airflow obstruction in COPD associated with chronic bronchitis. Other combinations have not been approved by the FDA. Combinations are not to be used for treatment of acute bronchospasm. Overdosage of combination can be fatal because of long-acting β_2 -agonist.

*COPD = chronic obstructive pulmonary disease; DPI = dry-powder inhaler; FDA = Food and Drug Administration; MDI = metered-dose inhaler; qid = four times daily; tid = three times daily.

22. Aaron SD, Vandemheen KL, Ferguson D et al; Canadian Thoracic Society/Canadian Respiratory Clinical Research Consortium. Tiotropium in combination with placebo, salmeterol, or fluticasone-salmeterol for treatment of chronic obstructive pulmonary disease: a randomized trial. *Ann Intern Med*. 2007;146:545-55. [PMID: 17310045]
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28. Poole PJ, Chacko E, Wood-Baker RW, et al. Influenza vaccine for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2006: CD002733. [PMID: 16437444]

in combination with albuterol. Metered-dose inhalers, dry-powder inhalers, and nebulizers are all equally efficacious, although all require appropriate patient education regarding proper technique to ensure adequate drug delivery.

Monotherapy with long-acting bronchodilators reduces exacerbations and slightly improves overall respiratory health status but does not significantly reduce hospitalizations or mortality (17). Approved long-acting β_2 -agonists include salmeterol, formoterol, and aformoterol, all of which require twice daily dosing. The only long-acting anticholinergic agent is tiotropium, which is given once daily. Salmeterol and tiotropium have a slow onset of action, whereas formoterol and aformoterol have a rapid onset of action. Long-acting bronchodilators should never be used as rescue therapy or in doses greater than those indicated on package inserts.

Oral β_2 -agonists have not been well studied in COPD. They may be effective but are slower in onset, have more side effects (1), and are generally avoided.

If monotherapy is insufficient, clinicians should consider using inhaled combination therapy with a β_2 -agonist and an anticholinergic agent. Most studies show that such combinations may improve levels of FEV₁ (18–21), but there are few data suggesting that combination therapy is significantly better than monotherapy in alleviating clinical symptoms, such as relieving shortness of breath, improving exercise tolerance, and reducing COPD exacerbations. A recent study suggests that combination therapy with tiotropium and salmeterol improves disease-specific quality of life (22).

When should clinicians prescribe corticosteroids in patients with COPD?

Clinicians should consider adding inhaled corticosteroids to regimens of inhaled long-acting bronchodilators in patients with moderate-to-severe COPD, usually with FEV₁ less than 60% predicted, who remain symptomatic or have had repeated exacerbations. When paired with a long-acting β_2 -agonist, inhaled corticosteroids afford even greater improvement in pulmonary function and clinical outcomes than either agent alone (17).

Data also indicate that combining the long-acting anticholinergic tiotropium with the long-acting β_2 -agonist salmeterol plus an inhaled corticosteroid improves quality of life compared with monotherapy with a long-acting anticholinergic (22).

A randomized, double-blind trial compared inhaled salmeterol plus fluticasone with placebo, salmeterol alone, or fluticasone alone for a period of 3 years in 6112 patients with an FEV₁ less than 60% predicted. The combination of salmeterol and fluticasone decreased the annual rate of moderate-to-severe exacerbations. A statistically significant effect on mortality was not seen (17).

Oral steroids should be reserved for acute exacerbations of COPD and should be avoided in patients with stable disease.

When should clinicians consider adding oral theophylline to inhaled drug therapy for COPD?

Methylxanthines, such as aminophylline or theophylline, can be considered in patients with COPD who remain symptomatic despite use of other bronchodilators with or without inhaled corticosteroids and who do not have potential risk factors for toxicity, such as seizures and tachydysrhythmias. In such patients, theophylline can be started at a low dose and titrated to effect. A therapeutic blood level is

generally between 5 and 14 µg/mL (2, 3). Theophylline should be discontinued if there is no improvement after several weeks, and it should not be used in treating acute exacerbations of COPD. Several RCTs have demonstrated oral theophylline to be a relatively weak bronchodilator (23–26). The narrow therapeutic window, multiple interactions with other medications, and potential toxicity necessitate frequent monitoring of serum theophylline levels.

What immunizations should clinicians administer to patients with COPD?

The Advisory Committee on Immunization Practices recommends influenza and pneumococcal vaccinations for persons who have chronic disorders of the pulmonary or cardiovascular systems, including COPD (27). Influenza vaccination should be administered yearly to all patients with COPD. This is supported by 3 meta-analyses (28–30).

In a Cochrane review of 11 RCTs, 6 of which were performed in patients with COPD, use of inactivated vaccine resulted in a significant reduction in the total number of exacerbations per vaccinated subject compared with those who received placebo (weighted mean difference, -0.37 [95% CI, -0.64 to -0.11]; P = 0.006) (28).

Pneumococcal vaccination should be given once before age 65 and again after age 65 if the previous vaccination was given more than 5 years earlier (27). If the patient was not vaccinated before age 65, then a 1-time vaccination is recommended.

How should clinicians manage patients with acute exacerbations of COPD?

Although there is no single definition of a COPD exacerbation, a frequently used approach is to apply the criteria shown in the Box on this page. Acute exacerbations of COPD frequently develop following an upper respiratory

Criteria and Classification of Acute COPD Exacerbation

Major criteria

- Increase in sputum volume
- Increase in sputum purulence (generally yellow or green)
- Worsening dyspnea

Additional criteria

- Upper respiratory infection in the past 5 days
- Fever of no apparent cause
- Increase in wheezing and cough
- Increase in respiratory rate or heart rate 20% above baseline

Mild exacerbation = 1 major criterion plus 1 or more additional criteria

Moderate exacerbation = 2 major criteria

Severe exacerbation = all 3 major criteria

(Adapted from ref. 31)

infection. Management includes prompt recognition of the exacerbation, adjustment of bronchodilator and steroid therapy, initiation of antibiotics, and assessment of the need for hospitalization.

Clinicians should strongly consider prescribing antibiotics for patients who meet the criteria for a moderate or severe exacerbation.

Although some exacerbations are due to viral infection or inhaled irritants, the most common bacterial causes are *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis* (32, 33). Antibiotic coverage should generally be directed toward these bacteria, taking into account local bacterial resistance patterns. To date, there are insufficient clinical data to recommend any single antimicrobial agent over another. However, there is consensus that the severity of the exacerbation, the degree of pulmonary function impairment, the history of exacerbations, and the response to previous treatment should be used to help guide therapy. For patients with moderate or severe exacerbations, a β-lactam/β-lactamase

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Indications for Hospital Assessment or Admission for Exacerbations of COPD

- Marked increase in intensity of symptoms, such as sudden development of resting dyspnea
- Severe underlying COPD
- Onset of new physical signs (for example, cyanosis or peripheral edema)
- Failure of exacerbation to respond to initial medical management
- Significant comorbid conditions
- Frequent exacerbations
- Newly occurring arrhythmias
- Diagnostic uncertainty
- Older age
- Insufficient home support

(Adapted from ref. 1)

37. Snow V, Lascher S, Mottur-Pilson C; Joint Expert Panel on COPD of the American College of Chest Physicians and the American College of Physicians-American Society of Internal Medicine. The evidence base for management of acute exacerbations of COPD: clinical practice guideline, part 1. *Chest*. 2001;119:1185-9. [PMID: 11296188]

38. Sachs AP, Koëter GH, Groenier KH, et al. Changes in symptoms, peak expiratory flow, and sputum flora during treatment with antibiotics of exacerbations in patients with chronic obstructive pulmonary disease in general practice. *Thorax*. 1995;50:758-63. [PMID: 7570411]

39. Wood-Baker RR, Gibson PG, Hannay M, et al. Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2005; CD001288. [PMID: 15674875]

40. Niewoehner DE, Erbland ML, Deupree RH, et al. Effect of systemic glucocorticoids on exacerbations of chronic obstructive pulmonary disease. Department of Veterans Affairs Cooperative Study Group. *N Engl J Med*. 1999;340: 1941-7. [PMID: 10379017]

inhibitor, an extended-spectrum macrolide, a second- or third-generation cephalosporin, or a fluoroquinolone can be used. Those with a mild exacerbation can be treated with tetracycline or trimethoprim-sulfamethoxazole. In any case, always consider antibiotics in patients with 1 major criterion and an abnormal chest X-ray or an FEV₁ less than 35% predicted. It is not necessary to routinely obtain sputum Gram stain and culture in patients with an exacerbation.

Previous meta-analyses and systematic reviews have provided support for the efficacy of antibiotics in patients with exacerbations of COPD (34–38). Specifically, antibiotics improve peak flow, reduce mortality, and reduce treatment failure. This effect appears to be most pronounced in patients with more severe exacerbations (36).

A Cochrane review of 11 RCTs included 917 patients with COPD. Of these, 10 trials used increased cough, sputum volume, and purulence as diagnostic criteria for a COPD exacerbation. Antibiotic therapy, regardless of antibiotic choice, significantly reduced mortality, treatment failure, and sputum purulence, with a number needed to treat of 8. There was a small increase in risk for diarrhea with antibiotics (relative risk, 2.86 [CI, 1.06 to 7.76]) (35).

Oral corticosteroids should be considered in patients with moderate-to-severe acute exacerbations of COPD. Although the appropriate dose is not well defined, 30 to 60 mg/d for up to 2 weeks is commonly used (39). There is good evidence to suggest that a 6-week course of systemic steroids is no more beneficial than a 2-week course and that the longer course increases the risk for adverse effects (40).

Tailoring therapy to prevent future exacerbations is difficult because there is no sufficiently accurate way to predict which subset of patients with COPD is at greatest risk. Most studies suggest that a history

of previous exacerbations, a baseline FEV₁ less than 50% predicted, and perhaps age may be the most useful predictors (41–43).

It is important to recognize patients in whom outpatient management of a COPD exacerbation is insufficient and hospitalization with possible intubation and mechanical ventilation may be necessary (see Box). Venous thromboembolism should be considered in patients with COPD exacerbations of unknown cause who do not have evidence of infection (44).

When should clinicians recommend pulmonary rehabilitation for patients with COPD?

Pulmonary rehabilitation is a multidisciplinary program of care that comprises a variety of interventions grouped into categories, including exercise training, education, and psychological and nutritional counseling. Although the individual components have benefits, the most effective approach is a comprehensive, integrated program (3). A team of health care practitioners usually provides pulmonary rehabilitation in a structured program administered to groups of patients with COPD.

Clinicians should recommend pulmonary rehabilitation for all symptomatic patients with COPD as part of their overall treatment plan as they are optimizing drug treatment. Patients who are most likely to benefit are those with impaired quality of life from COPD, who experience breathlessness and anxiety that limit activity, and who are willing to undertake an intensive education and exercise program (1–3).

Most studies involve patients with more severe disease, but patients with mild-to-moderate COPD may also benefit. More recent data suggest that pulmonary rehabilitation

may be helpful in patients after an acute exacerbation (45).

In a meta-analysis of 20 RCTs of 979 patients, including studies to the year 2000, it was concluded that pulmonary rehabilitation increased exercise ability and health-related quality of life and reduced dyspnea. Inspiratory muscle training, by itself, was not effective. Patients with severe COPD required a program lasting at least 6 months to achieve benefit. Patients with mild-to-moderate COPD could benefit from shorter programs (46).

What other adjunctive measures should clinicians consider in managing patients with COPD?

There are several other commonly used adjunctive therapies. Chest physiotherapy, percussion and vibration, and postural drainage are used to enhance clearance of sputum and alleviate shortness of breath. Relaxation techniques may reduce anxiety due to shortness of breath. Pursed-lip breathing and diaphragmatic breathing are used to reduce shortness of breath. Nutritional interventions aim to achieve ideal body weight and improve ability to perform daily activities and exercise (1, 3, 4). However, data to support the effectiveness of these measures are lacking.

When should clinicians prescribe oxygen therapy for patients with COPD?

Patients with moderate-to-severe COPD should be periodically evaluated for the need for supplemental oxygen. The Box lists criteria for initiation of long-term oxygen therapy. Measurement of PaO₂ after 30 minutes of breathing room air is the most accurate clinical standard for initiating therapy. Pulse oximetry can be used to qualify patients for long-term oxygen therapy. Oximetry can also be used to adjust oxygen delivery (for example, oxygen flow rates) after initial diagnosis and over time.

When long-term oxygen therapy is indicated, continuous oxygen should be used for a minimum of

Criteria for Initiation of Long-Term Oxygen Therapy

- Room air PaO₂ no greater than 55 mm Hg or between 55 and 60 mm Hg with cor pulmonale; signs of tissue hypoxia, such as polycythemia; or an SaO₂ no greater than 88% or 89% with signs of tissue hypoxia, OR
- Nocturnal hypoxemia with an SaO₂ no greater than 88% (use oxygen only at night), OR
- Exercise hypoxemia with a PaO₂ 55 mm Hg or less or an SaO₂ 88% or less (use oxygen only with exertion).

15 hours and ideally for 24 hours a day. Patients should have an initial follow-up within at least 3 months and yearly thereafter to guide subsequent oxygen therapy (47). However, the criteria of the Centers for Medicare & Medicaid Services do not generally require follow-up assessment if the qualifying PaO₂ was 55 mm Hg or less or the qualifying SaO₂ was 88% or less (48).

Long-term oxygen therapy can be used during exercise in persons with exertional desaturation to improve symptoms (49, 50) and during sleep in those who desaturate at night (51).

In a Cochrane review, meta-analysis of 6 RCTs showed that home long-term oxygen therapy improved survival in a select group of patients with COPD and severe hypoxemia (arterial PaO₂ less than 55 mm Hg [8.0 kPa]). Home oxygen therapy did not improve survival in patients with mild-to-moderate hypoxemia or in those with only arterial desaturation at night (50).

When should clinicians refer patients to a pulmonologist?

Clinicians should consider referring patients with COPD to a pulmonologist when there is diagnostic uncertainty or when patients are not responding well to treatment. Table 3 lists recommendations for referral adapted from guidelines.

Clinicians should consider pulmonary consultation in patients with COPD and severe disease undergoing surgery, those being considered for lung-volume

41. van der Valk P, Moninkhof E, van der Palen J, et al. Effect of discontinuation of inhaled corticosteroids in patients with chronic obstructive pulmonary disease: the COPE study. *Am J Respir Crit Care Med.* 2002;166:1358-63. [PMID: 12406823]
42. Jones PW, Willits LR, Burge PS, et al.; Inhaled Steroids in Obstructive Lung Disease in Europe study investigators. Disease severity and the effect of fluticasone propionate on chronic obstructive pulmonary disease exacerbations. *Eur Respir J.* 2003;21:68-73. [PMID: 12570111]
43. Niewoehner DE, Likhnygina Y, Rice K, et al. Risk indexes for exacerbations and hospitalizations due to COPD. *Chest.* 2007;131:20-8. [PMID: 17218552]
44. Tillie-Leblond I, Marquette CH, Perez T, et al. Pulmonary embolism in patients with unexplained exacerbation of chronic obstructive pulmonary disease: prevalence and risk factors. *Ann Intern Med.* 2006;144:390-6. [PMID: 16549851]
45. Puhan MA, Scharplatz M, Troosters T, et al. Respiratory rehabilitation after acute exacerbation of COPD may reduce risk for readmission and mortality—a systematic review. *Respir Res.* 2005;6:54. [PMID: 15943867]
46. Salman GF, Mosier MC, Beasley BW, et al. Rehabilitation for patients with chronic obstructive pulmonary disease: meta-analysis of randomized controlled trials. *J Gen Intern Med.* 2003;18:213-21. [PMID: 12648254]
47. Guyatt GH, Nonoyama M, Lachetti C, et al. A randomized trial of strategies for assessing eligibility for long-term domiciliary oxygen therapy. *Am J Respir Crit Care Med.* 2005;172:573-80. [PMID: 15901604]
48. Centers for Medicare & Medicaid Services. Evidence of medical necessity oxygen claims. Accessed at www.cms.hhs.gov/transmittals/downloads/r1742B3.pdf on 17 January 2008.

Table 3. When to Consider Referral to a Pulmonary Specialist*

Disease onset before 40 years of age
Frequent exacerbations (2 or more per year) despite adequate treatment
Rapidly progressive course of disease (decline in FEV ₁ , progressive dyspnea, decreased exercise tolerance, unintentional weight loss)
Severe COPD (FEV ₁ <50% predicted) despite optimal treatment
Need for oxygen therapy
Onset of comorbid condition (osteoporosis, heart failure, bronchiectasis, lung cancer)
Diagnostic uncertainty (for example, coexisting COPD and asthma)
Symptoms disproportionate to the severity of the airflow obstruction
Confirmed or suspected α_1 -antitrypsin deficiency
Patient requests a second opinion
Patient is a potential candidate for lung transplantation or lung-volume reduction surgery
Patient has very severe disease and requires elective surgery that may impair respiratory function

*Adapted and modified from American Thoracic Society/European Respiratory Society and Veterans' Affairs/Department of Defense guidelines (2, 3). COPD = chronic obstructive pulmonary disease.

49. Bradley JM, O'Neill B. Short-term ambulatory oxygen for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2005; CD004356. [PMID: 16235359]
50. Cranston JM, Crockett AJ, Moss JR, et al. Domiciliary oxygen for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2005; CD001744. [PMID: 16235285]
51. Fletcher EC, Luckett RA, Goodnight-White S, et al. A double-blind trial of nocturnal supplemental oxygen for sleep desaturation in patients with chronic obstructive pulmonary disease and a daytime PaO₂ above 60 mm Hg. *Am Rev Respir Dis*. 1992;145:1070-6. [PMID: 1586049]
52. American College of Physicians. Preoperative pulmonary risk stratification for noncardiothoracic surgery: systematic review for the American College of Physicians. *Ann Intern Med*. 2006;144:581-95. [PMID: 16618956]
53. Trayner E Jr, Celli BR. Postoperative pulmonary complications. *Med Clin North Am*. 2001;85:1129-39. [PMID: 11565490]
54. Ferreira IM, Brooks D, Lacasse Y, et al. Nutritional supplementation for stable chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2005; CD000998. [PMID: 15846608]
55. Fishman A, Martinez F, Naunheim K, et al. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. *N Engl J Med*. 2003;348:2059-73. [PMID: 12759479]
56. Hillerdal G, Löfdahl CG, Ström K, et al. Comparison of lung volume reduction surgery and physical training on health status and physiologic outcomes: a randomized controlled clinical trial. *Chest*. 2005;128:3489-99. [PMID: 16304304]

reduction surgery, and those who might be candidates for lung transplantation.

Preoperative Assessment

Patients with COPD have a 2.7- to 4.7-fold increase in the risk for postoperative pulmonary complications depending on the severity of COPD and the type, location, and urgency of the surgical procedure (52, 53). With COPD, patients undergoing thoracic and upper abdominal procedures are at greater risk. Patient-related risk factors include age, American Society of Anesthesiologists class, and cigarette smoking (52, 53).

A systematic review of interventions to reduce postoperative pulmonary complications after noncardiothoracic surgery found that a few are clearly effective. Effective measures include early ambulation; lung expansion maneuvers, such as incentive spirometry; deep breathing exercises; and continuous positive airway pressure to reduce pulmonary complications, such as atelectasis, pneumonia, and respiratory failure. Teaching patients about lung expansion maneuvers increases efficacy. Data that favor use of nasogastric tubes, epidural anesthesia and analgesia, laparoscopic operations, and enteral nutrition interventions are less clear-cut (52–54).

When should clinicians consider surgical therapies for COPD?

Lung-Volume Reduction Surgery

Lung-volume reduction surgery involves resection of up to 30% of diseased or nonfunctioning parenchyma to allow remaining lung to function more efficiently. It may be considered in patients with COPD who have completed a pulmonary rehabilitation program and meet the following criteria: 1) evidence of bilateral emphysema on CT scan; 2) postbronchodilator total lung capacity and residual volume greater than 150% and 100% predicted, respectively; 3) maximum FEV₁ no greater than 45% predicted; and 4) room air PaCO₂ no more than 60 mm Hg and a PaO₂ of at least 45 mm Hg. Patients with an FEV₁ no greater than 20% predicted and either homogeneous emphysema on CT scan or a carbon monoxide diffusing capacity of no more than 20% predicted should not be considered for lung-volume reduction surgery (55).

In patients with COPD who meet specific clinical criteria, lung-volume reduction surgery increases the chance for improved exercise capacity, lung function, dyspnea, and quality of life but does not improve overall survival compared with medical therapy alone. In a subgroup of patients with upper lobe emphysema and low exercise

capacity, lung-volume reduction surgery may improve survival, but definitive long-term data are not yet available (55–57).

Lung Transplantation

COPD disease-specific guidelines for candidate selection for lung transplantation include patient with a BODE index of 7 to 10 and at least 1 of the following (12): 1) history of hospitalization for exacerbation associated with acute hypercapnia (partial pressure of carbon dioxide greater than 50 mm Hg); 2) pulmonary hypertension, cor pulmonale, or both despite oxygen therapy; and 3) FEV₁ less than 20% predicted and either carbon monoxide diffusion in the lungs less than 20% or homogeneous distribution of emphysema. There are

also a number of relative and absolute contraindications to lung transplantation that are beyond the scope of this review (12).

Lung transplantation results in improved pulmonary function; exercise capacity; quality of life; and in highly selected patients, possibly survival (2). Average actuarial survival following single lung transplantation for patients with COPD is 82.9%, 59.7%, and 43.3% at 1, 3, and 5 years, respectively. Double lung transplantation survival is similar or slightly higher (58). By 5 years after lung transplantation, the prevalence of chronic allograft rejection (obliterative bronchiolitis), the leading cause of long-term morbidity and mortality, is as high as 50% to 70% among survivors (59).

Treatment... All patients with COPD who smoke should be urged to stop and to enter a smoking cessation program. Patients who have symptoms, such as dyspnea, can be treated with inhaled β_2 -agonists or anticholinergic agents alone or in combination. The greatest benefit from treatment with long-acting bronchodilators is achieved in patients with an FEV₁ less than 60% predicted with an improvement in health status and a reduction in COPD exacerbations. These benefits may be enhanced with the addition of an inhaled corticosteroid. Acute exacerbations should be treated by optimizing bronchodilator therapy and adding systemic corticosteroids or antibiotics when clinically indicated. All patients should be encouraged to exercise. Pulmonary rehabilitation should be offered to patients with moderate-to-severe COPD to improve dyspnea and health status. Continuous long-term oxygen therapy is recommended for patients with severe disease and hypoxemia. Eligible patients should be evaluated for lung-volume reduction surgery or lung transplantation.

CLINICAL BOTTOM LINE

What do professional organizations recommend with regard to prevention, screening, diagnosis, and treatment of COPD?

Guidelines from professional organizations include those from the Global Initiative for Chronic Obstructive Lung Disease, updated in 2007 (1); the American Thoracic Society/European Respiratory Society, updated in 2005 (2); the Veterans' Affairs and Department of Defense, updated in 2007 (3);

the National Institute of Clinical Excellence, published in 2004 (4); and the American College of Physicians (ACP), published in 2007 (16). The first 4 present a comprehensive approach to the diagnosis and management of COPD and draw information and evidence from a variety of sources, including RCTs; cohort studies; case-control studies; recommendations from public policy organizations, such as the Advisory Committee on Immunization

Practice Improvement

57. Ramsey SD, Shroyer AL, Sullivan SD, et al. Updated evaluation of the cost-effectiveness of lung volume reduction surgery. *Chest*. 2007;131:823-32. [PMID: 17356099]
58. United Network for Organ Sharing. The organ procurement and transplantation network. Accessed at www.optn.org/latestData/rptStrat.asp on 14 January 2008.

Practices; and expert opinion. The ACP guidelines are based almost solely on RCTs (9, 16). Although most guidelines suggest treating patients with COPD when they become symptomatic, the contribution of the ACP meta-analysis and guideline is to emphasize that the evidence indicates that inhaled drug therapy is most effective in patients in whom FEV₁ is less than 60% predicted.

What measures do stakeholders use to evaluate the quality of care for patients with COPD?

The Centers for Medicare & Medicaid Services has issued specifications for measures for the 2008 Physicians Quality Reporting Initiative. Of these measures, 2 relate to COPD. The first measure evaluates the percentage of patients age 18 years or older with a diagnosis of COPD who had spirometry evaluation documented in the measurement year. The second measure evaluates the percentage of patients age 18 years or older who had a diagnosis of COPD; an FEV₁/FVC ratio less than 0.70; symptoms, such as dyspnea, cough, sputum, or wheezing; and who were prescribed an inhaled bronchodilator.

What is the role of patient education in optimizing care of patients with COPD?

It is important that patients with COPD participate in the management of their disease by understanding the cause, treatment, course, and prognosis of COPD. They should be instructed in proper inhaler techniques, recognition of signs of deterioration, proper use of medications and exercise, smoking cessation, and precautions to take when traveling by air. Some of this education is available in multidisciplinary rehabilitation programs. Although some studies have shown that patient education programs have decreased hospitalizations and related measures, systematic reviews have documented less marked benefits (16).

According to the ACP guidelines on COPD, as of January 2005, the evidence shows that disease management and patient education efforts have not been effective in decreasing deaths, exacerbations, all-cause readmissions, lengths of stay, or number of visits to physicians or increasing improvements on health questionnaires, patient satisfactions, adherence to treatment, or self-management skills (16, 60).

59. Heng D, Sharples LD, McNeil K, et al. Bronchiolitis obliterans syndrome: incidence, natural history, prognosis, and risk factors. *J Heart Lung Transplant*. 1998;17:1255-63. [PMID: 9883768]

60. Monnikhof EM, van der Valk PD, van der Palen J, et al. Self-management education for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2003;1:CD002990. [PMID: 12535447]

in the clinic Tool Kit

Chronic Obstructive Pulmonary Disease

PIER Module

pier.acponline.org/physicians/diseases/d153/pdf/d153.pdf
Access PIER module on COPD.

COPD Pocket Card

www.oqp.med.va.gov/cpg/COPD/G/COPD_Pock.pdf
Download pocket card version of Veterans Administration/Department of Defense COPD Guidelines.

National Lung Health Education Project

www.nlbep.org/resources-medical.html
Pocket cards, wallet cards, posters, spirometry review materials, and other resources for physicians.

International COPD Coalition

www.internationalcopd.org/materials/professionals/default.aspx
COPD guidelines and patient information materials.

Joint Commission on Accreditation of Healthcare Organizations

www.jointcommission.org/CertificationPrograms/COPD
COPD certification program that lists a number of areas that should be in place for disease-specific care.

in the clinic

WHAT YOU SHOULD KNOW ABOUT CHRONIC OBSTRUCTIVE PULMONARY DISEASE

What is COPD?

- Chronic obstructive pulmonary disease (COPD) damages the lungs and the tubes that carry air from the nose and mouth to the lungs.
- COPD makes you cough and bring up mucus. It makes it hard to breathe and do the things you want to do.

How can you prevent COPD?

- Cigarette smoke is the most common cause of COPD. Stopping smoking can keep you from getting COPD.
- If you already have COPD, stopping smoking can keep it from getting worse.

How is COPD treated?

- Some people with COPD need medicines to open the airways. Most medicines are given by inhalers that deliver the medicine to the lungs in spray form.
- Sometimes antibiotics are needed to fight infections that make COPD worse.
- It is important to exercise and keep active.
- Some people need extra oxygen when COPD keeps them from getting enough.

How to Use an Inhaler

1. Take off the cap and shake the inhaler hard.
2. Breathe out all the way.
3. Hold the inhaler about 2 fingerwidths from your mouth.
4. Start to breath in slowly through your mouth as you press down on the inhaler once and keep breathing in slowly until you can't breathe in any more.
5. Hold your breath and count to 10 slowly.
6. Repeat steps 1 to 5 if your doctor has prescribed more than 1 puff of medicine, wait about 1 minute between puffs.

Web Sites with Good Information about COPD

MedlinePLUS

www.nlm.nih.gov/medlineplus/copdchronicobstructivepulmonarydisease.html#cat1

American Lung Association

www.lungusa.org/site/pp.asp?c=dvLUK900E&t=23050

International COPD Coalition

www.internationalcopd.org/materials/professionals/default.asp

1. Which of the following surgeries pose the greatest risk to patients with advanced chronic obstructive pulmonary disease?

- A. Ophthalmologic procedures
- B. Upper extremity surgical procedures
- C. Upper abdominal and thoracic surgical procedures
- D. Urologic surgical procedures using local anesthesia
- E. Endoscopic sinus surgery

2. A 65-year-old man with severe COPD is evaluated for worsening shortness of breath and ankle swelling. He does not have excessive daytime sleepiness or loud snoring. He uses a long-acting β -agonist in combination with an inhaled corticosteroid on a regular basis.

The patient's weight and vital signs are normal. There is neck vein distention at 30 degrees. Cardiac examination shows a regular rate and rhythm without murmur. The pulmonic closure sound is accentuated. An S_3 gallop was noted that varied with respiration. Examination of the lungs reveals faint wheezes bilaterally. The abdomen is nonobese without organomegaly. Examination of the legs and ankles reveals 1+ edema. Arterial blood gases with the patient breathing room air show pH 7.40, pO_2 65 mm Hg, and pCO_2 44 mm Hg. The hematocrit is 52%.

Which of the following is the most appropriate next step in the management of this patient?

- A. Nocturnal mechanical ventilation
- B. Phlebotomy
- C. Nocturnal pulse oximetry
- D. Ipratropium bromide therapy

3. A 57-year-old man with advanced COPD and systemic hypertension is evaluated because of a 6-day history of productive cough and shortness of breath. He uses inhaled albuterol and ipratropium bromide, a long-acting theophylline preparation, and lisinopril. He uses supplemental oxygen at night and during ambulation. Ciprofloxacin is prescribed for an exacerbation of COPD.

Three days later, having had nausea for 1 day, the man is brought to the emergency department after he is found nearly unconscious. Arterial oxygen saturation is 89%, with the patient breathing room air. Electrocardiogram shows normal sinus rhythm with nonspecific ST-T changes in the lateral chest leads.

Which of the following is likely to have interacted with ciprofloxacin and caused the symptoms that brought the man to the emergency department?

- A. Albuterol
- B. Theophylline
- C. Ipratropium bromide
- D. Lisinopril
- E. Oxygen

4. A 59-year-old man with advanced COPD is evaluated because of a daily cough productive of white or yellow sputum, dyspnea after climbing 1 flight of stairs, and a recent 4.5-kg (10-lb) weight loss with no associated change in appetite or food intake. The patient stopped smoking 4 years ago.

On physical examination, he has diminished breath sounds throughout all lung fields. Arterial oxygen saturation measured by pulse oximetry with the patient at rest, breathing room air, is 87%. Chest radiograph suggests hyperinflation of the lungs but shows no pulmonary infiltrates or abnormalities of the cardiac silhouette. Pulmonary function studies show a FEV_1 of 39% predicted and FVC of 78% predicted.

Which of the following may prolong life in this patient?

- A. Albuterol
- B. Ipratropium bromide
- C. Theophylline
- D. Supplemental oxygen

5. A 68-year-old man with severe COPD (FEV_1 , 32% predicted) is evaluated because of severe dyspnea and the inability to carry out his activities of daily living. He is on maximal bronchodilator and oxygen therapy.

Which of the following might pulmonary rehabilitation improve?

- A. Exercise tolerance
- B. FEV_1
- C. Oxygenation
- D. Survival

6. A 62-year-old woman with emphysema is evaluated during a routine visit. She has chronic dyspnea on exertion, but has no cough or sputum production. She uses supplemental oxygen, 2 L/min. She uses albuterol and ipratropium 4 times per day, and salmeterol and theophylline 2 times per day. She is enrolled in a pulmonary rehabilitation program and is concerned about "catching a cold" from other members of the program.

What is the best advice for this patient?

- A. Discontinue the rehabilitation program
- B. Obtain pneumococcal and annual influenza vaccination
- C. Take prophylactic ciprofloxacin
- D. Wear a surgical mask

Questions are largely from the ACP's Medical Knowledge Self-Assessment Program (MKSAP). Go to www.annals.org/intheclinic/ to obtain up to 1.5 CME credits, to view explanations for correct answers, or to purchase the complete MKSAP program.