

# Chronic Obstructive Pulmonary Disease: Diagnostic Considerations

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Chronic obstructive pulmonary disease is characterized by the gradual progression of irreversible airflow obstruction and increased inflammation in the airways and lung parenchyma that is generally distinguishable from the inflammation caused by asthma. Most chronic obstructive pulmonary disease is associated with smoking, but occupational exposure to irritants and air pollution also are important risk factors. Patients with chronic obstructive pulmonary disease typically present with coughing, sputum production, and dyspnea on exertion. However, none of these findings alone is diagnostic. The Global Initiative for Chronic Obstructive Lung Disease diagnostic criterion for chronic obstructive pulmonary disease is a forced expiratory volume in one second/forced vital capacity ratio of less than 70 percent of the predicted value. Severity is further stratified based on forced expiratory volume in one second and symptoms. Chest radiography may rule out alternative diagnoses and comorbid conditions. Selected patients should be tested for  $\alpha_1$ -antitrypsin deficiency. Arterial blood gas testing is recommended for patients presenting with signs of severe disease, right-sided heart failure, or significant hypoxemia. Chronic obstructive pulmonary disease also is a systemic disorder with weight loss and dysfunction of respiratory and skeletal muscles. (*Am Fam Physician* 2006;73:669-76, 677-8. Copyright © 2006 American Academy of Family Physicians.)

## ► Patient Information:

A handout on chronic obstructive pulmonary disease, written by the authors of this article, is provided on page 677.

► See related editorial on page 590.

The global burden of chronic obstructive pulmonary disease (COPD) is increasing; the disease is projected to be the third leading cause of death and fifth leading cause of overall disability worldwide by 2020.<sup>1</sup> Men and women seem to be at an equal risk, and the death rate attributable to COPD is increasing significantly in both sexes.<sup>1,2</sup> The economic consequences of COPD are substantial. In 2002, the estimated total societal cost of COPD in the United States was \$32 billion.<sup>2</sup>

## Definition

COPD is a heterogeneous disorder that encompasses traditional clinical entities such as emphysema and chronic bronchitis.<sup>3,4</sup> The Global Initiative for Chronic Obstructive Lung Disease (GOLD),<sup>5</sup> a collaborative effort from the National Heart, Lung, and Blood Institute; the National Institutes of Health; and the World Health Organization, defines COPD as a usually progressive disease with airflow

limitation that is not fully reversible and that is associated with an abnormal inflammatory response of the lungs to noxious particles or gases.

Patients with COPD present with a variety of clinical findings, including elements of chronic bronchitis and emphysema.<sup>6-8</sup> Although COPD and asthma are both associated with airflow obstruction and inflammation of the lung and airways, asthma-related airflow obstruction is more reversible and the disease course is more variable than with COPD.<sup>6,8,9</sup>

## Risk Factors

Exposure to tobacco smoke is the most significant risk factor for COPD, with 80 to 90 percent of all cases attributable to smoking.<sup>6</sup> Evidence linking tobacco smoke exposure and COPD predominantly comes from population-based studies that have consistently shown that smoking is associated with diminished lung function, more frequent respiratory symptoms, and increased COPD-related deaths.<sup>5,10-13</sup> Pipe and cigar smoking are associated with increased COPD risk,

**Smoking cessation can give a former smoker the same average ongoing loss of lung function as a never-smoker.**

**SORT: KEY RECOMMENDATIONS FOR PRACTICE**

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Spirometry should be used as the first-line diagnostic tool when evaluating patients for COPD. A FEV <sub>1</sub> /FVC ratio of less than 70 percent of the predicted value suggests COPD.	C	5, 6
Patients with suspected COPD should receive chest radiography to exclude other diagnoses and comorbidities.	C	6, 31
α <sub>1</sub> -Antitrypsin deficiency testing should be performed in select patients (e.g., COPD in never-smokers, idiopathic cirrhosis, family history of α <sub>1</sub> -antitrypsin deficiency, predominantly lower lung emphysema, "premature" COPD, and refractory asthma at a young age).	C	15
ABG testing should be performed if the patient presents with right-sided heart failure or has more severe COPD.	C	5

*COPD = chronic obstructive pulmonary disease; FEV<sub>1</sub> = forced expiratory volume in one second; FVC = forced vital capacity; ABG = arterial blood gas.*

*A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 573 or <http://www.AAFP.org/afpsort.xml>.*

but at a lesser rate than with cigarette smoking.<sup>5,6</sup> Although cigarette smoking is a significant risk factor for COPD, only about 20 percent of cigarette smokers develop clinically significant COPD.<sup>6,8,13</sup>

The second most significant documented risk factor for COPD is α<sub>1</sub>-antitrypsin deficiency. Although α<sub>1</sub>-antitrypsin deficiency increases the risks associated with smoking, COPD can develop in never-smokers with α<sub>1</sub>-antitrypsin deficiency. One percent of COPD cases are attributable to severe α<sub>1</sub>-antitrypsin deficiency.<sup>5,6,14,15</sup>

Certain occupational exposures are associated with increased risk of COPD (Table 1<sup>16-18</sup>). Exposure to solid biomass

fuels, commonly used for indoor cooking and heating, is a risk factor for COPD, particularly in the developing world.<sup>5,6,9,19,20</sup>

**Natural History**

Patients with COPD may present with loss of lung function beyond normal age-related decreases. Clinical disease develops fairly late in the disease course, after lung function drops below threshold values.

After 25 years of age, a nonsmoking adult's forced expiratory volume in one second (FEV<sub>1</sub>) decreases by an average of 20 to 40 mL per year. In some smokers, FEV<sub>1</sub> decreases by two to five times this amount, making them particularly susceptible to COPD.<sup>6,8,12,13,21,22</sup> Smoking cessation may cause slight initial improvement in FEV<sub>1</sub> (approximately 50 mL in the first year).<sup>21</sup> More importantly, smoking cessation can give a former smoker the same average ongoing loss of lung function as a never-smoker.<sup>13,21</sup> Figure 1<sup>13,21</sup> illustrates the progressive loss of lung function in a variety of settings.

Patients with COPD usually have a smoking history of at least 20 pack-years. Wheezing and dyspnea on exertion generally occur when the FEV<sub>1</sub> is less than 50 percent of the predicted value, and significant physical disability usually occurs when the FEV<sub>1</sub> is less than 35 to 40 percent of the predicted value.<sup>4,22,23</sup> Patients who started smoking in their 20s and have already sustained appreciable FEV<sub>1</sub> loss by their 40s are likely to

**TABLE 1  
Occupational Irritants That Increase the Risk of COPD**

<i>Occupation</i>	<i>Irritant</i>
Agricultural worker	Endotoxin
Coal miner	Coal dust
Concrete worker	Mineral dust
Construction worker	Dust
Gold miner	Silica
Hard rock miner	Mineral dust
Rubber worker	Industrial chemicals

*COPD = chronic obstructive pulmonary disease.  
Information from references 16 through 18.*

develop significant COPD if they continue to smoke. Those in their mid-40s who have normal FEV<sub>1</sub> values, however, probably will not develop symptomatic disease.<sup>13</sup>

### Pathophysiology

COPD involves a chronic inflammatory process, primarily in the peripheral airways and the lung parenchyma. Airway irritation causes mucous gland enlargement, hypersecretion, ciliary dysfunction, and squamous metaplasia early in the disease course. An ongoing cycle of inflammation and repair ultimately narrows the airway lumen and obstructs airflow. Patients with emphysema experience destruction of the structural constituents of the alveolar walls, causing permanent enlargement of the air spaces distal to the terminal bronchioles. In early COPD, emphyse-

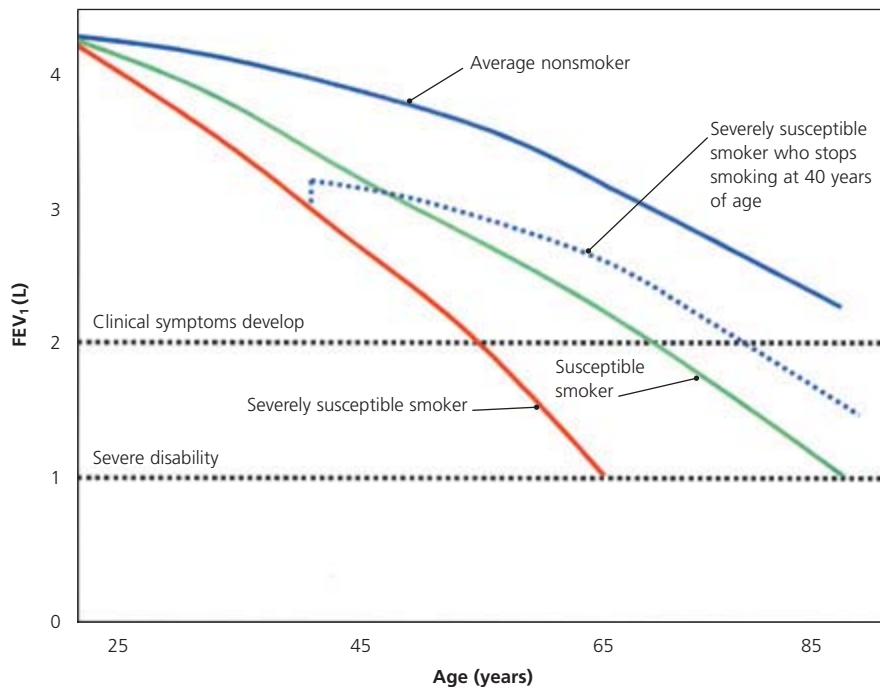
matous changes are most prominent in the upper lung fields. Loss of the structural supports that keep the airways open allows the bronchioles to collapse during expiration; the resulting nonfunctioning alveolar units reduce the amount of lung area available for gas exchange.<sup>4-6,24</sup>

Patients with COPD have high neutrophil, macrophage, and CD8<sup>+</sup> T-lymphocyte counts in the airways and lung parenchyma. These cells release inflammatory cytokines and proteases that cause an imbalance of the pro-inflammatory and protective mediators found in healthy lungs.<sup>5,8,20,25</sup>

### Diagnosis

Common differential diagnosis of COPD includes asthma, heart failure, bronchiectasis, bronchiolitis obliterans, cystic fibrosis,

## Lung Function Decline in Smokers and Nonsmokers



**Figure 1.** The natural history of lung function decline. Smokers who are susceptible to lung injury experience an increase in the rate of age-related loss in FEV<sub>1</sub> compared with nonsmokers (red, green, and blue lines). After lung function declines to threshold levels, clinical symptoms develop (black dotted lines). When a smoker stops smoking, the rate of FEV<sub>1</sub> loss again approximates to that of a nonsmoker (blue dotted line). (FEV<sub>1</sub> = forced expiratory volume in one second.)

Information from references 13 and 21.

and tuberculosis (Table 2). Clinical history; physical examination; and diagnostic testing, such as lung function measurements, can help diagnose COPD. Chest radiography may rule out alternative diagnoses and comorbid conditions.

#### CLINICAL HISTORY

Patients with COPD typically present with cough, sputum production, and dyspnea on exertion. A COPD diagnosis is likely if a patient with a significant history of tobacco smoke exposure has these symptoms. Patients with COPD also may experience orthopnea soon after reclining, unlike patients with heart

failure, in whom orthopnea typically occurs hours after reclining, when fluid mobilizes from the lower extremities. COPD-associated hemoptysis often is caused by airway mucosal erosion from coughing, but a coexisting cancer or underlying infection (e.g., tuberculosis) should be considered. Severe nocturnal hypoxia or hypercapnia should be considered if a patient with COPD presents with a persistent morning headache.

#### PHYSICAL EXAMINATION

Patients with COPD often present with diminished breath sounds, prolonged expiratory time, and expiratory wheezing that

TABLE 2  
COPD and Common Differential Diagnosis

Diagnosis	Characteristics	Clinical presentation	Pulmonary function test findings
COPD	Midlife to late-life onset; steadily progressive with exacerbations; associated with smoking history	Chronic productive cough, dyspnea, and wheezing	Predominantly fixed airflow obstruction, decreased DLCO
Asthma	Usually early-life onset; episodic; associated with other allergic disorders and family history	Episodic wheezing, cough, and dyspnea	Predominantly reversible airflow obstruction, normal DLCO
Bronchiectasis	Usually midlife onset; progressive with exacerbations	Productive cough with thick, purulent sputum; dyspnea; and wheezing	Obstructive airflow limitation, both fixed and reversible
Bronchiolitis obliterans	Onset at any age; may be associated with history of flu-like illness, collagen vascular disease, or toxic exposure	Often subacute presentation with dyspnea, cough, and fever	Decreased vital capacity, decreased DLCO, usually no obstructive component
Congestive heart failure	Midlife to late-life onset; associated with risk factors such as hypertension and coronary artery disease	Fatigue, exertional and paroxysmal nocturnal dyspnea, and peripheral edema	Decreased DLCO, predominantly used to exclude other diagnoses
Tuberculosis	Onset at any age; associated with history of exposure	Productive cough, hemoptysis, fever, and weight loss	Not used for diagnosis
Cystic fibrosis	Usually early-life onset; progressive with exacerbations; associated with pancreatic disease, failure to thrive, intestinal obstruction, cirrhosis, and steatorrhea	Predictive cough with purulent sputum, dyspnea, and wheezing	Predominantly fixed airflow obstruction

COPD = chronic obstructive pulmonary disease; DLCO = carbon monoxide diffusion in the lung; ABG = arterial blood gas; CT = computed tomography; ESR = erythrocyte sedimentation rate; BNP = brain natriuretic peptide; AFB = acid-fast bacillus.

TABLE 3  
**Signs and Symptoms to Predict Airflow Limitation  
 in Selected Patients with Suspected COPD\***

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<i>Chest radiography findings</i>	<i>Other recommended testing</i>
Hyperinflation, increased basilar markings, bronchial thickening	$\alpha_1$ -Antitrypsin testing, ABG testing, and chest CT in selected patients
Normal between episodes	Allergy testing, peak-flow monitoring
Focal pneumonia, atelectasis; dilated, thickened airways (ring shadow)	Bacterial, microbial, and fungal sputum culture, chest CT
Multifocal, bilateral alveolar infiltrates	ESR, high-resolution CT, lung biopsy
Increased heart size, pulmonary vascular congestion, pleural effusions	Echocardiography, BNP measurement, electrocardiography; cardiac catheterization in selected patients
Infiltrate, nodular lesions, hilar adenopathy	Sputum AFB culture
Bronchiectasis frequent in upper lobes	Sweat chloride test (diagnostic), Bacterial sputum culture

initially may occur only on forced expiration. Additional findings on physical examination include hyperinflation of the lungs with an increased anteroposterior chest diameter (“barrel chest”); use of accessory muscles of respiration; and distant heart sounds, sometimes best heard in the epigastrium. Patients with more advanced disease may have pursed lip breathing or postures that relieve dyspnea (e.g., leaning forward against outstretched palms). The presence of significant edema may indicate right-sided heart failure and cor pulmonale in patients with pulmonary hypertension from severe long-standing COPD.

The literature on the effectiveness of specific components of the patient history and physical examination as predictors of obstructive airway disease is of limited value. A history of COPD and a significant smoking history generally are strong predictors of airway obstruction, and the clinical likelihood of COPD is greater when multiple symptoms or signs suggesting COPD are present.<sup>24-28</sup> Table 3<sup>24</sup> lists the predictive values of common physical symptoms and signs for detecting airflow obstruction.

#### DIAGNOSTIC TESTING

The best diagnostic test for evaluating patients with suspected COPD is lung function measured with spirometry. The GOLD guidelines<sup>5</sup> characterize the severity of COPD according to clinical and spirometric measures (Table 4<sup>5</sup>). Key spirometric measures may be obtained with a portable office spirometer and should

include forced vital capacity (FVC) and FEV<sub>1</sub>. Patients with COPD typically present with obstructive airflow. According to the GOLD criteria, a FEV<sub>1</sub>/FVC ratio of less than 70 percent in a patient with a postbronchodilator FEV<sub>1</sub> of less than 80 percent of the predicted value is diagnostic for COPD.<sup>5</sup> Severity is further stratified based on symptoms and FEV<sub>1</sub> values. A patient with severe disease has a FEV<sub>1</sub> of less than 50 percent of the predicted value; values below 30 percent of the predicted value represent very severe disease.<sup>5,6,29</sup> Although some experts have proposed periodic FEV<sub>1</sub> testing for high-risk patients older than 45 years to facilitate risk factor reduction counseling, no evidence exists to support this recommendation.<sup>22</sup>

Beyond office spirometry, complete pulmonary function testing may show increased

total lung capacity, functional residual capacity, and residual volume. A substantial loss of lung surface area available for effective oxygen exchange causes diminished carbon monoxide diffusion in the lung (DLCO) in patients with emphysema. This finding may help distinguish COPD from asthma, because patients with asthma typically have normal DLCO values.<sup>5,6,30</sup>

Chest radiography usually is abnormal in patients with severe COPD but may not show changes in up to one half of patients with moderate disease.<sup>6,31</sup> Chest radiography in patients with COPD may show hyperinflation of the lungs, flattening of the domes of the diaphragm, and tapering of the pulmonary vessels as they move to the periphery of the lung fields. Increased basilar markings (“dirty lungs”) sometimes are visible on chest radiographs in patients with chronic bronchitis, and isolated bullae may be seen in patients with emphysema. A computed tomography (CT) scan of the chest should not be used routinely to diagnose COPD, but it may show findings that are highly correlated with the degree of COPD changes found on pathologic examination.<sup>31</sup>

Testing for  $\alpha_1$ -antitrypsin deficiency is appropriate in selected patients; testing involves measuring circulating  $\alpha_1$ -antitrypsin levels followed by phenotype testing if levels are abnormal. Patients with severe  $\alpha_1$ -antitrypsin deficiency usually are of European descent and develop clinical evidence of COPD approximately 10 years earlier than patients who are not  $\alpha_1$ -antitrypsin deficient.<sup>6</sup> Lung changes associated with severe  $\alpha_1$ -antitrypsin deficiency usually include lower lung field predilection.  $\alpha_1$ -Antitrypsin deficiency also may cause otherwise unexplained cirrhosis of the liver.<sup>6,14,15,19</sup> Clinical circumstances in which testing for  $\alpha_1$ -antitrypsin deficiency should be considered include COPD in never-smokers, idiopathic cirrhosis, family history of  $\alpha_1$ -antitrypsin deficiency, predominantly lower lung emphysema, “premature” COPD, and refractory asthma at a young age.<sup>6,15</sup>

Arterial blood gas measurement is recommended to rule out significant hypoxemia (partial pressure of oxygen less than 60 mm Hg) or hypercapnia in patients with

**TABLE 4**  
**GOLD Staging System for COPD Severity**

Stage	Description	Findings*
0	At risk	Risk factors and chronic symptoms but normal spirometry
I	Mild	FEV <sub>1</sub> /FVC ratio less than 70 percent FEV <sub>1</sub> at least 80 percent of predicted value May have symptoms
II	Moderate	FEV <sub>1</sub> /FVC ratio less than 70 percent FEV <sub>1</sub> 50 percent to less than 80 percent of predicted value May have chronic symptoms
III	Severe	FEV <sub>1</sub> /FVC ratio less than 70 percent FEV <sub>1</sub> 30 percent to less than 50 percent of predicted value May have chronic symptoms
IV	Very severe	FEV <sub>1</sub> /FVC ratio less than 70 percent FEV <sub>1</sub> less than 30 percent of predicted value or FEV <sub>1</sub> less than 50 percent of predicted value plus severe chronic symptoms

GOLD = Global Initiative for Chronic Obstructive Lung Disease; COPD = chronic obstructive pulmonary disease; FEV<sub>1</sub> = forced expiratory volume in one second; FVC = forced vital capacity.

\*—Classifications based on postbronchodilator FEV<sub>1</sub>.

Adapted from Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease [executive summary]. Updated 2005. Accessed online January 17, 2006, at: <http://www.goldcopd.com/Guidelineitem.asp?1=2&l2=1&intlD=996>.

more severe disease. This is based on FEV<sub>1</sub> (less than 40 percent of predicted value), signs of right-sided heart failure, and signs of hypoxemia.<sup>5</sup>

### Clinical Subtypes

Patients with COPD also may be grouped into clinical subtypes based on clinical findings. The most common clinical subtypes are chronic bronchitis and emphysema.

#### CHRONIC BRONCHITIS WITH AIRFLOW OBSTRUCTION

Pure chronic bronchitis is clinically defined as an otherwise unexplained chronic, productive cough for at least three months in each of two successive years. If fixed airway obstruction is present in a patient with chronic bronchitis, the patient also has COPD. Eighty-five percent of patients with COPD have chronic bronchitis.<sup>5</sup> These patients experience prominent cough and sputum production and frequently develop hypoxia and hypercarbia at rest and significant oxygen desaturation during sleep. Patients with chronic bronchitis and COPD often develop pulmonary hypertension, causing right-sided heart failure and cor pulmonale with marked peripheral edema.<sup>5-8</sup>

#### EMPHYSEMA

Dyspnea is the most prominent symptom associated with emphysema-related COPD. Hypoxia is less marked than in the bronchitic form of COPD, and hypercarbia is relatively uncommon until very late in the disease course.

Tidal breathing occurs at high lung volumes in patients with emphysema-related COPD to compensate for high pulmonary residual volumes and to open collapsed airways. This produces hyperinflation of the lungs and thorax, greatly increasing the total work required to breathe. Patients with emphysema-related COPD are less likely to have right-sided heart failure and cor pulmonale than patients with chronic bronchitis and COPD.<sup>5-7,30,32</sup>

### COPD as a Systemic Disease

COPD increasingly is considered a systemic disorder with important nonpulmonary

components. Weight loss in patients with COPD may be related to increased circulating levels of inflammatory mediators (e.g., tumor necrosis factor alpha, inflammatory cytokines). Pulmonary cachexia associated with severe COPD also causes profound weight loss, which is a predictor of increased mortality risk independent of lung function.<sup>5,6,8,25,33,34</sup>

Respiratory and skeletal muscle abnormalities accompany COPD. The respiratory muscles of patients with COPD are chronically overworked and fatigued, whereas the extremity muscles tend to be underworked and atrophied.

Members of various family medicine departments develop articles for "Problem-Oriented Diagnosis." This is one in a series from the Department of Family Medicine at the University of Florida College of Medicine, Gainesville. Coordinator of the series is R. Whit Curry, Jr., M.D.

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Author disclosure: Nothing to disclose.

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