

# Chronic Obstructive Pulmonary Disease (COPD)

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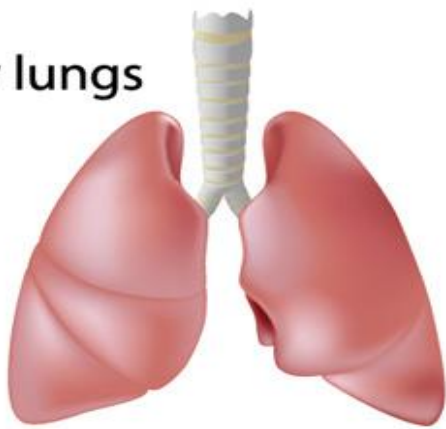
- In 2001, the National Institutes of Health (NIH) and the World Health Organization (WHO) collaborated to develop the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.

# Definition

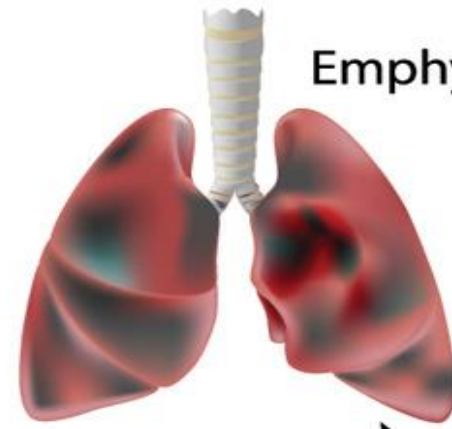
- Definition of COPD according to GOLD is as follows:
- “Chronic obstructive pulmonary disease (COPD) is characterized by chronic airflow limitation and a range of pathological changes in the lung, some significant extra-pulmonary effects, and important co-morbidities which may contribute to the severity of the disease in individual patients. Thus, COPD should be regarded as a pulmonary disease, but these significant comorbidities must be taken into account in a comprehensive diagnostic assessment of severity and in determining appropriate treatment.”

- COPD generally refers to emphysema or chronic bronchitis.
- Emphysema is pathologically defined and characterized by alveolar wall destruction and airspace enlargement.
- Chronic bronchitis is clinically defined as a chronic cough for at least 3 months for 2 consecutive years. Its pathologic hallmark involves inflammation and fibrosis of the small airways.
- Clearly, much overlap exists between these two conditions because both are primarily caused by cigarette smoking.

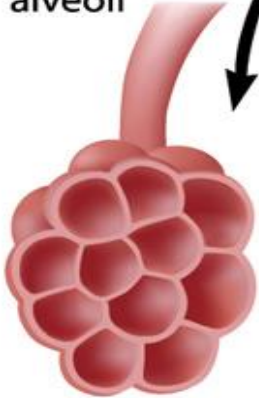
Healthy lungs



Emphysema



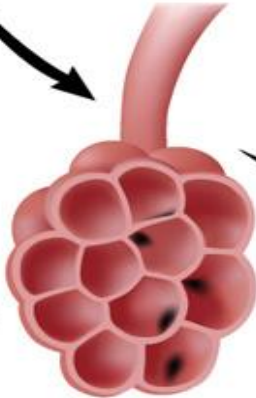
Healthy alveoli



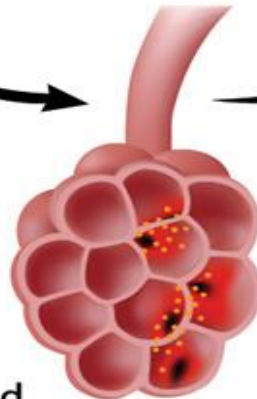
## Smoking and Emphysema



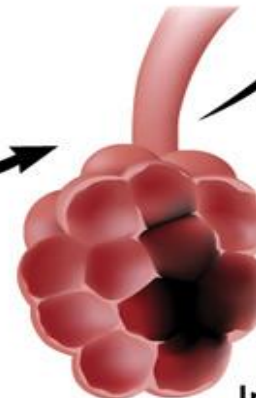
Harmful particles trapped in alveoli



Inflammatory response triggered



Inflammatory chemicals dissolve alveolar septum



Large air cavity lined with carbon deposits formed





# Risk factors

- Cigarette smoking
  - Air pollution
  - Respiratory viral infections
  - HIV
  - Genetic factors ( *$\alpha 1$ -antitrypsin deficiency*)
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- The risk of COPD from cigarette smoking is related to an accelerated loss of lung function. After age 35, nonsmokers experience a decline in forced expiratory volume in the first second of expiration (FEV1) of about 20 to 30 mL/year. In smokers, the decline may be 50 to 120 mL/year.

# Pathogenesis

- The exact mechanisms responsible for the pathogenesis of COPD are not entirely clear, but likely involve activation of the innate and adaptive immune system leading to chronic inflammation.



- An increase in numbers (hyperplasia) and enlargement (hypertrophy) of the submucosal glands and mucus-producing goblet cells within the surface epithelium.
- Overproduction of mucus in the large airways results in a chronic productive cough, as observed in chronic bronchitis, but this does not have a major impact on airflow limitation.
- Mucus hypersecretion coupled with impaired ciliary function reduces mucociliary clearance, increases the accumulation of secretions, and enhances the risk of bacterial colonization.

- The extent of inflammation, fibrosis, and airway exudate in the peripheral airway correlates best with the reduction in airflow as measured by a decrease in FEV1 or the FEV1 to forced vital capacity (FVC) ratio.

# Exacerbations

- Pulmonary hypertension
- Heart failure
- Cachexia
- Skeletal muscle dysfunction
- Osteoporosis
- Depression
- Anaemia

- In summary, although COPD is primarily a disease of the large and small airways and adjacent alveolar structures, it also includes important systemic consequences.
- The clinical consequences of the morphologic and pathophysiologic alterations include progressive dyspnea on exertion, chronic cough and sputum production, increased risk for respiratory infections, deconditioning, and an overall reduction in quality of life.

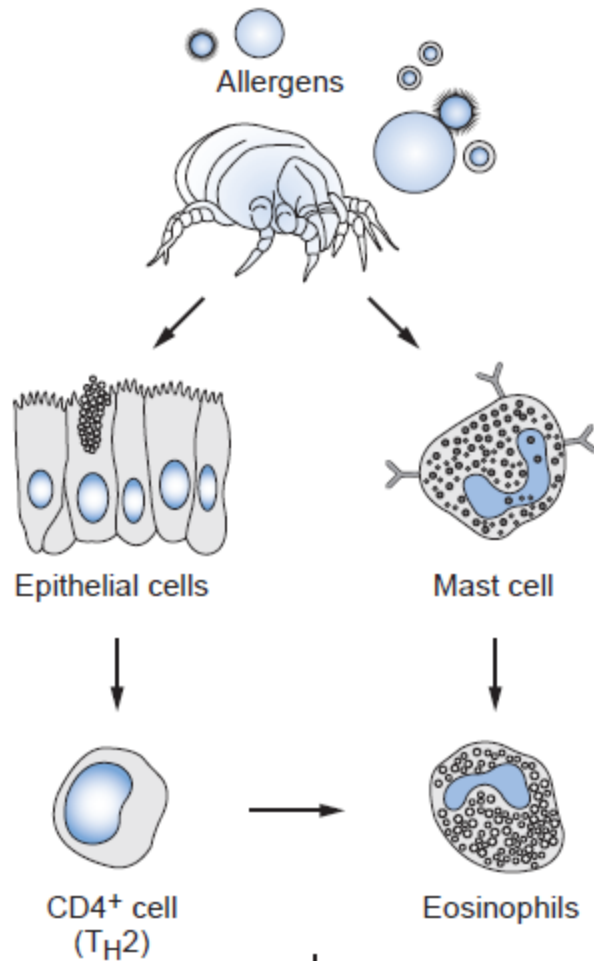
# COMPARISON WITH ASTHMA

- COPD and asthma are both common diseases, and both illnesses can coexist in the same patient.
- although inflammation is a key component of both conditions, the pattern of inflammation differs significantly.
- As a result, the pathophysiologic consequences, patient symptoms, and response to medications typically differ.

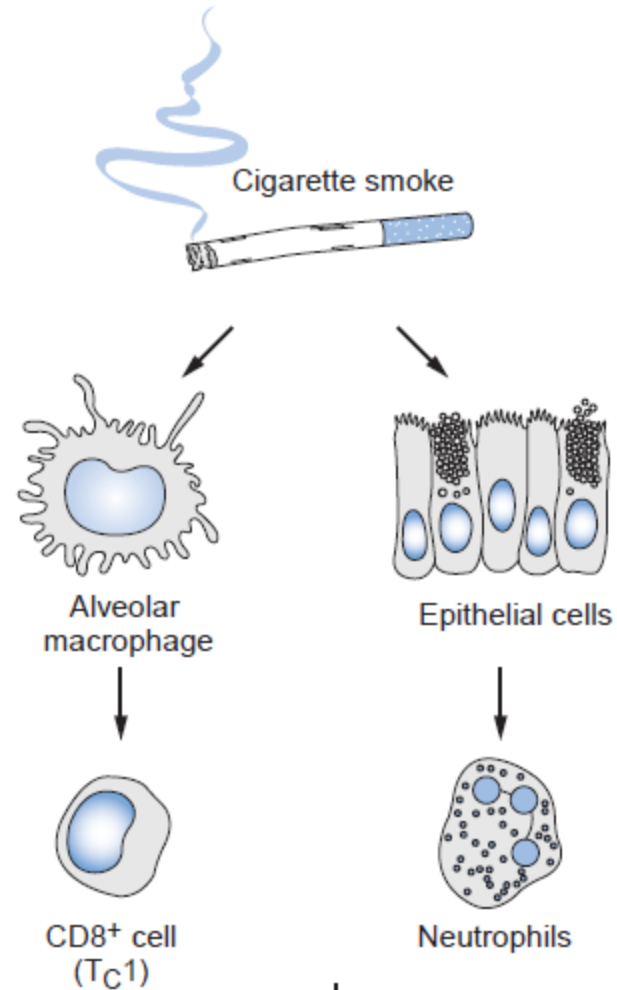
- Asthma is generally not progressive, and symptoms and airflow obstruction are often completely reversible. Patients with asthma respond well to anti-inflammatory medication, including inhaled corticosteroids.
- In the absence of an acute exacerbation, significant gas exchange abnormalities are uncommon.

- COPD, on the other hand, is a progressive and often fatal disorder. Although bronchodilators are clearly helpful in COPD, the degree of bronchodilator reversibility is typically less than that seen in asthma.
- The beneficial effects of anti-inflammatory medication, including inhaled corticosteroids, are much more modest.
- Patients with COPD, particularly those with emphysema, have substantial derangements in pulmonary gas exchange even at baseline.

## ASTHMA



## COPD





# DIAGNOSIS AND PATIENT ASSESSMENT

- The diagnosis of COPD is based on the presence of risk factors (generally smoking), clinical symptoms, and airflow obstruction on spirometric testing.
- Generally, individuals with COPD present in the sixth decade of life (or later) with symptoms of cough, wheeze, or dyspnea on exertion.
- Patients usually have at least a 20-pack-year history.
- Cough and sputum production may be present for many years before airflow limitation develops, but not everyone with those symptoms will develop COPD.
- Spirometry.

# GENERAL MANAGEMENT CONSIDERATIONS

- The only interventions that have proved to reduce mortality in COPD are:
  - Smoking cessation
  - Oxygen therapy for patients with severe hypoxemia at rest
  - Lung volume reduction surgery for very selective patients with advanced emphysema.
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- Immunizations (Pneumococcal vaccine)
  - Pulmonary rehabilitation

# Goals of therapy

- To prevent or control symptoms
- To reduce the frequency and severity of exacerbations
- To improve both health status and exercise tolerance.

# Management

- The number of medications will cumulatively increase as the disease worsens.
- Patients will eventually require daily maintenance therapy for sustained periods unless adverse effects of the medication(s) preclude further use.
- Interindividual variability in medication response is expected and requires careful monitoring over a continuum of time to ensure an acceptable benefit-to-risk ratio is achieved.

- When medications are initiated or modified, a minimal trial period of several weeks to a few months is usually recommended before determining their full benefit.
- FEV1
- Short-acting and long-acting  $\beta_2$ -agonists
- Short-acting and long-acting anticholinergic agents
- Theophylline

- Short acting  $\beta_2$ -agonists or ipratropium are given initially on as needed basis.
- If the disease progresses, the patient should be transitioned on to daily doses.
- Substitution with a long-acting agent of the same class can improve patient compliance if the patient uses short-acting agents more than once per day.
- However, the use of short-acting agents should still be recommended for acute symptomatic relief.

# Tiotropium:

- Tiotropium is a longer acting antimuscarinic agent which is taken by inhalation, and a single dose of 18 mcg has 24-hour duration of action.
- Daily inhalation of tiotropium has been shown not only to improve functional capacity of patients with COPD, but also to reduce the frequency of exacerbations of their condition.

# Methylxanthines

- Theophylline strengthens the contractions of isolated skeletal muscle in vitro and improve contractility and reverse fatigue of the diaphragm in patients with COPD.
- This may account for theophylline's ability to improve the ventilatory response to hypoxia and to diminish dyspnea even in patients with irreversible airflow obstruction.
- **Roflumilast:** orally administered PDE4 enzyme inhibitor reduces the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.



# Corticosteroids

- Daily use of inhaled corticosteroids can result in a reduction in the frequency of exacerbations and an improvement in overall health status, particularly in patients with more advanced disease.
- inhaled corticosteroid use in combination with a long-acting  $\beta_2$ -agonist is more effective than either agent alone in patients with advanced COPD.

- An acute exacerbation of COPD is defined as an acute worsening of a patient's chronic symptoms (dyspnea, cough, sputum production) necessitating treatment.
- They are associated with considerable morbidity; severe exacerbations are associated with an increased mortality.
- The cause of acute exacerbations is believed to be a result of respiratory tract infections, either viral or bacterial, air-pollution, or other environmental exposures

- Systemic corticosteroids are commonly given for a 7- to 10-day course.
- High-dose intravenous corticosteroids (methylprednisolone 125 mg every 6 hours) have been shown to be effective in hospitalized patients.
- Antibiotic use in the setting of an acute exacerbation should be made based on the presence of the following respiratory symptoms: increased dyspnea, sputum volume, and sputum purulence.

