

Chronic Obstructive Lung Disease - Dr. Kawa

Chronic Bronchitis & Emphysema

COPD Definition

- COPD is a chronic, slowly progressive disorder characterized by airflow obstruction.
- (FEV1 is less than 80% of the predicted value and FEV1/FVC < 70%) which does not change markedly over several months.
- The impairment of lung function is largely fixed (irreversible) but may be partially reversible by bronchodilator therapy.
- COPD is unlike asthma, is not fully reversible

Chronic bronchitis

- Is defined when a cough and sputum occur on most days for at least 3 consecutive months for at least 2 successive years (provided other causes of cough had been excluded).
- The blue bloaters (Chronic bronchitis) is characterized by chronic productive cough, likely to be heavy (obese) and cyanotic & develop hypercapnia earlier and may develop edema and secondary polycythemia.

Emphysema

- Referred to the pathological process of a permanent destructive enlargement of the airspaces distal to the terminal bronchioles.
 - The 'pink puffers' (emphysema) is characterized by chronic cough, are typically thin and breathless, and maintain a normal PaCO₂ (non-cyanotic) at rest until the late stage of disease. Have prominent use of accessory muscles.
- Although pure form of chronic bronchitis & Emphysema do exist, there is considerable overlap in the vast majority of patients.
- (COPD predominantly chronic bronchitis or COPD predominantly Emphysema)
- In practice, these phenotypes often overlap.

Aetiology of COPD

RISK FACTORS FOR DEVELOPMENT OF COPD

- Exposures
 - Tobacco smoking.
 - Occupation-coal miners.
 - Outdoor and indoor air pollution
 - Low birth weight-may reduce maximally attained lung function in young adult life
 - Lung growth-insults including childhood infections or maternal smoking may affect growth of lung during childhood, resulting in a lower maximally attained lung function in adult life
 - Infections-recurrent infection may accelerate decline in FEV1. Persistence of adenovirus in lung tissue may alter local inflammatory response predisposing to lung damage. HIV infection associated with emphysema
- Host factors
 - Genetic factors- α 1-antiproteinase deficiency
 - Airway hyper-reactivity

- A variety of factors appear to increase the risk of developing COPD, but the single most important cause is cigarette smoking.
- Smoking causes its effect by inducing persistent airway inflammation & causing a direct imbalance in oxidant/antioxidant capacity & proteinase/antiproteinase load in the lungs
- Only 15% of smokers likely to develop clinically significant COPD & there is a familial risk associated with the development of COPD.
- Stopping smoking slows the average rate of the decline in FEV1 from 50 – 70 ml/ year to 30 ml/year (i.e. equal to non-smokers).
- Susceptibility to cigarette smoke varies but both the dose and duration of smoking appear to be important, and it is unusual to develop COPD with less than 10 pack years (1 pack year = 20 cigarettes/day/year).
- Alpha 1-antitrypsin deficiency can cause emphysema in non-smokers but this risk is increased dramatically in enzyme-deficient patients who smoke. 1–2% of COPD patients are found to have severe 1AT deficiency as a contributing cause of COPD,

If people stop smoking, receive early diagnosis and the right care, COPD's progression can be slowed down, enabling people to live healthy and active lives for longer

- COPD is largely a preventable disease; approximately 80% of cases are attributable to smoking.
- Occupational and environmental factors account for approximately 15%, and there is a genetic element in a small number of cases.
- COPD will rise from the sixth to the third most common cause of death worldwide by 2020.
- COPD is the fourth leading cause of death

Leading causes of death:

- Heart disease
- Cancer
- Cerebrovascular disease (stroke)
- Respiratory diseases (COPD)
- Accidents
- Pneumonia and influenza
- Diabetes
- Suicide
- Nephritis
- Chronic liver disease
- All other causes of death

Pathogenesis of COPD

Pathogenesis

- Tobacco smoking is the main risk factor for COPD, although other inhaled noxious particles and gases may contribute.
- In addition to inflammation, an imbalance of proteinases and antiproteinases in the lungs, and oxidative stress are also important in the pathogenesis of COPD.

Pathophysiology

- The different pathogenic mechanisms produce the pathological changes which, in turn, give rise to the physiological abnormalities in COPD:
 - Mucous hypersecretion and ciliary dysfunction,
 - Airflow limitation and hyperinflation,
 - Gas exchange abnormalities,
 - Pulmonary hypertension,
 - Systemic effects.

Pathophysiology

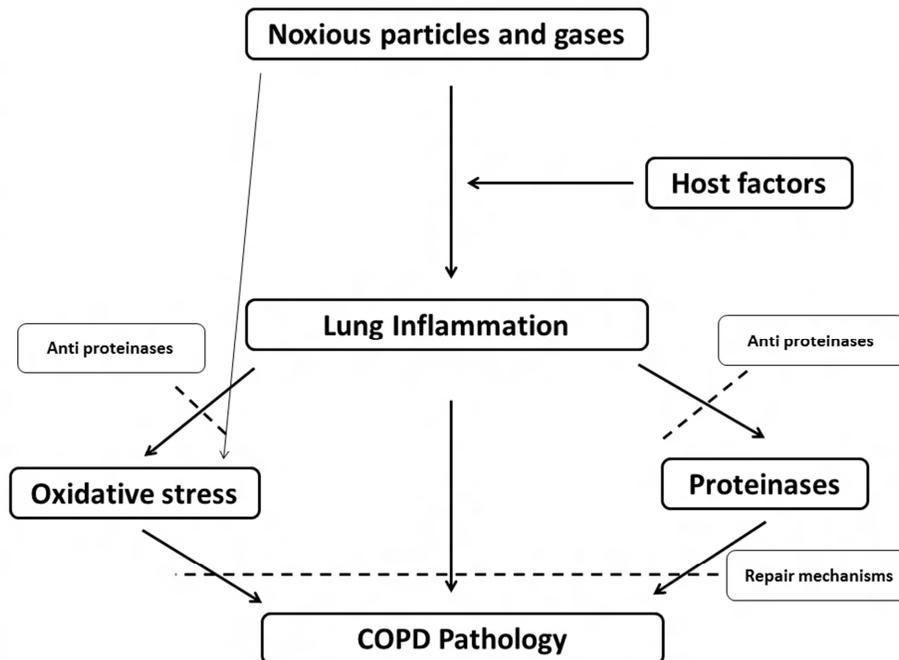
- COPD has both pulmonary and systemic components
- An enlargement of mucus-secreting glands and an increased number of goblet cells in the larger airways contribute to enhanced secretion of airway mucus that manifests as chronic bronchitis.
- Loss of elastic tissue surrounding the smaller airways, accompanied by inflammation and fibrosis in the airway wall and mucus accumulation within the airway lumen, results in airflow limitation, further increased by enhanced cholinergic tone.
- Premature airway closure leads to gas trapping and hyperinflation, which in turn decrease pulmonary and chest wall compliance.
- During exercise, the time available for expiration shortens, resulting in progressive hyperinflation.
- The work of breathing is therefore markedly increased, first on exercise but then, as the disease advances, at rest.
- In the alveolar capillary units the unopposed action of proteases and oxidants results in destruction of the alveoli and the appearance of emphysema
- Emphysema may be classified by the pattern of the enlarged airspaces: centriacinar, panacinar and periacinar.
- Bullae form in some individuals.
- In COPD there is often "air trapping" (increased residual volume and increased ratio of residual volume to total lung capacity) and progressive hyperinflation (increased total lung capacity) late in the disease.
- COPD may result in impaired gas exchange and respiratory failure.
- Inflammatory cells produce elastase
- Destroys connective tissue of alveolar walls
- Alpha-1 anti-trypsin (or alpha-1 protease inhibitor) is a protein produced by the liver that circulates in the blood and limits the action of elastase

Systemic effects of COPD

- Muscular weakness (cellular changes in skeletal muscles)
- Impaired salt & water excretion leading to peripheral edema.
- Altered fat metabolism contributing to weight loss
- Increased prevalence of osteoporosis.
- Increased circulating inflammatory markers.

Pathogenesis of COPD

Noxious Agent (tobacco smoke, pollutants, occupational agent) $\xrightarrow{\text{genetic factors, respiratory infection, other}}$ COPD



Clinical features of COPD

- Clinical features COPD should be suspected in any patient over the age of **40 years** who presents with symptoms of **persistent cough, sputum production, and breathlessness**.
- Many patients have such symptoms for months or years before seeking medical attention
- Depending on the presentation important differential diagnoses include asthma, tuberculosis, bronchiectasis and congestive cardiac failure.
- Chronic severe asthma may be difficult to distinguish from COPD.
- **Cough** is usually the first symptom but seldom prompts the patient to consult a doctor.
 - It is characteristically accompanied by small amounts of mucoid sputum.
 - Chronic bronchitis is formally defined when a cough and sputum occur on most days for at least 3 consecutive months for at least 2 successive years.
- **Haemoptysis** may complicate exacerbations of COPD but should not be attributed to COPD without thorough investigation.
- **Breathlessness** usually heralds the first presentation to the health professional.
- In advanced disease, enquiry should be made as to the presence of **edema** (which may be seen for the first time during an exacerbation) and **morning headaches** indicative of hypercapnia.

Physical signs

- The presence of pitting edema should be documented and the body mass index (BMI) recorded.
- Crackles may accompany infection but if persistent raise the possibility of bronchiectasis.
- Finger clubbing is not consistent with COPD and should alert the physician to potentially more serious pathology.
- Two classical phenotypes have been described: 'pink puffers' and 'blue bloaters'.
- The 'pink puffers (emphysema) are typically thin and breathless, and maintain a normal PaCO₂ (noncyanotic) at rest until the late stage of disease. have prominent use of accessory muscles,
- The 'blue bloaters (chronic bronchitis) likely to be heavy and cyanotic & develop hypercapnia earlier and may develop edema and secondary polycythaemia.
- In practice, these phenotypes often overlap.

Clinical Abnormalities in patients with advanced Airway obstruction (COPD)

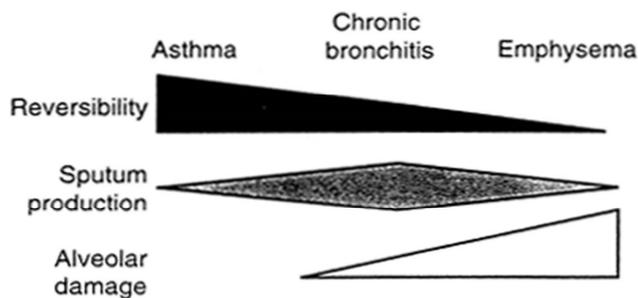
- A reduction in the length of the *trachea* palpable above the sternal notch.
- Tracheal descent during inspiration(*tracheal tug*)
- Contraction of the *sternomastoid and scalene* muscles on inspiration
- Excavation of the *suprasternal and supraclavicular fossae* during inspiration, together with indrawing of the costal margins and intercostal spaces.
- *Loss of weight* (often stimulates unnecessary investigation)
- *Pursed lip breathing* – physiological response to decrease air trapping.
- *Central cyanosis*
- *Flapping tremor and bounding pulse* (due to hypercapnia)
- Increased antero-posterior diameter of the chest relative to the lateral diameter (signs of hyperinflation include a *barrel chest*).
- Decreased *tactile vocal fremitus*.
- *Hyperresonant percussion note*
- *Loss of cardiac & hepatic dullness*
- *Decreased breath sounds*; prolonged expiratory phase and expiratory wheezing. (Rhonchi, especially on forced expiration).
- Peripheral *edema* which may indicate cor pulmonale
- *Raised JVP, right ventricular heave, loud pulmonary second sound, tricuspid regurgitation.*
- Advanced disease may be accompanied by *systemic wasting*, with significant weight loss, bitemporal wasting, and diffuse loss of subcutaneous adipose tissue. This syndrome has been associated with both inadequate oral intake and elevated levels of inflammatory cytokines (TNF-). Such wasting is an independent poor prognostic factor in COPD.
- *Clubbing* of the digits is not a sign of COPD, and its presence should alert the clinician to initiate an investigation for causes of clubbing. In this population, the development of lung cancer is the most likely explanation for newly developed clubbing

ASSESSMENT OF SEVERITY OF AIRFLOW OBSTRUCTION ACCORDING TO FEV1

(Classification of COPD according to the severity)

Severity	FEV1
• Mild	50-80% predicted
• Moderate	30-49% predicted
• Severe	< 30% predicted

CHRONIC OBSTRUCTIVE PULMONARY DISEASE:



Complications of COPD

Pulmonary bullae:

- Are thin-walled airspaces created by rupture of alveolar walls. They may be single or multiple, large or small & tend to be situated subpleurally, Rupture of subpleural bullae may cause pneumothorax, & occasionally bullae increase in size, compress functioning lung tissue & further embarrass pulmonary ventilation.
- Respiratory failure & cor pulmonale are generally late complications in COPD patients.

COPD Investigations

Pulmonary function tests

- The diagnosis of COPD requires objective demonstration of airflow obstruction by spirometry and is established when FEV1 is less than 80% of the predicted value and accompanied by FEV1/FVC < 70%
- normal FEV1 exclude the diagnosis of COPD
- Reversibility test is necessary to detect asthmatic cases.
- Lung volumes show an increase in TLC & RV due to gas trapping
- The carbon monoxide transfer factor & coefficient are markedly reduced in patients with severe emphysema component

Diagnosis of COPD

Symptoms

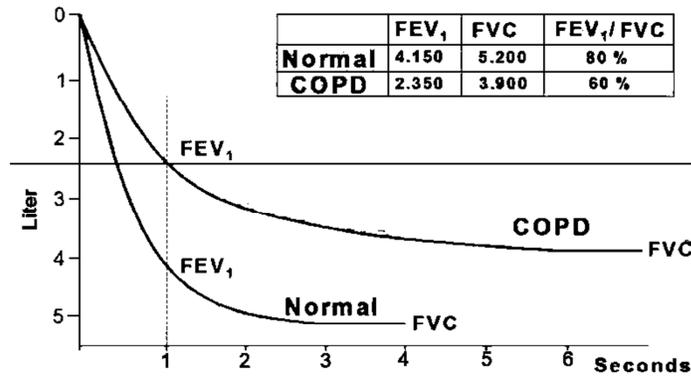
- Cough
- Sputum
- dyspnea

Exposure to risk factors

- Tobacco
- Occupation
- Indoor/outdoor pollution

Spirometry

Spirometry: Normal and COPD



Measurement of arterial blood gases

- Should be performed in all patients with severe COPD (FEV1 less than 40%)
- Alveolar underventilation causes a fall in paO₂ & often a permanent increase in PaCO₂.
- **Pulse oximetry** may prompt referral for a domiciliary oxygen assessment if less than 93%.

Imaging

1- Chest X-ray

- In moderate to severe COPD the chest X-ray typically shows :
 - Hypertranslucent lung fields
 - With disorganisation of vasculature
 - Low flat diaphragm
 - Prominent pulmonary artery shadows at both hila.
 - Bullae may also be observed.
- ❖ Chest X-ray is essential to identify alternative diagnoses such as cardiac failure, other complications of smoking such as lung cancer.

2- Scan of chest

- Can be used to quantify the extent & distribution of emphysema & for the assessment of bullous emphysema & the potential for lung volume reduction surgery or lung transplantation.
- CT is likely to play an increasing role in the assessment of COPD as it allows the detection, characterisation and quantification of emphysema and is more sensitive than the chest X-ray at detecting bullae
- Patients with α 1-antitrypsin deficiency typically display basal disease , compared with the predominantly apical disease seen in smokers with normal α 1-antitrypsin level

Haematology

- Polycythemia (secondary Polycythemia) may develop, but should not be assumed to be secondary without measurement of paO₂
- Venesection may be considered if the haematocrit is above 0.55
- In younger patients with predominantly basal emphysema, α ₁- antitrypsin level should be assayed.

Management of COPD

Reduction of bronchial irritation:

- Smoking cessation: Advise and assist the patient toward smoking cessation. Cessation is difficult but highly rewarding and remains the only intervention proven to decelerate the decline in FEV1.
- Dusty & smoke laden atmospheres should be avoided reduction of occupational exposure (this may involve a change of occupation).
- Reduction of total personal exposure to tobacco smoke, occupational dusts and chemicals, and indoor and outdoor air pollutants are important goals to prevent the onset and progression of COPD.
- Smoking cessation is the single most effective - and cost effective - intervention to reduce the risk of developing COPD and stop its progression.

Bronchodilators

- Bronchodilator therapy is central to the management of breathlessness in patients with COPD.
- The principal bronchodilator treatments are beta2-agonists, anticholinergics, theophylline, and a combination of these drugs
- The inhaled route is preferred.
- Short-acting bronchodilators may be used for patients with mild disease but longer-acting bronchodilators are more appropriate for patients with moderate to severe disease.
- Oral bronchodilator therapy may be used in patients who cannot use inhaled devices efficiently. .
- Bronchodilator therapy with regular inhaled anticholinergic agents & short acting B2 agonists taken as required provides useful symptomatic relief in the majority of patients.
- The choice between beta2-agonist, anticholinergic, theophylline, or combination therapy depends on availability and individual response in terms of symptom relief and side effects.
- Combining bronchodilators may improve efficacy and decrease the risk of side effects compared to increasing the dose of a single bronchodilator

Corticosteroids

- Inhaled corticosteroids (ICS) reduce the frequency and severity of **exacerbations**.
- They are currently recommended in patients with severe disease (**FEV1 < 50 %**) who report two or more exacerbations requiring antibiotics or oral steroids per year.
- The combination of ICS with long-acting β 2-agonists produces further improvement in breathlessness and reduces the frequency and severity of exacerbations.
- Oral corticosteroids are useful during exacerbations but maintenance therapy contributes to osteoporosis and impaired skeletal muscle function and should be avoided.

Other measures

- Exercise should be encouraged & outpatient based pulmonary rehabilitation programs, while not affecting the FEV1, can improve exercise performance & reduce breathlessness.
- Obesity, poor nutrition, depression & social isolation should be managed.
- Sedatives & opiate-based analgesic preparations are contraindicated.

LONG-TERM DOMICILIARY OXYGEN THERAPY

- In patients with COPD Long term low – concentration oxygen therapy (2 litres/min by nasal canulae for ≥ 15 hrs/day intermittently)
- It reduces secondary polycythemia, decrease pulmonary hypertension & improves neuropsychological health & most importantly prolongs life in hypoxemic COPD patients.
- The aim of therapy is to increase the PaO₂ to at least 8 kPa (60 mmHg) or SaO₂ at least 90%
- High concentrations of oxygen may cause respiratory depression and worsening acidosis

PRESCRIPTION OF LONG-TERM OXYGEN THERAPY (LTOT) IN COPD

- Arterial blood gases measured in clinically stable patients on optimal medical therapy on at least two occasions 3 weeks apart.
- PaO₂ ≤ 7.3 kPa (55 mmHg) irrespective of PaCO₂ and FEV₁ ≤ 1.5 liters
- PaO₂ 7.3 - 8 kPa (55-60 mmHg) plus pulmonary hypertension, peripheral edema or nocturnal hypoxemia
- Patient stopped smoking.
- Use at least 15 hours/day at 2-4 liters/min to achieve a
- PaO₂ > 8 kPa (60 mmHg) without unacceptable rise in PaCO₂

Treatment of respiratory infection:

- Respiratory infection should be treated promptly because it aggravate breathlessness & may precipitate type II respiratory failure in patients with severe airflow obstruction.
- Purulent sputum is treated with amoxicillin (or clarithromycin), cephalosporin pending sputum culture results.
- Co-amoxiclav should be used if there is no response or if a B-lactamase producing organism is cultured.
- The usual causative organisms are Streptococcus pneumoniae or Haemophilus influenzae.
- A 5-10 day course of treatment is usually effective.
- Influenza immunisation should be offered to all patients each year , and, as appropriate, pneumococcal vaccination

Surgical intervention

- A very small group of patients are suitable for surgical intervention.
- Young patient, particularly those with $\alpha 1$ - antitrypsin deficiency & severe disease, should be considered for lung transplantation (usually single lung)
- Bullectomy. Surgical removal of expanding or very large bullae
- Young patients with minimal airflow limitation and a lack of generalised emphysema, but in whom large bullae compress surrounding normal lung tissue, may be considered for bullectomy.
- Lung volume reduction surgery: the most severely affected areas of emphysematous lung are removed (removes peripheral emphysematous lung tissue) & this will reduce hyperinflation and decreasing the work of breathing.

Management of COPD by Severity of Disease

- Stage 0: At risk
- Stage I: Mild COPD
- Stage II: Moderate COPD
- Stage III: Severe COPD
- Stage IV: Very Severe COPD

Stage 0: At Risk

- **Characteristics:** Chronic symptoms (cough, sputum), No spirometric abnormalities
- **Recommended treatment:** Reduction of bronchial irritation

Stage I: Mild COPD

- **Characteristics:** $FEV_1/FVC < 70\%$, $FEV_1 > 80\%$ predicted, with or without chronic symptoms
- **Recommended treatment:** short-acting bronchodilator as needed

Stage II: Moderate COPD

- **Characteristics:** $FEV_1/FVC < 70\%$, $50\% < FEV_1 < 80\%$ predicted, with or without chronic symptoms
- **Recommended treatment:** short-acting bronchodilators as needed, regular treatment with one or more long-acting bronchodilators, rehabilitation

Stage III: Severe COPD

Characteristics: $FEV_1/FVC < 70\%$, $30\% < FEV_1 < 50\%$ predicted, with or without chronic symptoms

Recommended treatment: short-acting bronchodilators as needed, regular treatment with one or more long-acting bronchodilators, inhaled glucocorticosteroids if repeated exacerbations, rehabilitation

Stage IV: Very Severe COPD

- **Characteristics:** $FEV_1/FVC < 70\%$, $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure
- **Recommended treatment:** Short-acting bronchodilator as needed, Regular treatment with one or more long-acting bronchodilators, Inhaled glucocorticosteroids if repeated exacerbations, Treat complications, Rehabilitation, Long-term oxygen therapy if respiratory failure, Consider surgical options

Acute exacerbations of COPD

- Acute exacerbations of COPD are characterised by an increase in symptoms and deterioration in lung function and health status.
- They become more common as the disease progresses and may be caused by bacteria, viruses or a change in air quality.
- They may be accompanied by the development of respiratory failure and/or fluid retention and represent an important cause of death

Management of acute COPD exacerbations

- **Causes of COPD exacerbation:** The most common causes of exacerbation are infection of the tracheobronchial tree and air pollution, but the cause of about one-third of severe exacerbations cannot be identified
- **Features of acute exacerbation of COPD:** Acute exacerbation of COPD can present as increased sputum volume & purulence, increased breathlessness & wheeze, chest tightness & sometimes fluid retention.
- **The differential diagnosis includes:** pneumonia, pneumothorax, left ventricular failure, pulmonary embolism, lung cancer & upper airway obstruction.

Indications for hospital admission:

- Severe breathlessness
- Cyanosis
- Worsening edema
- Impaired conscious level

Lines of management of acute COPD exacerbation

In the community

- Add or increase bronchodilator therapy.
- Antibiotics:
 - Patients experiencing COPD exacerbations with clinical signs of airway infection (e.g., increased volume and change of color of sputum, and/or fever) may benefit from antibiotic treatment.
- Oral corticosteroids:
 - If the patient already on oral corticosteroid
 - If previous response to such treatment
 - If airflow obstruction fails to respond to bronchodilator therapy
 - If first presentation of disease
- (Prednisolone 30 mg daily for 1 week)

In hospital

- **Investigations:** Check arterial blood gases, CXR, ECG, full blood count, urea & electrolytes, measure FEV1 + peak flow, send sputum for culture.
- **Oxygen:** 24 – 28 % via mask, 2 litres/min, Check arterial blood gases within 60 mins & adjust according to p_aO₂ (try to keep equal or more than 7.5 kpa) & CO₂ / pH. (High concentrations of oxygen may cause respiratory depression and worsening acidosis).
- **Bronchodilators:** nebulised B2 agonist (+ ipratropium bromide if severe) 4-6 hourly. If no response consider i.v. aminophylline infusion.
- **Antibiotics**
- **Oral corticosteroid.**
- **Diuretics:** indicated if JVP elevated & edema present
- **Ventilatory support:** If pH less than 7.35 & p_aCO₂ more than 6, consider ventilatory support (invasive or non-invasive IPPV).
- **Doxapram:** If patient continuing to deteriorate despite non-invasive ventilatory support, & endotracheal intubation not indicated (e.g. significant comorbidity), doxapram can be considered. may be useful for a limited period in selected patients with a low respiratory rate.
- **Heparin:** Prophylactic subcutaneous low molecular weight heparin.

Air travel

- Medical assessment is required in all patients who are dyspnoeic on walking 50 m.
- All patients with resting paO_2 on air of less than 9.0 kpa will require supplemental oxygen since at usual in-flight cabin pressures equivalent to an altitude of 5000-8000 feet the paO_2 of such patient will fall below 7 kpa
- Hypercapnia or gross hypoxaemia while breathing air (PaO_2 less than 6.7 kpa) is a relative contraindication to air travel.
- Additional hazards include expansion of emphysematous bullae & abdominal gases & drying of bronchial secretions.

Prognosis of COPD

- The best guide to the progression of COPD is the decline in FEV1 over time(normally 30 ml/year).
- The prognosis is inversely related to age & directly related to the post-bronchodilator FEV1 .
- Poor prognostic indicators include:
 - Pulmonary hypertension
 - Weight loss (survival is negatively correlated with BMI)
- The mean survival of patients admitted with an acute exacerbation of COPD associated with an elevated paCO_2 that reverts to normal on recovery is **3 years**.
- Factors may improve survival in patients with COPD:
 - Stop smoking
 - Long term oxygen therapy
 - Yearly Influenza vaccination