

# Chronic Obstructive Pulmonary Disease II: A Case-Based Approach to Management

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**C**hronic obstructive pulmonary disease (COPD) is a slowly progressive disease that usually advances over a period of 30 to 40 years. Although it most commonly becomes symptomatic in the fifth and sixth decades of life, symptoms may occur earlier, particularly in women. COPD now ranks as the fourth most common cause of death in the United States. It is the only disease among the top 10 killers of Americans that continues to rise in prevalence.<sup>1,2</sup>

COPD refers to a spectrum of diseases including asthmatic bronchitis, chronic bronchitis, and emphysema. COPD is used as an all-inclusive term to include these designations, which usually occur in combinations.<sup>2</sup> This article is the second of a 2-part series on COPD. The epidemiology, clinical presentation, evaluation, and diagnosis of COPD were examined in the first article.<sup>3</sup> This article will use a case-based approach to review the management of mild, moderate, and severe COPD. The emphasis will be on the maintenance management of patients at these various stages of the disease. Recent advances in our understanding of the pathophysiology of the disease are also discussed, along with their implications in the treatment of COPD. The goal is to provide practical information for primary care physicians and others who may be increasingly involved in the evaluation and management of growing numbers of patients with COPD, as the population of the United States ages.

## ETIOLOGY AND PATHOGENESIS

The causes of COPD are multifactorial. COPD is related to smoking in approximately 90% of patients.<sup>2</sup> In addition, genetic and environmental factors, including  $\alpha_1$ -antitrypsin deficiency, passive smoking, certain occupations, and probably air pollution, result in airway inflammation and damage to alveolar walls, which together cause premature losses in ventilatory function, as measured by the forced expiratory volume in 1 second (FEV<sub>1</sub>).

Recent studies strongly indicate that the pathogenesis of COPD involves inflammatory mechanisms of the con-

ducting airways that are quite different from those in asthma.<sup>4,5</sup> In COPD, the inflammatory process involves CD8+ T lymphocytes, as well as macrophages and neutrophils.<sup>4,5</sup> Interleukin (IL)-8 and tumor necrosis factor (TNF)- $\alpha$  are involved in tobacco-induced airways inflammation and fibrosis in susceptible individuals. By contrast, asthma involves CD4+ lymphocytes; activated mast cells; increased eosinophils; and IL-4, IL-5, and IL-13.<sup>4,5</sup> These differences in pathogenesis have important implications in management. Although corticosteroids reduce the eosinophilic inflammation of asthma, they have little effect on the inflammatory process characteristic of COPD.<sup>6</sup> Thus, responses to therapy from antiinflammatory agents for COPD are different from those for asthma. However, corticosteroids are effective in acute exacerbations of COPD. In these exacerbations, eosinophilic mechanisms are probably involved.

Alveolar damage is apparently a noninflammatory process. Recent evidence points to increased apoptosis of alveolar structures, resulting from decreased expression of vascular endothelial growth factor (VEGF), in the lungs of experimental animals and in patients with emphysema.<sup>7,8</sup> Thus, while airway changes are mediated by inflammation, alveolar damage and loss of alveolar walls apparently have different mechanisms. Once these mechanisms are better understood, new strategies in therapy will emerge.

## STAGING SYSTEMS

Spirometric testing is required to confirm the diagnosis of COPD, to assess the severity of the disease, and to assess responses to therapy. Several clinically useful staging systems are in use around the world (**Tables 1 and 2**). The American Thoracic Society (ATS),<sup>9</sup> British Thoracic Society (BTS),<sup>10</sup> and European Respiratory

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**Table 1.** Staging Systems for Stable COPD

System	FEV <sub>1</sub> (% of predicted)		
	Mild	Moderate	Severe
ATS*	≥ 50	35–49	< 35
BTS†	60–79	40–59	< 40
ERS‡	≥ 70	50–69	< 50
GOLD§	≥ 80	30–79¶	< 30

FEV<sub>1</sub> = forced expiratory volume in 1 sec; FVC = forced vital capacity.

NOTE: For all classification systems listed, the criteria for all stages of COPD includes FEV<sub>1</sub>/FVC ratio < 70%.

\*American Thoracic Society. Data from Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1995;152:83S.

†British Thoracic Society. Data from The COPD Guidelines Group of the Standards of Care Committee of the British Thoracic Society: BTS guidelines for the management of chronic obstructive pulmonary disease. *Thorax* 1997;52:S1–S28.

‡European Respiratory Society. Data from Siafakas NM, Vermeire P, Pride NB, et al. Optimal assessment and management of chronic obstructive pulmonary disease (COPD). The European Respiratory Society Task Force. *Eur Respir J* 1995;8:1398–420.

§Global Initiative for Chronic Obstructive Lung Disease. Data from Pauwels RA, Buist AS, Calverley PM, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care Med* 2001;163:1256–76.

¶GOLD further classifies moderate COPD into stage IIA (FEV<sub>1</sub>, 50%–79% of predicted) and stage IIB (FEV<sub>1</sub>, 30%–49% of predicted).

Society (ERS),<sup>11</sup> have all offered somewhat different staging systems for the characterization of mild, moderate, and severe stages of COPD. More recently, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) has put forth a classification system.<sup>12</sup> (The GOLD criteria are discussed in detail in the first article of this series.<sup>3</sup>) Spirometric testing is fundamental to all of these classification systems. **Table 3** lists clinical criteria for acute exacerbations of COPD.

These classifications are arbitrary; however, they are quite useful in the stratification of the severity of illness. For example, patients with severe COPD are at greater risk of acute respiratory failure and its complications when acute exacerbations occur than are those with mild to moderate severity.

#### GENERAL MEASURES APPLICABLE TO ALL PATIENTS

##### Smoking Cessation

All patients with COPD absolutely must stop smok-

**Table 2.** British Thoracic Society Scoring System for Symptoms for Stable Chronic Obstructive Pulmonary Disease

Clinical Findings	Stage		
	Mild	Moderate	Severe
Cough	“Smoker’s cough”	Cough with or without sputum	Prominent cough
Dyspnea	Minimal	On exertion	On exertion or at rest
Lung examination results	Normal	With or without wheeze	Hyperinflation, wheeze
Other examination results	Normal	Normal	Cyanosis, edema

Data from The COPD Guidelines Group of the Standards of Care Committee of the British Thoracic Society: BTS guidelines for the management of chronic obstructive pulmonary disease. *Thorax* 1997; 52:S1–S28.

ing. Details of strategies for smoking cessation go beyond the scope of this presentation. The reader is referred to a succinct review on this topic.<sup>13</sup>

Approximately 3% of people who smoke will stop smoking, simply on the advice by a physician or a physician equivalent that this is imperative.<sup>14</sup> It is important for patients to modify their behavioral patterns associated with their cues to light up a cigarette. Deciding to quit and choosing a quit date are fundamental principles. A growing number of drugs, available both over the counter and by prescription, are available to deal with nicotine withdrawal symptoms (**Table 4**). These factors taken together—the physician’s advice, the decision on the part of the patient to quit, the selection of a quit date, and the use of pharmacologic strategies during the initial 2 weeks of nicotine withdrawal—may lead to successful cessation in up to 30% of patients.<sup>14</sup>

##### Vaccination

All patients with any stage of COPD should receive influenza virus vaccine each fall. Because of antigenic shift and waning immunity, a newly constituted vaccine given before the influenza season, usually beginning in October or November, is required annually. Pneumococcal vaccine should be given at least once in a lifetime. A community outreach program designed to reach all persons age 65 and older with both influenza and pneumococcal vaccines has been

**Table 3.** Severity Scale for Acute Exacerbations of Chronic Obstructive Pulmonary Disease

Severity of Exacerbation			Cardinal Clinical Findings
Mild	Moderate	Severe	
1 of 3 cardinal clinical findings <i>plus at least 1 of the following:</i> URI in the past 5 days Fever w/out other apparent cause ↑ wheezing ↑ cough ↑ RR or HR (20% above baseline)	2 of 3 cardinal findings	All 3 cardinal findings	Worsening dyspnea Increased sputum purulence Increased sputum volume

HR = heart rate; RR = respiratory rate; URI = upper respiratory infection.

Adapted from Anthonisen NR, Manfreda J, Warren CP, et al. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med* 1987;106:196–204.

judged to be cost-effective, and more cost-effective than promoting either vaccine alone.<sup>15</sup>

#### THE GROWING THERAPEUTIC ARMAMENTARIUM FOR COPD

Bronchodilators are the mainstay of drug therapy for most patients with symptomatic COPD. A growing number of bronchodilators, including inhaled anticholinergics and  $\beta_2$ -agonists, used alone or in combination, are available to deal with symptomatic stages of COPD.<sup>6</sup> Most patients with COPD have some degree of airflow improvement with the use of inhaled bronchodilators. A combination of ipratropium with albuterol is a convenient formulation. Long-acting  $\beta_2$ -agonists can be used in conjunction with anticholinergics in maintenance management of the disease. In addition, both inhaled and oral corticosteroids are available for acute exacerbations. For most patients with COPD, inhaled corticosteroids are not indicated. In general, inhaled corticosteroids are only appropriate for COPD patients in whom significant relief of symptoms is achieved. Antibiotics are indicated for episodes of purulent bronchitis.

Oxygen is useful for the maintenance management of patients with chronic stable hypoxemia and for exacerbations of disease.<sup>6</sup> Pulmonary rehabilitation is effective in increasing exercise tolerance and in improving quality of life.<sup>16,17</sup> Both noninvasive and invasive mechanical ventilation can be lifesaving. Surgical approaches, including lung volume reduction surgery and lung transplantation, may be palliative in selected patients.<sup>18,19</sup>

#### CASE-BASED APPROACHES TO MANAGEMENT

The following case examples give practical advice on the management of various stages of COPD. When

ever possible, the strategies of therapy suggested are evidence based.

#### Patient 1 Presentation

Patient 1 is a 59-year-old man who visits a respiratory medicine clinic 1 month following discharge from an intensive care unit (ICU). The patient had been previously diagnosed by his primary care physician as having COPD. He had been advised to stop smoking but had failed on several attempts. He had received influenza virus vaccine the past fall.

Following a holiday shopping outing, patient 1 developed a cold, which “settled in his chest.” Increased sputum production with purulence and fever were followed by worsening dyspnea. He suddenly became extremely dyspneic and was admitted to the ICU via the emergency department. Following treatment with oxygen, antibiotics, and corticosteroids, the patient was discharged on home oxygen delivered by a concentrator. Corticosteroids were not continued after discharge.

When seen in the clinic 1 month later, patient 1 is accompanied by his daughter, who is wheeling the E cylinder that was prescribed for portability. The patient reports that he remains severely short of breath and has been unable to regain the 10 pounds that he lost during the acute exacerbation. He comments on being “depressed” over the fact that he needs to be on oxygen. His appetite is poor and he has had difficulty sleeping. He has rarely gone outside of his home since discharge. The patient has been receiving albuterol (a short-acting  $\beta_2$ -agonist) by metered-dose inhaler 3 times daily; ipratropium (an anticholinergic bronchodilator) by metered-dose inhaler 3 times daily; and theophylline, 600 mg at bedtime.

The patient is moderately short of breath. He is alert and cooperative. Physical examination reveals decreased

**Table 4.** Drugs Used for Smoking Cessation

Drug and Method of Administration	Unit Dose	Dose Interval
Nicotine polacrilex (oral)	2 to 4 mg	Every 1 to 2 hours*
Transdermal nicotine patch	21,14, and 7 mg	24 hours
	15, 10, and 5 mg	16 hours
	22 and 11 mg	24 hours
Nasal nicotine spray	0.5 mg/inhalation/nostril	8 to 40 mg/day in hourly or prn dosing
Nicotine inhaler	10 mg/inhaler	Continuous puffing for 20 minutes 6 to 16 times/day
Bupropion sustained-release tablets	150 mg	150 mg for 3 days, then 300 mg/day
Buspirone tablets	15, 10, and 5 mg	7.5 mg twice daily, starting dose; 60 mg/day, maximum dose

prn = as required.

\*Fifteen to 30 pieces may be chewed over a 24-hour period.

breath sounds. Results of cardiac and extremity examinations are normal. Edema is absent. The patient's spirometry results are as follows: FEV<sub>1</sub>, 1.10 L (29% of expected); forced vital capacity (FVC), 3.42 (76% of expected); FEV<sub>1</sub>/FVC ratio, 46%. (No previous spirometric tests had been performed.) The patient's oxygen saturation, measured by pulse oximetry, is 97% while receiving oxygen by nasal cannulae at 2 L/min. Which of the following treatment options would be most valuable at this time?

- A) Prescribe a selective serotonin reuptake inhibitor antidepressant
- B) Prescribe oral corticosteroids
- C) Measure theophylline blood level
- D) Prescribe a salmeterol metered-dose inhaler
- E) Stop oxygen administration and repeat pulse oximetry after 20 minutes
- F) Continue the current treatment and see the patient again in 3 months

#### Discussion

Patient 1 has severe COPD and has just recovered from his first bout of acute respiratory failure. The patient, now depressed and on oxygen, is in need of aggressive systematic therapy with bronchodilators to prevent relapse and readmission.<sup>20</sup> Of equal importance, however, is the challenge of improving the patient to a state of general health.

The treatment option listed above that is least likely to be helpful is to prescribe an antidepressant (option A). Depression, anxiety, and somatic preoccupation are common in patients with advanced COPD.<sup>21</sup> In most

cases, however, the depression is reversible through methods of pulmonary rehabilitation and adjustments in therapy.<sup>21</sup> More recent studies of patients who receive home oxygen have shown a high prevalence of depression.<sup>22</sup> This depression may be a result of reduced mobility and opportunities for social interaction.<sup>22</sup>

One might be tempted to add corticosteroids once again to patient 1's treatment regimen (option B) because they have been shown to be helpful in acute exacerbations of disease. In fact, the results of some uncontrolled clinical trials have suggested that corticosteroids may slow the rate of decline in ventilatory function, but no randomized controlled clinical trials have shown an improvement in survival.<sup>23,24</sup>

Theophylline often has a beneficial effect on respiratory muscle function and usually does not lead to insomnia in patients with COPD.<sup>25</sup> The effect on respiratory muscle function is not directly related to blood levels of the drug. Furthermore, blood level measurements are expensive. Thus, in the absence gastrointestinal upset or cardiac arrhythmias, measurement of theophylline blood levels (option C) is not commonly used to guide theophylline therapy.

Salmeterol, a long-acting  $\beta_2$ -agonist, may be useful in the maintenance management of COPD (option D).<sup>26</sup> In comparisons with ipratropium, salmeterol has shown equal clinical benefit.<sup>26</sup> However, salmeterol cannot be used for breakthrough attacks because of its prolonged action. Thus, either albuterol or ipratropium would still be required for this purpose. The combination of albuterol with ipratropium in a single metered-dose inhaler would be a reasonable and useful strategy in either exacerbations or in maintenance management.<sup>27</sup>

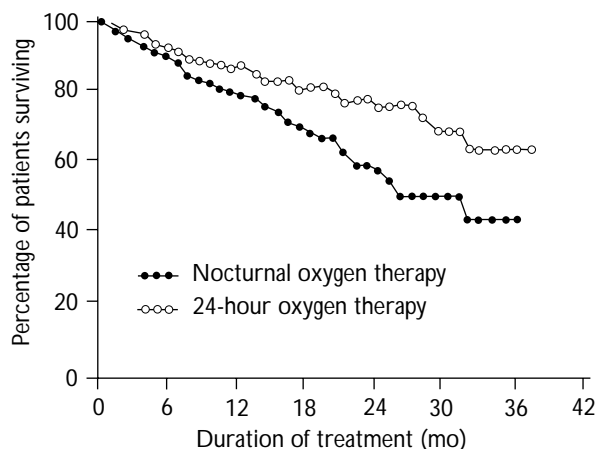
Stopping oxygen for 20 minutes and repeating pulse oximetry (option E) would be the most beneficial strategy at this point. Because this patient has a 97% oxygen saturation while on 2 L/min supplemental oxygen, it could be that room air hypoxemia is not present. Too many patients with COPD are encumbered by supplemental oxygen, often inappropriately delivered via a stationary system. This may, in fact, promote depression and lead to reduced performance of activities of daily living.<sup>22</sup>

Oxygen is useful in selected patients, but only those patients with chronic stable hypoxemia.<sup>28</sup> The Nocturnal Oxygen Therapy Trial (NOTT), which evaluated oxygen therapy in patients with hypoxemic COPD, clearly showed a survival benefit from long-term ambulatory administration of oxygen, as compared to shorter periods of oxygen therapy delivered via a stationary system (Figure 1).<sup>29</sup> Whether or not the improved survival with ambulatory oxygen in the NOTT study was a result of the duration of oxygen administration or the method of delivery has not been adequately studied. A recent reevaluation of the NOTT study<sup>30</sup> strongly suggests that in patients who had better walk tolerance during exercise training prior to receiving oxygen, compared to those with poorer walk tolerance, the rate of survival was substantially better with ambulatory oxygen than with stationary oxygen. Even patients with poor exercise tolerance did better with ambulatory oxygen, compared with stationary oxygen.<sup>30</sup> Today, for patients with chronic hypoxemia, ambulatory oxygen is the standard of care, allowing them to increase their activities and level of exercise both inside and outside of the home.<sup>31</sup>

Continuing with the same treatment and seeing the patient again 3 months later (option F) might be the treatment option selected by many clinicians. However, this would probably encourage a further period of unnecessary self-exile because of the patient's preoccupation with the need for oxygen therapy. The continued use of an inappropriate home oxygen system would not be desirable. A more active treatment strategy is more appropriate.

### Management of Patient 1

During the current clinic visit, the supplemental oxygen was stopped for 20 minutes, an interval necessary to reach an oxygen saturation steady state. Pulse oximetry was repeated, and room air oxygen saturation at this time was 92%. On walking around the clinic while breathing room air, the patient's oxygen saturation was 90% with an accompanying pulse of 88 bpm. Based on the results of this trial, patient 1's home oxygen therapy was discontinued.



**Figure 1.** Comparison of survival in patients on nocturnal oxygen therapy compared to those on continuous oxygen therapy. Survival differences began to appear at 1 year, and achieved statistical significance at 3 years. Adapted with permission from Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease. A clinical trial. Nocturnal Oxygen Therapy Trial Group. *Ann Intern Med* 1980;93:394.

Stopping supplemental oxygen at this point—3 months after discharge—is important in the management of patient 1 because it helps both the physician and the patient understand that oxygen is no longer necessary, at least at present. By discovering this fact, the patient can be encouraged to gradually increase walking to at least 20 to 30 minutes daily. The patient can walk outside during good weather, or inside shopping malls or within other covered structures when the weather is poor. Regular daily exercise is the key ingredient of pulmonary rehabilitation.<sup>16,17</sup> Pulmonary rehabilitation can briefly be described as focusing on patient education, breathing retraining, physical reconditioning, and the adjustment of pharmacologic agents.<sup>16,17</sup> However, the details of pulmonary rehabilitation go beyond the scope of this discussion.

The prognosis of patients with advanced COPD has been improving in recent years.<sup>32</sup> There are probably several reasons for this trend, including more meticulous therapy given to prevent exacerbations of COPD, which helps to prevent acute respiratory failure; better treatment of acute respiratory failure; more effective smoking cessation programs; and the more widespread use of ambulatory oxygen therapy and pulmonary rehabilitation.

### Patient 2 Presentation

Patient 2 is a 41-year-old woman who visits a respiratory medicine clinic because of her concerns about

emphysema. Her mother, who has severe emphysema, has recently been found to have lung cancer, which is inoperable because of its location near the carina. Her mother is receiving radiation therapy in an attempt to improve the staging with the possibility of a lung resection later.

Patient 2 started smoking at age 13 and has consumed, on average, 1.5 packs of cigarettes per day (42 pack-years). She reports a “cigarette cough,” and poor “pep” and energy. In spite of her symptoms, she is still able to work as a secretary in a large law firm. Because smoking in the office is prohibited, she takes numerous “coffee breaks” and smokes outside of the building to deal with her nicotine craving.

Results of patient 2’s physical examination are normal. Which of the following diagnostic procedures would be appropriate at this time?

- A) Chest radiograph
- B) Arterial blood gas analysis
- C) Spirometry
- D) Evaluation for  $\alpha_1$ -antitrypsin deficiency
- E) Sputum cytology

### Discussion

Because patient 2’s mother has lung cancer, and lung cancer has a familial component, one might be tempted to order a chest radiograph (option A), even given the patient’s young age. In fact, most physicians are now beginning to realize that women are more susceptible than men to developing lung cancer at a given age and level of smoking<sup>33</sup> and that women tend to have lung cancer at a younger age than men. A chest radiograph, however, is not nearly as sensitive as computed tomographic (CT) scanning.<sup>34</sup> In this patient, low-radiation dose spiral CT scanning would be appropriate if airflow obstruction were present. The risk of lung cancer is 4- to 6-fold greater in patients with airflow obstruction, compared with those with normal airflow, all other background factors (ie, smoking, occupational risk, and family history) being equal.<sup>35,36</sup>

There would be no point in doing arterial blood gas analysis in this patient (option B) before assessing the degree of airflow obstruction by spirometry.  $\alpha_1$ -Antitrypsin deficiency (option D) could be considered in view of the family history of emphysema, but only approximately 3% of COPD cases are due to  $\alpha_1$ -antitrypsin deficiency. In the assessment of patients with a family history of emphysema, it is much more important to identify airflow obstruction by spirometry. Sputum cytology to evaluate for malignancy (option E)

could also be considered, but it would not be the first option in this patient.

Spirometric testing (option C) is the appropriate step to take at this point in the evaluation of patient 2. Spirometry is the most important method of diagnosing COPD and assessing responses to therapy.

### Results of Spirometry for Patient 2

Patient 2’s spirometry results are as follows: FEV<sub>1</sub>, 2.05 (67% of predicted); FVC, 4.10 (110% of predicted); and FEV<sub>1</sub>/FVC ratio, 51%. Thus, with an FEV<sub>1</sub> that is less than 70% of the predicted value, this patient clearly has airflow obstruction. This patient’s disease would be classified as moderate severity by ERS and GOLD criteria, but only mild by ATS and BTS guidelines. In view of her young age and significant loss of airflow, most experienced clinicians would consider the severity as moderate. This illustrates the fact that the boundaries between mild and moderate stages are not distinct.

It is interesting to note that the FVC for patient 2 is 110% of predicted. Studies have shown that in relatively early stages of emphysema, the total lung capacity and FVC actually increase owing to loss of elastic recoil.<sup>37</sup> This is why the FEV<sub>1</sub>/FVC ratio is so exquisitely sensitive in identifying patients at risk of premature losses in ventilatory function, as judged by FEV<sub>1</sub>.<sup>38</sup>

In view of this patient’s heavy smoking and airflow obstruction, she is a candidate for both sputum cytology and CT scanning, particularly in light of her family history of lung cancer. Her young age does not exclude her from the possibility of having lung cancer.

### Management of Patient 2

The most important therapy for patient 2 is smoking cessation. The Lung Health Study has clearly shown that patients between the ages of 35 and 60 years exhibit a significant improvement in FEV<sub>1</sub> following smoking cessation. In comparison, patients who continue to smoke experience an accelerated loss of lung function over a 5-year period (**Figure 2**).<sup>39</sup> Today, strategies for smoking cessation are more effective than those of several years ago, with a growing number of pharmacologic agents available to use before or on the quit date (Table 4).

Assuming patient 2 had normal ventilatory function at age 20 (which may not be true because she started smoking as a teenager), she has lost a total of approximately 1000/mL of FEV<sub>1</sub> in 21 years, for a loss of more than 48 mL/year. Normal losses for a person this age and height (5 ft 5 in) are approximately 25 mL of FEV<sub>1</sub> per year. Thus, given a corresponding decline over the next 20 years with continued smoking, by the time patient 2 is 61 years old (her mother’s age), she will

have lost another 960/mL of FEV<sub>1</sub>. By age 61 years, her FEV<sub>1</sub> will have declined to 1.09 L (Figure 3), which is in the range of far advanced and disabling emphysema. By contrast, if she stops smoking and only loses FEV<sub>1</sub> at the rate of 25 mL /year, she will lose 500 mL, and her FEV<sub>1</sub> will be 1.55 L at age 61, which is compatible with a state of reasonably good health (see Figure 3). Thus, smoking cessation is key in the management of this patient to prevent a disastrous outcome.

Because patient 2 is symptomatic, she should receive inhaled bronchodilators. Ipratropium, an anticholinergic bronchodilator, would be the drug of first choice. Ipratropium remained effective throughout the 5 years of the Lung Health Study.<sup>39</sup> Salmeterol would be an alternative.<sup>26</sup>

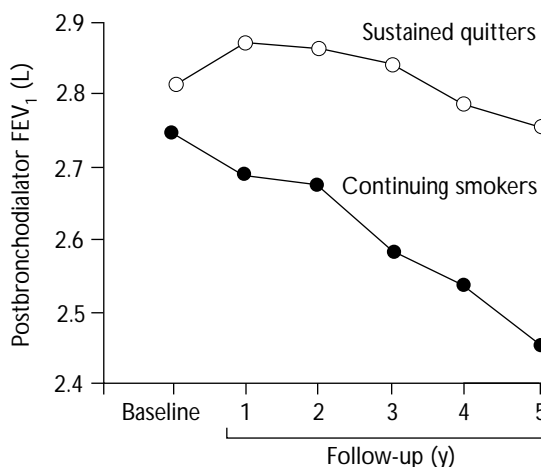
### Continued Clinical Course of Patient 2

Patient 2 succeeds in stopping smoking and is seen again for a follow-up visit 1 year later. Her FEV<sub>1</sub> is now 2.20 L (72% of predicted). She is concerned about a 12-pound weight gain and has further concerns about the future, because her mother has died of a massive hemorrhage. Which of the following steps would now be appropriate in the management of patient 2?

- A) Sputum cytology
- B) CT scan
- C) Reassurance that her smoking cessation at a young age will be sufficient to substantially reduce the likelihood of developing lung cancer
- D) Chest radiograph
- E) Appetite suppressants

### Discussion

Patient 2 is certainly at high risk for lung cancer, even though she has stopped smoking. Today, lung cancer is found more frequently in former smokers than in current smokers.<sup>40</sup> Option C is incorrect. Although controversial, it would be appropriate, based upon recent studies, to order a low-radiation dose spiral CT scan (option B) for patient 2 to look for an occult peripheral nodule, and sputum cytology (option A) to find indications of dysplastic, preneoplastic, or neoplastic lesions.<sup>34</sup> Today, the combination of sputum cytology and CT scanning offers the greatest promise in early identification of lung cancer. Both sputum cytology and CT scans identify patients in early stages of lung cancer, when the likelihood of cure is 60% to 80%. Conversely, when lung cancer is diagnosed by accident when chest radiographs are done for other reasons or on the basis of symptoms, the 5-year survival rate is a dismal 14%.<sup>41</sup>



**Figure 2.** Effect of continued smoking on mean postbronchodilator forced expiratory volume at 1 second (FEV<sub>1</sub>) in smokers with mild chronic obstructive pulmonary disease. Sustained quitters are compared to continuing smokers. The two curves diverge sharply after baseline. Adapted with permission from 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 FEV<sub>1</sub>. The Lung Health Study. JAMA 1994;272:1502.

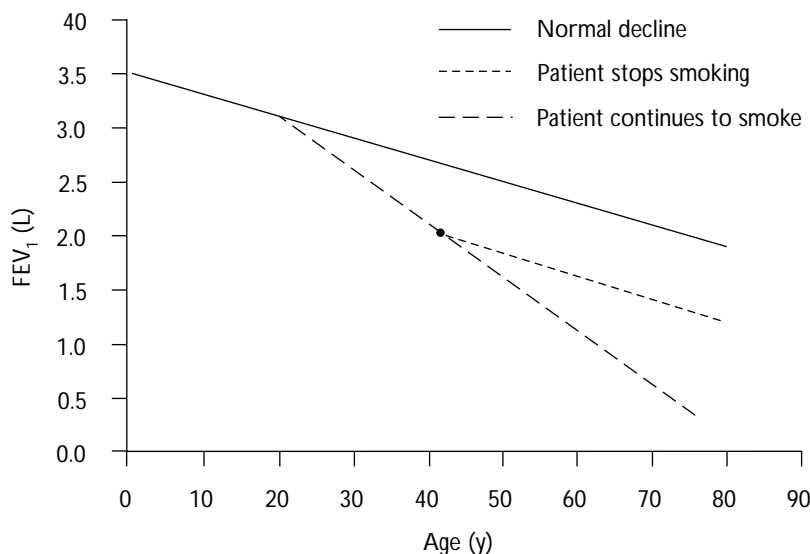
Chest radiographs (option D) are not as sensitive as CT scans in the diagnosis of early lung cancer.<sup>34</sup>

Many smokers gain some weight on stopping, but this occurs in the initial stage of quitting and often does not progress. Dietary counseling for patient 2 would be appropriate because of the weight gain, but not anorectic agents (option E).

### Patient 3 Presentation

Patient 3 is a 45-year-old man who visits his primary care physician for a routine physical examination. He prides himself on a state of good physical fitness. He plays golf each weekend, and jogs at least 30 minutes daily. This fitness program was begun 2 years ago, after an earlier diagnosis of hypertension, hypercholesterolemia, and insulin resistance. Following the exercise and weight loss program, the patient's blood pressure returned to normal. His most recent serum lipid levels are as follows: high-density lipoprotein cholesterol (HDL), 60 mg/dL; low-density lipoprotein cholesterol (LDL), 105 mg/dL; fasting triglyceride level, 200 mg/dL; and fasting blood glucose, 90 mg/dL. He had smoked a pack of cigarettes daily for 21 years but stopped 2 years ago.

The patient's medical records include the results of a chest radiograph, electrocardiogram, and 22-channel serum chemistry panel that were performed in the past



**Figure 3.** FEV<sub>1</sub> projections for patient 2. This graph illustrates the accelerated losses of FEV<sub>1</sub> that have occurred by age 41 years, assuming that the patient's lung function was normal at age 20 years. The 2 projections portray a slower decline in FEV<sub>1</sub> if the patient stops smoking, compared with a more rapid decline if she continues to smoke. FEV<sub>1</sub> = forced expiratory volume in 1 second.

year as a part of an insurance evaluation, all of which were within normal limits. Spirometric tests have never been performed on this patient. His height is 5 ft 11 in.

Spirometry is performed, and reveals the following values: FEV<sub>1</sub>, 3.43 L (80% of predicted); FVC, 5.28 L (100% of predicted); and FEV<sub>1</sub>/FVC ratio, 65%. The clinician recognizes that patient 3 has mild COPD because the FEV<sub>1</sub>/FVC ratio is less than 70%, even though his FEV<sub>1</sub> is only borderline low. In response to albuterol, the patient's FEV<sub>1</sub> elevates by 350 mL to 3.84 L, an increase of 12%. The patient would like to know if there is any therapy that will prevent the decline of his FEV<sub>1</sub> over his lifetime. Which of the following options are appropriate for patient 3 at this time?

- A) Advising the patient that stopping smoking is all that can be done
- B) Ipratropium, 2 puffs 3 times daily
- C) Salmeterol, 2 puffs twice daily
- D) Inhaled corticosteroids
- E) A trial of theophylline with a follow-up of pulmonary function tests

### Discussion

Option A is correct. Re-emphasizing to the patient that he has already made a major investment in his future health will likely encourage him to remain smoke-free for the rest of his life.

Although patient 3 meets the criterion of a 12% improvement of FEV<sub>1</sub> in response to an inhaled bronchodilator, there is no evidence that the long-term use of either a  $\beta_2$ -agonist (option C) or an anticholinergic agent

(option B) will alter the rate of decline in ventilatory function. During the Lung Health Study, ipratropium remained effective during the 5 years that it was used, but it did not change the rate of decline of baseline FEV<sub>1</sub>.<sup>39</sup> Another study, however, showed that ipratropium had the effect of elevating baseline lung function. Thus, if a bronchodilator were to be used, ipratropium would probably be superior to a  $\beta_2$ -agonist.<sup>42</sup> It would also have fewer side effects of tremor, tachycardia, or palpitations.<sup>20</sup> Theophylline (option E) is not indicated in asymptomatic patients with mild airflow obstruction.

Recently, there has been great interest in determining whether inhaled corticosteroids (option D) can slow the rate of decline in FEV<sub>1</sub>. Five studies have failed to show a sustained benefit in baseline FEV<sub>1</sub> with the use of inhaled steroids.<sup>43-47</sup> One study of smokers with mild COPD showed a slight improvement initially, but the long-term rate of decline was equal to that of patients given placebo.<sup>45</sup> At least 2 studies have shown an improvement in symptoms and quality of life,<sup>46,47</sup> although one of these showed a statistically significant reduction in bone density.<sup>47</sup> In patient 3, who has previously demonstrated insulin resistance, corticosteroids' systemic effects might worsen insulin resistance and ultimately result in diabetes. Thus, corticosteroids should not be used in this patient.

Judged by his FEV<sub>1</sub> and state of physical fitness, this patient does not face premature morbidity and mortality from COPD. He does not require any medications for his lungs as long as he remains asymptomatic and maintains a near-normal FEV<sub>1</sub> (ie,  $\geq 80\%$ ). For now, maintaining his nonsmoking status is the most important action the patient can take to maintain his lung function. New

drugs are under study which may slow the rate of decline in FEV<sub>1</sub> by opposing the inflammatory and other damaging mechanisms which result in airway inflammation and loss of alveolar walls.<sup>4,6</sup>

#### THE NATIONAL LUNG HEALTH EDUCATION PROGRAM

A national healthcare initiative, the National Lung Health Education Program (NLHEP), was launched in 1998<sup>2,48</sup> ([www.nlhep.org](http://www.nlhep.org)). Its aim is to involve all primary care physicians in early identification of and intervention in COPD and related disorders. The NLHEP recommends spirometric testing in all smokers age 45 years or older, and in adults with chronic cough, mucus hypersecretion, dyspnea, or wheeze.<sup>49</sup> Today, the NLHEP is promoting the widespread use of simple office spirometry. Industry has responded with the production of several simple, handheld units that are highly accurate. In evaluating the results of spirometry, the NLHEP recommends substituting the forced expiratory volume in 6 seconds (FEV<sub>6</sub>) for FVC (ie, using the ratio of FEV<sub>1</sub>/FEV<sub>6</sub>) because it is a useful surrogate.<sup>50</sup> Spirometric testing for only 6 seconds is much easier for the patient and for the person who performs the spirometry. **“Test Your Lungs, Know Your Numbers”** is the battle cry of the NLHEP.

#### SUMMARY

COPD is recognized as the United States' most rapidly growing health problem. COPD is a smokers' disease that clusters in families and worsens with age. COPD also occurs in some nonsmokers. Today, the challenge is to identify patients early in the disease process and to intervene through smoking cessation. Bronchodilators are indicated for symptomatic airway obstruction. Additional therapies include the use of vaccines and the treatment of exacerbations of disease. New drugs designed to deal with the specific inflammatory mechanisms involved in COPD are currently being developed. It is hoped that the future will bring this devastating healthcare crisis under control. The key to success is the involvement of primary care physicians in the early identification and intervention before symptomatic stages develop. **HP**

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