COPD

- It is a progressive disease characterized by airflow limitations (irreversible).
- It adds to the heart work.
- Progression of the disease

**First**
Chronic bronchitis with an obstructive ventilatory pattern that is defined by the existence of chronic bronchitis with permanent obstruction of airways (FEV1/FVC<70%)

**Second**
Chronic respiratory failure, which is defined by the existence of chronic obstructive bronchitis with hypoxaemia. (not hypoxia)

**Third**
Emphysema with or without α1-anti-trypsin deficiency (imbalance due to increase in proteases)

- COPD is characterized by
  1) 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.
  2) Permanent enlargement of airspaces distal to the terminal bronchioles, emphysema, accompanied by destruction of their walls and without obvious fibrosis.

الفيبيسم بس مش في الfibrosis
**Epidemiology**

It was the 6th cause of death in USA in 1990

2000: 130,000 died from COPD

2002: 12.1 million were reported having COPD

2020: is expected to be the 3rd cause of death

However, the exact prevalence of COPD is under-estimated, due to it is an underdiagnosed (and undertreated) disease, because most patients do not present for medical care until the disease is in a late stage.

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**ETIOLOGY**

- Cigarette smoking (the leading cause, 80-90%)
- Occupational exposure to dusts & chemicals (fumes, vapors, irritants, cadmium)
- Environmental air pollution (exact role is still unknown)
- Genetic factors: deficiency of α1 antitrypsin (AAT) is not a major cause but helps the factors in progression.
- Asthma & hyper-responsiveness are risk factors, but how they cause COPD is unknown
- Recurrent infections &/or exposure to tobacco smoke during childhood → ↑ risk to COPD
- Intravenous drug use of methadone or methylphenidate leads to pulmonary vascular damage that results from the insoluble filler (e.g., cornstarch, cotton fibers, cellulose, and talc) contained in them.

**Pathologic changes**

- Chronic inflammation due to repeated exposure to noxious particles & gases
- Oxidative stress (ROS, tobacco + inflammation)
- Proteinases ≠ Anti-proteinases
- in Peripheral airways
- in Lung Parenchyma
- in Pulmonary vasculature
- Pathologic changes in Central airways

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1- Chronic inflammation is mediated primarily by the activation of inflammatory cells, e.g. neutrophils, macrophages, CD8+T-lymphocytes and eosinophils (during exacerbation) inflammatory mediators (LTB4, IL-8, TNF-α).

2- Imbalance between Proteinases and Anti-proteinases leading to unopposed proteinase activity (elastase, proteinase-3, etc…….)

3- Increase in oxidative stress
   - ROS & RNS (reactive nitrogen) → damage of cell macromolecules & cell dysfunction
   - oxidants constrict airway smooth muscle → narrowing airways
   - Promotes inflammation & prot./anti-prot. Imbalance

Central Airways (trachea, bronchi, bronchioles >2mm diameter) [mainly hypersecretory phase]

Hyperplasia & hypertrophy of mucus secretory glands & goblet cells ↑ mucus secretion → ciliary dysfunction → chronic cough & sputum production + susceptibility to respiratory infections (viral followed by bacterial, Steptococcus pneumoniae and Haemophilus influenzae).

Peripheral Airways obstruction (bronchioles<2mm diameter) Obstruction phase

1- Inflammatory exudates & mucus hypersecretion → cell remodeling “fibrosis” + thickening the airway walls + narrowing of the airways.

2- Advanced chronic bronchitis: squamous metaplasia and fibrosis → ↑ fixed limitation of airflow.

3- Loss of alveolar wall & elasticity → closure of small airways during expiration & fixed obstruction.
Worsened airflow obstruction leads to slow emptying of the lung leading to lung hyperinflation (1st upon exercise, then even at rest).

Airflow obstruction + damaged alveoli & bronchioles + pulmonary vascular abnormality (inadequate ventilation/ perfusion = V/Q) leads to hypoxemia/hypercapnia.

Severe hypoxemia → pulmonary artery V.C. → pulmonary H.T. → right-sided HF (Cor-pulmonale)

Cor-pulmonale leads to venous stasis, thrombosis and pulmonary embolism.
Hypoxic pulmonary vasoconstriction

Hypoxic pulmonary vasoconstriction is a paradoxical, physiological phenomenon in which pulmonary arteries constrict in the presence of hypoxia (low oxygen levels) without hypercapnia (high carbon dioxide levels), redirecting blood flow to alveoli with higher oxygen content.

The process might at first seem illogical, as low oxygen levels should theoretically lead to increased blood flow to the lungs to receive increased gaseous exchange. However, it is explained by the fact that constriction leads to redistribution of blood flow to better-ventilated areas of the lung, which increases the total area involved in gaseous exchange.

Types of respiratory failure

<table>
<thead>
<tr>
<th>Type one respiratory failure</th>
<th>Type two respiratory failure</th>
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<tbody>
<tr>
<td>caused by a ventilation-perfusion mismatch</td>
<td>Caused by alveolar hypoventilation, e.g. patient with an exacerbation of COPD may not be able to ventilate alveoli sufficiently to remove CO2 leading to retention of CO2, with hypercapnia and hypoxaemia (chronic, ventilatory or hypercapnic respiratory failure).</td>
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<tr>
<td>This process impairs oxygen transfer in the lung &amp; causes hypoxaemia (acute or hypoxaemic respiratory failure) → hypoxaemia.</td>
<td>Treatment is a high conc. of O2 despite a high CO2 level.</td>
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<tr>
<td>Treatment: correction of hypoxaemia with a high conc. of O2 to establish a PaO2 &gt; 60 mmHg to ensure O2 saturation is maintained above 92 %, as tissue hypoxia will not occur at this level.</td>
<td>The aim is to achieve acceptable PaO2 without a fall in pH below 7.35. A pH below 7.26 is predictive of a poor outcome, so monitoring O2 saturation alone is not advisable &amp; blood gas analysis is recommended to detect rise in PaCO2.</td>
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Normal Arterial Values Range:  
- pH 7.35-7.45,  
- pCO2 35-45,  
- pO2 80-100,  
- O2 Sat. 95-100% ,  
- HCO3 22-26  

Abnormal values:  
- pH 7.30 (acidotic),  
- pCO2 58 (acidotic),  
- pO2 50 (low)  
- O2 Sat. 80% (low)  

In case of respiratory failure we can use resp. stimulants as I.V. infusion of Doxapram (1-4 mg/min).

S.E. narrow therap. index, HT, tachycardia, convulsion.

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A diagnosis of COPD should be considered in:

- patients over the age of 35 who have a risk factor (generally smoking)
- Who presents with exertional breathlessness, chronic cough, regular sputum production, frequent winter ‘bronchitis’ or wheeze.
- The presence of airflow obstruction should be confirmed by performing spirometry.

A suspected diagnosis of COPD should be based on the patient’s symptoms and/or history of exposure to risk factors.

<table>
<thead>
<tr>
<th>History:</th>
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<tbody>
<tr>
<td>Do you smoke?</td>
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<tr>
<td>Have you had chronic exposure to dust or air pollutants?</td>
</tr>
<tr>
<td>Do you get short of breath with exercise?</td>
</tr>
<tr>
<td>Do you have chronic cough and/or wheezing?</td>
</tr>
<tr>
<td>Do you cough up excess mucus?</td>
</tr>
<tr>
<td>Are you short of breath?</td>
</tr>
<tr>
<td>Do other members of your family have lung disease?</td>
</tr>
</tbody>
</table>

COPD is asymptomatic at first, then symptoms develop when FEVI/FVC post-bronchodilator<70%. This’ll confirm airflow limitation that is not fully reversible.

**SYMPTOMS & SIGNS:**

- Initial:
  - chronic cough > 3 months in 2 successive years
  - chronic sputum production
  - dyspnea on exertion
- As COPD progresses
  - dyspnea at rest develops
  - decreased ability to perform daily activities

N.B. Breathlessness is one of the 1ry symptoms of COPD graded by “The Medical Research Council (MRC) dyspnea scale.

**Signs:**

Observation of the patient:

- patient starts to respire in a see-saw movement and starts use of accessory muscles
- pursed-lips breathing
- Hyperinflation of the chest with increased anterior-posterior diameter (barrel chest).
On auscultation of the lungs:

- Wheezing
- a prolonged expiratory phase
- Rhonchi (breathing sound as snoring, due to obstructed airways with mucus & swollen mucus membrane).

In advanced COPD: cyanosis & tachycardia (signs of hypoxemia) occurs

Cor-pulmonale signs:

- jugular venous distention (JVD),
- lower extremity edema
- hepatomegaly

Infection signs: yellowish or greenish sputum, which involves bacteria, macrophages & epithelial cells with no fever.

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**GOLD Spirometric Criteria for COPD Severity**

<table>
<thead>
<tr>
<th>Stage</th>
<th>FEV1/FVC</th>
</tr>
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<tbody>
<tr>
<td>I. Mild COPD</td>
<td>FEV1 &lt; 0.7</td>
</tr>
<tr>
<td></td>
<td>* FEV1 &gt; or = 80% predicted</td>
</tr>
<tr>
<td>II. Moderate COPD</td>
<td>FEV1 &lt; 0.7</td>
</tr>
<tr>
<td></td>
<td>* FEV1 50% to 79% predicted</td>
</tr>
<tr>
<td>III. Severe COPD</td>
<td>FEV1 &lt; 0.7</td>
</tr>
<tr>
<td></td>
<td>* FEV1 30% to 49% predicted</td>
</tr>
<tr>
<td>IV. Very Severe COPD</td>
<td>FEV1 &lt; 0.7</td>
</tr>
<tr>
<td></td>
<td>* FEV1 &lt; 30% predicted OR FEV1 &lt; 50% predicted with chronic respiratory failure</td>
</tr>
</tbody>
</table>

**At this stage, the patient is probably unaware that lung function is starting to decline.**

**Symptoms during this stage progress, with shortness of breath (SOB) developing upon exertion.**

**SOB becomes worse at this stage & COPD exacerbations are common.**

**Quality of life at this stage is gravely impaired. COPD exacerbations can be life threatening.**

**GOLD: Global Initiative for Obstructive Lung Disease**
GOLD I: Mild COPD

- There may be mild airflow limitation, but one may be unaware that lung function has started to decline.
- FEV1 ≥ 80% of the predicted normal values with an FEV1/FVC < 70%. One may not yet have any COPD symptoms, or may have symptoms of chronic cough and excessive mucus.
- People at this stage are not likely to associate symptoms with the disease process and therefore, rarely seek treatment.

GOLD II, Moderate COPD

- Airflow limitation worsens and one may start to notice symptoms, particularly shortness of breath (SOB) upon exertion along with cough and sputum production.
- FEV1 will be anywhere between 50% - 79% of the predicted normal values and FEV1/FVC < 70%.
- During this stage most people seek medical treatment.

GOLD III, Severe COPD

- Limitation of airflow significantly worsens, shortness of breath becomes more evident and COPD exacerbation is common.
- FEV1 will be between 30% - 49% predicted and FEV1/FVC < 70%.
- This stage, is accompanied by ↓ in activity tolerance & ↑ in fatigue-ability.

GOLD IV, Very Severe COPD

- Quality of life is greatly impaired & COPD exacerbations are life threatening.
- Airflow limitation is severe (FEV1 < 30% predicted, FEV1/FVC < 70%).
- Chronic respiratory failure is often present at this stage, and may lead to complications with heart, such as cor-pulmonale and/or eventually, death.

<table>
<thead>
<tr>
<th>GROUP</th>
<th>SYMPTOMS</th>
<th>RISK</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Mild or infrequent</td>
<td>FEV1 ≥ 80% predicted &amp; 0-1 exacerbations within the past year, mMRC dyspnea score: 0-1</td>
</tr>
<tr>
<td>B</td>
<td>Moderate to severe</td>
<td>FEV1 ≥ 50% predicted &amp; 0-1 exacerbations within the past year, MRC ≥ 2</td>
</tr>
<tr>
<td>C</td>
<td>Mild or infrequent</td>
<td>FEV1 &lt; 50% predicted &amp; ≥ 2 exacerbations within the past year or ≥ 1+ hospitalization, MRC: ≥ 2</td>
</tr>
<tr>
<td>D</td>
<td>Moderate to severe</td>
<td>FEV1 &lt; 30% predicted &amp; ≥ 2 exacerbations within the past year or ≥ 1+ hospitalization, mMRC ≥ 2</td>
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### The MRC breathlessness scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Degree of breathlessness related to activities</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Not troubled by breathlessness except on strenuous exercise</td>
</tr>
<tr>
<td>2</td>
<td>Short of breath when hurrying or walking up a slight hill</td>
</tr>
<tr>
<td>3</td>
<td>Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace</td>
</tr>
<tr>
<td>4</td>
<td>Stops for breath after walking about 100 m or after a few minutes on level ground</td>
</tr>
<tr>
<td>5</td>
<td>Too breathless to leave the house, or breathless when dressing or undressing</td>
</tr>
</tbody>
</table>

Zero for no breathlessness
In COPD there is decrease in all lung volumes
Laboratory tests:
- Hematocrit (polycythemia: no. of RBCs may be >55%). (compensatory mechanism)
- Arterial blood gases (ABGs) [sp. in patients with an FEV1 less than 40% predicted [severe] or respiratory failure (hypoxemia with or without hypercapnia) or S&S of cor-pulmonale.
- A1-antitrypsin level [sp. pat. <45 years, with COPD S&S, & family history of emphysema].
- Sputum bacterial analysis in case of patients with infection signs.

Non-Pharmacological:

I- Smoking Cessation

- slow the rate of decline in pulmonary function
- Reduce cough & sputum
- decrease airway reactivity
- Patients should be treated with a combination of counseling on behavioral and cognitive strategies and pharmacotherapy (mainly nicotine replacement therapy).
II- Pulmonary Rehabilitation

- It should cover a range of non-pulmonary problems including:
  - exercise de-conditioning,
  - relative social isolation,
  - altered mood states (especially depression),
  - muscle wasting, and
  - Weight loss.

III- Long-term O2 therapy

✓ In patients with chronic respiratory failure: give O2 therapy > 15 hrs/day to reduce mortality & improve life quality.

✓ Very severe COPD with:
  i) Resting PaO2 at or below 55 mm Hg
  ii) PaO2 between 55 and 60 mm Hg & evidence of pulmonary hypertension, peripheral edema (suggesting CHF), or polycythemia.

Use the dual-prong nasal cannula to deliver continuous O2 flow to O2 baseline saturation to at least 90% to oxygenate vital organs.

The flow rate (L/minute), must be during exercise, sleep & air travel (2L/min).

Oxygen therapy should be continued indefinitely.

IV- Surgery

Bullectomy & lung transplantation in very severe COPD improved spirometry, lung volumes, exercise capacity, dyspnea, health-related quality of life, and possibly survival.