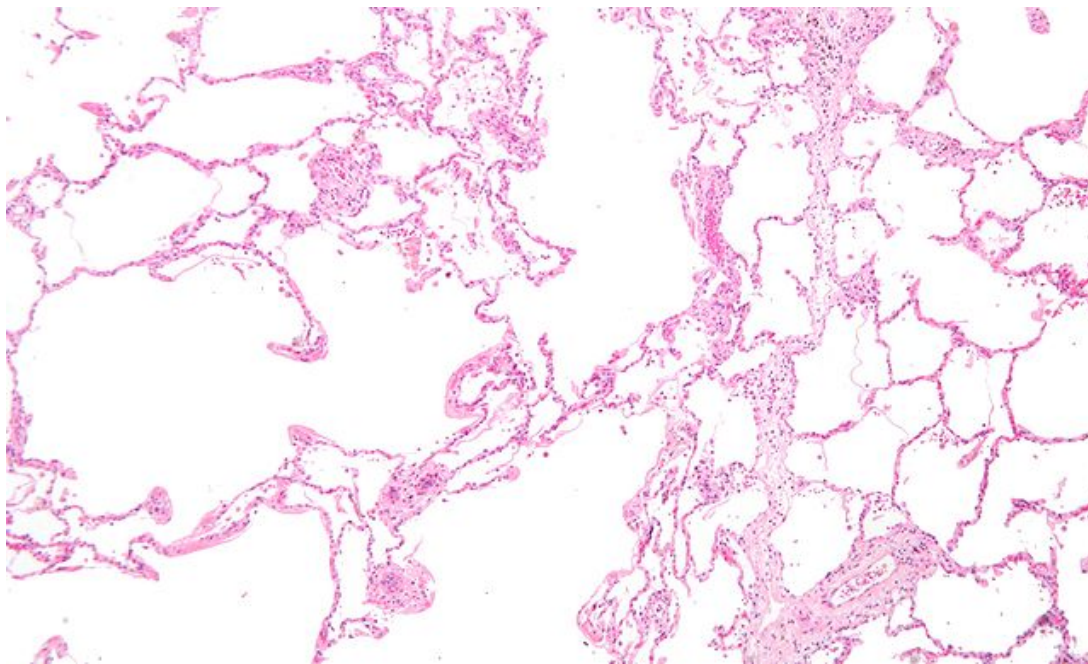


## Chronic Obstructive Pulmonary Disease (COPD) — Classification, Symptoms and Diagnosis

[See online here](#)

**Chronic obstructive pulmonary disease (COPD) is the most common chronic disease of the airways that is caused in 90 % of cases by smoking. COPD is a preventable and treatable disease. However, many patients do not know that they suffer from the disease, so the number of unreported cases of patients is very high. In this article, you will find important information on the epidemiology, etiology, pathophysiology and diagnosis, as well as the differential diagnosis and treatment of COPD.**



### Definition of COPD



**Image:** "A chest X-ray demonstrating severe COPD. Note the small size of the heart in comparison to the lungs." by James Heilman.  
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The term COPD refers to a **chronic obstructive pulmonary disease** and thus summarizes chronic respiratory diseases, where an **airflow limitation** occurs. A distinction must be done between the definition of the WHO and the global initiative for chronic obstructive lung disease (GOLD).

## WHO definition

The WHO defines COPD as a lung disease **characterized by chronic obstruction of lung airflow that interferes with normal breathing and is not fully reversible**. The more familiar terms 'chronic bronchitis' and 'emphysema' are no longer used but are now included within the COPD diagnosis.

## GOLD definition

According to the global initiative for chronic obstructive lung disease, COPD is a **preventable and treatable disease of the airways**, which is accompanied by a **restriction of the respiratory flow**. The disease is progressive and associated with a **chronic inflammatory reaction** of the lung to noxious particles or gases.

## Causes and Risk Factors of COPD

Almost 3 million people suffer from COPD in the United Kingdom. Roughly 900,000 patients among them have a confirmed diagnosis of COPD while about 2 million people have undiagnosed COPD. **90 % of COPD patients are smokers**. People **above the age of 50** are most affected. Heavy smokers can develop COPD after the age of 35.

The major cause of COPD is smoking, either active or passive. Other causes include **long-term inhalation of chemical fumes**, dust, and air pollutants. Genetic **alpha 1 antitrypsin deficiency** can also damage the lungs and lead to COPD. Smoking is a risk factor for these people as well.

Almost all preterm babies need long-term oxygen therapy as their lungs are still

underdeveloped. This can lead to [lung](#) injury (neonatal chronic lung disease) increasing the risk for COPD later in adult age. [Chronic bronchitis](#) is defined on the basis of history as a chronic productive cough for at least 3 months in two consecutive years. Emphysema is defined by the loss of alveoli.

## Epidemiology of COPD

The prevalence of COPD in the United States of America is about 5% among individuals over 45 years of age, but due to the unreported cases, a much higher number can be estimated. In the seventh decade of life, the prevalence is the highest. Worldwide, COPD is the third leading cause of death among men and women. Men and women are equally affected.

## Etiology of COPD

The causes of COPD include exogenous and endogenous factors. The main exogenous factor is cigarette smoking, which is responsible for COPD in approximately 90 % of cases. However, **air pollution** by ozone or fine dust is a trigger of COPD. Miners are often affected.

**Recurrent bronchopulmonary infections** aggravate the progression of COPD. In addition, a **disturbed lung maturation** in embryogenesis is known as a cause of later COPD. Important endogenous factors are an  **$\alpha$ 1-antitrypsin deficiency** and **IgA deficiency** which may contribute to the development of COPD – especially at younger age.

## Classification of COPD

COPD can be divided into different levels of severity. According to the global initiative for chronic obstructive lung disease (GOLD), the following grades can be distinguished:

Severity	Result
GOLD I (easy)	$FEV_1 \geq 80 \%$ , $FEV_1/VC < 70 \%$
GOLD II (medium)	$FEV_1 50 - 79 \%$ , $FEV_1/VC < 70 \%$
GOLD III (severe)	$FEV_1 30 - 49 \%$ , $FEV_1/VC < 70 \%$
GOLD IV (very severe)	$FEV_1 < 30 \%$ , $FEV_1/VC < 70 \%$

Spirometry is done every two years after the initial diagnosis. The patient is also **evaluated for other associated conditions** like [anemia](#), cancer, anxiety/depression, [ischemic heart disease](#), congestive heart failure, metabolic syndrome, peripheral muscle dysfunction, osteopenia, [osteoporosis](#), etc.

The [Medical Research Council](#) (MRC) has proposed a dyspnea scale:

1. **Grade 1:** No breathlessness except with strenuous exercise
2. **Grade 2:** Breathlessness when walking up a slight hill or walking fast on a flat level
3. **Grade 3:** The patient walks relatively slower than normal people on a flat level because of shortness of breath or has to catch for breath while walking at own pace on a flat level.
4. **Grade 4:** The patient stops to catch a breath after roughly 100 yards (90 m) walk or after a few minutes on a flat level.
5. **Grade 5:** The patient is not able to leave his house due to breathlessness or breathless during dressing or undressing.

# Pathogenesis of COPD

Airway limitation is the main feature of this disease. Initial stages of COPD are without any significant symptom. People consider a mild cough and shortness of breath on exertion as a normal part of aging. COPD can take years to complicate and produce significant symptoms; however, complications lead to permanent damage to the lungs. Although the damage caused by COPD cannot be undone, it is still possible to prevent further damage and manage the patients.

**COPD includes chronic bronchitis and emphysema.** **Chronic bronchitis** is the inflammation of the airways in response to smoking or pollutants leading to narrowing of the airway and increased mucous deposition, which causes excess cough. Narrowed or blocked airways disturb effective respiration, making the patient symptomatic.

**Emphysema** is the breakdown of the air sacs (alveoli) and alveolar membranes. Alveolar walls lose their elastic strength, the air entering the lungs is trapped, occupies space not used in the exchange of gas, leading to [dyspnea](#).

The deficiency of alpha 1 antitrypsin can lead to COPD. Emphysema occurs in these patients after the age of 30. Deficiency of the alpha 1 antitrypsin protein, an antiprotease that controls inflammation in the lungs, leads to the destruction of lung tissue by the WBCs.

## Pathophysiology of COPD

After **years of damage caused by inhaled toxic material** such as cigarette smoke, there is **hypertrophy and hyperplasia of goblet cells** in the mucosa of the bronchi. This results in an **increased production of mucus** whose removal can no longer be guaranteed by the ciliated epithelium. The **lumen of the bronchi is constricted** and therefore promotes a **lasting inflammatory reaction**.

This inflammation leads to a **remodeling process**, so the obstruction is both functionally and structurally permanent. Another consequence of chronic inflammation is a **non-physiological ratio between proteases and protease inhibitors** so that there is a destruction of connective tissue leading to **damage to the supporting structures** of the [lung](#) and development of **pulmonary emphysema**.

**The elasticity of the lung decreases, the residual volume increases.** The affected patients have to **increase their work of breathing**. The obstruction of the respiratory tract causes interference in the distribution of air, which leads to pulmonary vasoconstriction of the hypoxic areas according to the Euler-Liljestrand mechanism. If the total cross-section of all pulmonary vessels continues to decrease, this may cause **pulmonary hypertension** or even **pulmonary heart disease (cor pulmonale)**.

Additionally, there is a non-specific **bronchial hyper-responsiveness**. During forced expiration, (for example during physical exertion), a **bronchial collapse** occurs that contributes to **hyperinflation of the lung**. This creates a massive **performance limitation** of patients.

## Signs and Symptoms of COPD

COPD produces symptoms, disability and impaired quality of life which may respond to pharmacological and other therapies that have an impact on the airflow obstruction.

Symptoms of COPD include:

1. **Shortness of breath** or breathlessness on exertion or at rest (in late stages)
2. **Chest tightness** on exertion or at rest (in late stages)
3. **Chronic Cough with sputum**, a feature of chronic bronchitis
4. **Wheezing**, particularly on expiration
5. Other symptoms like **weight loss, ankle swelling, low appetite**

## Signs seen on examination

COPD patients can have the following signs depending upon the severity of the disease:



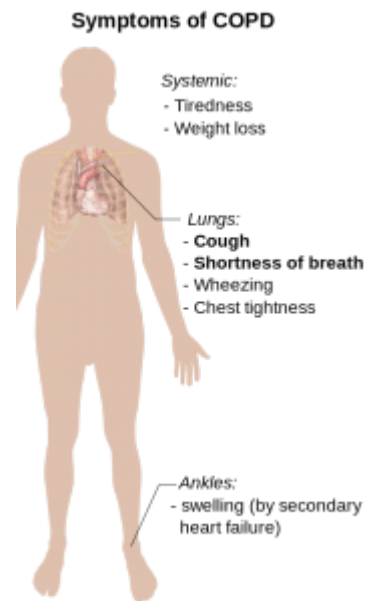
1. **Image:** "A lateral CXR of a person with emphysema. Note the barrel chest and flat diaphragm" by James Heilman, MD. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

**Barrel-shaped chest** due to hyperinflation and labored breathing using accessory muscles of respiration

2. **Cyanosis of the lips** and/or nail beds due to impaired lung function
3. **Wheeze with breathing**, particularly with expiration
4. **Distant breath sounds** on auscultation of the chest
5. **Scattered rhonchi** on auscultation of the chest
6. **Hyper-resonance** of the lungs on percussion
7. **Pulmonary hypertension** can develop and produce signs of cor pulmonale like ankle swelling, orthopnea, chest tightness, raised JVP, etc.

## GOLD Algorithm

Asthma and COPD have a different pathogenesis. **Asthma is triggered by allergens** in the environment and **airway inflammation is caused by CD4+ T cells**, lymphocytes, eosinophil, and ILs-4. However, the symptoms of asthma are **completely reversible**, while COPD develops in response to noxious agents. **Airway inflammation in COPD is caused by CD8+ T-lymphocytes and CD68+ macrophages/PMNS but airway obstruction is permanent and irreversible.**



**Image:** "Main symptoms of Chronic obstructive pulmonary disease." by Mikael Häggström. License: [Public domain](#)

The typical presentation of COPD is a **chronic cough** with whitish or purulent sputum to **expectoration and dyspnea**. Frequently COPD follows simple chronic bronchitis. Two types can be distinguished in their clinical picture:

- **Pink puffer:** emphysemic COPD type with strong dyspnoea and late pulmonary heart disease
- **Blue bloater:** bronchial COPD type with low dyspnea, cyanosis, and pronounced edema

## Diagnosis of COPD

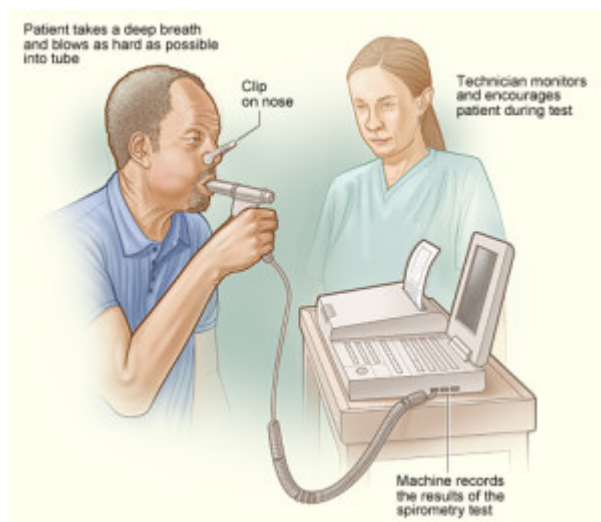
### History and physical examination

History is essential for existing **risk factors**, particularly asking about **smoking behavior** and already known **respiratory diseases** such as asthma. You can determine the severity of the disease from history by asking about the degree of distress with daily activities.

At physical examination, evidence of COPD (for example **cyanosis** or **barrel chest**) can already be found by inspection. A reduced vocal fremitus may be detected upon palpation, and during percussion, a hyper-resonant sound can be heard due to the hyperinfiltration of the lungs.

During auscultation, a **prolonged expiratory phase** can be heard, which is accompanied by **whistling** and also by **wheezing** and **humming**. Reduced breathing sounds can be heard in the hyperinflated lungs. Fine rales can also be heard accompanying pneumonia.

### Pulmonary functions tests



**Image:** "The image shows how spirometry is done. The patient takes a deep breath and blows as hard as possible into a tube connected to a spirometer. The spirometer measures the amount of air breathed out. It also measures how fast the air was blown out." by National Heart Lung and Blood Institute (NIH). License: Public Domain

A patient presenting with shortness of breath, cough with sputum and chest tightness should be thoroughly evaluated and tests for COPD should be performed.

Initially, **clinical history and physical examination** should be done. Baseline blood chemistry and hematology investigations should be sent to the laboratory and an **ECG with a chest x-ray** is advised to rule out other causes like lung cancer or cardiac disease. **Pulmonary function tests** are performed using a spirometer.

**Spirometry** is the most important test to diagnose obstructive and restrictive lung disease. FEV1 and FVC are calculated using spirometry. FEV1 is the forced expiratory volume of the air in one sec while FVC is the forced vital capacity. FEV1 measures the rate at which air moves out of the lungs. **Arterial blood gases** are done to measure the content of oxygen, carbon dioxide, and  $H^+$  ions. Oxygen saturation is also monitored regularly for COPD patients.

An alpha 1 antitrypsin test is done rarely to rule out the inherited cause of COPD. A CT scan, plain or HRCT (High-Resolution CT) of the chest is done to see a detailed picture of the lungs.

After inhalation of salbutamol, only **slight reversibility** of less than 200 ml/or less than 15 % appears in the post-bronchodilation test. A **reduced transfer coefficient** (DLCO/VA) sheds light on the severity of existing emphysema. A **decreased MEF**<sub>25-75</sub> shows obstruction of the small airways.

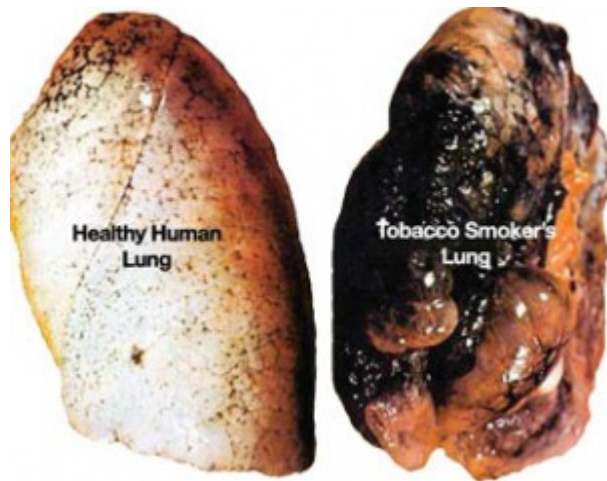


Image: "A Healthy lung compared to a smoker's lung." by United States: NIH, National Institute on Drug Abuse. License: [Public domain](#)

In smokers, the **CO content in the exhaled air** may be determined, which increases with cigarette consumption (> 50 ppm). In addition, the HbCO in blood gas analysis is increased in smokers. The arterial blood gas analysis also gives information about whether there is a partial respiratory insufficiency counteracted with hyperventilation ( $p\text{CO}_2$  decreased) or a generalized respiratory insufficiency ( $p\text{O}_2$  decreased and  $p\text{CO}_2$  increased).

#### Type of respiratory failure:

- $\text{Pco}_2$  increased → if the patient is hypercapnic only: type 1 respiratory failure.
- $\text{Po}_2$  decreased and  $\text{pco}_2$  decreased → if the patient is hypoxic and hypercapnic: it's type 2 respiratory failure.

Arterial blood gases and oximetry may demonstrate resting exertional hypoxemia. Arterial blood gases provide additional information about alveolar ventilation and acid-base status by measuring arterial  $\text{Pco}_2$  and pH.

In addition, certain patterns can be identified in spirometry, which are typical of COPD. Typical in the flow-volume graph is the **emphysema bend** and in the resistance loop the image of a **golf club** shown below.

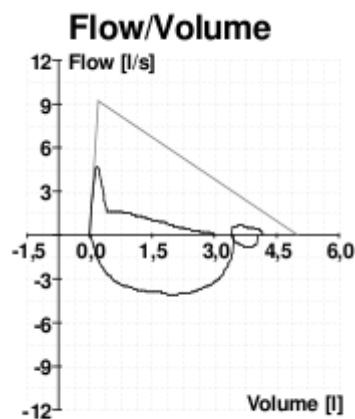


Image: "Flow Volume Curve from a spirometry test from a patient with COPD, Chronic Obstructive Pulmonary Disease" by Evgenios Metaxas MD MSc,



## Laboratory diagnostics

In the laboratory diagnosis, it is necessary to investigate the  **$\alpha$ 1-antitrypsin deficiency**, especially in younger patients who do not smoke. A complete blood count may show an elevated hematocrit, which suggests the presence of chronic hypoxemia.

## Microbiology

In cases of recurrent severe exacerbations or treatment failure, **sputum culture** should be obtained. A morning expectoration should be collected, but obtaining endobronchial secretions as part of bronchoscopy is even better. **Potential pathogens are frequently Haemophilus influenza, pneumococcus or Moraxella catarrhalis** and different virus types.

## Diagnostic radiology

Characteristic radiographic findings:

- Hyperinflation with → 1- flattened hemidiaphragms 2- increased anteroposterior chest diameter
- Parenchymal destruction produces attenuated peripheral vascular markings.
- Pulmonary hypertension produces proximal pulmonary artery dilation .
- Cardiac size may be increased, suggesting the right heart volume overload.
- Cystic or bullous changes.

On chest X-ray, small opacities may suggest **inflammatory infiltrates** or **restricted ventilation**. Changes due to **emphysema** or **cor pulmonale** can be detected, and other diseases such as lung cancer or pneumonia are excluded. Since chronic bronchitis is a diagnosis of exclusion, an X-ray image is always needed before a diagnosis is made.

## Bronchoscopy

In addition, bronchoscopy should be entertained to exclude various differential diagnoses that result in symptoms similar to COPD such as haemoptysis and dyspnoea. During bronchoscopy, biopsies may be obtained for histological examination.

**Note:** If differential diagnoses, such as lung cancer cannot be excluded with an X-ray or CT, bronchoscopy should be done.

## Diagnostic criteria

There is no single diagnostic test for COPD. Physicians rely on clinical judgment based on a **combination of history, physical examination, and confirmation of the presence of airflow obstruction using spirometry**. COPD is characterized by airflow obstruction that is not fully reversible. Airflow obstruction is defined as a reduced FEV<sub>1</sub>/FVC ratio such that the diagnosis of COPD is made when the FEV<sub>1</sub>/FVC ratio is less than 0.7 and the FEV<sub>1</sub> is less than 80% of predicted. Additionally, a diagnosis of COPD should only be made in the presence of respiratory symptoms, for example, breathlessness or cough.

# Differential Diagnosis of COPD

Differential diagnosis of COPD is **bronchial asthma**. Unlike COPD, asthma is prevalent mostly in childhood or adolescence, and is accompanied by paroxysmal dyspnoea, allergies and a good response to corticosteroids and is completely reversible in the post-bronchodilation test.

Other lung diseases must be excluded. To exclude **bronchiectasis** a greater amount of sputum is necessary as well as a High-Resolution CT scan. **Tracheal or laryngeal stenosis** may be differentiated by laryngoscopy or bronchoscopy. An otolaryngologist may establish the diagnosis of a **sinobronchial syndrome**, a combination of sinusitis and the resulting lower respiratory tract symptoms such as chronic bronchitis or asthma.

To exclude a **left ventricular failure** that occurs especially with nocturnal cough and cardiac asthma, cardiac diagnostics are necessary. **Cystic fibrosis** can be diagnosed through a sweat test. The detection of **bronchial carcinoma** is important, therefore X-rays and CT scans with a bronchoscopy-guided biopsy may be necessary. In addition, a **pulmonary embolism** and the presence of **gastroesophageal reflux disease** should be excluded.

## In summary:

- **Asthma**
- Cardiovascular or pulmonary vascular disease
- Obesity
- Severe exercise deconditioning
- **Anemia**
- Interstitial lung disease
- Neuromuscular disease

# Acute Exacerbation of COPD

**A sudden attack of shortness of breath, wheezing and cyanosis with signs of respiratory distress** in a patient with diagnosed COPD is called acute exacerbation of COPD. **Infections** caused by bacteria or viruses, or body response to **environmental pollutants** can be the triggers of an acute attack. Management includes systemic and inhaled corticosteroids with oxygen therapy and regular monitoring with antibiotic cover if required.

# Therapy of COPD

The treatment of COPD is divided into a medical and conservative approach. The basis of conservative therapy is the **absolute nicotine abstinence** and the **elimination of other inhaled noxious agents**. **Patient training** and **breathing exercises** combined with **training to improve cardiopulmonary capacity** are also necessary.

**Vaccination against pneumococcal and influenza viruses** is indicated for the prevention of infections. Furthermore, **prophylaxis of osteoporosis** with calcium and vitamin D3 is useful as it counteracts glucocorticoid-induced osteoporosis. Existing infection sources have to be eliminated and comorbidities need to be treated.

Drug therapy is structured according to a graduate scheme.

The first group of patients with GOLD 1 to 2, 0 to 1 exacerbations per year and a few

symptoms can be treated with a **short-acting anticholinergic or short-acting  $\beta_2$ -sympathomimetic as needed**. Alternative or adjunctive to this regime is therapy with theophylline.

The second group of patients with GOLD 1 to 2, from 0 to 1 exacerbations per year but with stronger symptoms is **treated with a long-acting anticholinergic or a long-acting  $\beta_2$ -sympathomimetic**. Supplementary in this stage is therapy with short-acting anticholinergics and/or short-acting  $\beta_2$ -sympathomimetics and theophylline.

The third group of patients with GOLD 3 to 4, with two or more exacerbations per year and few symptoms, is treated with an **inhaled glucocorticosteroids and a long-acting anticholinergic, or a long-acting  $\beta_2$ -sympathomimetic**. Alternative or supplement to this stage is therapy with short-acting anticholinergics and/or short-acting  $\beta_2$ -sympathomimetic and theophylline.

The fourth group of patients with GOLD 3 to 4, two or more exacerbations per year and stronger symptoms get **inhaled glucocorticosteroids and a long-effective  $\beta_2$ -sympathomimetic and/or a long-acting anticholinergic**. Alternative or supplement to this stage is therapy with short-acting anticholinergics and/or short-acting  $\beta_2$ -sympathomimetic and theophylline and carbocysteine.

## Therapy of acute recurrent exacerbations

In this case, hospitalization is often sought, especially if strong dyspnoea and/or tachypnoea or older age of the patients occur. In infection-related exacerbations, antibiotic therapy is indicated based on antibiotic susceptibility of the suspected pathogens as well as the patient's clinical condition. Patients with mild exacerbations can be treated as outpatients with **aminopenicillin** (alternatively doxycycline, macrolides).

Patients with moderate to severe exacerbations need hospital admission and treatment with **aminopenicillin with beta-lactamase inhibitor or parenteral cephalosporin of the 2nd or 3rd generation** (alternatively anti-pneumococcal fluoroquinolones). In patients with suspected *P. aeruginosa* infections or in patients in intensive care, **pseudomonas effective carbapenems, cephalosporin or fluoroquinolones** should be used.

The **bronchodilator therapy may be temporarily intensified** and combined with **intravenous glucocorticoids**. There are also **aerosol treatments**, an apparatus inhalation therapy with 0.9 % NaCl,  $\beta_2$ -sympathomimetics such as salbutamol, and an oxygen treatment so that the pO<sub>2</sub> is maintained above 60 mmHg.

## Complications of COPD

**Acute recurrent exacerbations** are complications of COPD that require an adjustment of therapy. Viral or bacterial infections may cause a more severe deterioration that may last longer than 24 hours. Also, co-morbidities such as **cardiovascular disease** or **metabolic syndrome, lung carcinoma, muscle weakness** and **osteoporosis** (due to catabolic mechanisms requiring an increased work of breathing) and **depression** are complications of COPD.

**Weight loss** with increased work of breathing is typical. Among the late complications, **respiratory failure** is common and **cor pulmonale** is due to the Euler-Liljestrand mechanism and direct vascular loss. Pulmonary hypertension may lead to **right heart failure** with hepatomegaly and ascites.

# Prevention of COPD

The most effective preventive method is risk factors avoidance. It has been shown that middle-aged smokers who were able to successfully stop smoking experienced a significant improvement in their prognosis with a slower progression of the disease. For this purpose, the detailed medical **reconnaissance** and **surveillance** are essential as well as assisting with substitution drugs and anti-depressants in order to facilitate the cessation.

In occupational COPD, immediate **avoidance of inhaled noxious substances** is crucial. Also, **vaccines against pneumococcal and influenza** are indexed to avoid acute exacerbations due to these infections.

## Learn more about COPD

To learn more about this topic you may [test the course "Respiratory Medicine" by Prof. Jermeý Brown for free!](#) An extra lecture about COPD is included!

## Review Questions

The answers are below the references.

### 1. What does not belong to the symptoms of COPD?

- A. Dyspnoea
- B. Cyanosis
- C. Sputum production
- D. Cough
- E. Chest pain

### 2. Which is the best diagnostic tool for COPD?

- A. Anamnesis
- B. Auscultation
- C. Chest X-ray
- D. Biopsy
- E. Laboratory diagnostics

### 3. Which is the best to describe the Pink buffer?

- A. bronchial COPD type
- B. strong dyspnea
- C. Cyanosis
- D. pronounced edema
- E. pyknic type



**Image:** "A chest X-ray demonstrating severe COPD. Note the small size of the heart in comparison to the lungs." by James Heilman, MD. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

**4. A 62-year-old male smoker for the last 35 years came to the emergency with excessive sweating and difficulty breathing with productive cough. He has a history of difficulty breathing and a productive cough from the past 3 years. On physical examination, the temperature is 101° Fahrenheit, pulse 124/min and BP 130/90 mm hg. He was pale and his lips were bluish. On auscultation of the chest, bilateral crepitations were present on the base of the lungs, more on the right side. Chest X-ray was done in the emergency, shown in the figure. Which is the correct statement?**

- A. The patient is having acute asthma, as a chest x-ray shows hyperinflation.
- B. The patient is having emphysema due to active smoking.
- C. The patient is having chronic bronchitis along with lobar pneumonia.
- D. The patient is having right heart failure and pulmonary edema.

**5. What are the findings in the chest x-ray (image)?**

- A. Hyperinflation and infiltration showing bronchopneumonia
- B. Hyperdense is in the right lung due to pulmonary edema and bronchopneumonia.
- C. Hyperinflation of the lungs, narrow mediastinum, hyperlucency through lung fields bilaterally
- D. Calcification of the hilar lymph nodes, 2-3<sup>rd</sup> rib fracture on the right side

## References

[GOLD-Definition](#)

[What causes COPD?](#) via [nhlibi.nih.gov](http://nhlibi.nih.gov)

[COPD Diagnosis and Management Algorithm](#) via The Lung Association Ontario

**Correct answers:** 1E, 2D, 3B, 4B, 5C

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