

An Evidence-Based Approach to COPD: Part 1

A review of current guidelines on the diagnosis and management of chronic obstructive pulmonary disease. The first of a two-part article.

OVERVIEW: Chronic obstructive pulmonary disease (COPD) is the third leading cause of death in the United States, affecting as many as 24 million Americans and resulting in 1.5 million ED visits, 700,000 hospital admissions, and 124,000 deaths annually. This article, the first in a two-part series on COPD, outlines current guidelines and other evidence-based recommendations on diagnosing and managing stable COPD in the outpatient setting. Part 2 will appear in a future issue of *AJN* and will focus on managing acute exacerbations of COPD.

Keywords: chronic bronchitis, chronic obstructive pulmonary disease, emphysema, patient education, respiratory disease

Miranda Pierce, age 55, tells her NP that for the past three years, shortness of breath and increased sputum production have caused her to cough up about two teaspoons of clear phlegm each morning. (This patient is a composite of cases we've encountered in our clinical practice.) An investment banker for 30 years, she says she's been relatively active most of her life but is now easily fatigued and breathless when walking one or two blocks. She lives in a two-story home and becomes short of breath when climbing even one flight of stairs. She has never been hospitalized or treated in an ED for respiratory problems, but several times a week she uses an albuterol inhaler to relieve episodic wheezing. She has smoked since the age of 15 and currently smokes one pack of cigarettes per day; until about three years ago, she

smoked two packs per day. She says she has no other significant medical history.

On physical examination her vital signs are blood pressure, 138/78 mmHg; heart rate, 88 beats per minute; respiratory rate, 22 breaths per minute; temperature, 98°F (36.6°C). Her body mass index (BMI) is 21 kg/m², and her arterial oxygen saturation (SaO₂) level, while she's at rest and breathing room air, is 94%. She's alert, oriented, and in no acute distress while resting. Her cardiac examination is unremarkable. Chest auscultation reveals slightly diminished breath sounds with a prolonged expiratory phase and scattered end-expiratory wheezes. She has neither peripheral edema nor digital clubbing.

Office spirometry shows a forced expiratory volume in the first second (FEV₁) of exhaling from full lung capacity to be 60%—consistent with moderate expiratory airflow obstruction. The ratio between FEV₁ and forced vital capacity (FVC)—the total volume exhaled as forcefully and completely as possible, starting at full lung capacity—is 65% (normally, it's 70% to 80%). On a six-minute walk test, in which Ms. Pierce walks 300 meters (about 1,000 ft.), pulse oximetry shows no significant oxygen desaturation. Her score on the chronic obstructive pulmonary disease (COPD) assessment test (CAT), a simple questionnaire that measures health status in patients with COPD,¹ is 17, representing a moderate impact on health. The NP diagnoses Ms. Pierce with COPD, a disease that's estimated to affect as many as 24 million adults in the United States and accounts for 1.5 million ED visits and 700,000 hospital admissions annually.² In 2008 more than

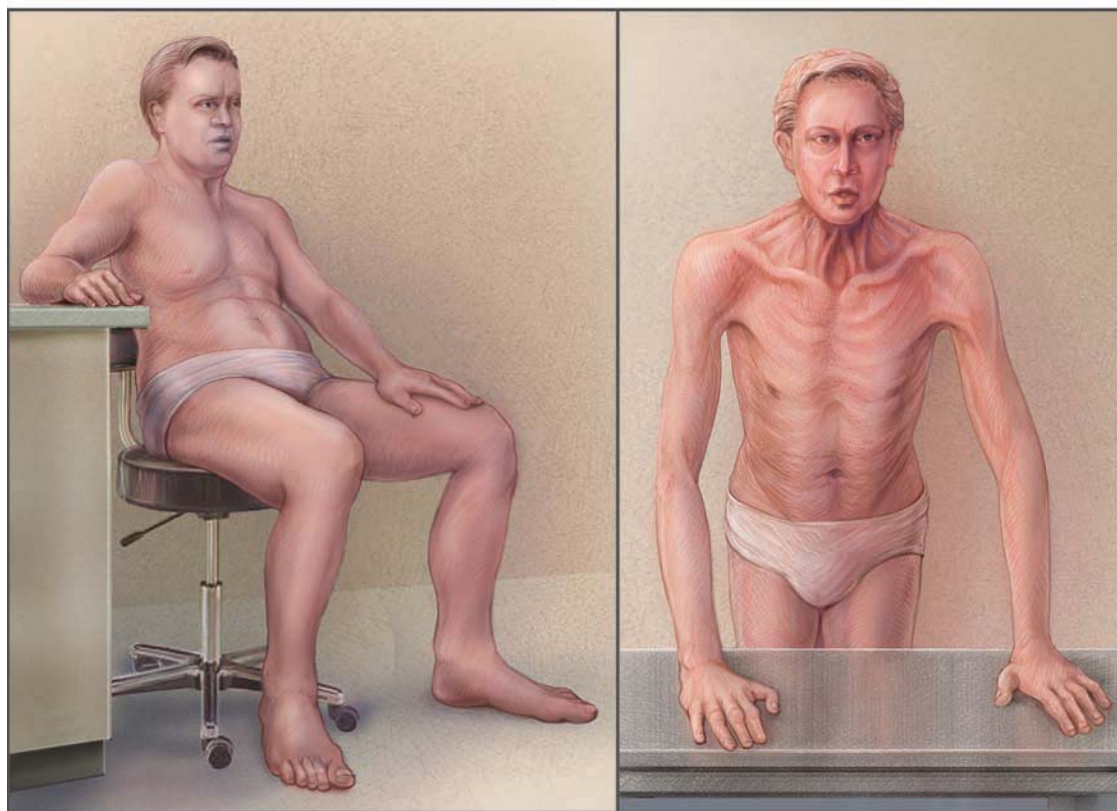


Figure 1. Most patients with COPD have features of both chronic bronchitis and emphysema, but some present with more features of one than the other. The patient on the left has signs and symptoms of chronic bronchitis: hypoxemia, pulmonary hypertension, right-sided heart failure, and peripheral edema. The patient on the right has signs and symptoms of emphysema: pulmonary cachexia, dyspnea, and pursed-lip breathing. Image courtesy of the *New England Journal of Medicine*.

124,000 U.S. deaths were attributed to COPD, making it the third leading cause of death.³

The NP strongly encourages Ms. Pierce to quit smoking and refers her to a smoking-cessation program, prescribes a long-acting bronchodilator, orders influenza and pneumonia vaccinations, and enrolls her in a pulmonary-rehabilitation program. After explaining the pathophysiology of COPD, he goes over patient education materials that detail the proper use of COPD medications; how to monitor symptoms; and the importance of smoking cessation, good nutrition, and general wellness in COPD management (see *What You Need to Know if You're Diagnosed with COPD: Pointers for Patients*, also available online at <http://links.lww.com/AJN/A40>). He also instructs Ms. Pierce to return for a follow-up visit in one month.

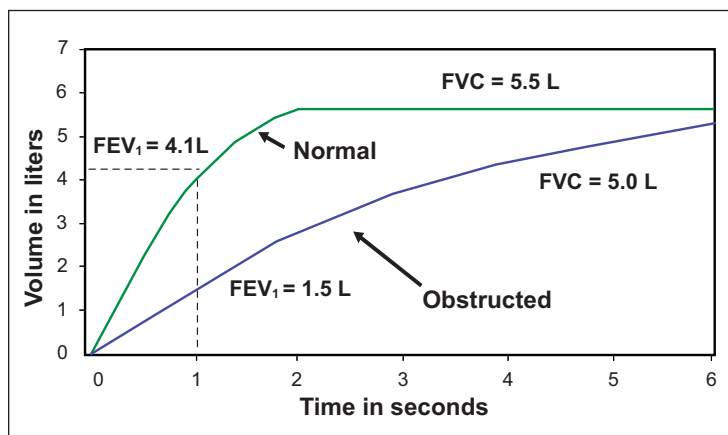
The NP responded to a case of moderate, stable COPD in accordance with current, evidence-based guidelines—using a range of measures to assess disease severity, prescribing accordingly, fully explaining the disease to the patient, and providing important

information on symptom management. This article will review the evidence and recommendations on which these clinical actions were based; discuss the essential features, pathogenesis, diagnosis, and management of COPD; and provide an education tool for patients.

THE ESSENTIAL FEATURES OF COPD

In 2004 the American Thoracic Society (ATS) and the European Respiratory Society (ERS) released a joint position paper on the diagnosis and management of COPD.⁴ In it they define COPD as a respiratory disease with features of both chronic bronchitis and emphysema (but not asthma, which they consider a separate diagnosis). Chronic bronchitis inflames and alters airway structures, causing cough, excessive phlegm, wheezing, and breathlessness. It can be diagnosed when a productive cough is present on most days for at least three months in each of two consecutive years and cannot be attributed to another cause. Emphysema refers to the destruction

Figure 2. Obstruction as Seen on Spirometry



During simple spirometry, the patient exhales as forcefully and completely as possible, starting at full lung inflation (bottom left of the above curve). Exhaled volume (in liters) is plotted on the Y axis against exhalation time (in seconds) on the X axis to generate the volume–time curve. The total volume exhaled during this maneuver is called the forced vital capacity (FVC). The forced expiratory volume in the first second of the FVC maneuver is called the FEV₁. Under normal conditions (green line), the FVC is completed in three or four seconds (as indicated by a plateauing of the volume–time curve), and 70% to 80% of the FVC is exhaled in the first second (so the FEV₁–FVC ratio is normally 0.7 to 0.8). In the sample shown here, the patient’s exhalation (signified by the blue line) demonstrates an abnormally low FEV₁, suggestive of expiratory airflow obstruction. Typically, in COPD, the FEV₁ drops lower than the FVC does, which reduces the FEV₁–FVC ratio. An FEV₁–FVC ratio of less than 0.7 suggests airflow obstruction. An FEV₁–FVC ratio that remains less than 0.7 after administration of a short-acting bronchodilator suggests airflow obstruction that isn’t fully reversible.

of lung parenchyma, including alveolar attachments and alveolar-capillary units. It causes breathlessness, but in and of itself, produces no cough or excessive phlegm. Most patients with COPD have aspects of both chronic bronchitis and emphysema, working together to obstruct expiratory flow; such obstruction can be detected through simple spirometry.

Bronchodilators may improve but cannot fully reverse airflow limitation in COPD, as they often can in asthma. In fact, the distinction between COPD and asthma may be complicated because asthma that causes airway remodeling and fixed airflow obstruction is also irreversible.

Risk factors. Most, but not all, patients who develop COPD are current or ex-smokers.^{5,6} The greater the amount smoked over a lifetime, the more likely the patient is to develop COPD.⁷ Even in the absence of clinical symptoms, COPD should be considered in all patients over age 40 who have a smoking history of 10 or more pack-years. (Pack-years are calculated by either multiplying the number of packs smoked per day by the number of years of smoking or multiplying the number of cigarettes smoked daily by the

number of years of smoking and dividing by 20, the number of cigarettes in a pack.) In a Polish study in which free spirometric evaluation was provided to 11,027 subjects (8,827 current or former smokers and 2,200 who had never smoked), airway obstruction was found in nearly 31% of those who were over age 40 and had smoked for at least 10 pack-years.⁸

Other risk factors for COPD include exposure to secondhand smoke, occupational dusts and chemicals, biofuels, and other indoor and outdoor pollutants.^{5,6} Genetics also plays a role: deficiency of α_1 -antitrypsin, a protein found in the blood that’s produced in the liver and protects against lung damage, is known to elevate risk.^{5,6} Patients with α_1 -antitrypsin deficiency (serum levels below 20% of normal) are prone to emphysema even if they’ve never smoked.^{5,9,10}

Not all cigarette smokers develop clinically apparent COPD.⁶ This suggests that tobacco smoke alone is insufficient to cause COPD and that other relevant factors play a role. In addition to α_1 -antitrypsin deficiency, a number of other risk factors have been identified, including other susceptibility genes, female sex, recurrent respiratory infection, low socioeconomic status, poor nutrition, and asthma.^{5,6}

Pathogenesis. Regular tobacco smoking creates a cycle of repeated respiratory injury and attempted repair that can restrict airways. An accumulation of intraluminal mucus and infiltration by inflammatory cells further elevates airway resistance.^{4,11} With the destruction of alveoli, elastin is lost.^{4,11} Reduced pulmonary elasticity contributes to hyperinflation and impairs expiratory flow, causing airways to collapse. Alveolar collagen deposition leads to fibrosis of the remaining alveolar tissue.¹²

Clinical presentation. Although most patients with COPD have features of both chronic bronchitis and emphysema, some present with a purer phenotype—COPD characterized predominantly by either chronic bronchitis or emphysema. In cases of COPD characterized predominantly by chronic bronchitis, hypoxemia develops from the airflow obstruction, which decreases ventilation to perfused lung units, precipitating hypoxic pulmonary vasoconstriction, pulmonary hypertension, and possibly right-heart strain and peripheral edema.^{4,13} In cases marked predominantly by emphysema, airways aren’t inflamed. Loss of elasticity may cause airway collapse during exhalation, but ventilation is maintained because airways are pulled open again during inspiration. When at rest and breathing room air, patients with emphysema may have sufficient oxygen saturation levels—and may be able to sustain them when dyspneic, if they breathe through pursed lips (a technique for preventing airway collapse).

Emphysema often leads to pulmonary cachexia, a loss of weight and muscle mass⁶ that’s thought to result from the release of proinflammatory mediators,¹⁴

What You Need to Know if You're Diagnosed with COPD: Pointers for Patients

Chronic obstructive pulmonary disease, or COPD, is a lung disease that affects about 24 million adults in the United States alone. Although there is no cure for COPD, there are many ways to reduce symptoms and stop the disease from getting worse. If you've been diagnosed with COPD, or someone you love has, it's important for you to learn how COPD affects the lungs and other parts of the body and what you or your loved one can do to continue living a full and active life.

Understanding COPD. COPD develops when toxic elements in the air—like smoke or pollution—irritate the lungs' air sacs and the cells lining the airways, causing them to swell. After repeated injury, the air sacs lose their elasticity (their ability to expand and contract), causing the lungs to overexpand and reducing their ability to empty. The narrowed airways further limit the amount of air that can flow into and out of the lungs. The loss of elasticity and the narrowed airways cause breathlessness and coughing, but the coughing is ineffective in removing irritants and mucus. The excess mucus further narrows the airways and invites infection.

Preventing further lung injury and flare-ups (exacerbations). The damage caused by COPD can't be fully reversed, but there's a lot you can do to relieve symptoms and prevent further lung injury and COPD flare-ups.

- If you smoke (the major cause of COPD), enroll in a smoking-cessation program, and talk to your primary health care provider about medications that can help you quit.
- Avoid lung irritants, such as secondhand smoke and fumes from cars or harsh chemicals.
- Remember that you are especially vulnerable to infection and should avoid people who are sick.
- Wash your hands thoroughly, often—and always before eating.
- Get an annual flu vaccination.
- Follow the medication and exercise plan recommended by your health care provider.

When to call your health care provider. A number of situations can lead to COPD flare-ups—a cold or flu, a change in medication, drinking more fluids than usual, exposure to air pollution or extreme weather conditions, or other illnesses that strain the lungs. Because frequent

exacerbations can cause a rapid decline in lung function, call your health care provider if you experience any of the following changes:

- an increase in shortness of breath—a need for more pillows while sleeping or more time to get dressed, a decrease in the distances you can walk
- more frequent use of your inhalers
- increased wheezing or chest tightness
- a more frequent or more severe cough
- a change in the color, odor, thickness, or amount of your mucus
- ankle swelling that doesn't go away after a night's sleep
- an increase in weight of 3 to 5 lbs. per week
- a fever, especially with cold or flu-like symptoms
- unexplained fatigue or extreme weakness lasting more than one day
- confusion or a change in mood or your ability to think clearly or concentrate

Proper medication use. Medications are prescribed to relax the muscles around the airways and prevent swelling within them. Some medications need to be used regularly to prevent and control symptoms. Others are to be used only as you need them to control symptoms.

Carefully review your medication plan with your health care provider to make sure you understand how your medications are used and that you're using an appropriate delivery device. Your provider will want to recheck your inhaler technique at every visit, so always bring your inhalers with you.

If you use a nebulizer, clean it after every use and allow it to air dry (to avoid contamination). If your COPD is stable, you may be able to achieve the same medication effectiveness, while lowering your risk of infection, using a metered-dose inhaler.

Oxygen therapy can reduce breathlessness, make you more alert, and increase endurance. Your provider will prescribe different flow rates for rest, activity, and sleep. It's crucial that you follow the prescribed flow rates to avoid straining your heart.

Oxygen is safe and nonaddictive. It won't explode or burst into flames, although it will feed a flame, causing things to burn faster. Don't use flammable products, such as aerosol sprays or petroleum jelly, around your oxygen-delivery unit.



What You Need to Know if You're Diagnosed with COPD: Pointers for Patients

Pursed-lip breathing can help to slow your breathing rate and reduce breathlessness. First, you inhale slowly through the nose, then exhale through pursed lips for twice as long as you inhaled. Pursed-lip breathing may be particularly helpful during tasks that involve bending, lifting, or stair climbing.

Energy conservation. There are a number of ways to simplify everyday tasks that drain energy.

- Work at waist level when possible, avoiding extended reaches from the floor or above the shoulder.
- Pace yourself with each task.
- While sitting, keep your feet on the floor, lean your chest forward slightly, and rest your elbows on your knees and your chin on your hands.
- When standing, lean your chest slightly forward and rest your hands on your thighs.
- While showering, sit on a stool instead of standing, or shower in a bathtub, using a sprayer hose connected to the faucet.
- To cut down on the reaching required with towel drying, wear a long, terry cloth robe after showering.
- While shaving, brushing teeth, or applying make-up, sit in a chair at the sink.
- Wear comfortable clothing and avoid such restrictive garments as belts, pantyhose, and ties.
- Wear slip-on shoes and use a long shoehorn to reduce the labor and time needed for dressing.

Good nutrition is a key aspect of managing COPD, but mealtime can make breathing more difficult. To ensure you're getting the extra energy you need to breathe, preserve strength, and fight infection, the following simple steps can ease breathing during meals.

- Keep utensils and appliances at counter level or at the front of cabinets, reducing the need to reach and bend.
- Gather ingredients and supplies before sitting down to prepare food.
- Plan meals in advance so you're not too tired or too hungry to cook.
- Prepare enough food to freeze for future use.
- Eat five or six small meals each day to prevent your stomach from pushing up on your diaphragm.
- Put utensils down between bites to slow your eating and avoid overeating.

- Avoid gas-producing foods that cause bloating.
- If you've been prescribed oxygen therapy, use it during meals, when you need more oxygen for digestion.
- Use breathing medication about one hour before meals.
- Eat when well rested.

Sleep and rest. COPD can disrupt your sleep: coughing, phlegm, too little oxygen, depression, anxiety, and some medications all have an effect. The following strategies can help:

- Set regular bedtime and waking hours.
- Create a sleep environment that's dark, quiet, and warm or cool enough for you to sleep comfortably.
- Avoid stimulants (such as caffeine or nicotine) and alcohol two to four hours before bedtime.
- Exercise regularly, but complete activity at least three hours before bedtime.
- Relax during daytime rest periods, but don't fall asleep; daytime napping can disrupt nighttime sleep.
- Limit the fluids you drink after dinner to reduce the need for bathroom trips.
- Practice relaxation techniques as part of your bedtime routine.

Mood and stress. COPD may cause you to feel isolated or experience depression or anxiety. Discuss such feelings with your health care provider in the same way you would discuss physical concerns. Many people with COPD find counseling or a support group to be helpful.

Intimate relationships. Intimacy and sexual function are important, and you don't have to avoid them because you have COPD. If your symptoms or medication effects interfere with sexual function, plan ahead.

- Use bronchodilators before sexual activity.
- Use supplemental oxygen during sexual activity.
- Choose positions that require less energy and chest pressure.
- Avoid sex immediately after a meal.

If you're too tired for sex, holding your partner's hand, touching, massaging, and talking are all ways to be intimate without the physical demands of sexual intercourse.

as well as from the increased work of breathing and insufficient nutrition. In addition to cachexia, osteoporosis, depression, anxiety, anemia, thrombophilia, and cardiovascular disease are often concomitant with COPD.^{6, 15, 16}

ESTABLISHING THE DIAGNOSIS

Spirometry can be used to confirm the presence of airflow obstruction and determine its severity.^{6, 17} The key spirometric measures are the FVC and the FEV₁ (see Figure 2). The airway resistance and loss of elasticity that occur in COPD delay patients' exhalation on spirometry, as signified by a low FEV₁. When airflow is obstructed, the FEV₁ is usually substantially lower than the FVC; motivated patients can exhale for longer than the normal three to five seconds typically required to complete the FVC maneuver. In such cases, the FEV₁-FVC ratio is below the normal value of 70% to 80%.

The FEV₁ correlates with disease severity: the lower the FEV₁, the sicker the patient,⁶ but regardless of FEV₁ value, exercise capacity, dyspnea, and quality of life may vary widely among patients. When assessing disease severity or response to therapy, other measures such as the patient's CAT score, BMI, SaO₂, and the BODE (Body-Mass Index, Degree of Airflow Obstruction and Dyspnea, and Exercise Capacity) index should be considered.

Once a patient has COPD, management goals are to slow disease progression, ease symptoms, improve health status and exercise tolerance, prevent and treat exacerbations and complications, and reduce the risk of dying from the disease.

CAT scores range from 0 to 40 and represent disease impact; scores below 10 represent a low level of impact and scores above 20 a high level. A change in score of two or more points is considered clinically significant.¹⁸ Exercise-induced hypoxemia is common in COPD, and pulse oximetry readings should therefore be taken both when the patient is at rest and during a six-minute walk test. Patients whose values are 88% or lower when at rest and breathing room air are eligible for continuous oxygen therapy.⁶ Arterial blood gases (ABGs) should be measured in patients with an FEV₁ below 50%. In addition to defining the severity of hypoxemia, ABGs reveal the patient's acid-base status. The BODE index, a validated grading system designed to predict the risk of death from COPD based on the four factors for which it was named—BMI, obstruction, dyspnea, and exercise capacity—can also be used to

assess the respiratory and systemic components of COPD.¹⁹ Full pulmonary function testing can detect a drop in the diffusing capacity for carbon monoxide, indicating a loss of alveolar capillary units.

Chest X-ray cannot be used to diagnose COPD, but it may reveal diaphragm flattening, a sign of lung hyperinflation, which is considered a hallmark of the disease. Although computed tomography isn't used routinely to diagnose or evaluate COPD, in patients with emphysema it often shows enlarged alveolar spaces in the lung apices, thickening of the airway walls, and air trapping.

MANAGEMENT GOALS

COPD is preventable and treatable. Once a patient has COPD, management goals are to slow disease progression, ease symptoms, improve health status and exercise tolerance, prevent and treat exacerbations and complications, and reduce the risk of dying from the disease.⁶

Risk reduction is the first step in accomplishing these goals. To prevent exacerbations, patients should avoid contact with those who are sick, practice good handwashing techniques, use medications as prescribed, obtain appropriate vaccinations, exercise regularly, and maintain a healthy weight.

Remind patients who smoke of the benefits of quitting and refer them to individual or group counseling.

Discuss the use of pharmacologic smoking-cessation aids, such as nicotine replacement, bupropion (Zyban), and varenicline (Chantix). Strategies for promoting smoking cessation can be found in the U.S. Department of Health and Human Services guidelines, *Treating Tobacco Use and Dependence: 2008 Update*, available online at <http://1.usa.gov/tDWy30>.

Ongoing assessment is essential in preventing the downward spiral of inactivity and deconditioning. Monitoring disease progression involves a simple spirometry test annually (or more frequently, if there is a change in status) and evaluation of the impact of dyspnea, cough, and sputum production on patients' daily life.⁶

Breathlessness, which is progressive in COPD, is the symptom that most commonly limits activity.⁶ To assess its severity, use the Modified Medical Research Council Dyspnea Scale, which asks patients

Table 1. Classes of Medications Used in COPD Treatment⁶

Therapeutic Class	Comment	Examples
Short-acting bronchodilators		
Short-acting β_2 -agonist	Available as MDI and nebulizer solution	Albuterol (Ventolin, ProAir, Proventil) Levalbuterol (Xopenex)
Short-acting anticholinergic agent	Available as MDI and nebulizer solution	Ipratropium (Atrovent)
Combination short-acting β_2 -agonist and short-acting anticholinergic agent	Bronchodilation lasts about six hours; avoid MDIs in patients with peanut or soybean allergy	Albuterol and ipratropium (Combivent Respimat, DuoNeb)
Long-acting bronchodilators		
Long-acting anticholinergic agent	Capsules are for inhalation with an inhaler	Tiotropium (Spiriva)
Long-acting β_2 -agonist	Inhalation solution offers no benefit over DPI unless patient is unable to use DPI	Formoterol (Foradil, Perforomist) Salmeterol (Serevent) Arformoterol (Brovana) Indacaterol (Arcapta)
Methylxanthine	Beneficial for patients with COPD and pulmonary hypertension	Theophylline
Antiinflammatory agents		
Inhaled corticosteroids	Avoid use without a long-acting β_2 -agonist unless the patient has asthma and COPD	Beclomethasone (Qvar) Budesonide (Pulmicort, Pulmicort Respules) Ciclesonide (Alvesco) Fluticasone (Flovent) Mometasone (Asmanex)
Combination long-acting β_2 -agonist and inhaled corticosteroid	Recommended for patients with multiple COPD exacerbations	Salmeterol–fluticasone (Advair Diskus) Formoterol–budesonide (Symbicort)
Oral corticosteroid	Avoid long-term use	Prednisone, methylprednisolone
Phosphodiesterase type 4 enzyme inhibitor	Recommended in severe COPD to treat the symptoms of cough and excess mucus linked to bronchitis	Roflumilast (Daliresp)
Augmentation therapy (for α_1-antitrypsin deficiency)		
α_1 -proteinase inhibitor		Aralast, Aralast NP, Prolastin, Zemaira, Glassia

COPD = chronic obstructive pulmonary disease; DPI = dry-powder inhaler; MDI = metered-dose inhaler; NP = nanofiltration process.

to characterize their dyspnea on a scale ranging from 0 (“I only get breathless with strenuous exercise”) to 4 (“I am too breathless to leave the house or I am breathless when dressing or undressing”).⁶ In addition to worsening dyspnea, increased coughing or a change in the amount or character of sputum may signal the start of an exacerbation or of an upper respiratory infection, in which wheezing, chest tightness, and fatigue are common.²⁰⁻²² Assess the level of social and family support, especially for patients in the later stages of COPD.

Provide information and referrals as appropriate to patients with associated comorbid conditions. A drop in BMI elevates the risk of death in COPD.⁶

If patients have lost weight, identify reasons and help them improve their nutritional status. Research suggests that increased calorie intake may work best when accompanied by anabolic exercise.⁶ In people at all stages of COPD, exercise has been shown to reduce breathlessness and fatigue while improving strength, exercise tolerance, and the ability to accomplish daily activities.⁶

Sleeping difficulties are common in people with COPD and may be related to hypoxia associated with sleep apnea, nighttime hypopnea (unusually shallow breathing), anxiety, depression, breathlessness, cough, or an increase in sputum. Refer patients with such sleep problems to a sleep specialist.

PHARMACOTHERAPY FOR COPD

Although there is no cure for COPD and, to date, no COPD medication has been shown to prevent disease progression or reduce death rates,⁶ a number of medications can be used to manage symptoms (see Table 1⁶).

When current smokers who have COPD should start inhaler use is controversial because, although bronchodilators provide symptom relief, only smoking cessation can slow disease progression. The clinical practice guidelines for the diagnosis and management of stable COPD, recently updated by the American College of Physicians, the American College of Chest Physicians (ACCP), the ATS, and the ERS, suggest that patients with stable COPD who have respiratory symptoms and a predicted FEV₁ between 60% and 80% may be treated with inhaled bronchodilators (although they note that the evidence supporting this is “limited and conflicting”).¹⁷ A short-acting bronchodilator, such as albuterol (Proventil and others, a β_2 -agonist) or ipratropium (Atrovent, an anticholinergic) is typically prescribed as a “rescue” inhaler to be used as needed for dyspnea.⁶ By decreasing airflow obstruction and hyperinflation, short-acting bronchodilators may improve exercise endurance and reduce dyspnea. A combination of ipratropium and albuterol (Combivent Respimat, DuoNeb) is available as both a metered-dose inhaler and inhalation solution. The combination product is less expensive and easier to use because the two medications can be delivered in fewer puffs through a single inhaler or together in one nebulizer session. High doses of albuterol are associated with adverse effects such as hypokalemia, tremors, and insomnia,²³ whereas long-term ipratropium use is associated with dry mouth, urinary retention, and elevated cardiovascular risk.²⁴⁻²⁷ Recent research suggests that short- and long-acting β_2 -agonists may be used safely by patients who have COPD and take cardioselective β -blockers, such as atenolol (Tenormin) or metoprolol (Lopressor, Toprol), to treat hypertension, but further research is necessary.²⁸

When patients have a predicted FEV₁ below 60% and are experiencing symptoms, monotherapy with a long-acting bronchodilator (either a β_2 -agonist or an anticholinergic) is recommended.^{6,17} In COPD, unlike in asthma, long-acting β_2 -agonist monotherapy isn't contraindicated.²⁹

The long-acting β_2 -agonist salmeterol (Serevent) combined with ipratropium improves bronchodilator response and reduces exacerbations more than salmeterol alone, but it doesn't improve symptom control or lessen the need for rescue medication.³⁰ Another long-acting β_2 -agonist, formoterol (Foradil, Perforomist), acts more quickly than salmeterol and is available both as a capsule to be used with an aerolizer inhaler or as an inhalation solution.^{31,32} Both

salmeterol and formoterol are taken twice daily. A once-daily, long-acting β_2 -agonist, indacaterol (Arcapta), was recently approved by the U.S. Food and Drug Administration (FDA) for use in COPD. In clinical trials, indacaterol has been shown to be as effective as the long-acting (24-hour) anticholinergic tiotropium (Spiriva) and slightly more effective than formoterol.^{33,34}

Tiotropium achieves maximal effect one week after initiation. In clinical trials, tiotropium decreased COPD exacerbations, improved quality of life, reduced rates of hospitalization and produced greater bronchodilation and symptom control than either ipratropium or salmeterol.³⁵⁻³⁷ Theoretically, the combined use of ipratropium and tiotropium should increase adverse drug effects and decrease the selectivity of tiotropium, but this hasn't been seen in clinical research.³⁸ Tiotropium use hasn't been associated with an elevated risk of adverse cardiovascular events.³⁹⁻⁴¹ Inhalers that combine long-acting β_2 -agonists with long-acting anticholinergic agents are on the horizon for COPD treatment.

In COPD, unlike in asthma, inhaled corticosteroids can cause more harm than benefit if used alone—such use is associated with elevated risks of hospitalization and pneumonia.

A low dose of theophylline combined with an inhaled corticosteroid, such as fluticasone (Flovent), may benefit a small percentage of patients with COPD who don't respond to inhaled therapy.⁴² Risks of serious adverse effects from interactions with a number of drugs, including tobacco smoke, limit the use of theophylline as a long-acting bronchodilator.

Combined treatment with long-acting β_2 medications, long-acting anticholinergic agents, and inhaled corticosteroids may benefit symptomatic patients with stable COPD and a predicted FEV₁ below 60%.¹⁷ Adding an inhaled corticosteroid to long-acting bronchodilator therapy is recommended in patients who have a history of repeated exacerbations or are at high risk for exacerbations.⁴³ In COPD, unlike in asthma, inhaled corticosteroids can cause more harm than benefit if used alone—such use being associated with elevated risks of hospitalization and pneumonia, for instance⁴⁴—and not in combination with a long-acting β_2 -agonist. Using a long-acting β_2 -agonist in conjunction with an inhaled corticosteroid reduces the number of hospitalizations and

improves quality-of-life scores, although its ability to prevent COPD exacerbations doesn't differ from that of tiotropium.⁴⁵ Products containing both a long-acting β_2 -agonist and an inhaled corticosteroid simplify prescribing and use. A triple therapy regimen including tiotropium and fluticasone-salmeterol improves spirometry performance and reduces albuterol use, compared with either agent alone.⁴⁶

In people with COPD and resting hypoxemia, long-term, continuous oxygen therapy is associated with increased survival.

Augmentation therapy, infusions of α_1 -antitrypsin derived from human plasma, is used, rarely, in patients diagnosed with α_1 -antitrypsin deficiency to slow the decline of lung function.⁶ The plasma-derived products are available as weekly infusions. Common adverse effects include fever, chills, allergic reactions, and flu-like symptoms.

Recently, the FDA approved roflumilast (Daliresp), the first phosphodiesterase type 4 enzyme inhibitor approved to treat COPD. Administered orally, it's used to reduce the frequency of exacerbations in patients with severe COPD associated with chronic bronchitis. Although it increases cyclic adenosine monophosphate in the lung tissue by inhibiting the phosphodiesterase 4 enzyme, roflumilast isn't a bronchodilator; rather, it's thought to act as a nonsteroidal antiinflammatory drug, decreasing the numbers of neutrophils and eosinophils in the airway.⁴⁷ Data support the assertion that roflumilast reduces exacerbations and improves lung function when added to first-line maintenance therapy, which in patients with severe COPD associated with chronic bronchitis and a history of exacerbations would include both a long-acting bronchodilator and an inhaled corticosteroid. Roflumilast is contraindicated in patients with liver impairment. The most commonly reported adverse effects are diarrhea, weight loss, nausea, abdominal pain, and headache. Patients taking roflumilast should be monitored for changes in mood, behavior, or thought, including suicidal ideation.^{47,48} Antibiotics and oral corticosteroids are the cornerstones of therapy for COPD exacerbations. Oral corticosteroid burst therapy for 10 to 14 days improves lung function, reduces hospitalization time and the 30-day relapse rate, and prolongs time to an exacerbation.^{49,50} Using oral corticosteroids for more than 14 days isn't beneficial and increases the risk of adverse effects.⁶ Antibiotics are indicated when the

patient is having COPD symptoms with signs of infection such as increased dyspnea, increased sputum volume, and sputum purulence.⁶ In such cases, antibiotic use upon hospital admission reduces the risk of dying of or being rehospitalized for COPD and requiring mechanical ventilation.⁵¹

Annual influenza immunization in patients with COPD from October through March has been shown to halve the rates of illness and death.⁵² Smokers are at four times greater risk for contracting pneumonia than nonsmokers.⁵³ Pneumococcal vaccination is recommended for all smokers 19 years of age and older and all patients with COPD.⁵⁴ Another pneumococcal vaccination can then be provided after the age of 65.⁵⁴

OXYGEN THERAPY

In people with COPD and resting hypoxemia, long-term, continuous oxygen therapy (more than 15 hours per day) is associated with increased survival and improved hemodynamics, hematology, exercise capacity, lung mechanics, mental status, motor speed, and hand grip strength.^{6,55,56} Oxygen therapy can be administered by face mask, nasal cannula, or (in specialized centers) by transtracheal catheter. At-home oxygen is usually provided by concentrator with a portable supply for outings. The goal is to keep the SaO₂ level at or above 90% during activity. Long-term oxygen is usually introduced when the partial pressure of arterial oxygen (PaO₂) is at or below 55 mmHg or the SaO₂ is at or below 88% in patients who are at rest and breathing room air.⁶ Prescriptions for oxygen therapy should specify how it will be supplied (gas or liquid); how it will be delivered (mask or cannula); how long it will be used; and the flow rates at rest, during exercise, and during sleep. Patients should be told why supplemental oxygen is used and the importance of safety, including not changing the flow rate unless told to do so by the prescriber and notifying that provider if headaches, confusion, or increased sleepiness occur.

NONPHARMACOLOGIC INTERVENTIONS

Ventilatory support. Although it's often used to treat exacerbations, noninvasive ventilation (positive-pressure ventilation accomplished, usually, with a nasal mask) isn't indicated in the routine, long-term management of COPD. It has demonstrated no effect on shortness of breath, exercise tolerance, arterial blood gases, respiratory muscle strength, or quality of life, although a small subset of patients with daytime hypercapnia may benefit from the combination of noninvasive, positive-pressure ventilation and long-term oxygen therapy.⁶

Surgical treatments. The goals of medical and surgical treatments for emphysema are to extend life and to improve the quality of life. Surgical treatments

are recommended only for carefully selected patients with severe COPD.⁶

Bullectomy is the surgical removal of large bullae (essentially blisters, which don't contribute to gas exchange). It makes room for compressed lung parenchyma to reexpand. Performed thoracoscopically, this procedure can reduce dyspnea and improve lung function.⁶

In lung volume reduction, small sections of the lung are removed, reducing hyperinflation and improving elastic recoil pressure and expiratory flow rates. The National Emphysema Treatment Trial showed that a select subset of patients with predominantly upper-lobe emphysema and reduced exercise tolerance had a greater life expectancy and higher health-related quality-of-life scores after undergoing this procedure, compared with similar patients who didn't have the surgery but received medical therapy.⁶

Lung transplantation can improve quality of life and functional capacity in a select group of patients with very severe COPD. Limitations of lung transplantation include donor organ shortage, cost, and complications from postoperative immunosuppressive medications.⁶

aims to break the cycle commonly seen in patients with COPD: dyspnea leading to poor fitness, immobility, social isolation, and depression, all of which further contribute to dyspnea and immobility.

The team approach—using professionals with expertise in exercise training, psychosocial evaluation and counseling, respiratory medication and oxygen therapy, breathing exercises and retraining, patient education, nutrition, energy conservation, and smoking cessation—is used to develop individualized, long-term programs. Coordinated by a pulmonary nurse or respiratory therapist, the team often includes a medical director (pulmonologist), an occupational therapist, a physical therapist, a dietician, a psychologist, and a social worker.

Patients benefit from pulmonary rehabilitation whether it's conducted in an outpatient, inpatient, or home setting. The decision to participate, however, may be influenced by insurance reimbursement, out-of-pocket expenses, transportation, and location. Highly motivated patients receive the most benefit from participation. Patients with grade 4 dyspnea on the Modified Medical Research Council Dyspnea Scale and those who are chairbound may not

Exercise training programs both improve exercise tolerance and reduce symptoms of dyspnea and fatigue in patients with COPD.

Clinical trials of experimental, minimally invasive, surgical procedures for COPD are currently under way. One is testing the bronchoscopic placement of a valve designed to reduce lung volume, thereby decreasing shortness of breath. For participation information, refer patients and caregivers to www.clinicaltrials.gov.

PULMONARY REHABILITATION

In conjunction with medical management, all patients with COPD can benefit from exercise training programs. Extensive research confirms that participation in pulmonary rehabilitation improves exercise tolerance, reduces patients' perceptions of dyspnea, improves health-related quality of life, reduces the numbers of hospitalizations and hospital days, reduces anxiety and depression associated with COPD, improves arm function (through strength and endurance training), and improves survival.⁶

In 1974 the ACCP's Committee on Pulmonary Rehabilitation defined pulmonary rehabilitation as "an individually tailored, multidisciplinary program" that "attempts to return the patient to the highest possible functional capacity."⁵⁷ Pulmonary rehabilitation

achieve the same functional benefit. There's no evidence that nonsmokers achieve better results, but experts agree that smokers should be enrolled in a smoking-cessation program to participate in rehabilitation.⁶ Although components of pulmonary rehabilitation programs vary, all include exercise training and patient education. Sessions are conducted in small groups, two to three times per week, for a minimum of 28 sessions.⁶

EXERCISE TRAINING

Exercise training programs both improve exercise tolerance and reduce symptoms of dyspnea and fatigue in patients with COPD. Bicycle ergometry and treadmill exercise are used most commonly, with duration and intensity being dependent on the individual's tolerance. Endurance training, continuing until the patient is experiencing 60% to 80% of maximum symptoms, is the preferred measure in a patient with COPD, rather than a target heart rate.⁶ When that goal is achieved, the patient rests for a bit, then continues again until at least 20 minutes of exercise is completed.⁵⁸ Pulse oximetry is used throughout exercise training to monitor SaO₂. Exercise improvement

can be monitored objectively, using pulse oximetry, dyspnea scales, heart rate surveillance, and the six-minute walk test.^{59,60}

The benefits of such exercise programs will be lost without continued participation in at-home exercise or a maintenance program. A home program combining strength and endurance training includes a five-minute warm-up of stretching for flexibility, upper-extremity strengthening, lower-extremity strengthening, aerobic conditioning on a treadmill or a stationary bicycle, followed by a five-to-10-minute cool down. The health care provider prescribes the oxygen flow rate, target intensity level, and duration of the specific home exercises.

END-OF-LIFE DISCUSSIONS

Near the end of life, patients with COPD need additional support and information that will help them make decisions about treatment, symptom management, and comfort. Allowing patients and family members or significant others to talk about their feelings may help minimize the anxiety and depression often associated with end-of-life care. In addition to offering guidance and information on treatments, clinicians can discuss such subjects as advanced directives, caregiver support, and hospice care, which will help patients and family members through difficult decisions.

FOLLOW-UP

When Ms. Pierce returns to the NP for a one-month follow-up visit, she says that, with the help of her prescribed oral smoking-cessation medication and nicotine replacement therapy, she hasn't smoked in two weeks. She's continuing with individual and group counseling in the smoking-cessation program and says she has less dyspnea and phlegm and doesn't need to use her rescue inhaler as often. She has been taking the long-acting bronchodilator initially prescribed by the NP and demonstrates its correct use. She started a pulmonary rehabilitation program near her home this week.

On examination, she's in no distress. Her cardiac examination is unremarkable. On chest auscultation, her breath sounds are still somewhat diminished, and her expiratory phase remains prolonged, but no end-expiratory wheezing is audible.

The NP reinforces patient education, including signs and symptoms of exacerbation that warrant immediate attention. He supports Ms. Pierce's initial success with smoking cessation and pulmonary rehabilitation and instructs her to continue with the medication regimen and return for follow-up in three months. ▼

Susan Corbridge is director of the Acute Care Nurse Practitioner and Clinical Nurse Specialist programs at the University of Illinois at Chicago College of Nursing and a clinical assistant professor in the Department of Pulmonary and Critical Care Medicine at the University of Illinois at Chicago Medical Center. Lori Wilken is a clinical assistant professor at the University of Illinois at Chicago College of Pharmacy and a clinical pharmacist in the Department of Pulmonary Medicine at the University of Illinois at Chicago Medical Center. Mary C. Kapella is a research assistant professor at the University of Illinois at Chicago College of Nursing. Cindy Gronkiewicz is adjunct faculty at the University of Illinois at Chicago College of Nursing. Contact author: Susan Corbridge, sjsmith@uic.edu. The authors have disclosed no potential conflicts of interest, financial or otherwise.

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