Chronic Obstructive Pulmonary Disease (COPD)

There are two commonly recognized types of emphysema:

1. **Emphysema**
   - Two recognized causes of emphysema:
     - Polycythemia:
     - Arterial blood gases:
       - Productive cough:
       - Inflammation & fibrosis of the bronchial wall,
       - Hypothesis of thick, purulent sputum owing to:
         - Excess protease production
         - Inadequate antiprotease

2. **Chronic bronchitis**
   - Hypoxia:
     - Inadequate antiprotease
     - Increased elastase production
     - Persistent airway narrowing
     - Reduced elastic recoil in lung tissue supporting the airways results in increased
     - Hypercapnia, Cyanosis

Typically, the cough has been present for many years, with a gradual increase in acute exacerbations that produce frankly purulent sputum.

**Types**
- Chronic obstructive bronchitis
- Chronic bronchitis without airflow obstruction.

**Causes**
- It is associated with chronic irritation from smoking & recurrent infections.

In chronic bronchitis, airflow obstruction is caused by:
- Hypertrophy of the submucosal glands and small airways.
- There is edema and hyperplasia of submucosal glands and excess mucus secretion into the bronchial tree.

**Clinical Manifestations**

1. **Reduced elastic recoil:**
   - The lung's reduced ability to retract (deflate lung) can lead to obstructive lung disease, because:
     - Reduced elastic recoil (increased compliance) of the lung requires an increase in intrathoracic pressure for expiration, resulting in compression of the intrathoracic airways
     - Massive increase in flow resistance.

2. **Positive pressure in alveoli:**
   - Reduced lung's elastic recoil generates the positive pressure in the alveoli:
     - With loss of lung elasticity and hyperinflation of the lungs
     - Greater intrathoracic pressure is necessary for expiration because compliance and resistance are increased:
       - This causes compression of the bronchioles, hypoxia, airway pressure increases further.
     - The airways often collapse during expiration because pressure in surrounding lung tissue exceeds airway pressure, making it harder to breathe on expiration, producing an increase in the anteroposterior dimensions of the chest.
     - A bocca barrel

3. **External compression:**
   - Elastic recoil can be restored by increasing the inspiratory volume leading to a shift in the resting position toward inspiration (barrel chest).
   - Purpuric breathing:
     - Increases the resistance to the outflow of air, preventing airway collapse by increasing airway pressure.

**Histology**

Maximal expiratory flow rate (FEV1) is a function of the ratio between the elastic recoil (RE) and resistance (R).

- **Respiratory function:**
  - If tidal volume (TV) remains constant:
    1. Functional residual capacity (FRC)
    2. Residual volume (RV)
    3. Dead space

- Vital capacity (VC) because of the reduced expiratory volume.

1. **Homeostatic function:**
   - Resulting in a decrease in the ratio of the elastic recoil to resistance.
   - Reduced elastic recoil (increased compliance) of the lung requires an increase in intrathoracic pressure for expiration, resulting in compression of the intrathoracic airways
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1- Lung function tests:
- Show evidence of airflow limitation: FEV1/FVC ratio is reduced and/or PEF is low.
  - In many patients the airflow limitation is partly reversible (usually a change in FEV1 of ≥15%), and it can be difficult to distinguish between COPD and asthma.
- Lung volumes: be normal or increased.
- Carbon monoxide gas transfer factor: is low when significant emphysema is present.

2- Chest X-ray: see above in clinical manifestations.

3- High-resolution CT scans: when the plain chest X-ray is normal.

4- Haemoglobin level and PCV: can be elevated as a result of persistent hypoxaemia (2% polythraemia).

5- Blood gases:
  - Arterial normal: On exercise = patients desaturate.
  - In more advanced cases: 1- resting hypoxaemia and 2- hypercapnia.

6- Sputum examination:
  - Strip, pneumococcal and H. influenzae are the only common organisms to produce acute exacerbations.
  - Occasionally, Moraxella catarrhalis may cause infective exacerbations.

7- Electrocardiogram: Is often normal, but in advanced pulmonary hypertension:
  - P wave is tall (P pulmonale).
  - Right bundle branch block (RBBB) - RV hypertrophy.

8- Echocardiogram: Is useful to assess cardiac function where there is disproportionate dyspnoea.

9- α1-Antitrypsin: Levels & genotype are worth measuring in: 1- premature disease or 2- lifelong non-smokers.

Acute exacerbations of COPD:
- Invasive Mechanical Ventilation:
  - Bronchodilators:
    - Nebulised short-acting β2-agonists (salbutamol), combined with anticholinergic agent (ipratropium).
    - These may be administered separately or together.
  - Glucocorticoids:
    - 1- Reduce length of stay.
    - 2- hasten recovery.
    - 3- reduce chance of subsequent exacerbation or relapse for a period of up to 6 months.
  - The GOLD guidelines recommend oral prednisolone (30 mg) for a period of 2 weeks.
  - Antibiotics:
    - Patients with COPD are frequently colonized with potential respiratory pathogens. (pneumococcal, H. influenzae, M. catarrhalis).
    - Indications: Currently recommended for patients reporting increase in sputum purulence, sputum volume or breathlessness.
    - Regimens: Aminopenicillin or a macrolide. Co-amoxiclav or β-lactamase-producing organisms susceptible.
  - Mechanical Ventilatory Support:
    - Indications: 1- Severe respiratory distress despite initial therapy.
    - 2- Life-Threatening hypoxaemia.
    - 3- Severe hypercapnia or acidosis.
    - 4- Markedly impaired mental status.
    - 5- Respiratory arrest.
    - 6- Hemodynamic instability.

Pharmacotherapy

Reducing exposure to noxious particles & gases:
- Complete cessation of smoking is accompanied by:
  - 1- improvement in lung function.
  - 2- desaceleration in the rate of FEV1 decline.
- Pharmacologic approaches: 1- Bioprop  2- Nicotine replacement therapy as: gum, transdermal patch, inhaler 3- Varenicline, nicotin acid receptor agonist/antagonist.

Bronchodilators:
- Bronchodilator therapy is central to the management of breathlessness.
  - Compound bronchodilators, a selective β2 agonist and an antimuscarinic agent, are used.
  - Oral bronchodilator therapy may be used in patients who cannot use inhaled devices efficiently.
  - Significant improvements in breathlessness may be reported, despite minimal changes in FEV1 reflecting improvements in lung emptying that reduce dynamic hyperinflation.

β-Mimetic agents:
- In mild COPD: Short-acting β2-agonists: Salbutamol or Terbutaline.
- In moderate & severe COPD: Long-acting β2 agonists: Formotérol or Salmeterol.

Antimuscarinic drugs:
- In moderate & severe COPD: Long-acting anticholinergic agents: Ipratropium bromide.
  - Use: improve breathlessness and quality of life, but their use is limited by:
    - 1- side-effects: 2- unpredictable metabolism: 3- drug interactions.

Phosphodiesterase inhibitors:
- Roflumilast is an inhibitor with anti-inflammatory properties.
  - It is used as an adjunct to bronchodilators for the maintenance treatment of COPD patients.

Corticosteroids

Combination of:
- Corticosteroid with long-acting β agonist may protect against lung function decline BUT does not improve overall mortality.

Inhaled Corticosteroids (ICS):
- Indications:
  - Recommended in patients with severe disease (FEV1 < 50%) who report two or more exacerbations requiring antibiotics or oral steroids per year.
- Effects:
  - Reduces the frequency and severity of exacerbations.
  - Regular use is associated with a small improvement in FEV1 (but ICS do not alter the natural history of the FEV1 decline).

Oral Corticosteroids:
- Prednisolone 30 mg daily should be given for 2 weeks.

Oxygen therapy

Long-term domiciliary oxygen therapy (LTOT) will benefit patients who have:
- Arterial blood gases measured in clinically stable patients on optimal medical therapy at at least two occasions 3 weeks apart:
  - PaO2 < 55 mmHg irrespective of PaCO2 and FEV1 < 1.5L.
  - PaO2 55-60 mmHg, secondary polycythemia, pulmonary hypertension, peripheral oedema or nocturnal hypoaxemia.
  - Carbonylhaemoglobin of ≥3% (i.e. patients who have stopped smoking).

Use: at least 15 hrs/day at ≥4 L/min.
- A fall in pulmonary artery pressure: was achieved if oxygen was given for 15 hours daily.
- Substantial improvement in mortality: was only achieve if oxygen was given for 19 hours daily.

Other measures

Nonpharmacologic Therapies

Pulmonary rehabilitation:
- Exercise should be encouraged at all stages.
- Multidisciplinary programmes that incorporate:
  - 1- Physical training.
  - 2- Education and nutritional counselling.
  - 3- Improve health status and enhance confidence.

Surgical intervention
- Buv秘诀: Patients in whom large bullae compress surrounding normal lung tissue, who otherwise have minimal airflow limitation and a lack of generalised emphysema, are considered for bullectomy.
- Lung volume reduction surgery (LVRS): Patients with:
  - Predominantly upper lobe emphysema.
  - With preserved gas transfer.
  - No evidence of pulmonary hypertension.
  - Benefit from lung volume reduction surgery (LVRS), in which peripheral emphysematous lung tissue is resected with the aim of reducing hyperinflation and decreasing the work of breathing.

Lung Transplantation
- Candidates for lung transplantation: 1- < 65 years.
- 2- have severe disability despite maximal medical therapy.
- 3- free of comorbid conditions (liver, renal diseases).
- In contrast to LVRS, the anatomic distribution of emphysema AND presence of pulmonary hypertension are not contraindications to lung transplantation.