

## PRACTICE

# Chronic obstructive pulmonary disease: Diagnosis and management

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### Abstract

**Purpose:** The purpose of this article is to provide a comprehensive review of the current modalities employed in diagnosing and treating chronic obstructive pulmonary disease (COPD). Special emphasis is placed on current guidelines, as defined by the Global Initiative for Chronic Obstructive Lung Disease.

**Data source:** A comprehensive literature review for COPD serves as the basis for this article.

**Conclusions:** According to the National COPD Coalition (2004), there are nearly 24 million Americans who suffer from COPD. The incidence of COPD is rising globally and is associated with increased morbidity and mortality. COPD is characterized by progressive decline in function, resulting in concomitant diseases, which increase healthcare dollar expenditures, thus making COPD a concern for healthcare providers in the United States and abroad.

**Implications for practice:** Once a diagnosis of COPD is made, healthcare providers should explore multiple treatment options in an effort to find the most beneficial regimen. It is only when the treatments are individualized, including physiological therapies and cognitive approaches to lessen risks as well as to reduce exacerbations, that the patient with COPD is able to potentially experience a reasonable quality of life.

### Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality in the United States and is currently ranked as the fourth leading cause of death in the world (Pauwels, Buist, Calverley, Jenkins, & Hurd, 2001). There are more than 24 million people suffering from COPD in the United States, with more than 110,000 persons dying from COPD annually. The mortality rate for COPD continues to rise in contrast to that for cardiovascular disease, which has seen a steady decline in mortality over the past two decades. As the population ages, the incidence of COPD is expected to rise. Associated with this debilitating disease is an increase in work absences, hospital admissions, and outpatient office visits (Zielinski & Bednarek, 2001). The incidence of COPD and its associated

morbidity warrant special consideration by healthcare providers.

### Definition

Several problems are encountered when defining COPD. The first relates to the term chronic obstructive pulmonary disease because this is not truly a disease but a constellation of diseases. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) program, COPD is defined as a disease state characterized by airflow limitation that is not fully reversible (Pauwels et al., 2001). The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases. Traditionally,

COPD has been divided into several pathophysiologic entities, each sharing the common physiologic features of airflow obstruction and abnormal inflammatory response. These groups include chronic bronchitis, emphysema, asthma, and bronchiectasis (McCorry, Brown, Gelfand, & Bach, 2001). The GOLD program standardizes the term COPD by incorporating each entity into the diagnosis of COPD. Additionally, clinicians may experience difficulty differentiating COPD from asthma, particularly the syndrome of poorly reversible airway obstruction in older patients with chronic asthma (D'Alonzo, 2004).

According to the American Thoracic Society, chronic bronchitis is defined as sputum production on most days for at least 3 months in at least 2 consecutive years in the absence of any other identifiable cause (Rennard, 2005). Emphysema is defined as abnormal, permanent enlargement of the air spaces distal to the terminal bronchioles—that is, the gas-exchanging unit of the lung, accompanied by destruction of their walls and without obvious fibrosis. As with chronic bronchitis, the definition of emphysema does not require the presence of airflow limitation (Niimi et al., 2005). Asthma is a condition characterized by reversible airflow limitation; however, persistent asthma, especially in older adults, is difficult to distinguish from COPD (D'Alonzo, 2004). Chronic inflammation and hypertrophy of the bronchial smooth muscle result in poor airway reversibility and fixed airflow obstruction, therefore making persistent asthma difficult to distinguish from COPD. Bronchiectasis is characterized as an abnormal inflammatory response of the lungs, which produces airflow limitations and should be considered in the differential of COPD.

COPD is as a result of a wide variety of environmental, behavioral, and genetic conditions. Approximately 85%–90% of all cases of COPD arise from cigarette smoking, with the remaining 10%–15% arising from second-hand smoke exposure, occupational exposure, air pollution, genetic disturbances, and possibly from hyperresponsive airways (Tzortzaki, Tsoumakidou, Makris, & Sifakas, 2005).

### Pathophysiology of COPD

The pathologic changes associated with COPD are complex and occur in the central conducting airways, the peripheral airways, the lung parenchyma, and the pulmonary vasculature, resulting in permanent airway remodeling. Inflammation underlies the majority of pathologic lesions associated with COPD. Inflammation leads to corresponding physiological changes of COPD, which include mucus hypersecretion, ciliary dysfunction, airflow limitation, pulmonary hyperinflation, gas exchange abnormalities, pulmonary hypertension, and cor pulmonale.

In chronic bronchitis, mucus hypersecretion and ciliary dysfunction lead to chronic cough and sputum production. The productive cough is characterized by chronic hypersecretion of mucus resulting in the central airways—the trachea, the bronchi, and the bronchioles greater than 2–4 mm in diameter. Mucus is produced by mucus glands in the larger airways and by goblet cells in airway epithelium. Hypertrophy of the mucus glands occurs, and the number of goblet cells increases, extending more peripherally (Poole & Black, 2001). The volume of sputum produced correlates with the degree of stimulation to mucus glands. Airway wall changes include squamous metaplasia of the airway epithelium, loss of cilia and ciliary function, and increased smooth muscle and connective tissue. Transbronchial biopsies during an acute exacerbation show an influx of eosinophils and neutrophils. The influx of proinflammatory mediators results in airway inflammation and subsequently increases airflow limitation. Expiratory airflow limitation, best measured through spirometry, is the hallmark physiological change of COPD and the key to diagnosis of the disease (Buffels, Degryse, Heyrman, & Decramer, 2004). The limitations are primarily because of fixed airway obstruction, the increase in airway resistance, and the destruction of alveolar attachments, which inhibits the ability of the small airways to maintain patency. The latter plays only a smaller role in the disease. Over time, peripheral airway obstruction, parenchymal destruction, and pulmonary vascular abnormalities reduce the lung's capacity for gas exchange, producing hypoxemia and, over time, hypercapnia. Pulmonary hypertension and the resulting cor pulmonale are common cardiovascular complications that develop late in COPD and portend a poor prognosis (Nausser & Stittes, 2001).

### Clinical features

Patients with COPD characteristically complain of breathlessness or dyspnea on exertion, often accompanied by wheezing and cough. Dyspnea develops gradually and may not be noticed until its severity impacts activities of daily living or quality of life. The cough is usually productive and is present for many years, usually in the morning, with varying degree of purulent sputum, and the patient may relay a history of a “smoker's cough.” In addition, a reported smoking history of at least 20 pack years is normal (packs per day multiplied by number of years of smoking) (Buffels et al., 2004).

Usually, dyspnea is observed during more strenuous activities such as stair climbing or hurrying to complete an activity. This usually relates to moderate obstruction on pulmonary function testing. The other common complaint is a cough, which may exacerbate during the night. Bursts

of coughing coupled with severe airway obstruction may result in elevated intrathoracic pressures, which can produce syncope and “cough fractures” of the ribs. Wheeze is common but is not specific to COPD (McCrary et al., 2001).

Substernal chest pain is common in patients with COPD and may be the result of underlying ischemic heart disease or gastroesophageal reflux disease. Chest tightness is a common complaint during an exacerbation of COPD or with periods of worsening breathlessness or exercise. Hemoptysis can occur in COPD and may be the result of a wide variety of etiologies, including airway inflammation and infection, and it is imperative to rule out bronchial neoplasm.

Other comorbidities such as anorexia, weight loss, and malnourishment may result from COPD and are thought to result from both decreased caloric intake and hypermetabolism (Ferreira, Brooks, Lacasse, & Goldstein, 2001). In addition, a heightened sensation of dyspnea while eating or sensation of fullness may hinder the patient from eating. Psychiatric conditions, especially depression, are common in patients with COPD. This is often related to impaired physical abilities and may be worsened by poor sleep quality and sexual dysfunction (Wagena, Arrindell, Wouters, & van Schayk, 2005). The clinician should be careful to record pertinent historical information as it relates to COPD (Table 1).

### Physical examination

Patients typically present in the fifth decade of life and often have a completely negative exam early in the course of the disease. Physical examination generally offers

limited clues regarding airflow changes until the disease is significantly progressed: the respiratory rate may be increased and there may be evidence of dyspnea with exertion. A forced expiratory time greater than 5 s strongly suggests the presence of airflow limitation. The prolonged expiration, with or without the pursed lip breathing, is characteristic of COPD. Use of accessory muscles of respiration, particularly the sternocleidomastoids, is often seen in advanced disease. In addition, these patients may adopt a body position in that they lean forward and support themselves on their arms to fix the shoulder girdle, allowing the use of the pectorals and latissimus dorsi to increase chest wall movement. In earlier stages of the disease, spirometry can show changes not always evident by the physical exam, so it is the “gold standard” of care. In addition, spirometry detects airflow limitation in smokers without symptoms and in nonsmokers who complain of cough or sputum production. In the later stages of the disease, patients often develop a barrel-chested appearance with kyphosis, resulting in an increased anterior to posterior diameter, horizontal ribs, prominence of the sternal angle, and a wide subcostal angle. These are all signs of overinflation. There may be decreased dullness during hepatic or cardiac percussion, indicating overinflation. Breath sounds may have a prolonged expiratory phase or may be uniformly diminished, particularly in the advanced stages of the disease. Wheezes may be present on both inspiration and expiration, or crackles may be heard, particularly in the posterior lung bases, and may vary with coughing (Rennard, 2005).

Tar stains on the fingers, teeth, or tongue are evidence of smoking in many patients. In advanced disease, cyanosis may be present, indicating hypoxemia, but it may be accentuated by anemia or polycythemia. Weight loss may also be apparent in advanced disease, as well as a reduction in muscle mass. Finger clubbing is not associated with COPD; if present, the possibility of bronchial neoplasm or bronchiectasis should be entertained.

The cardiovascular examination is important in patients with COPD. Air trapping decreases venous return and compresses the heart, resulting in tachycardia. Common cardiac physical exam findings include soft heart sounds, difficulty in discerning jugular venous pulsations as a result of large fluctuations in venous pressure in relation to respirations, and the use of accessory muscle may cloud the ability to interpret findings. Signs of right ventricular failure and pulmonary hypertension may be evidenced by a right ventricular heave palpated at the left sternal edge or the subxiphoid region. A right ventricular gallop may be auscultated in the fourth intercostal space to the left of the sternum. The liver may also be palpable below the right costal margin as a result of overinflation of the lungs. Peripheral vasodilatation accompanies hypercapnia,

**Table 1** COPD historical data

Personal respiratory history
Asthma
Allergy
Respiratory infection in childhood
Presence of respiratory disease such as tuberculosis
Family history
COPD
Allergic diseases
Other respiratory diseases
Pattern of dyspnea
Number of exacerbations
Activities that alleviate or exacerbate dyspnea
Frequency of hospitalizations
Comorbidities
Risk factors—smoking, noxious gases or dust, and occupational exposure
Smoking-related diseases
Coronary artery disease
Peripheral artery disease
Diabetes mellitus
Cerebral vascular disease

producing warm peripheries with a high-volume pulse. Pitting peripheral edema may also be present as a result of fluid retention (Rennard, 2005).

### Diagnostic criteria for COPD

A diagnosis of COPD should be entertained in any person with a history of chronic progressive cough, wheeze, or breathlessness, with little variation in these symptoms, and the presence of causative risk factor such as cigarette smoke or occupational and environmental dust and/or gaseous exposure. The diagnosis of COPD is confirmed by spirometry: If airflow measurement of forced expiratory volume in 1 s (FEV-1) is at or below 80% of predicted value, and the ratio of FEV-1 to forced vital capacity (FVC), FEV-1/FVC, is less than 70% of predicted value postbronchodilator treatment, the diagnosis of COPD is confirmed (Pauwels et al., 2001).

COPD is further categorized as at risk, mild, moderate, severe, and very severe as determined by spirometry results (Table 2). Mild COPD is characterized by mild airflow obstruction and is often accompanied by chronic cough and sputum production. Moderate and severe COPD are characterized by further decline in pulmonary function as measured by spirometry. Very severe COPD is characterized by severe airflow limitation or the presence of chronic respiratory acidosis (Pauwels et al., 2001).

COPD does not produce any specific features on a plain chest radiograph (CXR) unless features of emphysema are present. Generally, CXR is used to rule out other pathological processes. Table 3 lists common radiographic signs of emphysema (Coxson & Rogers, 2005).

### Treatment of COPD

#### Common treatment modalities

This section discusses only the common treatments employed to treat COPD. Table 4 summarizes common medications used in the treatment of COPD, while Table 5

**Table 2** COPD severity

Stage	Pulmonary function
0: at risk	Complaints of cough, sputum production
I: mild COPD	FEV-1/FVC $\leq$ 70%, FEV-1 $\geq$ 80% predicted value
II: moderate COPD	FEV-1/FVC $\leq$ 70%, 50% < FEV-1 < 80%
III: severe COPD	FEV-1/FVC $\leq$ 70%, 30% < FEV-1 < 50%
IV: very severe COPD	FEV-1/FVC $\leq$ 70% and FEV-1 < 30%. Or the presence of chronic respiratory acidosis

Note. From Pauwels et al. (2001).

**Table 3** Radiographic findings of COPD

1. A low, flattened diaphragm
2. Increased retrosternal space, visible on the lateral film at a point 3 cm below the manubrium, is present when the horizontal distance from the posterior surface of the aorta to the sternum exceeds 4.5 cm
3. An obtuse costophrenic angle on the posterior–anterior or lateral CXR
4. An inferior margin of the retrosternal air space 3 cm or less from the anterior space of the diaphragm
5. Reduction in the number or size of the pulmonary vessels, particularly to the periphery of the lung
6. Vessel distortion, producing increased branching angles and excess straightening or bowing of vessels
7. Areas of increased lucency

provides a stepped approach to treating COPD. The pharmacological treatment of COPD is aimed at reducing inflammation and decreasing airflow limitation, while adjuvant therapies are used to improve patient's functional capacity and quality of life. The goals of managing COPD should include the following: establish a correct diagnosis and determine severity of disease with spirometry, reduce the risk for disease progression by encouraging smoking cessation and avoidance of other causative agents, reduce dyspnea by appropriate administration of

**Table 4** COPD medications by classification

Generic name	Formulation
Short-acting $\beta$ -2-agonists	
Albuterol	MDI, DPI, LFN, and tablets
Bambuterol	Tablets
Fenoterol	MDI, DPI, and LFN
Isoetherine	MDI, LFN
Isoproterenol	MDI, LFN
Levalbuterol	MDI, LFN, and tablets
Metaproterenol	MDI, LFN, and tablets
Pirbuterol	MDI
Terbutaline	MDI, DPI, LFN, and tablets
Tornalate	MDI, LFN
Long-acting $\beta$ -2-agonists	
Formoterol	DPI
Salmeterol	MDI, DPI
Short-acting anticholinergic	
Ipratropium bromide	MDI, DPI, LFN
Oxipropium bromide	MDI, DPI
Long-acting anticholinergic	
Tiotropium	DPI
Inhaled glucocorticosteroids	
Beclomethasone/beclometasone	MDI, DPI
Budesonide	MDI, DPI, LFN
Flunisolide	MDI
Fluticasone propionate	MDI, DPI
Triamcinolone	MDI

DPI, dry powder inhaler; LFN, liquid for nebulizer.

bronchodilators, and prevent and treat complications such as hypoxia and acute exacerbations (McCrory et al., 2001).

Risk reduction is important in the treatment of COPD. A clear, concise smoking cessation message should be delivered during each visit. Smoking cessation is the most effective tool to preserve lung function and functional capacity. Discontinuing smoking markedly reduces the decline in FEV-1, essentially to that of a nonsmoker, but it does not reverse airway remodeling damage done. The key features of a successful smoking cessation program are vigilance, inquiry about smoking status, assessment of preparedness to quit, and continued support of the process (West, McNeill, & Raw, 2000). Whenever possible, the patient should be instructed regarding the availability of smoking cessation aids (i.e., nicotine replacement patches). Hospitalizations for acute exacerbations provide an optimal time period for the introduction of smoking cessation aids, besides providing literature on the benefits of smoking cessation; literature explaining the potential usage of smoking cessation pharmacological aids is imperative.

### Bronchodilators for COPD management

Inhaled bronchodilators are currently considered the most effective first line of treatment. Nebulized bronchodilators have not been shown to provide any benefit over metered-dose inhalers (MDI) or dry powder delivery devices; however, patients may perceive the MDI as inferior. The choice of which bronchodilator to use should be based on availability, achievement of the desired response, and adverse outcomes. Combining bronchodilators from different classes may improve their effectiveness and lessen the side effects compared with the use of higher doses of a single agent (Tashkin & Cooper, 2004). Long-acting agents are more convenient and their use may increase compliance with the prescribed regimen (Cazzola & Matera, 2004). Table 4 summarizes the various medications available for the treatment of COPD.

There are a variety of bronchodilators, each working on specific receptor sites to partially reverse airflow limitation. Each medication has a variable duration of action. Classically, anticholinergic bronchodilators, such as ipratropium bromide (Atrovent), act on muscarinic receptors on airway smooth muscles and submucosal gland receptors, resulting in relaxation of airway musculature and providing improvement in airflow. The duration of action is usually from 4 to 6 h; thus, this treatment requires frequent dosing. Longer acting formulations are now available; tiotropium (Spiriva) is a long-acting anticholinergic bronchodilator, with a lasting effect of 24 h. Hence, the medicine is given once daily. Other forms of bronchodilators are available including  $\beta$ -2-agonist bronchodilators. These medications cause smooth muscle relaxation

**Table 5** COPD therapy by stage

Stage	Therapy
0: at risk	Avoid risk factors, influenza vaccination
I: mild COPD	Add short-acting bronchodilator as needed
II: moderate COPD	In addition to therapy in stage I, add regular treatment with one or more long-acting bronchodilator. Add pulmonary rehabilitation
III: severe COPD	In addition to therapy in stage II, add inhaled glucocorticosteroids if repeated exacerbations
IV: very severe COPD	In addition to therapy in stage III, add long-term oxygen if there is chronic respiratory failure. Consider surgical options

Note. From Pauwels et al. (2001).

by direct stimulation of  $\beta$ -2 receptors. The prototype of this class is albuterol sulfate (Albuterol). Albuterol has a rapid onset of action, usually within 5–15 min, and its duration of action lasts for 4–6 h. Albuterol, like ipratropium bromide, can be delivered via nebulizer. A longer formulation of  $\beta$ -2-agonist is available and includes salmeterol (Serevent) and formoterol (Foradil). Salmeterol (Serevent) binds to the lipophilic site of the  $\beta$ -receptor, takes 30–60 min to reach maximum bronchodilatation, and lasts for up to 12 h. Formoterol (Foradil) is amphiphilic and binds with equal avidity to the hydrophilic and lipophilic sites on the  $\beta$ -receptors. This provides a relatively rapid onset of action from 5 to 15 min and 12-h duration of action (Barnes, 1999).

The combination of  $\beta$ -2-agonists and anticholinergic agents had proved to provide superior bronchodilatation and improvement in health status compared with using either of these agents individually. In patients who remain symptomatic with persistent dyspnea, despite the use of a single class of bronchodilators, a combination of  $\beta$ -2-agonists and anticholinergics can be used (Barnes, 1999).

### Corticosteroids in the management of COPD

Corticosteroids have been studied to determine their efficacy in the treatment of COPD. Clinical trials have supported the use of these agents in the management of this chronic disease (Wright, Brocklebank, & Ram, 2002). A number of clinical trials suggest that chronic use of inhaled steroids reduces the frequency of acute exacerbations, particularly for patients with an FEV-1 of <50% of predicted value. Current international guidelines suggest that inhaled steroids be used in this patient population, although there are no predictors of which patients will be steroid responsive. During an acute exacerbation, large randomized controlled clinical trials have shown that systemic steroids improved clinical response to treatment, decreased hospital stay, and documented rapid improvement in FEV-1 (Stanbrook & Goldstein, 2001).

### The role of mucolytics in COPD management

Mucolytics have shown to be of modest benefit in the treatment of COPD. Guaifenesin is used to promote mucus clearance by thinning secretions and making secretion more mobile and easily expectorated. The methylxanthines, such as theophylline, are modest bronchodilators but have other properties that improve breathing in patients with COPD. There is considerable potential for adverse side effects; however, theophylline should be considered in patients who remain symptomatic, despite the use of inhaled bronchodilators (Poole & Black, 2001).

### The role of oxygen in COPD management

Oxygen therapy is used in the treatment of COPD to correct hypoxemia. The goals of oxygen therapy in patients with COPD are to increase survival, reduce dyspnea, and improve exercise by eliminating exercise-induced hypoxemia. The indications for continuous oxygen therapy to improve survival are a PaO<sub>2</sub> of less than or equal to 50 mmHg or a PaO<sub>2</sub> of 56–59 mmHg when there is evidence of end-organ dysfunction secondary to chronic hypoxemia (such as peripheral edema without another cause, pulmonary hypertension, or polycythemia) or ambulatory pulse oximetry less than 89%. The assessment for long-term oxygen therapy should be performed with the patient seated, at rest, breathing room air when they are in optimal medical condition rather than when they are having an acute exacerbation. The goal of chronic oxygen therapy is to increase the PaO<sub>2</sub> to above 60 mmHg—or SpO<sub>2</sub> to 90%. Pulse oximetry can be used to titrate oxygen flow rates to maintain adequate saturation. Oxygen therapy should be ordered in patients with hypoxemia and should include the number of hours of daily use, the need for oxygen required for ambulation, the type of oxygen system to use, and the method of delivery (Rennard, 2005).

Patients frequently do not understand the role of supplemental oxygen. Some of the more common misunderstandings are that oxygen is required only for control of dyspnea and that higher doses will eliminate dyspnea. In addition, concerns over body image and misconceptions of oxygen dependency may occur. Thus, patient education is a prerequisite for proper use and adherence to therapy.

In addition to maximizing medications, patients should be considered for pulmonary rehabilitation. There are numerous benefits to pulmonary rehabilitation, including the reduction of dyspnea and the improvement in exercise capacity. The improvement in symptoms leads to an increased ability to perform daily activities, with an associated improvement in health-related quality of life (Hui & Hewitt, 2003).

### Summary

The burden of COPD on the healthcare system is enormous because it is a major source of morbidity in the United States. Often, a diagnosis of COPD is not made until advanced disease is present; thus, the importance of prevention, early detection, and use of appropriately combined therapies cannot be underscored. Once a diagnosis of COPD is made, healthcare practitioners should explore multiple treatment options in an effort to find the most beneficial regimen. It is only when the practitioner is successfully able to individualize the combined physiological therapies and cognitive approaches lessening risks, as well as reduce exacerbations, that the patient with COPD is able to potentially experience the full promise for quality of life. In short, reducing rates of hospitalization, morbidity, and mortality among this aggregate patient population with COPD will lower healthcare costs, improve individual disease burden, and promote better management of COPD, which will remain a major concern for our healthcare system.

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