Seventh Edition

CLINICAL MANIFESTATIONS AND ASSESSMENT OF RESPIRATORY DISEASE

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CHAPTER

12 Chronic Obstructive Pulmonary Disease, Chronic Bronchitis, and Emphysema

Chapter Objectives

After reading this chapter, you will be able to:

- Describe the American Thoracic Society (ATS) guidelines for chronic obstructive pulmonary disease (COPD), chronic bronchitis, and emphysema.
- Describe the Global Initiative for Chronic Obstructive Lung Disease (GOLD) *definition* of COPD.
- Explain the anatomic alterations of the lungs associated with chronic bronchitis and emphysema.
- Describe the etiology and epidemiology of COPD.
- Discuss the risk factors associated with COPD.
- Describe the GOLD guidelines for the *diagnosis* and

Panlobular Emphysema
"Pink Puffer"
Pulmonary Rehabilitation
Pulmonary Rehabilitation Protocol
Transitional Care Specialists
ZZ Alpha$_1$-Antitrypsin Phenotype

Chapter Outline

Introduction

The **American Thoracic Society (ATS)** guidelines for **chronic obstructive pulmonary disease (COPD), chronic bronchitis,** and **emphysema** provide the following definitions:

> *Chronic obstructive pulmonary disease* is a preventable and treatable disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive, is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, and is primarily caused by cigarette smoking. Although COPD affects the lungs, it also produces significant systemic consequences.
>
> *Chronic bronchitis* is defined clinically as chronic productive cough for 3 months in each of 2 successive years in a patient in whom other causes of productive chronic cough have been excluded.
>
> *Emphysema* is defined pathologically as the presence of permanent enlargement of the air spaces distal to the terminal bronchioles, accompanied by destruction of bronchiole walls and without obvious fibrosis.
>
> *In patients with COPD, both chronic bronchitis and emphysema are present.* However, the relative contribution of each to the disease process is often difficult to discern. Note that the ATS definition for *chronic bronchitis* is based on the major clinical manifestations associated with the disease (i.e., productive cough). Also note that the ATS definition for *emphysema* is based on the pathology, or the anatomic alterations of the lung associated with the disorder.

The **Global Initiative for Chronic Obstructive Lung Disease** (GOLD) now provides the following working definition:[1]

> *Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases.*

Note that the GOLD definition does not use the terms *chronic bronchitis* and *emphysema*. GOLD explains that *chronic bronchitis* is defined as the presence of cough and sputum production for at least 3 months in each of 2 consecutive years (i.e., clinical manifestations), and is not always associated with airflow limitation. GOLD also points out that *emphysema* is defined as destruction of the alveoli and is a pathologic term (i.e., anatomic alteration of the lung) that is sometimes—and incorrectly—used to describe only *one* of several structural abnormalities present in patients with COPD.[2]

The bottom line is this: even though chronic bronchitis and emphysema can each develop alone, they often occur together as one disease entity. When this happens, the disease entity is called *chronic obstructive pulmonary disease—that is, COPD*. In other words, *COPD* is a term referring to two lung diseases—chronic bronchitis and emphysema—occurring simultaneously. Patients with COPD demonstrate a variety of clinical manifestations associated with both disorders, although the relative contribution of each respiratory disorder is often difficult to ascertain. For this reason the treatment of chronic bronchitis, emphysema, or a combination of both disorders (COPD) is very similar in clinical practice.

Anatomic Alterations of the Lungs Associated with Chronic Bronchitis

The conducting airways (particularly the bronchi) are the primary structures that undergo change in chronic bronchitis. As a result of chronic inflammation the bronchial walls are narrowed by vasodilation, congestion, and mucosal edema. This condition is often accompanied by bronchial smooth muscle constriction. In addition, continued bronchial irritation causes the submucosal bronchial glands to enlarge and the number of goblet cells to increase, resulting in excessive mucus production. The number and function of cilia lining the tracheobronchial tree are diminished, and the peripheral bronchi are often partially or totally occluded by inflammation and mucous plugs, which in turn leads to hyperinflated alveoli (Figure 12-1). Figure 12-2 shows two microscopic views of chronic bronchitis.

To summarize, the following major pathologic or structural changes are associated with chronic bronchitis:

- Chronic inflammation and thickening of the walls of the peripheral airways.
- Excessive mucous production and accumulation.
- Partial or total mucous plugging of the airways.
- Smooth muscle constriction of bronchial airways (bronchospasm)—a variable finding.
- Air trapping and hyperinflation of alveoli may occur in late stages.

Anatomic Alterations of the Lungs Associated with Emphysema

Emphysema is characterized by a weakening and permanent enlargement of the air spaces distal to the terminal bronchioles and by destruction of the alveolar walls. As these structures enlarge and the alveoli coalesce, many of the adjacent pulmonary capillaries also are affected, and this results in a decreased surface area for gas exchange across the alveolar-capillary membrane. Furthermore, the distal airways, weakened in the process, tend to collapse during expiration in response to increased intrapleural pressure. This traps gas in the alveoli. There are two major types of emphysema: Panacinar (panlobular) emphysema and centriacinar (centrilobular) emphysema.

In **panacinar emphysema**, or **panlobular emphysema** there is an abnormal weakening and enlargement of all alveoli distal to the terminal bronchioles, including the respiratory

[1] Modified from GOLD, Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, Revised 2014. (www.goldcopd.org). GOLD is recognized as a worldwide leading authority for the diagnosis, management, and prevention of COPD.

[2] It should be noted that a chapter on the diagnosis of **Asthma and COPD Overlap syndrome (ACOS)** is in preparation by the Science Committee of the Global Initiative for Asthma (GINA) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD). It is expected to be available with the release of GINA 2014 document Global Strategy for Asthma Management and Prevention in the spring of 2014 (www.ginasthma.org). A full chapter with references will be posted on the GOLD website when it available. It will also appear in full in the Appendix of the 2015 GOLD update (www.goldcopd.org).

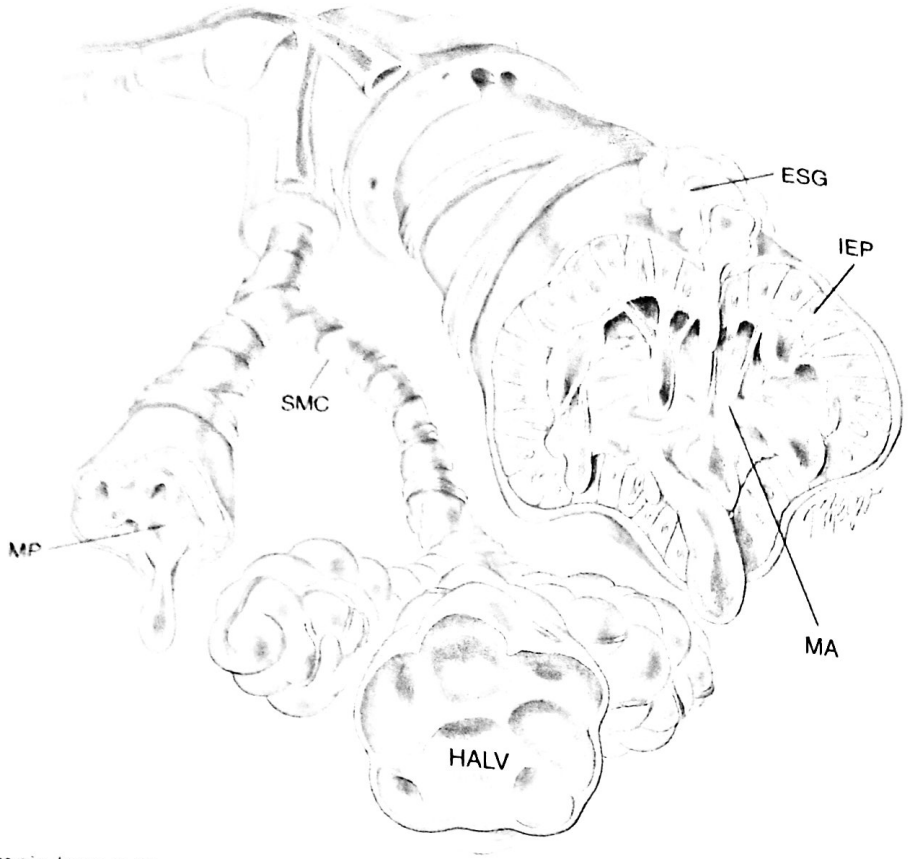


FIGURE 12-1 Chronic bronchitis, one of the most common airway diseases. *SMC*, Smooth muscle constriction; *ESG*, enlarged submucosal gland; *HALV*, hyperinflation of alveoli (distal to airway obstruction); *IEP*, inflammation of epithelium; *MA*, mucous accumulation; *MP*, mucous plug.

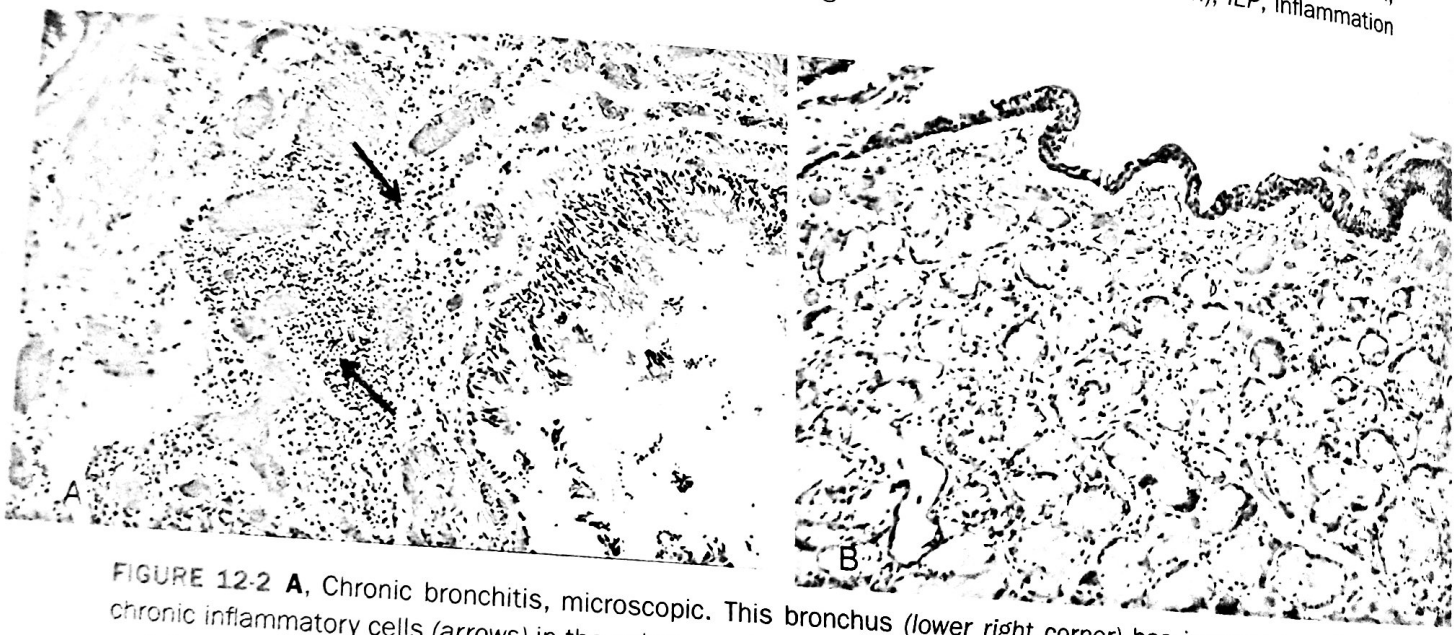


FIGURE 12-2 **A**, Chronic bronchitis, microscopic. This bronchus *(lower right corner)* has increased numbers of chronic inflammatory cells *(arrows)* in the submucosal bronchial region. (Figure was obtained from: Klatt: Robbins and Cotran Atlas of Pathology, 2nd edition, 2010, Elsevier/Saunders.) **B**, Chronic bronchitis. The lumen of the bronchus is above. Note the marked thickening of the mucous gland layer (approximately twice normal) and squamous metaplasia of lung epithelium. (Figure was obtained from: Robbins Basic pathology, by Kumar, Abbas, and Aster, 2013, Elsevier/Saunders.)

bronchioles, alveolar ducts, alveolar sacs, and alveoli—the entire acinus is affected by dilatation and destruction. The alveolar-capillary surface area is significantly decreased (Figure 12-3). Panlobular emphysema is commonly found in the lower parts of the lungs and is sometimes associated with a deficiency of the protease inhibitor alpha$_1$-antitrypsin.

Panlobular emphysema is one of the more severe types of emphysema and therefore the most likely to produce significant clinical manifestations.

In **centriacinar emphysema**, or **centrilobular emphysema**, the pathology involves the respiratory bronchioles in the proximal portion of the acinus. The respiratory

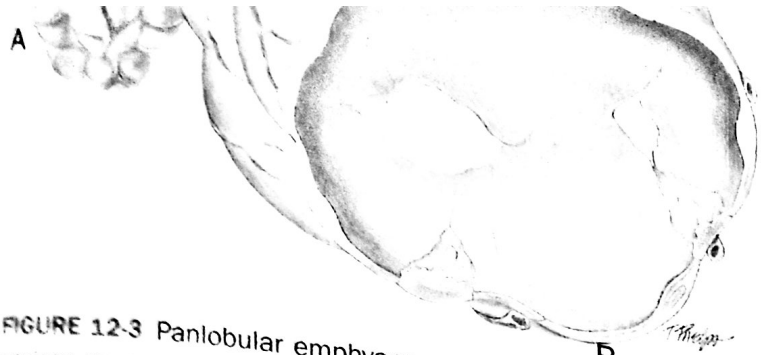


FIGURE 12-3 Panlobular emphysema. **A**, Normal alveoli for comparison purposes. **B**, Panlobular emphysema: Abnormal weakening and enlargement of all air spaces distal to the terminal bronchioles.

FIGURE 12-4 Centrilobular emphysema. Abnormal weakening and enlargement of the respiratory bronchioles and alveoli in the proximal portion of the acinus.

bronchiolar walls enlarge, become confluent, and are then destroyed. A rim of parenchyma remains relatively unaffected (Figure 12-4). Centriacinar emphysema is the most common form of emphysema and is strongly associated with cigarette smoking and with chronic bronchitis. Figure 12-5 shows a microscopic view of pulmonary emphysema.

To summarize, the following are the major pathologic or structural changes associated with emphysema:

- Permanent enlargement and destruction of the air spaces distal to the terminal bronchioles.
- Destruction of the alveolar-capillary membrane.
- Weakening of the distal airways, primarily the respiratory bronchioles.
- Air trapping and hyperinflation.

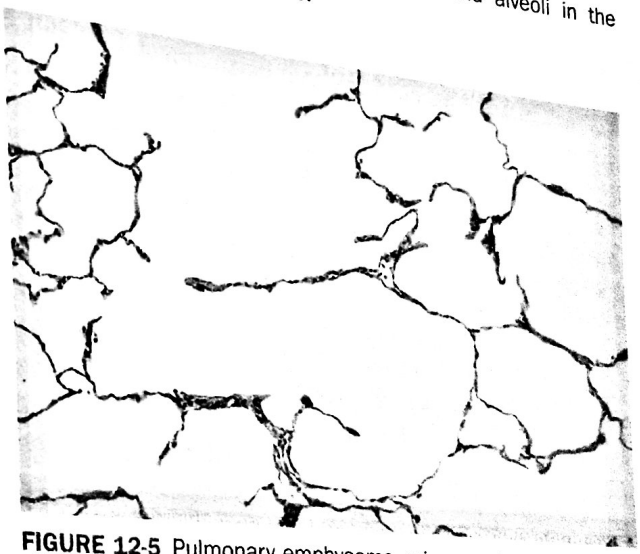


FIGURE 12-5 Pulmonary emphysema, microscopic. There is loss of alveolar ducts and alveoli with emphysema, and the remaining air spaces become dilated. There is less surface area for gas exchange. Emphysema leads to loss of lung parenchyma, loss of elastic recoil, increased lung compliance, and increased pulmonary residual volume with increased total lung capacity, mainly from an increased residual volume. (Figure was obtained from: Klatt: Robbins and Cotran Atlas of Pathology, 2nd edition, 2010, Elsevier/Saunders.)

Etiology and Epidemiology

Although the precise incidence of COPD is not known, it is estimated that 10 to 15 million people in the United States have chronic bronchitis, emphysema, or a combination of both. Most authorities agree that COPD is underdiagnosed. It is felt that if you take into account the people who have not been "officially" diagnosed with COPD, the incidence would be over 20 million people in the United States. It is generally accepted that more people have chronic bronchitis than emphysema. For example, the National Center for Health Statistics estimates that in the United States about 9.5 million people have chronic bronchitis and 4.1 million people have emphysema. COPD claims more that 138,000 Americans each year. It is the third leading cause of death in the United States. Recent data show that COPD prevalence and mortality is now about equal in men and women, which likely reflects the changing patterns of smoking.

Risk Factors

According to GOLD, although the current understanding of the risk factors associated with COPD is incomplete, the following factors influence the development and progression of COPD:

- **Genes—Alpha$_1$–antitrypsin deficiency** (also known as alpha$_1$-proteinase inhibitor deficiency, A_1AD, AATD, ATT deficiency, AP_1 deficiency, and alpha-1 inherited

emphysema) is a genetic disorder affecting the lung, liver, and rarely, the skin. Alpha$_1$-antitrypsin is made in the liver and one of its functions is to protect the lungs from neutrophil elastase, an enzyme that can break down connective tissue. When the alpha$_1$-antitrypsin deficiency level is low, the elastase is free to attack and destroy the elastic tissue of the lungs. A severe deficiency of alpha$_1$-antitrypsin poses a strong risk factor for early onset of emphysema—especially **panacinar emphysema** (see Figure 12-3). The premature development of emphysema is the hallmark of alpha$_1$-antitrypsin deficiency. Cigarette smoking significantly increases the risk factor for early onset emphysema in patients with alpha$_1$-antitrypsin deficiency—for example, the onset of dyspnea around 30 years of age.

The normal level of alpha$_1$-antitrypsin ranges between 150 to 350 mg/dL (1.5 to 3.5 g/L) when measured via radial immunodiffusion. Patients with normal levels of alpha$_1$-antitrypsin are referred to genetically as having an **MM phenotype** or simply an M phenotype (homozygote). The phenotype associated with severely low serum concentrations is the **ZZ phenotype**, or simply Z. The heterozygous offspring of parents with the M and Z phenotypes have an **MZ phenotype**. The **MZ phenotype** results in an intermediate deficiency of alpha$_1$-antitrypsin. The precise effect of the intermediate level of alpha$_1$-antitrypsin is unclear. It is strongly recommended, however, that individuals with this phenotype do not smoke or work in areas having significant environmental air pollution. Although alpha$_1$-antitrypsin deficiency is considered to be rare, it is estimated that 80,000 to 100,000 individuals in the United States have severe deficiency of alpha$_1$-antitrypsin.

- **Age**—As a person ages, the risk of COPD increases. Although the precise connection between age and COPD is unclear, it is suggested it may be related to the sum of cumulative exposures throughout life.
- **Lung Growth and Development**—Any condition that affects lung growth during gestation and childhood (e.g., low birth weight, respiratory infections) has the potential for increasing an individual's risk for developing COPD.
- **Exposure to Particles**
  - **Tobacco** smoke—Cigarette smoking is the most commonly encountered risk factor for COPD worldwide. Other types of tobacco (e.g., pipe, cigar, water pipe) are added risk factors for COPD. Passive exposure to cigarette smoke may also cause COPD. Smoking during pregnancy may affect lung growth and development of the fetus.
  - **Occupational exposure**—Organic and inorganic dusts and chemical agents and fumes (e.g., asbestos, coal dust, moldy hay, bird droppings, or paints) may cause COPD.
  - **Indoor Air Pollution**—Wood, animal dander and dung, crop residues, and coal, commonly burned in open fires or poorly functioning stoves, may lead to very high levels of indoor pollution. Research data continues to grow that indoor pollution from biomass cooking and heating in poorly ventilated areas is an important risk factor for COPD. It is estimated that about 3 billion people around the world use biomass and coal as their primary source of energy for cooking, heating, and basic household needs.
  - **Outdoor Air Pollution**—Although high levels of air pollution (e.g., silicates, sulfur dioxide, the nitrogen oxides, and ozone) are known to be harmful to individuals with existing heart and lung disease, the role of outdoor pollution in causing COPD is unclear.
- **Socioeconomic Status**—Poverty is clearly a risk factor for COPD, although the precise components associated with poverty and COPD are unclear. Likely factors include exposure to indoor and outdoor air pollutants, crowding, poor nutrition, and infection. Current CDC data (2012) strongly indicates that the risk of developing COPD is inversely related to an individual's socioeconomic status.
- **Asthma/Bronchial HyperReactivity**—Asthma may be a risk factor for the development of COPD.
- **Chronic Bronchitis**—May be a risk factor for the development of COPD. In other words, chronic bronchitis may lead to emphysema. When both chronic bronchitis and emphysema are present, the patient is said to have COPD.
- **Respiratory Infections**—A history of severe childhood respiratory infections is associated with decreased lung function and increased respiratory complications in adulthood. Susceptibility to respiratory infections may lead to COPD.
- **Tuberculosis**—Has been shown to be a risk factor for COPD.

Diagnosis and Assessment of Chronic Obstructive Pulmonary Disease

According to GOLD, the diagnosis of COPD should be considered for any patient who is over 40 years of age and who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease—especially cigarette smoking. The primary indicators and their descriptions for considering a COPD diagnosis are listed in Table 12-1. Although these indicators are not diagnostic by themselves, the presence of any combination of these clinical markers significantly increases the possibility of a diagnosis of COPD. A **pulmonary function test** (PFT) is required to confirm the airflow limitation (see below).

Pulmonary Function Testing

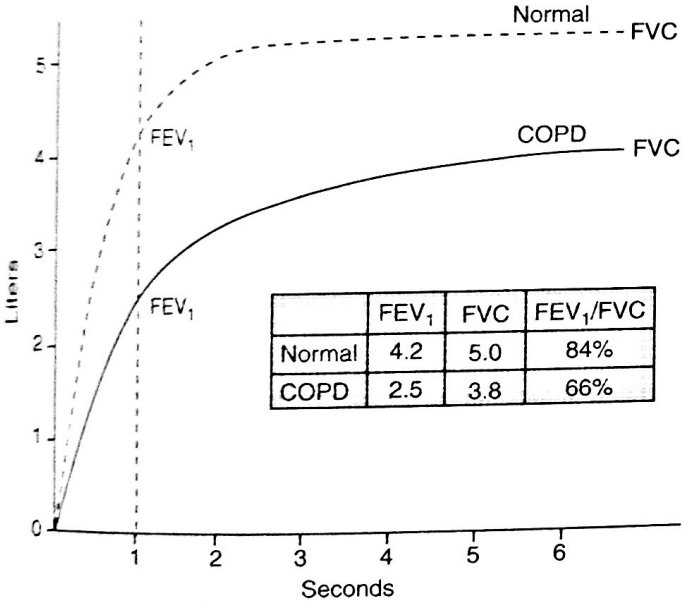
The three main pulmonary function tests used to measure the severity of airflow limitation in the COPD patient are the spirometric **forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), and forced expiratory volume in 1 second/forced vital capacity ratio (FEV_1/FVC ratio)**. Clinically, the FEV_1/FVC ratio is also commonly called the **forced expiratory volume 1 second percentage (FEV_1%)**. Figure 12-6 illustrates a normal FEV_1 and the FEV_1 that is typically seen in the spirogram of patients with mild to moderate COPD.

An FEV_1/FVC ratio of less than 0.70 usually indicates the presence of airway obstruction. A diagnosis of COPD

TABLE 12-1 Primary Indicators of COPD in Patients Over age 40

Indicator	Description
Dyspnea	Progressive shortness of breath over time, worse with exercise. Persistent
Chronic Cough	Can be intermittent or unproductive
Chronic Sputum Production	Any display of persistent sputum production may suggest COPD
History of Exposure to Risk Factors	Tobacco smoke Smoke from home cooking and/or heating fuels Work-related dusts and/or chemicals
Family History of COPD	Alpha$_1$-antitrypsin deficiency

Note: The above indicators are not diagnostic themselves. However, the presence of multiple key indicators increases the likelihood of a diagnosis of COPD. A pulmonary function study is required to establish a diagnosis of COPD.
(Modified from GOLD. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, Revised 2014; www.goldcopd.org.)



	FEV_1	FVC	FEV_1/FVC
Normal	4.2	5.0	84%
COPD	2.5	3.8	66%

Postbronchodilator FEV_1 is recommended for the diagnosis and assessment of severity of COPD

FIGURE 12-6 Normal spirogram and spirogram typical of patients with mild to moderate chronic obstructive pulmonary disease.

made when the patient demonstrates (1) any combination of the COPD indicators (see Table 12-1), (2) an FEV_1/FVC ratio of less than 0.70 and an FEV_1 less than 80%, and (3) there is no alternative explanation for the symptoms and airflow obstruction (e.g., bronchiectasis, vocal cord paralysis, and tracheal stenosis).

Other important PFT values associated with COPD include the following:

- Decreased inspiratory capacity (IC) and vital capacity (VC).

TABLE 12-2 Modified Medical Research Council Questionnaire for Assessing the Severity of Breathlessness

Score	Circle the score box that best applies to you (one box only)
0	I only get breathless with strenuous exercise.
1	I get short of breath when hurrying on level ground or walking up a slight hill.
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace.
3	I stop for breath after walking about 100 meters or after a few minutes on level ground.
4	I am too breathless to leave the house or I am breathless when dressing.

- Increased total lung capacity (TLC), functional residual capacity (FRC), and residual volume (RV), and residual volume/total lung capacity ratio (RV/TLC).
  - These PFT values confirm alveolar hyperinflation.
- The carbon monoxide diffusing capacity (DLCO) decreases in proportion to the severity of emphysema. The DLCO is normal in pure chronic bronchitis.

Severity Assessment of COPD

According to GOLD, before an effective treatment plan for COPD can be constructed, a thorough COPD assessment must first be performed. The primary goals of COPD assessment are to determine (1) the severity of the disease, (2) the impact the disease has on the patient's health status, and (3) the risk of future events—that is, number of exacerbations and hospital admissions, and death. To achieve this goal, GOLD recommends assessing the following aspects of the disease independently:

- Symptoms
- Severity assessment based on degree of airflow limitation
- Risk of exacerbations
- Comorbidities

Symptom Evaluation—There are several validated questionnaires available to assess symptoms in patients with COPD. GOLD recommends using either the **COPD Assessment Test (CAT)**, or the **Modified British Medical Research Council (mMRC) Breathlessness Scale**. The mMRC questionnaire relates well to other health conditions and predicts future mortality risks. An mMRC score of less than one is classified as a low-risk patient; a score greater than two is considered a high-risk patient. Table 12-2 shows an mMRC questionnaire.

The CAT is an eight-item one-dimensional assessment of health status in COPD. This questionnaire is applicable worldwide and there are validated translations available in a wide range of languages (see example of CAT questionnaire at http://www.catestonline.org). A score less than 10 is classified as a low-risk patient; a score greater than 10 is identified as a high-risk patient.

TABLE 12-3 Severity of Airflow Limitation in COPD Based on Post-Bronchodilator FEV_1

(Only in Patients with FEV_1/FVC Ratio < 0.70)

GOLD 1	Mild	FEV_1 ≥80% predicted
GOLD 2	Moderate	FEV_1 50%–79% predicted
GOLD 3	Severe	FEV_1 30%–49% predicted
GOLD 4	Very Severe	FEV_1 29% or less than predicted

Modified from GOLD: Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, Revised 2014; www.goldcopd.org.)

Severity of Airflow Limitation Evaluation—As shown in Table 12-3, GOLD has established a classification of airflow limitation severity in COPD. This classification defines the severity of the disease according to airflow limitation. The PFT measurements used to evaluate the patient's airflow limitation are the *forced expiratory volume in one second (FEV_1)* and the *forced expiratory volume in one second (FEV_1) to forced vital capacity ratio (FEV_1/FVC ratio)*.

Note: The Centers for Medicare and Medicaid Services (CMS) now require pulmonary rehabilitation patients to qualify for service based on airway limitation severity. Only patients with GOLD 3 or 4 severities qualify for CMS reimbursement at present.

Risk of Exacerbations Assessment—According to GOLD, an exacerbation of COPD is defined as *an acute event, characterized by a worsening of the patient's respiratory symptoms, that is beyond normal day-to-day variations and leads to a change in medication*. The best forecaster of having a risk of exacerbation is the patient's past history—a history of two or more exacerbations per year is considered a high risk for more exacerbations. A worsening FEV_1 increases the occurrence of exacerbations in COPD patients and risk of death.

Comorbidities Assessment—Because COPD often develops in middle-aged chronic tobacco smokers, the patient often has a variety of other health problems related to either smoking or aging. Diseases commonly associated with COPD include cardiovascular disease, osteoporosis, depression and anxiety, skeletal muscle dysfunction, the metabolic syndrome, and lung cancer.

Combined COPD Assessment

GOLD recommends combining all the above assessments—that is, the symptoms assessment, airflow limitations assessment, and risk of exacerbations assessment. Combining these three areas helps to determine the impact of COPD on the patient, and improves the ability to develop and manage a treatment plan that is specifically designed to meet the individual patient's needs.

GOLD recommends using a *scoring rubric*[3] *measurement* system to objectively assess the patient's COPD related symptoms, the severity of airflow limitation, and the risk of exacerbations. A representative example of a Combined COPD Assessment Rubric Scoring Tool, similar to the one developed by GOLD, is shown in Figure 12-7.

[3]A scoring *rubric* is defined as an explicit set of criteria used for assessing a particular type of work or performance.

How to Use the Combined COPD Scoring Rubric

To assign a patient to either Group A, B, C, or D (see Fig. 12-7)—and to subsequently develop and manage a treatment plan that is specifically designed to meet the individual patient's needs—follow these steps:

1. First evaluate the patient's **Symptoms** with the mMRC or CAT score to determine if the patient belongs on the "left" side of the box—Less Symptoms (mMRC 0–1; CAT < 10); or the "right" side of the box—More Symptoms (mMRC ≥ or CAT ≥ 10).
2. Next, evaluate the **Risk of Exacerbations** to determine if the patient belongs on the "lower" part of the box (Low Risk), or the "upper" part of the box (High Risk). This can be established by either of the following two methods:
   a. **GOLD Classification of Airflow Limitation**—Determine the GOLD grade of airflow limitation. GOLD 1 and 2 indicate Low Risk, whereas GOLD 3 and 4 indicate High Risk.
   b. **Number of Exacerbations during Last 12 Months**—Identify the number of exacerbations the patient experienced during the last 12 months. Zero to one exacerbation indicates Low Risk, whereas two or more exacerbations indicate High Risk.

Finally, it should be noted that in some COPD patients, the above two methods of assessing the risk of exacerbations may not lead to the same severity of risk. In these cases, select the highest risk according to either the GOLD grade or the exacerbation history. For example, consider the case in Box 12-

Additional Screening Methods Used to Diagnosis COPD

The following are additional diagnostic procedures that may be helpful in the diagnosis and assessment of COPD:

BODE index—To evaluate the patient's extrapulmonary manifestations associated with COPD more closely, the BODE index may also be used. The **BODE index** or BODE score, which is short for "**B**ody-mass index, airflow **O**bstruction, **D**yspnea and **E**xercise capacity index in chronic obstructive pulmonary disease," is a multidimensional, 10-point scale that provides better prognostic information than the FEV_1 alone. Changes in the BODE index can also be used to evaluate the patient's response to therapy.

Chest Radiographs

A chest radiograph has a poor sensitivity in establishing the diagnosis of COPD. However, it is useful in eliminating other cardiopulmonary disorders—such as pulmonary fibrosis, bronchiectasis, and cardiomegaly. Radiographic features associated with COPD in the advanced stages include:

- Increased radiolucency of the lungs, rapidly tapering vascular shadows, flat diaphragms, a long and distended heart shadow, widened intercostal spaces, and flattened costophrenic angles on a frontal radiograph. These findings are caused by hyperinflation.
- Bullae, which are radiolucent areas on the lung greater than 1 cm in diameter and surrounded by

shadows. Bullae may or may not be present on a chest radiograph.

- Prominent hilar vascular shadows caused by pulmonary hypertension and cor pulmonale, which are secondary to COPD.

Computed Tomography of the Chest

Although a computed tomography (CT) scan of the chest has a greater sensitivity than the chest radiograph in detecting emphysema, it is not effective for confirming the presence of chronic bronchitis or asthma. The CT scan can determine whether the emphysema is centriacinar or panacinar.

Lung Volume and Diffusing Capacity

Patients with COPD exhibit air trapping (e.g., increased residual volume and functional residual capacity). These measurements help in assessing the severity of COPD. The measurement of the carbon monoxide diffusing lung capacity (DLCO) can provide information regarding the overall impact of emphysema on COPD. The DLCO is helpful in evaluating the patient whose dyspnea may appear out of proportion with the degree of his/her airflow limitation.

Oximetry and Arterial Blood Gas Measurement

Rest and exercise pulse oximetry and arterial blood gas (ABG) measurements are helpful in determining the patient's oxygenation and acid-base status. These measurements are useful in determining the severity of COPD, qualifying the patient for supplemental oxygen therapy and, importantly, the general management of acute exacerbations and stable COPD. For example, an ABG of a "stable" COPD patient could be the following: pH 7.36, $PaCO_2$ 79, HCO_3^- 43, and PaO_2 61, or an ABG example that shows the COPD patient is in "impending ventilatory failure" (or chronic ventilatory failure) could be the following: pH 7.52, $PaCO_2$ 52, HCO_3^- 40, and PaO_2 46 (mild or moderate acute exacerbation); or an ABG example that shows the COPD patient is in "acute ventilatory failure" (or chronic ventilatory failure) could be the following: pH 7.28, $PaCO_2$ 99, HCO_3^- 45, and PaO_2 34 (severe acute exacerbation). (See Chapter 4 for further discussion.)

Alpha$_1$-Antitrypsin Deficiency Screening

When a younger patient (<45 years old) presents with a history and clinical indicators associated with COPD, an alpha$_1$-antitrypsin deficiency screen should be considered. A serum concentration below 15% to 20% of normal value is highly suggestive of emphysema caused by alpha$_1$-antitrypsin deficiency.

Exercise Testing

The objective assessment of exercise impairment, measured by means of a reduction in self-paced walking distance, or by an incremental exercise test in the laboratory, is a powerful evaluation of the patient's health and employment status and is a valid predictor of prognosis. More complex cardiopulmonary exercise tests (e.g., aerobic stress tests) are helpful in the differential diagnosis of dyspnea, and may reveal congestive heart failure, cardiac arrhythmias, deconditioning, pulmonary embolic disease, and pulmonary hypertension.

Key Distinguishing Features between Emphysema and Chronic Bronchitis

Even though chronic bronchitis and emphysema often occur as one disease complex called COPD, they can develop alone. A complete presentation of all the specific signs and symptoms associated with emphysema and chronic bronchitis is provided in the Overview of the Cardiopulmonary Clinical Manifestations section on pages 180–185.

An abbreviated and handy overview of the key distinguishing features between emphysema and chronic bronchitis is provided as follows:

Clinically, the patient with emphysema is sometimes classified as a **"pink puffer,"** or a patient with type A COPD, and the patient with chronic bronchitis is sometimes classified as a **"blue bloater,"** or a patient with type B COPD. These general, older terms are primarily based on the clinical manifestations commonly associated with each respiratory disorder.

"Pink Puffer" (Type A Chronic Obstructive Pulmonary Disease)

The term *pink puffer* is derived from the reddish complexion and the "puffing" (pursed-lip breathing) commonly seen in the patient with emphysema. The major pathophysiologic mechanisms responsible for the red complexion and puffing are the following:

- Emphysema is caused by the progressive destruction of the distal airways and pulmonary capillaries.
- The progressive elimination of the distal airways and pulmonary capillaries leads to ventilation-perfusion mismatches.
- To compensate for these ventilation-perfusion ratio mismatches, the patient hyperventilates.
- The increased respiratory rate, in turn, works to maintain a relatively normal arterial oxygenation level and causes a ruddy or flushed skin complexion. During the end stage of emphysema, however, the patient's oxygenation status decreases and the carbon dioxide level increases.
- Thus, the patient with emphysema, who has both a ruddy complexion and a rapid respiratory rate, is called a *pink puffer*.

In addition to the marked dyspnea and ruddy complexion, the pink puffer tends to be thin (because of the muscle wasting and weight loss associated with the increased work of breathing), has a barrel chest (because of hyperinflated lungs), uses accessory muscles of inspiration, and exhales through pursed lips.

"Blue Bloater" (Type B Chronic Obstructive Pulmonary Disease)

The term *blue bloater* is derived from the cyanosis—the bluish color of the lips and skin—commonly seen in the patient with chronic bronchitis. The bluish complexion is caused by the following:

- Unlike emphysema, the pulmonary capillaries in the patient with chronic bronchitis are not damaged. The patient with chronic bronchitis responds to the increased airway obstruction by decreasing ventilation and increasing cardiac output—that is, a decreased ventilation-perfusion ratio.
- The chronic hypoventilation and increased cardiac output (decreased ventilation-perfusion ratio) leads to a decreased arterial oxygen level, an increased arterial carbon dioxide level, and a compensated (normal) pH—or chronic ventilatory failure arterial blood gas values (also called *compensated respiratory acidosis*). The respiratory drive is depressed in patients with chronic ventilatory failure.
- The persistently low ventilation-perfusion ratio and depressed respiratory drive both contribute to a chronically reduced arterial oxygenation level and polycythemia that, in turn, causes cyanosis. In addition, the blue bloater tends to be stocky and overweight, has a chronic productive cough, and frequently has swollen ankles and legs and distended neck veins as a result of pulmonary hypertension and right-sided heart failure (cor pulmonale).

Table 12-4 provides an overview of the more common distinguishing features between emphysema and chronic bronchitis.

The clinical features of emphysema and chronic bronchitis are not always clear-cut because many patients have a combined disease process, COPD. This is especially the case during the late stages of emphysema and chronic bronchitis.[4]

[4]It should be noted that the current definition for these respiratory disorders (i.e., chronic bronchitis and emphysema), even if occurring as a singular disease, is often called COPD if there is airflow limitation.

TABLE 12-4 Key Features Distinguishing Emphysema from Chronic Bronchitis*

Clinical Manifestation	Emphysema (Type A COPD: Pink Puffer)	Chronic Bronchitis (Type B COPD: Blue Bloater)
Inspection		
Body build	Thin	Stocky, overweight
Barrel chest	Common, classic sign	Normal
Respiratory pattern	Hyperventilation and marked dyspnea; often occurs at rest Late stage: diminished respiratory drive and hypoventilation	Diminished respiratory drive Hypoventilation common, with resultant hypoxia and hypercapnia
Pursed-lip breathing	Common	Uncommon
Cough	Uncommon	Common; classic sign
Sputum	Uncommon	Common; classic sign Copious amounts, purulent
Cyanosis	Uncommon (reddish skin)	Common
Peripheral edema	Uncommon	Common Right-sided heart failure
Neck vein distention	Uncommon	Common Right-sided heart failure
Use of accessory muscles	Common	Uncommon
Auscultation	Decreased breath sounds, decreased heart sounds, prolonged expiration	Wheezes, crackles, depending on severity of disease
Percussion	Hyper resonance	Normal
Laboratory Tests		
Chest radiograph	Hyperinflation, narrow mediastinum, normal or small vertical heart, low flat diaphragm, presence of blebs or bullae	Congested lung fields, densities, increased bronchial vascular markings, enlarged horizontal heart
Polycythemia	Uncommon	Common
Infections	Occasionally	Common
Pulmonary Function Study		
DLCO and DL/VA	Decreased	Often normal
Other		
Pulmonary hypertension	Uncommon	Common
Cor pulmonale	Uncommon	Common Right-sided heart failure

*The clinical features of emphysema and chronic bronchitis are not always clear-cut because many patients have a combined disease process (COPD—this is especially the case

Oxygenation Indices[g] for Chronic Bronchitis and Emphysema
Moderate to Severe Stages

Qs/Qt	DO_2	VO_2	$C(a-\bar{v})O_2$	O_2ER	$S\bar{v}O_2$
↑	↓	N	N	↑	↓

Hemodynamic Indices[i] for Chronic Bronchitis and Emphysema
Moderate to Severe Stages

CVP	RAP	$\overline{PA}$	PCWP	CO
↑	↑	↑	N	N
SVI	**cardiac index**	**RVSWI**	**LVSWI**	**PVR**
N	N	↑	N	↑

Laboratory Tests and Procedures

Test	Emphysema	Chronic Bronchitis
Hematocrit and hemoglobin	Normal—mild to moderate stage Elevated—late stage	Polycythemia common during early a late stages
Electrolytes (abnormal)	Late stage: • Hypochloremia (Cl^-) when chronic ventilatory failure is present • Hypernatremia (Na^+)	Early and late stages: • Hypochloremia (Cl^-) (when chron ventilatory failure is present) • Hypernatremia (Na^+)
Sputum examination (culture)	Normal	Streptococcus pneumoniae Haemophilus influenzae Moraxella catarrhalis

Radiology Findings

Test	Chronic Bronchitis
Chest radiograph	Lungs may be clear if only large bronchi are affected. Occasionally • Translucent (dark) lung fields • Depressed or flattened diaphragms Common • Right ventricle (cor pulmonale) and/or left ventricle enlargement No radiographic abnormalities may be present in chronic bronchitis if only the large bronchi are affected. This often explains why the diagnosis is delayed. Although the situation is uncommon, if the more peripheral bronchi are involved, air trapping may occur. This is revealed on x-ray film as areas of translucency or areas that are darker appearance. In addition, because of the increased functional residual capacity, the diaphragms may be depressed or flattened and are seen as such on the radiograph (Figure 12-8). Because bronchial wall thickening is common in chronic bronchitis, increased, diffuse fibrotic-appearing lung markings are often seen. This is commonly referred to as a "dirty chest x-ray."

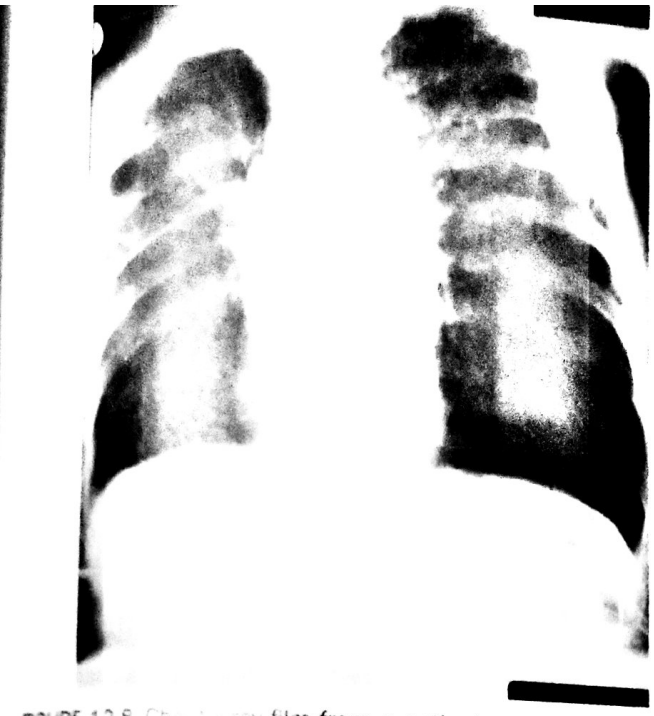


FIGURE 12-8 Chest X-ray film from a patient with chronic bronchitis. Note the translucent (dark) lung fields at the bases, depressed diaphragms, and long and narrow heart.

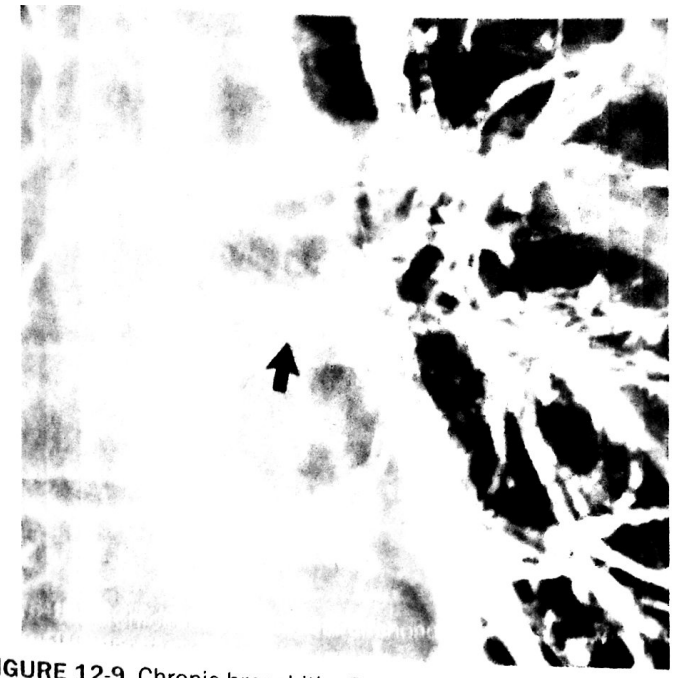


FIGURE 12-9 Chronic bronchitis. Bronchogram with localized view of left hilum. Rounded collections of contrast lie adjacent to bronchial walls and are particularly well demonstrated below the left main stem bronchus (*arrow*) in this film. They are caused by contrast in dilated mucous gland ducts. (From Hansel DM, Armstrong P, Lynch DA, McAdams HP, eds: *Imaging of the diseases of the chest*, ed 4, St Louis, 2005, Mosby.)

Test	
	Chronic Bronchitis
	Finally, because right and left ventricular enlargement and failure are commonly associated with chronic bronchitis, in the late stage an enlarged heart may be seen on the chest radiograph.
Bronchogram Computed tomography (CT) scan	Although rarely done today, small spikelike protrusions ("train tracks" appearance of airways) from the larger bronchi could often be seen on the bronchograms of patients with chronic bronchitis. It is believed that the spikes result from pooling of the radiopaque medium in the enlarged ducts of the mucous glands (Figure 12-9). Since the advent of the computed tomography (CT) examination, bronchograms are seldom done today on patients with chronic bronchitis. A "thin-section" CT exam is even more helpful.
Chest radiograph	**Emphysema** Common • Translucent (dark) lung fields. • Depressed or flattened diaphragms. • Long and narrow heart (pulled downward by diaphragms). • Increased retrosternal air space (lateral radiograph). Occasionally • Cor pulmonale (signs of cardiomegaly). • Emphysematous bullae.