

Lecture 10

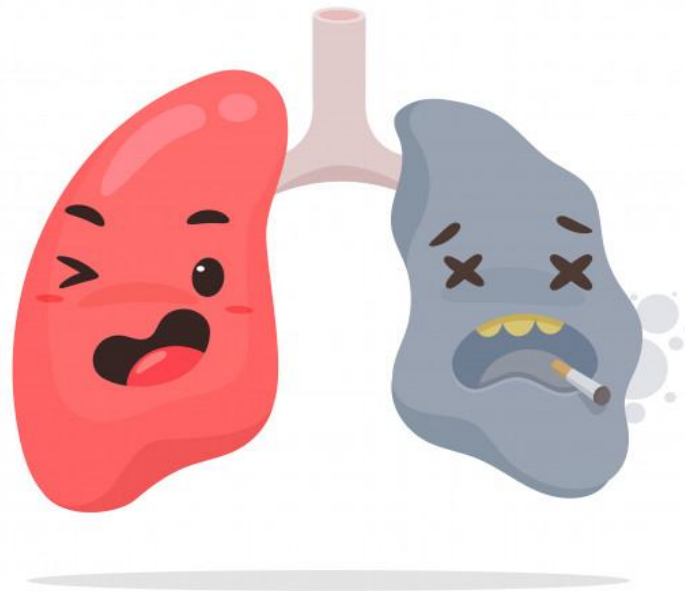
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Reviewed By



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COPD and Bronchiectasis

Objectives:

- ★ What's COPD
- ★ The definition of airway obstruction
- ★ Causes of COPD
- ★ Clinical presentation and diagnosis
- ★ Management of COPD
- ★ To know the definition of bronchiectasis
- ★ Discuss the radiological features and etiology
- ★ To know the principles of management

Color index:

Original text Females slides Males slides
Doctor's notes Textbook Important Golden notes Extra

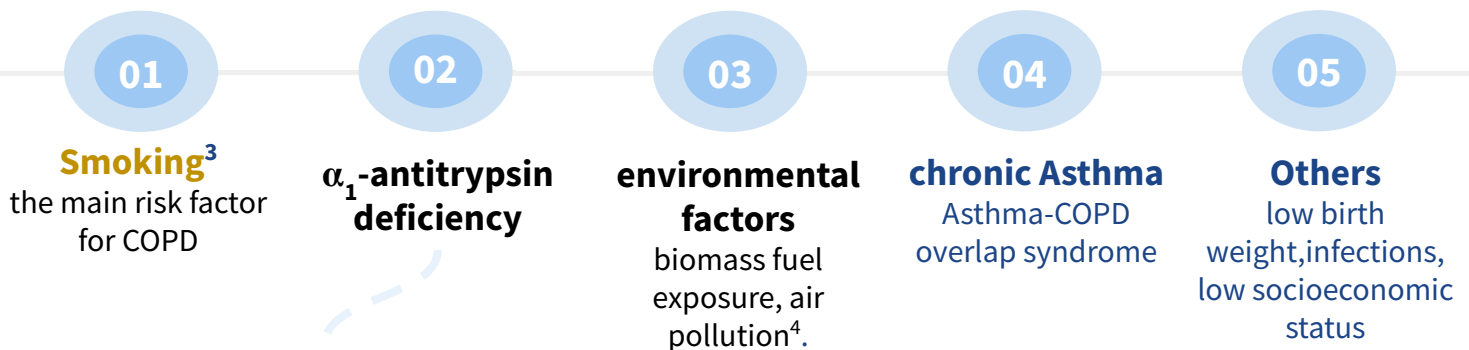
Definition

Chronic Obstructive Pulmonary Disease (COPD) is a common, **preventable** and **treatable** but not fully reversible disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

◀ Epidemiology

- higher in **smokers** and ex-smokers compared to non-smokers, **cigarette smoking accounts for 90% of cases in developed countries. However, only 10-20% of smokers develop COPD, indicating individual susceptibility (host factors).**
- **Higher ≥ 40 year group** compared to those < 40 , Higher in men than women¹
- Estimated 384 million COPD cases in 2010.
- **The prevalence of smoking is increasing all over the world²**
- Three million deaths annually by COPD, predicted to increase to 4.5 million by 2030.

◀ Risk factors



➔ α_1 -antitrypsin deficiency (AATD):

- Alpha-1-antitrypsin is a protease inhibitor that is synthesized in the liver and protects elastin from breakdown by neutrophil elastase. (Elastin is essential for the lung elasticity and recoiling).
- AATD patients are typically < 45 years with **panlobular basal emphysema** (destruction of airways due to relative excess in protease (elastase) activity that is released by PMNs, or relative deficiency of antiprotease (AATD) activity in the lung.)
- There are 2 types of A1AD:
 - **Functional A1AD:** occurs due to **tobacco smoking**. Smoking induces the release of ROS which may eventually inactivate alpha1-antitrypsin leading to increased elastase (Protease-antiprotease imbalance) which will lead to destruction of lung parenchyma.
 - **Congenital A1AD:** Autosomal co-dominant disorder due to a mutation in SERPINA1 gene, patients usually present with hepatitis and liver cirrhosis
- WHO recommends that all patients with a diagnosis of COPD should be screened once especially in areas with high AATD prevalence.
- Delay in diagnosis in older AATD patients presents as more typical distribution of emphysema (centrilobular apical).
- A low concentration ($< 20\%$ normal) is highly suggestive of homozygous deficiency

1: Nowadays this might have changed, as the prevalence of smoking is increasing among women

2: Is using E-cigarettes to quit tobacco smoking effective? Studies have shown that those who try to use E-cigarettes to stop tobacco smoking usually end up smoking both (Tobacco and E-cigarettes), so...no.

3: **Smoking is the most common cause of COPD.** Tobacco smoking increases number of activated PMNs and macrophages and digests human lungs, this is inhibited by α_1 -antitrypsin

4: climate and air pollution are lesser causes of COPD, but mortality from COPD increases dramatically during periods of heavy atmospheric pollution.

Pathology & pathophysiology¹

- COPD is characterized by: **structural changes** (emphysema) and **chronic inflammation** (chronic bronchitis) leading to:

1 Airflow limitation and gas trapping

2 Gas exchange abnormalities

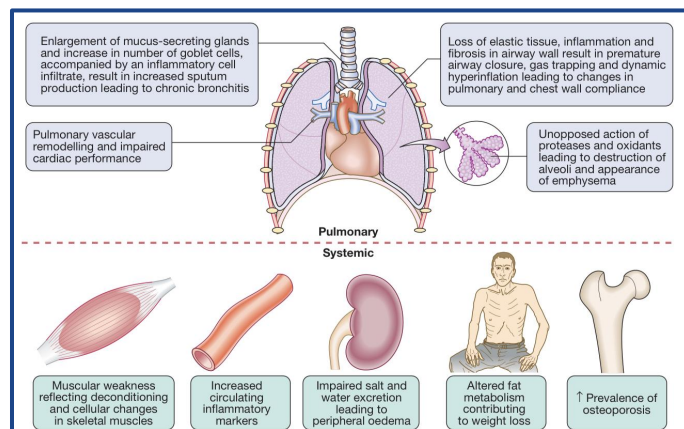
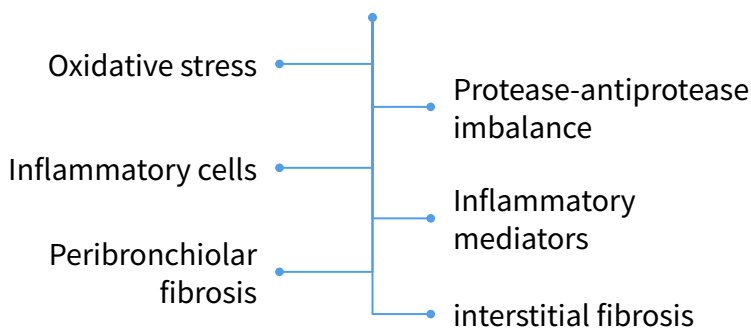
3 mucus hypersecretion²

4 Pulmonary hypertention³

→ Cor Pulmonale

- Definition:** symptoms and signs of fluid overload secondary to lung disease. The fluid retention and peripheral oedema is due to failure of excretion of sodium and water by the hypoxic kidney rather than heart failure.
- Characteristics:**
 - Pulmonary hypertension
 - Right ventricular hypertrophy.
- Signs and Symptoms:**
 - Initially there may be a prominent parasternal heave (due to right ventricular hypertrophy) and a loud pulmonary second sound.
 - central cyanosis (owing to the lung disease) → patient later becomes more breathless
 - ankle oedema.
- In case of very severe pulmonary hypertension → the pulmonary valve becomes incompetent.
- In case of severe fluid overload → tricuspid incompetence may develop → elevated jugular venous pressure (JVP), ascites and upper abdominal discomfort due to liver swelling.

Pathogenesis⁴



1- Pathology: Damage to the airways. Pathogenesis: the inflammatory process. Pathophysiology: the outcomes of the disease

2- due to increased numbers of goblet cells, especially in larger bronchi, narrows the airway and causes productive cough.

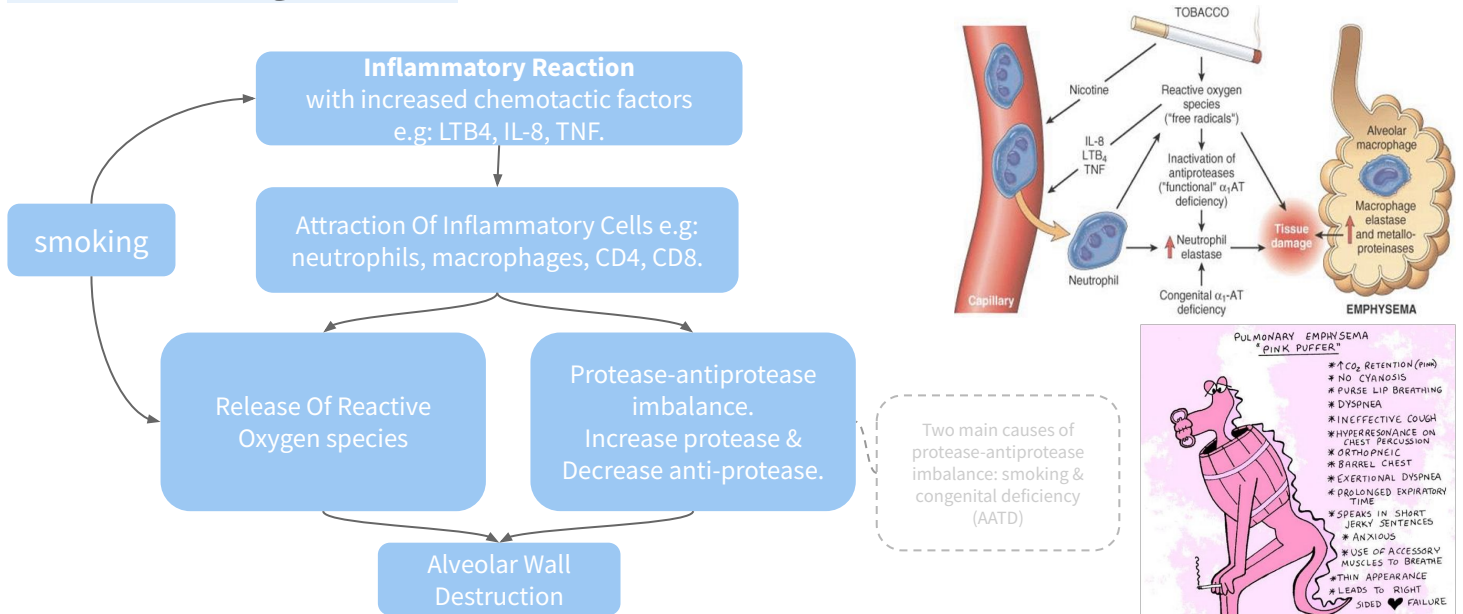
3- flattens the diaphragm, leads to increasingly horizontal alignment of intercostal spaces resulting in right sided HF (cor pulmonale)

4- COPD isn't just limited to the lungs, you could have inflammation elsewhere in the body (as seen in the pic). What are the most common causes of death in COPD patients? Lung cancer, Cardiovascular diseases and respiratory failure

Definition

Permanent **enlargement of the airspaces** distal to the terminal bronchioles accompanied by destruction of their walls, **without obvious fibrosis**. (Associated with loss of recoil and support of small airways → tendency to collapse with obstruction)

Pathogenesis



Two main causes of protease-antiprotease imbalance: smoking & congenital deficiency (AATD)



Types of emphysema

	Centriacinar (centrilobular) "Most common"	Panacinar (panlobular)	Distal acinar (paraseptal)	Irregular
Location	Central or Proximal alveoli of the acini.	Uniform injury, total damage of the alveoli.	The distal alveoli of the acinus.	Can affect any part of the respiratory tract.
Cause	Smoking	Genetic condition: Alpha-1 antitrypsin deficiency	Unknown	Invariably associated with scarring such as that resulting from healed inflammatory diseases.
Features	Common in upper Lobes.	- Common in lower lobes. - leads to V_A / Q mismatch	- adjacent to areas of fibrosis or atelectasis. - More severe in the upper half of the lungs	Asymptomatic.

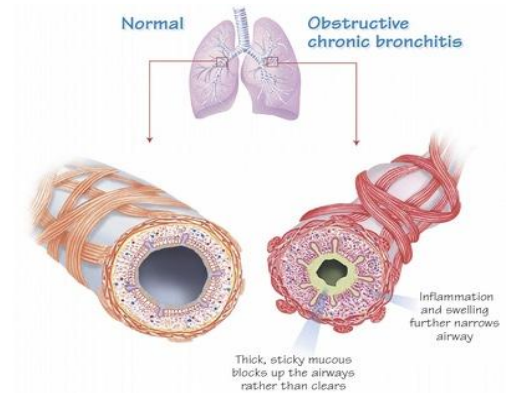
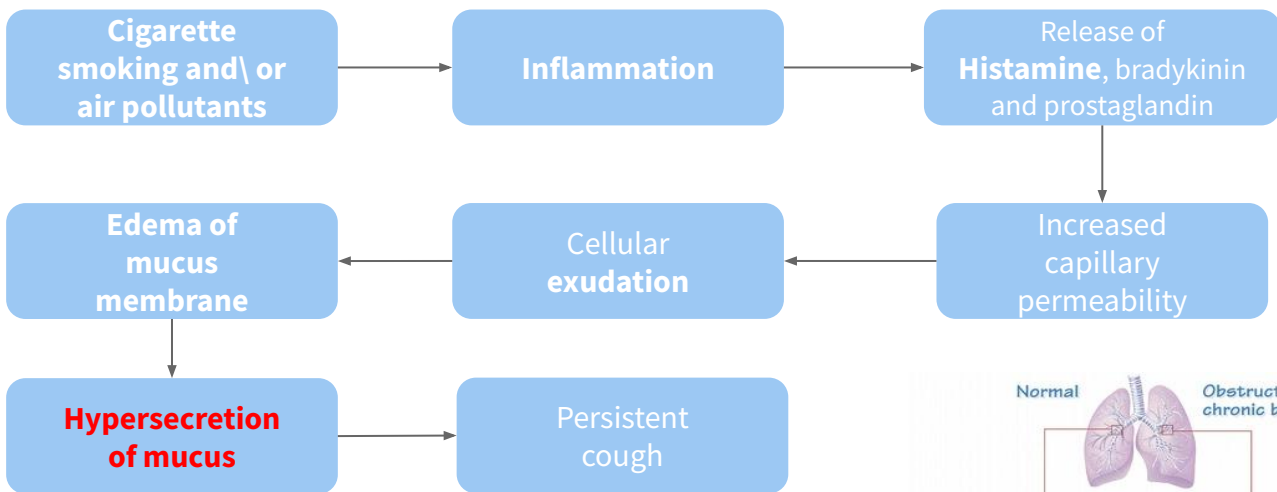
- Emphysema leads to **expiratory airflow limitation** and **air trapping**. The loss of lung elastic recoil results in an **increase in TLC**. Premature closure of airways limits expiratory flow while the loss of alveoli decreases capacity for gas transfer.
- **V_A / Q mismatch**: due to damage and mucus plugging of smaller airways from chronic inflammation, and partly due to rapid closure of smaller airways in expiration owing to loss of elastic support. The mismatch leads to a fall in PaO₂ and increased work of respiration.

Definition

A chronic obstructive airway disease characterized by the presence of chronic productive cough that Persists for at least 3 consecutive months in at least 2 consecutive years.

Pathogenesis

The distinctive feature of chronic bronchitis is **hypersecretion of mucus**, beginning in the large airways.



An area for your notes



Clinical features

Signs & symptoms

chronic and prgressive dyspnea

cough

sputum production

wheezing & chest tightness

fatigue, weight loss, anorexia, syncope¹,
rib fractures², ankle swelling, depression
& anxiety

tachypnea, prolonged expiration, pursing
of the lips on expiration, and loss of the
normal cardiac and liver dullness.

Other causes of chronic cough

Intrathoracic

- Asthma
- Tuberculosis
- lung cancer
- bronchiectasis
- left heart failure
- interstitial lung disease
- cystic fibrosis
- idiopathic cough

Extrathoracic

- chronic allergic rhinitis
- post nasal drip syndrome (PNDS)
- Upper airway cough syndrome (UACS)
- Gastroesophageal reflux disease (GEGD)
- Medication (eg: ACEI)

diagnosis and investigations



Pulmonary function tests

The only diagnostic investigation

- **Reduced FEV1: FVC ratio**
- Reduced PEFR.
- In many patients the airflow limitation is partly reversible (usually a change in FEV 1 of <15%), and it can be difficult to distinguish between COPD and asthma.
- Lung volumes may be normal or increased.
- Carbon monoxide gas transfer factor is low when significant emphysema is present.
- Recall that asthma is reversible, and to diagnose asthma we do a bronchodilator test, so to rule-out asthma all your measures should be post bronchodilator.

Classification of airflow limitation severity in COPD (Based on post Bronchodilator)

In Patients with FEV1/FVC < 70%		
Gold 1:	mild	FEV1 ≥ 80% of predicted
Gold 2:	moderate	50% ≤ FEV1 < 80% of predicted
Gold 3:	severe	30% ≤ FEV1 < 50% of predicted
Gold 4:	very severe	FEV1 < 30% of predicted

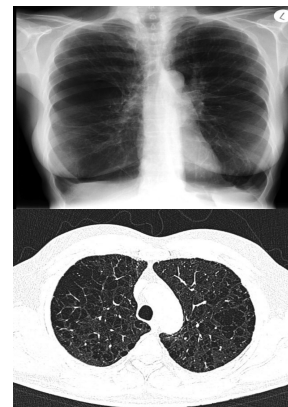
1: This may occur due to severe bouts of coughing which may induce valsalva maneuver leading to syncope.

2: The cough in COPD will be so bad that the amount of force generated in the chest is very high leading to rib fracture.



Radiological studies

- **CXR**
 - often **normal**, even when the disease is advanced.
 - The classic features are overinflation¹ of the lungs with low, flattened diaphragms, and sometimes the presence of large bullae.
 - Blood vessels may be ‘pruned’ with large proximal vessels and relatively little blood visible in the peripheral lung fields.
 - **Hyperlucent lungs: Less lung markings**
- **CT**
 - Might be helpful when CXR is normal.
 - **Tissue destruction: if you compare the trachea and the lung tissue, it’s almost the same**




Choices of threshold

➔ **Modified Medical Research Council (mMRC) questionnaire:**

Modified Medical Research Council (MRC) dyspnoea scale	
Grade	Degree of breathlessness related to activities
0	No breathlessness, except with strenuous exercise.
1	Breathlessness when hurrying on the level or walking up a slight hill
2	Walks slower than contemporaries on level ground because of breathlessness or has to stop for breath when walking at own pace.
3	Stops for breath after walking about 100 m or after a few minutes on level ground.
4	Too breathless to leave the house, or breathless when dressing or undressing

➔ **COPD Assessment Test (CAT™):**



Your name: _____
 Today's date: _____

How is your COPD? Take the COPD Assessment Test™ (CAT)
 This questionnaire will help you and your healthcare professional to measure the impact that COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers and test score can be used by you and your healthcare professional to help improve the management of your COPD and gain the greatest benefit from the treatment.

For each item below, place a mark (X) in the box that best describes your current situation. Please ensure that you only select one response for each question.

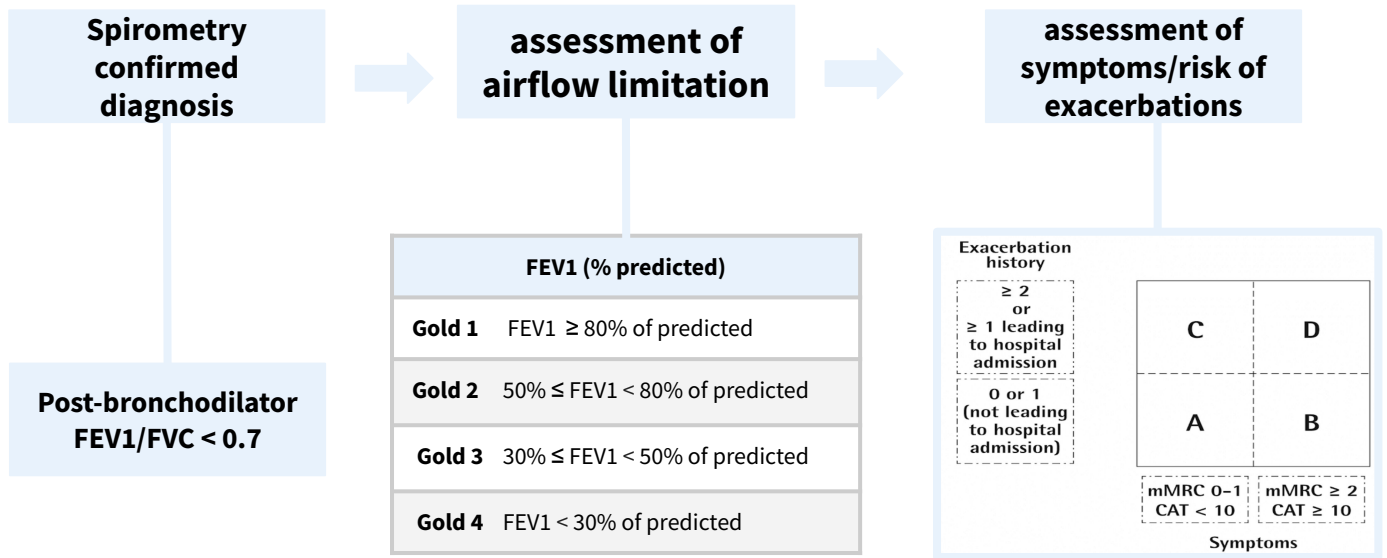
Example: I am very happy 1 2 3 4 5 I am very sad

		SCORE
I never cough	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I cough all the time <input type="checkbox"/>
I have no phlegm (mucus) on my chest at all	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	My chest is full of phlegm (mucus) <input type="checkbox"/>
My chest does not feel tight at all	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	My chest feels very tight <input type="checkbox"/>
When I walk up a hill or a flight of stairs I am not out of breath	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	When I walk up a hill or a flight of stairs I am completely out of breath <input type="checkbox"/>
I am not limited to doing any activities at home	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I am completely limited to doing all activities at home <input type="checkbox"/>
I am confident leaving my home despite my lung condition	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I am not confident leaving my home at all because of my lung condition <input type="checkbox"/>
I sleep soundly	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I do not sleep soundly because of my lung condition <input type="checkbox"/>
I have lots of energy	<input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I have no energy at all <input type="checkbox"/>
TOTAL SCORE		<input type="checkbox"/> <input type="checkbox"/>

A COPD assessment test was developed by an interdisciplinary group of international COPD experts with support from GSK. GSK's activities in connection with the COPD assessment test are monitored by a supervisory council that includes external, independent experts, one of which is chair of the council. CAT, the COPD assessment test and the CAT logo are trademarks that belong to the GSK group of companies. ©2009 GSK. All rights reserved.

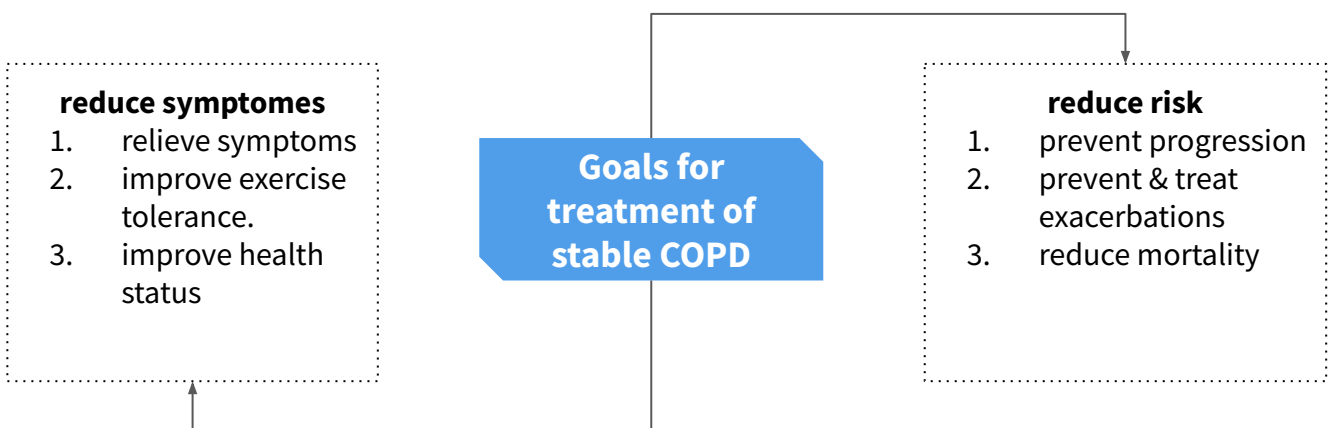
1: If you count the ribs you'll find 11 posterior ribs at the midclavicular line above diaphragm (Sign of hyperinflation).

ABCD of COPD¹




Management of COPD

- Once COPD has been diagnosed, effective management should be based on an individualized assessment to reduce both **current symptoms** and **future risks of exacerbations**.



¹: It's important to understand this, as it will guide you in management

1- non-pharmacological treatment

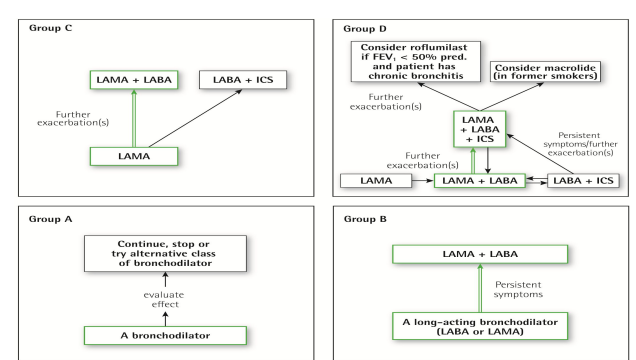
<h3>Smoking cessation¹</h3>	<ul style="list-style-type: none"> ● Smoking cessation has the greatest capacity to influence the natural history of COPD. ● If effective resources and time are dedicated to smoking cessation, long-term quit success rates of up to 25% can be achieved. Reduces mortality. ● May slow down the rate of deterioration and prolong time before disability and death even in advanced disease.  <p>The graph plots the percentage of FEV1 value at age 25 years against age in years (25, 50, 75). Three curves are shown: 1) 'Never smoked or not susceptible to its effects' (blue line) which remains at 100% until age 40 and then slowly declines. 2) 'Stopped at 45' (orange line) which follows the blue line until age 45, then declines more steeply. 3) 'Stopped at 65' (purple line) which follows the blue line until age 65, then declines very steeply. A horizontal line at approximately 25% FEV1 is labeled 'Disability', and a horizontal line at 0% is labeled 'Death'. The 'Stopped at 65' curve crosses the 'Disability' line around age 75 and reaches 'Death' around age 80.</p>
<h3>Long term oxygen therapy²</h3>	<p>Long term oxygen therapy has proven to reduce mortality. Indicated for stable patients who have:</p> <ul style="list-style-type: none"> ● PaO₂ ≤ 7.3 kPa (55 mmHg) or SaO₂ ≤ 88%, with or without hypercapnia confirmed twice over a three week period. <p>or</p> <ul style="list-style-type: none"> ● PaO₂ (7.3 kPa (55 mmHg) - 8.0 kPa (60 mmHg)) or SaO₂ of 88%, if there is evidence of : <ul style="list-style-type: none"> ● pulmonary hypertension, ● peripheral edema suggesting congestive cardiac failure, ● or polycythemia (hematocrit > 55%).
<h3>Vaccination (Evidence B)</h3>	<ul style="list-style-type: none"> ● Influenza vaccination: reduces: <ul style="list-style-type: none"> ○ serious illness (such as lower respiratory tract infections requiring hospitalization) ○ death in COPD patients. ● Pneumococcal vaccinations: recommended for all patients ≥ 65 years of age. <ul style="list-style-type: none"> ○ PCV13: has demonstrated significant efficacy in reducing bacteremia and serious invasive pneumococcal disease in adults ≥ 65 years. ○ PPSV23: has been shown to reduce incidence of CAP in COPD patients aged < 65 yrs with FEV₁ < 40% predicted in those with comorbidities.
<h3>Pulmonary rehabilitation³</h3>	<ul style="list-style-type: none"> ● Improves dyspnea, health status & exercise tolerance (evidence A) ● reduces hospitalization among patients who have recurrent exacerbations (≤ 4 wks from prior hospitalization) (evidence B)
<h3>other measures</h3>	<ul style="list-style-type: none"> ● education: ineffective (evidence C) ● self management: intervention with communication with health care professional improves health status & decrease hospitalization and ER visits. (evidence B) ● Exercise training: 6-12 wks (longer program = larger effects). 20-30 min walking per session, no limits of symptoms. ● Patient education about: <ul style="list-style-type: none"> ○ Smoking cessation ○ COPD natural history and management ○ self-management ○ exacerbations ● Nutritional support

1: Normally if you don't smoke your lung functions will be maintained until the age of 40, after 40y/o there will be a slow down-hill regression (loss of 15-20ml of lung capacity/yr). If the person is a smoker, there will be a RAPID deterioration of his lungs functions (about 100ml of lung capacity/yr) and by the age of 75 his lungs will not be able to sustain his life, unless he quits smoking early (the earlier the better).

2: The aim in COPD patients is to keep their PaO₂ 88-92%

3: Pulmonary rehabilitation has shown to be more effective in reducing dyspnea in patients with COPD than all other medications.

2- Pharmacological treatment

<h3>Bronchodilators</h3>	<ol style="list-style-type: none"> Short acting bronchodilators for mild disease: <ul style="list-style-type: none"> Inhaled Beta 2 agonists: Salbutamol, Terbutaline Long acting bronchodilators for moderate to severe disease: <ul style="list-style-type: none"> formoterol, salmeterol Inhaled Anticholinergics (muscarinic antagonists) are more appropriate and effective for patients with moderate to severe disease: <ul style="list-style-type: none"> Tiotropium bromide (LAMA), Ipratropium bromide (SAMA). Oral Bronchodilators can be given to patients who cannot inhale efficiently: Theophylline <ul style="list-style-type: none"> not commonly used due to its side effects, drug interactions and Narrow therapeutic index. Improves mucociliary clearance and central respiratory drive. <p>Combinations are commonly used:</p> <ul style="list-style-type: none"> short acting beta 2 agonist (Salbutamol) with anticholinergic (ipratropium bromide) <i>more efficacious than either agent alone</i> long acting beta 2 agonist (formoterol) with anticholinergic (aclidinium) long acting beta 2 agonist (formoterol) with corticosteroids (budesonide) <p>pharmacological treatment algorithm by GOLD:</p> <div style="border: 1px dashed green; padding: 5px; margin-bottom: 10px;"> <p>Group A: SABA or SAMA prn Group B: LABA or LAMA (Or both) Group C: LAMA or combination of LAMA and LABA or combination of LABA and ICS Group D: You basically give them everything</p> </div> 
<h3>Corticosteroids</h3>	<ol style="list-style-type: none"> Inhaled corticosteroids: usually given in combination with LABA¹ Oral corticosteroids: used in management of acute exacerbations.
<h3>Other drugs</h3>	<ol style="list-style-type: none"> Methylxanthines: aminophylline, theophylline Phosphodiesterase-4 inhibitors: Roflumilast: <i>work by:</i> <ol style="list-style-type: none"> inhibiting PDE4 → increase cAMP → open the airway Reducing inflammation
<h3>Surgery</h3>	<p>May be beneficial in selected patients (with damaged lungs); carefully weigh potential benefits with risks:</p> <ul style="list-style-type: none"> Surgical or endoscopic Lung resection (LVRS)² Bullectomy³ Lung transplantation⁴

1: Benefits: 1- Improve lung functions 2- Reduce inflammation 3- Prevents exacerbation

2: If the patient has severe emphysema affecting top of the lung, then you can use this to remove the emphysematous tissue.

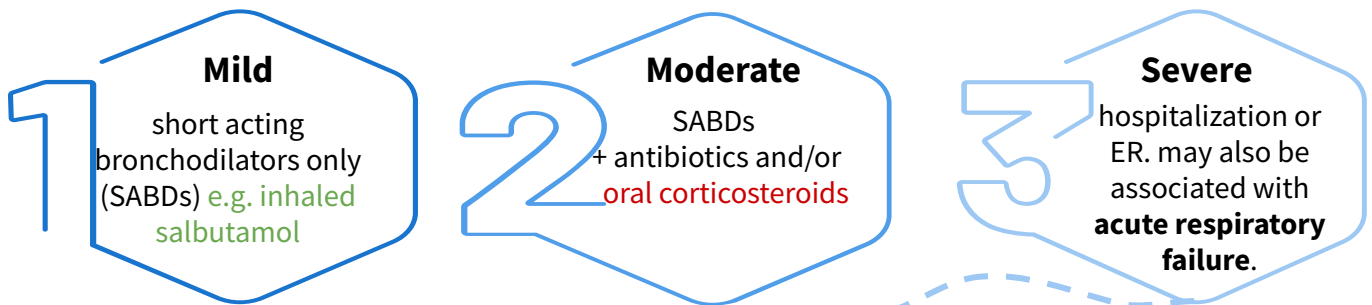
3: To get rid of a big bullae (Big, useless, air filled sac) in the lung.

4: Last option, when the lung are unfixable.

Definition

COPD exacerbations are defined as: an acute worsening of respiratory symptoms that result in additional therapy.

Classifications



classification of hospitalized patients

No respiratory failure

- 01**
- Respiratory rate: 20-30 breaths per minute
 - No use of accessory respiratory muscles
 - No changes in mental status
 - Hypoxemia improved with supplemental oxygen given via Venturi mask 28-35% inspired oxygen (FiO_2);
 - No increase in $PaCO_2$.

Acute respiratory failure (non- life threatening)

- 02**
- Respiratory rate: >30 breaths per minute
 - **Using accessory respiratory muscles**
 - **No changes in mental status**
 - Hypoxemia improved with supplemental oxygen given via Venturi mask 25-30% inspired oxygen (FiO_2)
 - hypercarbia (i.e. $PaCO_2$ increased compared with baseline or elevated 50-60 mmHg)

Acute respiratory failure (life threatening)

- 03**
- Respiratory rate: >30 breaths per minute
 - Using accessory respiratory muscles
 - **Acute changes in mental status**
 - Hypoxemia not improved with supplemental oxygen given via Venturi mask or requiring >40% inspired oxygen (FiO_2)
 - hypercarbia (i.e. $PaCO_2$ increased compared with baseline or elevated >60 mmHg) or presence of acidosis ($pH \leq 7.25$).

management of exacerbations

1 Pharmacological management

1 Bronchodilators

- Inhaled or nebulizer
- salbutamol and ipratropium bromide are given 4–6 hourly together

2 Corticosteroids

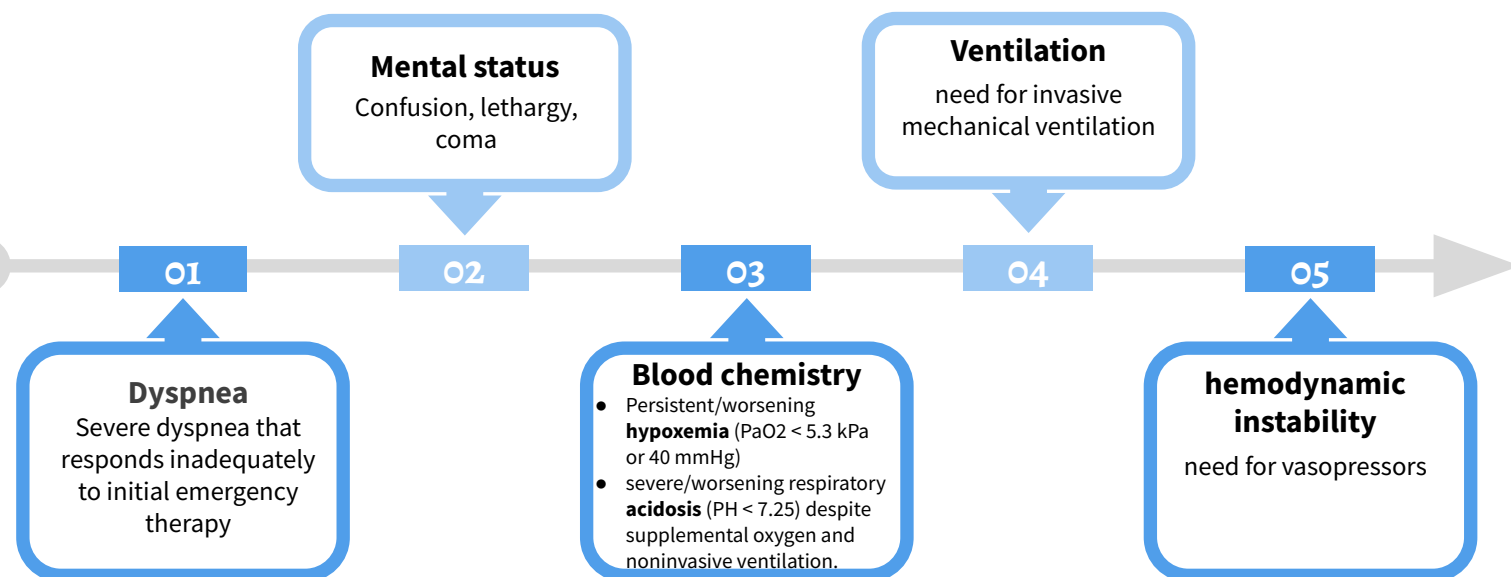
OCS e.g. 30-40 mg
Prednisolone for 5-7 days

3 Antibiotics¹

Given if there's evidence of infection (confirm by CXR or sputum)

2 Respiratory support

→ **indications for respiratory or medical intensive care unit admission:**



3 Non-invasive ventilation

→ **indications for noninvasive mechanical ventilation (NIV)²:**

Noninvasive ventilation (NIV): in the form of noninvasive positive pressure ventilation (NPPV) is the standard of care for decreasing morbidity and mortality in patients hospitalized with an exacerbation of COPD and acute respiratory failure

At least one of the following:

- Respiratory acidosis (PaCO₂ ≥ 6.0 kPa or 45 mmHg and arterial PH ≤ 7.35)
- Severe dyspnea with clinical signs suggestive of respiratory muscle fatigue, increased work of breathing or both such a respiratory accessory muscles, paradoxical motion of the abdomen or retraction of the intercostal spaces
- persistent hypoxemia despite supplemental oxygen therapy

1: cefaclor or co-amoxiclav, are given if there is a history of more purulent sputum production or with chest X-ray changes. Antibiotic treatment is modified depending on sputum culture results.

2: NIV: delivery of oxygen via a face or nasal mask and therefore eliminating the need of an endotracheal airway. The patient wears a tight-fitting nasal (Mouth have to be kept close if you're using a nasal mask) or face mask, which is connected to a CPAP unit. The treatment provides a larger tidal volume with the same inspiratory effort, thus improving alveolar ventilation and decreasing the work of breathing.

Bronchiectasis

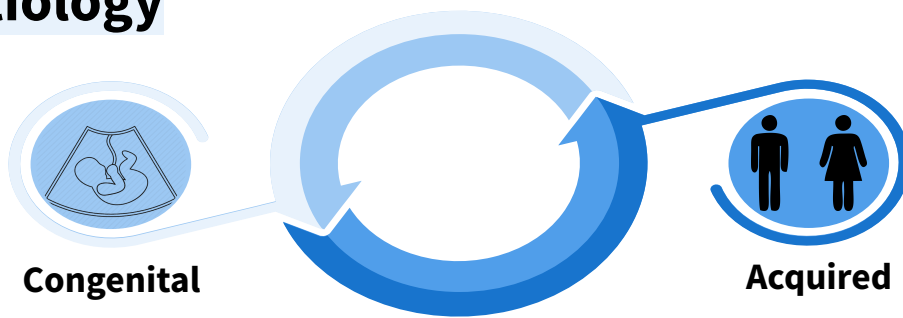
Definition

This term describes abnormal and permanently dilated airways. Bronchial walls become inflamed, thickened and irreversibly damaged. The mucociliary transport mechanism is impaired and **frequent bacterial infections ensue**. originally described by Laennec in 1819 as **chronic debilitating disease**.

Characteristics

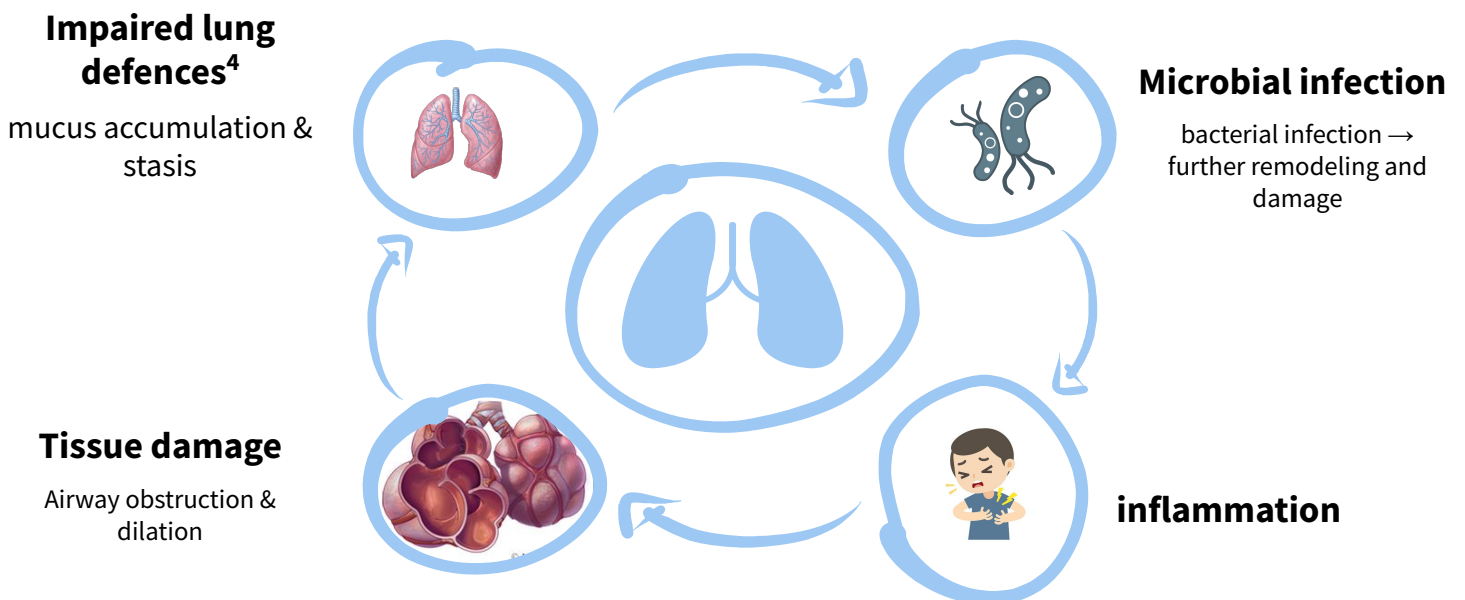
- 1** Persistent cough
- 2** Excessive sputum secretions¹
- 3** Recurrent airway infection¹

Etiology



- **Kartagener's syndrome** (primary ciliary dyskinesia or immotile cilia syndrome)
 - **Hypogammaglobulinemia**
 - **Cystic fibrosis**
 - Abnormal cartilage formation
 - Pulmonary sequestration.
- **Recurrent pulmonary infection** (eg: bacterial and viral pneumonia)
 - **Bronchial obstruction**²
 - **Childhood infection** e.g measles, pertussis
 - Aspiration (eg: GERD)
 - Granulomas (eg: TB & sarcoidosis)

Pathogenesis³



1: Bronchiectasis is similar to COPD except for these two features
 2: Can be intrinsic (e.g.: foreign body, post TB stenosis, tumor) or extrinsic (e.g.: lymph node, tumor), this will lead to accumulation of secretions distal to the obstruction leading to inflammation and infection
 3: The onset of bronchiectasis could be anywhere in this circle e.g. Severe infection will lead to inflammation and tissue damage and eventually bronchiectasis. The principle of management is to interfere with this vicious cycle.
 4: e.g. If cilia are non-motile (Unable to clear secretions, bacteria) or Immunodeficiency

Definition

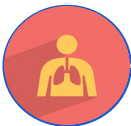
CF is a hereditary autosomal recessive disorder caused by defective **CFTR** (cystic fibrosis transmembrane conductance regulator) protein due to mutation in the *CFTR* gene located on the long arm of **chromosome 7**.

Pathophysiology



In general

Mutated CFTR gene → **misfolded protein** → retention for degradation of the defective protein in the rough endoplasmic reticulum (rER) → **absence of ATP-gated chloride channel** on the cell surface of epithelial cells throughout the body (e.g., intestinal and respiratory epithelia, sweat glands, exocrine pancreas, exocrine glands of reproductive organs)



In GIT and lungs

Defective ATP-gated chloride channel → inability to transport intracellular Cl⁻ across the cell membrane → reduced secretion of Cl⁻ and H₂O → accumulation of intracellular Cl⁻ → ↑ Na⁺ reabsorption (via ENaC) → ↑ H₂O reabsorption → formation of hyperviscous mucus → accumulation of secretions and blockage of small passages of affected organs → chronic inflammation and remodeling → organ damage

Clinical features

Clinical features



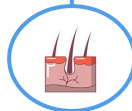
Gastrointestinal

- Meconium ileus (in newborn)
- Failure to thrive (due to malabsorption)



Respiratory

- COPD with bronchiectasis
- Chronic sinusitis
- Recurrent pulmonary infections



Sweat glands

- Salty sweat



Musculoskeletal

- Kyphoscoliosis



Urogenital

- **Men: usually infertile**
(Obstructive azoospermia is common; spermatogenesis may be intact, vas deferens may be absent.)
- **Women:** reduced fertility

Diagnosis: What's the best initial test? Sweat chloride test (A chloride concentration ≥ 60 mmol/L indicates a likely diagnosis of cystic fibrosis)

Definition

This is rare **autosomal recessive** disorder characterized by **absent or dysmotile cilia** caused by a defect in the **dynein arm** of microtubules

Clinical features

Clinical features

Chronic productive cough

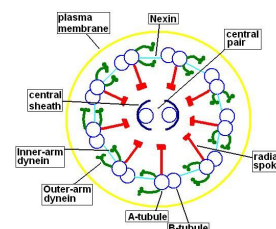
Recurrent otitis, sinusitis, and nasal polyps

Bronchiectasis

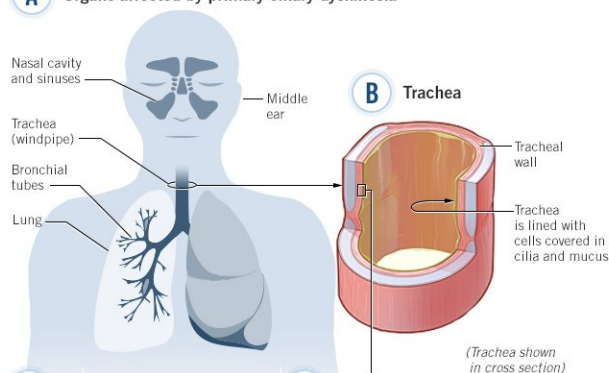
Conductive hearing loss

Infertility in men due to decreased sperm motility as a result of defective flagella

Reduced fertility in women (and rarely ectopic pregnancy) due to defective cilia in fallopian tubes



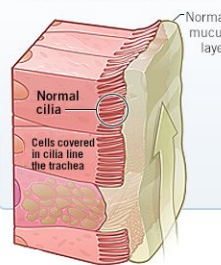
A Organs affected by primary ciliary dyskinesia



(Trachea shown in cross section)

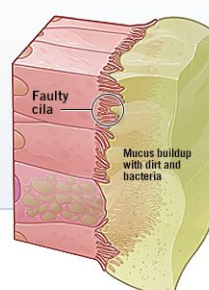
C Normal cilia lining trachea

Cilia move together in wave-like motions to transport mucus toward the mouth. The mucus contains dirt and bacteria.



D Faulty cilia lining trachea

Cilia are deformed and do not move together, causing a buildup of mucus. The mucus contains dirt and bacteria.



Kartagener syndrome:

Kartagener syndrome is a subtype of primary ciliary dyskinesia characterized by the **triad** of **situs inversus**, **chronic sinusitis**, and **bronchiectasis**.

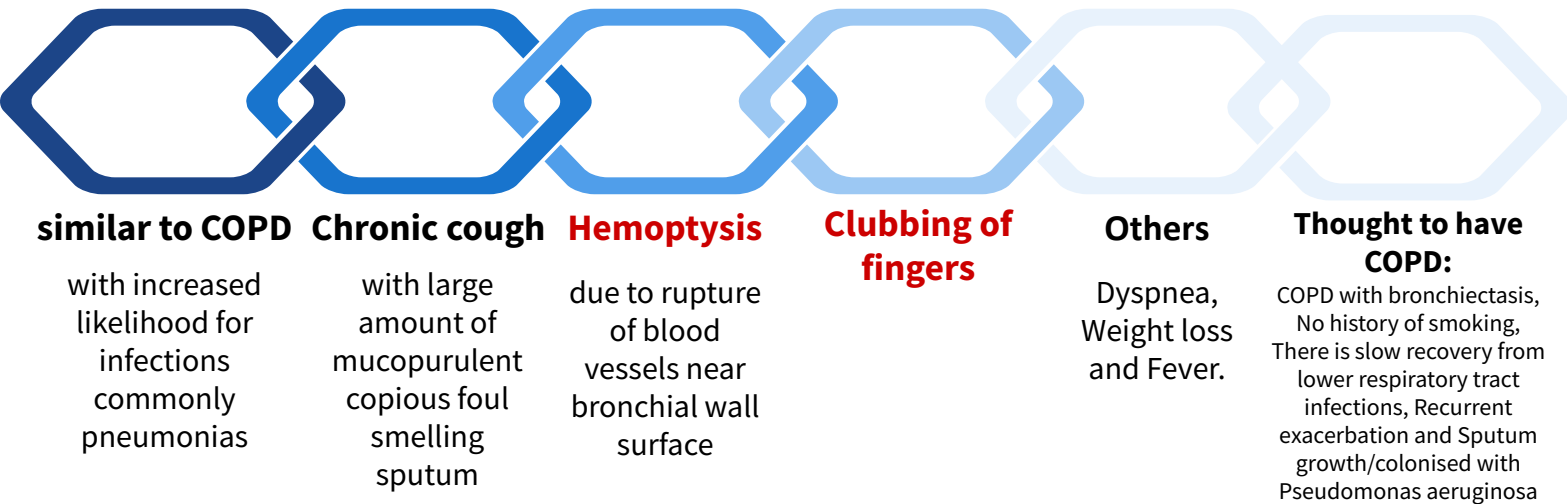
Tip: You can memorize the cause of Kartagener syndrome by thinking of **Kartagener's** restaurant that only has 'take-out' service because there is no **dine-in (dynein)**!

Diagnosis

- **Nasal nitric oxide test:** reduced nasal nitric oxide (screening test)
- **Genetic tests** for dynein arm mutations
- **Chest x-ray:** **bronchiectasis**, dextrocardia, and **situs inversus** (suggests Kartagener syndrome)
- **Electron microscopy:** abnormal cilia

Bronchiectasis

Clinical features¹



When to suspect bronchiectasis?



chronic productive cough²

especially if:

- young age at presentation .
- symptoms over many years.
- absence of smoking history.
- daily expectoration of large volumes of sputum.
- hemoptysis.



Past history of:

- Recurrent LRTI.
- Chronic productive cough.
- Breathlessness, wheeze.
- haemoptysis.
- Chest pain
- Tiredness
- (ENT,infertility,GI,ILD)³



consider:

only when other ddx are excluded, consider unexplained:

- hemoptysis.
- non-productive cough

1: As the condition worsens, patients suffer persistent halitosis, recurrent febrile episodes with malaise, and episodes of pneumonia. coarse crackles can be heard over the infected areas, usually the lung bases. When the condition is severe there is continuous production of foul-smelling, thick, khaki-coloured sputum. Haemoptysis can occur either as blood-stained sputum or as a massive haemorrhage. Breathlessness may result from airflow limitation.

2: Usually increased in the morning.

3: If ENT (e.g. deafness, recurrent sinusitis) or Infertility think of PCD and CF. For GI symptoms think of CF.

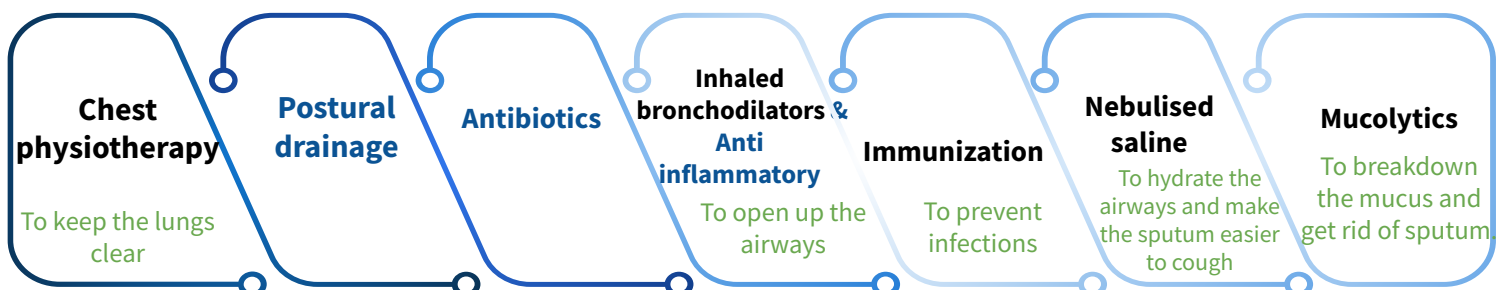
Investigations

<p>Sputum Culture</p>	<ul style="list-style-type: none"> • Sputum examination and culture are essential for adequate treatment. • The major pathogens are: <ul style="list-style-type: none"> ○ Staph. aureus. ○ Pseudomonas aeruginosa. ○ H. influenzae ○ anaerobes. • Other pathogens: Strep.pneumoniae, Klebsiella pneumoniae, Aspergillus fumigatus¹ & Mycobacterium avium-intracellulare complex (MAI). • Sputum microscopy culture sensitivities are done when patient is stable or at the onset of exacerbating².
<p>High resolution-CT (HR-CT scan) (Gold standard)</p>	<ul style="list-style-type: none"> • thickened, dilated bronchi • cysts at the end of the bronchioles. • Characteristically, the airways are larger than their associated blood vessels. • Gives an idea of the degree of bronchiectasis
<p>CXR</p>	<p>Can be normal, but sometimes shows:</p> <ul style="list-style-type: none"> • dilated bronchi with thickened bronchial walls • sometimes multiple cysts containing fluid
<p>Other investigations</p>	<p>Spirometry³, Sinus x-ray, Serum immunoglobulins, Sweat electrolytes (when CF is suspected) & Mucociliary clearance</p>



Dilated airways at the bottom of the left lung

Management

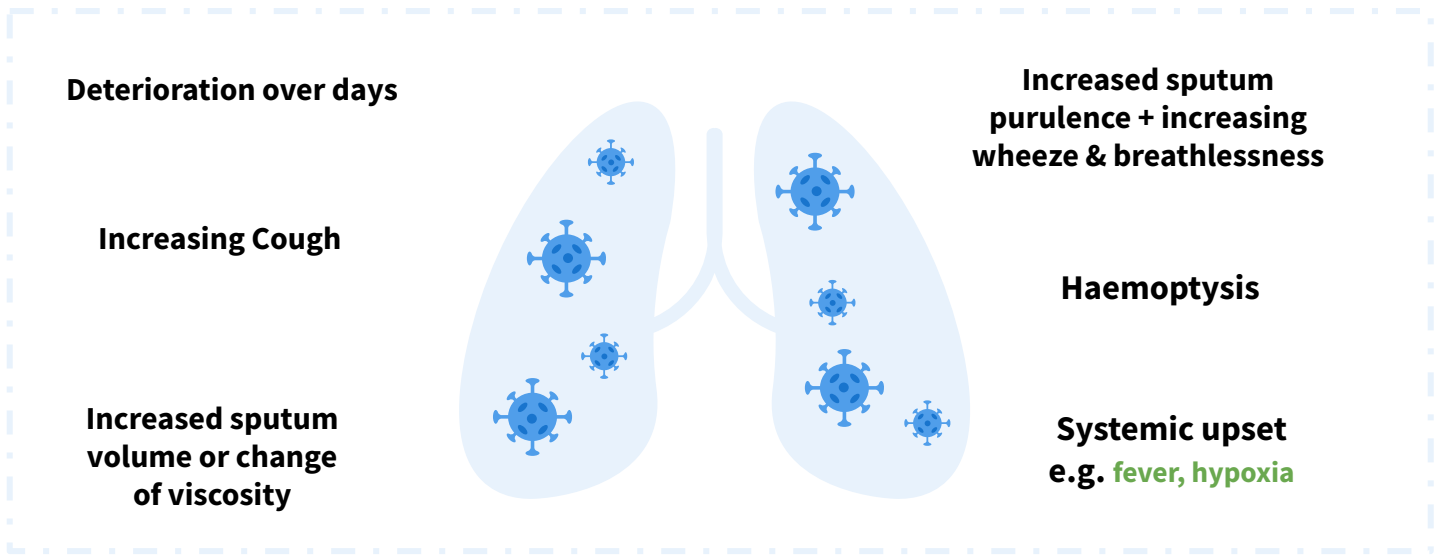


1: Aspergillus fumigatus can be isolated from 10% of sputum specimens in cystic fibrosis, but the role of this organism in producing infection is uncertain. Treatment of Aspergillus is prednisolone 30 mg daily (± Antifungal agent (itraconazole, voriconazole) if high doses of steroids are used).

2: tells you what the patient is infected with at the onset of exacerbation

3: to establish the amount of damage the bronchiectasis has caused to the lung (the amount of damage is parallel to the abnormalities in PFTs)

How to spot a Bronchiectasis exacerbation?¹



Management of Bronchiectasis exacerbation

1 Antibiotics

→ 1st: Empiric therapy

Drug	dose		duration
Amoxicillin	500mg tds		14 days
	H.influenzae:	1g tds	
		3g bd	
clarithromycin	500 bd		
ciprofloxacin	Pseudomonas	500/750 bd	

→ 2nd: Long term antibiotics

- **Used in case of:**
 - 3 or more Exacerbations/yr.
 - Fewer Exacerbation in patients with significant morbidity.
- **Use:**
 - Nebulised antibiotics (Gentamicin/tobramycin/colistin)
 - Long term Macrolides²

1: **First Q:** Does the pt have an exacerbation? Check the features listed. If the answer is YES, your **Second Q** must be what's the antibiotic of choice? Usually in Bronchiectasis we give high doses for long duration (14 days).

2: Macrolides have both anti-microbial and anti-inflammatory activity.

➔ **3rd: Common organisms associated with acute exacerbation of bronchiectasis and their suggested antimicrobial agents:**

Streptococcus pneumoniae	<ul style="list-style-type: none"> ● Amoxicillin 500 mg three times per day (tds) ● Clarithromycin 500 mg two times per day (bd) for 14 days
Haemophilus influenzae (b-lactamase negative)	<ul style="list-style-type: none"> ● Amoxicillin 500 mg tds ● Amoxicillin 1 g tds ● Amoxicillin 3 g bd ● Clarithromycin 500 mg bd
Haemophilus influenzae (b-lactamase positive)	<ul style="list-style-type: none"> ● Co-amoxiclav 625 mg tds ● Clarithromycin 500 mg bd ● Ciprofloxacin 500 mg bd
Moraxella catarrhalis	<ul style="list-style-type: none"> ● Co-amoxiclav 625 mg tds ● Ciprofloxacin 500 mg bd
Staphylococcus aureus (MSSA)	<ul style="list-style-type: none"> ● Flucloxacillin 500 mg qds ● Clarithromycin 500 mg bd
Other organisms:	MRSA → Vancomycin, Coliforms (gram - rods) → Ciprofloxacin, Pseudomonas → Ceftazidime

When to admit the patient?

- Cyanosis
- Confusion
- Breathlessness (RR >25/minute)
- Circulatory & respiratory failure
- Temperature >38°C
- Patient unable to take oral therapy
- Patient unable to cope at home
- Haemoptysis >25mls/day

Use:

Intravenous therapy in patients with clinical failure after oral antibiotics

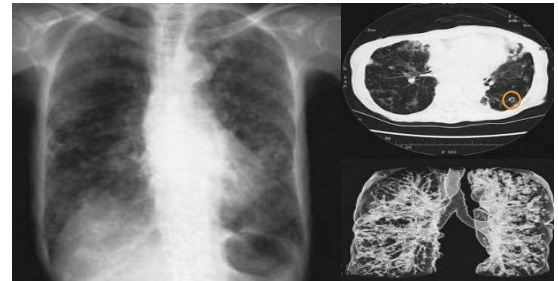
How to monitor a bronchiectasis patient?

- Symptoms.
- Sputum Volume 24hrs/Purulence.
- Frequency of Exacerbations/yr.
- Frequency of Antibiotic use.
- FEV1/ FVC annually.
- CXR only if indicated.

Case study 1:

- An 81-year-old woman was admitted with weight loss (18 kg in 27 months), hemoptysis, and tubular and diffuse granular shadows on her chest radiograph.

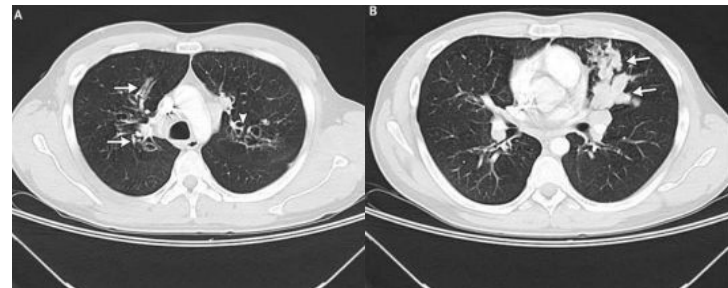
- Features:**
 - CT: Dilated airways & Signet ring sign
- What is your diagnosis?** Mycobacterium avium complex (MAC) infection of bronchiectasis



Case study 2:

- A 26-year-old man who smoked and had a long history of **poorly controlled asthma** and **severe environmental allergies** was admitted for an exacerbation of asthma. Total IgE 5000 Aspergillus IgE raised Aspergillus antibody raised.

- What is your diagnosis?** Allergic bronchopulmonary aspergillosis (ABPA)
- Features:**
 - Pic A:** Dilated airways
 - Pic B:** Airways are plugged with mucus (Finger in glove appearance)



Case study 3:

- 42-year-old man with recurrent respiratory infections and Chest problems since childhood. he told that he had asthma but inhalers are not effective. He struggled at school due to frequent absence due to "chest infections". He is married but no children¹. His sister and Cousin have similar chest problems

- What is your diagnosis?** Cystic fibrosis (CF)
- Features:**
 - CT:
 - Dilated airways
 - Airways full with secretion



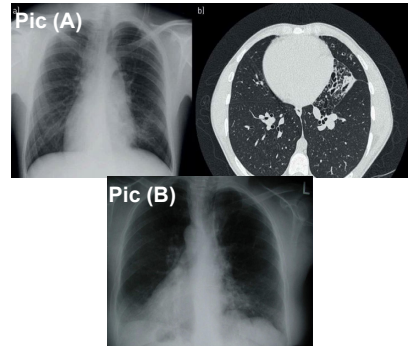
1: CF male patients are infertile

Bronchiectasis cases

Case study 4:

❖ A 17-Year-old with **Respiratory problems since childhood**. His grand parents describe him as a small child with **chronic cough from birth, Recurrent ear and sinus infections** which have led to partial deafness. **His brother and one of his cousins are similarly affected**

- **What is your diagnosis?** PCD (Katergener's)
- **X-ray: both pictures show dextrocardia**
 - **Pic (A): Enlarged cardiac compartment**
 - **Pic (B): Heart is completely pushed to the right**
- **CT: Dilated airways**

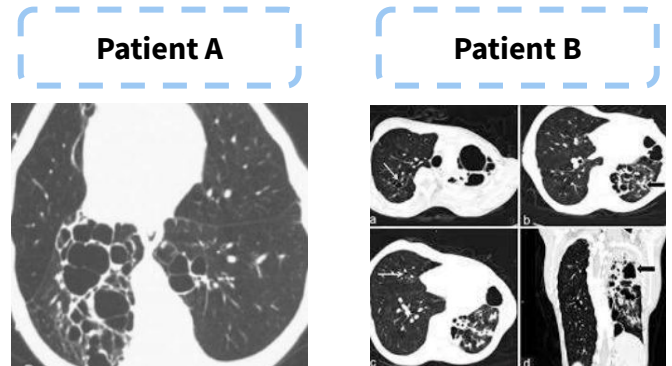


Case study 5:

❖ **Patient A:** 75 year old lady had TB 55 years ago, Chronic cough and SOB. Recurrent LRTI and Sputum production.

❖ **Patient B:** 79 year old man presents Cough, sputum production and recurrent LRTI.

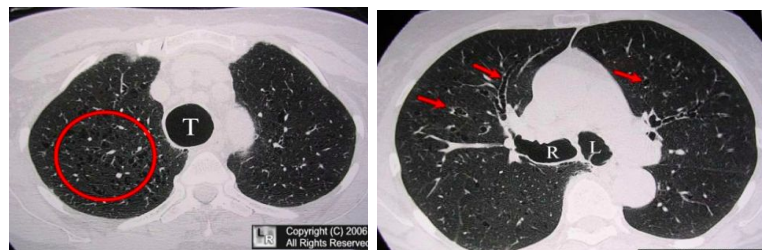
- **What is your diagnosis?** Post TB
- **CT: Left lung is destroyed with thickened airways**



Case study 6:

❖ 35-year-old man with chronic cough, increased sputum production, breathlessness with fever. Computed tomography of chest showed tracheal dilation (diameter, 31 mm) and emphysematous changes. Fiberoptic bronchoscopy revealed enlarged trachea and main bronchi. Pulmonary function testing showed combined ventilatory defect.

- **What is your diagnosis?** Mounier-kuhn syndrome
- **These patients have very large non-functioning airways making them prone to some infections.**
- **CT: Tracheobronchomegaly**



Summary

Chronic obstructive pulmonary disease

<p>Definition</p>	<ul style="list-style-type: none"> ● Emphysema: permanent enlargement of airspaces due to destruction of alveolar walls. ● Chronic Bronchitis: inflammation and scarring in airways, and excess mucus production narrowing the airways.
<p>Risk factor</p>	<ul style="list-style-type: none"> ● Smoking ● α_1-antitrypsin deficiency ● Environmental factors ● Chronic Asthma
<p>Clinical Features</p>	<ul style="list-style-type: none"> ● Signs: <ul style="list-style-type: none"> ○ Prolonged expiratory time ○ Wheezing ○ Tachypnea, tachycardia ○ Cyanosis ○ Use of accessory respiratory muscles ○ Hyperresonance on percussion ○ Signs of Cor Pulmonale ● Symptoms: <ul style="list-style-type: none"> ○ Chronic and progressive dyspnea ○ Cough ○ Sputum production ○ Wheezing and chest tightness
<p>Diagnosis</p>	<ul style="list-style-type: none"> ● Pulmonary function testing (Spirometry): \downarrow FEV₁ and \downarrow FEV₁/FVC ratio. ● CXR: overinflation of the lungs with low, flattened diaphragms. ● α_1-antitrypsin: in patients with a personal or family history of premature emphysema (≤ 50 years old). ● Arterial blood gas (ABG): chronic PCO₂ retention, decreased PO₂.
<p>Management</p>	<p>The flowchart illustrates the management of COPD based on FEV₁ levels. It is divided into three main sections: Supplemental therapy, Stepwise drug therapy, and Healthcare. Supplemental therapy includes Lung reduction surgery, Single lung transplantation, Evaluation and treatment of hypoxaemia (e.g. home oxygen), and Pulmonary rehabilitation. Stepwise drug therapy includes Single short-acting inhaled β_2-agonist bronchodilator, Short-acting inhaled β_2-agonist bronchodilator for acute relief of symptoms, Long-acting inhaled β_2-agonist bronchodilator, Combination of muscarinic and β_2-agonist bronchodilator, Consider theophylline, and Combination of inhaled corticosteroid and long-acting β_2-agonist. Healthcare includes Pneumococcal and annual influenza vaccination, Smoking cessation, and Regular assessment of lung function. Symptoms are indicated at the bottom.</p>
<p>Complications</p>	<ul style="list-style-type: none"> ● Acute exacerbations: <ul style="list-style-type: none"> ○ Mild \rightarrow short acting bronchodilators SABD ○ Moderate \rightarrow SABD plus antibiotics and/or oral corticosteroids ○ Severe \rightarrow patient requires hospitalization and may also be associated with acute respiratory failure. ● Respiratory failure ● Pulmonary hypertension/Cor pulmonale

Summary

Bronchiectasis	
Definition	Permanent dilation of bronchi and bronchioles caused by destruction of the muscle and supporting elastic tissue, resulting from or associated with chronic necrotizing infections.
Causes	<ul style="list-style-type: none">● Acquired bronchiectasis:<ul style="list-style-type: none">○ Recurrent pulmonary infection (e.g. pneumonia, and tuberculosis)○ Bronchial obstruction caused by (e.g. asthma, and chronic bronchitis)● Congenital bronchiectasis:<ul style="list-style-type: none">○ Kartagener's syndrome (primary ciliary dyskinesia)○ Hypogammaglobulinemia○ Cystic fibrosis
Clinical Features	<ul style="list-style-type: none">● Persistent cough● Excessive sputum secretions● Recurrent airway infection● Clubbing of fingers● Hemoptysis● Dyspnea, Weight loss and Fever
Diagnosis	<ul style="list-style-type: none">● Culture patient's sputum● HR-CT scan (Gold Standard)● CXR shows dilated bronchi with thickened bronchial walls● Spirometry reveals an obstructive pattern.
Management	<ul style="list-style-type: none">● Empiric Antibiotic therapy (in acute exacerbations)● Chest physiotherapy (postural drainage, chest percussion) to help remove the mucus● Immunization● Inhaled bronchodilators● Mucolytics● Nebulised saline

Lecture Quiz

Q1: You see a 46-year-old woman on your ward who has been diagnosed with bronchiectasis following a three-month history of a mucopurulent cough. Which of the following from the list below is not a cause of bronchiectasis?

- A- Cystic fibrosis
- B- Pneumonia
- C- Bronchogenic carcinoma
- D- Left ventricular failure

Q2: You see a 68-year-old man in clinic, with a 40 (cigarette) pack year history, who has been experiencing breathlessness on exertion and a productive cough of white sputum over the last four months. You assess his spirometry results which reveal an FEV1/FVC of 51 percent with minimal reversibility after a 2-week trial of oral steroids. Cardiological investigations are normal. Which of the following is the most likely diagnosis?

- A- Asthma
- B- Chronic obstructive pulmonary disease (COPD)
- C- Chronic bronchitis
- D- Lung fibrosis

Q3: A 30-year-old man presents to your clinic with a cough and finger clubbing. From the list below, which of these answers is not a respiratory cause of finger clubbing?

- A- Empyema
- B- Cystic fibrosis
- C- Bronchogenic carcinoma
- D- COPD

Q4: A 68-year-old woman is admitted to accident and emergency with shortness of breath and cough. She has been a smoker for 25 years, smoking on average 20 cigarettes a day, and is a known COPD patient with home oxygen. The observations read a pulse rate of 101, blood pressure of 100/60, respiratory rate of 20, oxygen saturations of 88 percent on air and temperature of 37.2°C. On auscultation you hear bilateral expiratory wheeze. She is prescribed nebulizers (salbutamol 5 mg + ipratropium 500 µg) with oxygen and chest x-ray requested. Intravenous access has been established and bloods sent for analysis. From the list below, select the most appropriate next step in this patient's management plan?

- A- Arterial blood gas sampling
- B- Peak flow assessment
- C- Start non-invasive ventilation (e.g. BIPAP)
- D- Obtain sputum for microscopy, culture and sensitivity (MC&S)

Q5: The severity of COPD is assessed using post bronchodilator spirometry analysis. From the list below, select the values that you would expect to see in a patient with moderate COPD?

- A- FEV1/FVC <0.7, FEV1 percent predicted **30–49** percent
- B- FEV1/FVC <0.7, FEV1 percent predicted **50–79** percent
- C- FEV1/FVC <0.7, FEV1 percent predicted **<30** percent
- D- FEV1/FVC <0.7, FEV1 percent predicted **60–70** percent

THANKS!!

NO WORDS COULD DESCRIBE OUR GRATITUDE TO EVERYONE THAT WORKED ON THIS LECTURE IN SUCH A SHORT NOTICE, YOU GUYS ARE HEROS!

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*Send us your feedback:
We are all ears!*

