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Chronic Obstructive lung Disease & Bronchiectasis

★ **Objectives:**

1. Definition of the two conditions
2. Clinical and radiological diagnosis
3. Differential diagnosis
4. General outline of management
5. Create a link to 341 clinical teaching

★ **Resources Used in This lecture:**

Davidson, Guyton and Becker step 1 lecture notes

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Chronic Obstructive Pulmonary Diseases (COPD)

COPD contains two diseases which are chronic **bronchitis** and **emphysema**

- COPD is classified under obstructive pulmonary diseases (no kidding!) along with other diseases such as asthma and bronchiectasis
- Chronic bronchitis and emphysema are grouped together under COPD because they are both mainly caused by smoking and they *usually present together.*
- Brainless pathology textbooks (Robbins) try to confuse us students with "Pink Puffers" and "Blue Bloaters". Forget about that as it is not clinically relevant[1].

Let us quickly point out some points (pathology) that are relevant to each disease (chronic bronchitis and emphysema) and then we will discuss the clinical presentation, management, etc. of COPD

Chronic bronchitis

It is mainly a *clinical* diagnosis patients cough up lots of sputum for a long period of time
"3 months per year for at least 2 consecutive years[2]"

- **Pathogenesis**: Cigarette smoke causes hyperplasia of mucus glands which increase the secretion of mucus → mucus plugs cause obstruction of bronchioles→ COPD

Emphysema

It is mainly a *pathological* diagnosis.

- **Pathogenesis:**
    1. Pollutants (smoking)→ increased inflammatory mediators in the lung that destroy the lung parenchyma (trypsin and elastase)
    2. We have defense mechanisms to fight these inflammatory mediators (alpha1 antitrypsin)
        - However, the amount of inflammatory mediators exceeds our ability to counteract them
    3. Pulmonary capillaries are destroyed (decreased DL_{CO})
    4. Elastic tissue that helps push air out during expiration is destroyed → ↓ ↓ FEV1 & ↓ FVC → obstructive pulmonary diseases
- Some patients have an inherited deficiency of alpha 1 antitrypsin→ emphysema at a younger age

[1] Look Davidson 22nd edition page 674-675: "In practice, these phenotypes often overlap."
[2] No gap between the years: meaning that they are two consecutive years

What is the difference between chronic bronchitis, emphysema, and COPD?

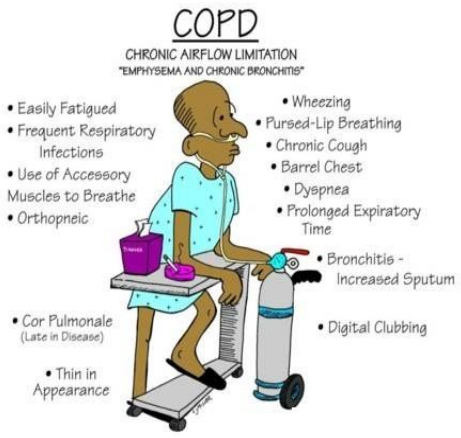
1) Chronic bronchitis is a clinical diagnosis of increased sputum over a period of time
2) Emphysema is a pathological diagnoses which is defined by loss of alveolar capillaries
3) COPD is a clinical syndrome which requires a history of smoking, wheezing, and spirometry (decreased FEV1/FVC ratio)

COPD

We might think of COPD of being exclusively a pulmonary disease; however, COPD also has **systemic** components:

- Muscle weakness
- Impaired salt and water excretion → peripheral edema
- Weight loss
- Osteoporosis

Clinical features



1. *Over 40* with symptoms of chronic bronchitis and/or *dyspnea***.**
   a. Differential: chronic asthma, TB, bronchiectasis & CHF
2. *Cough* with or without *hemoptysis*.

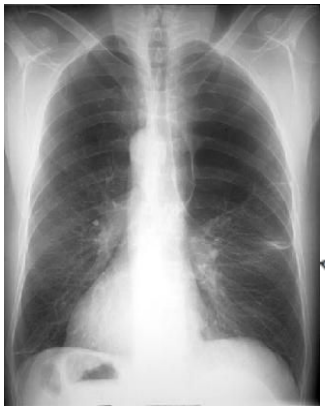
Hemoptysis is a serious clinical presentation and must be worked up; you can't say "I'll leave it alone it is probably due to the patient's COPD."

   a. Exclude lung cancer and other causes of hemoptysis[3].
3. *Shortness of breath:* ask about the level of exertion before the shortness of breath presents,
4. On auscultation:
   a. End expiratory *wheezes.*
   b. Decreased breath sounds.
   c. +/- Inspiratory *crackles*.
5. On percussion:
   a. *Hyperresonance* (as lungs are hyperinflated with air)
6. Other signs and symptoms are nonspecific
   a. *Clubbing* of fingers is not associated with COPD
      i. Must exclude lung cancer or fibrosis if clubbing is present.
7. *Tachypnea* and *tachycardia*
8. *Cyanosis*

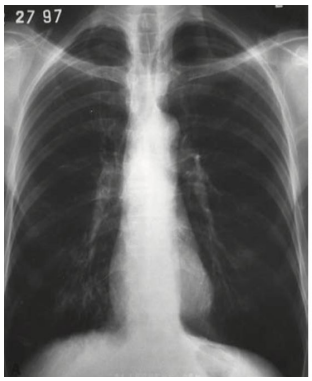
[3] More details about hemoptysis can be found in Davidson p658

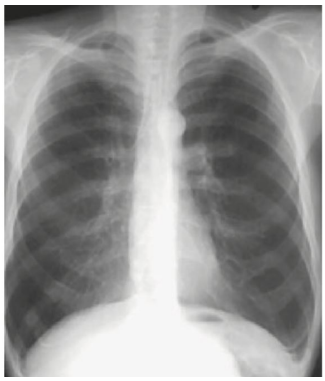
Investigations

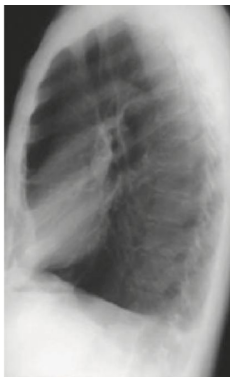
1. Chest X-ray
    a. To look for other diseases: lung cancer, CHF, and bullae[4]



Plain chest radiograph in severe cases of emphysema might show "*barrel chest*"







Advanced emphysema shows: *Hyperinflated*, flattened diaphragm, *enlarged retrosternal* space and *diminished vascular markings.*

Pulmonary function tests (PFTs)

**Definitions*

a) FEV1: the volume exhaled in the first second
b) FVC: the total volume exhaled
c) FEV1/FVC: the ratio is normally 0.8 (i.e: 80% of the total expired lung volume is expired in the first second). It can help us a lot in diagnosing pulmonary diseases
    i) These are measured using a spirometry: a video if you want to see how it looks https://www.youtube.com/watch?v=6kbgZWS5wH0

**PFTs in obstructive pulmonary diseases:*

- Obstructive pulmonary diseases have a problem with expiring air out of the lung (hence the name "obstructive"); there is obstruction to airflow out of the lungs (due to mucus in COPD or inflammatory response in asthma).
- We expect that the amount of air expired in the first second to be severely decreased (↓ ↓ FEV1)
- We would also expect the FVC, which is the total amount of expired air, to be also decreased because there is airflow obstruction (↓ FVC)
- Note that the degree of reduction of FEV1 (↓ ↓ FEV1) is much more severe than FVC (↓ FVC)
- Now if we plug in the numbers (↓ ↓ FEV1 / ↓ FVC) the end result is a decrease in FEV1/FVC ratio

Bottom line: in obstructive pulmonary diseases there is a decrease in the FEV1/FVC ratio
In restrictive pulmonary diseases there is a normal (or slightly increased) FEV1/FVC ratio

[4] A bulla is defined as an air space in the lung measuring more than one centimeter in diameter in the distended state.

Note: one of the ways to differentiate asthma from the other obstructive diseases is to measure FEV1/FVC (which should be decreased) and then remeasure these values **after giving the patient corticosteroids**. Patients with asthma will have significant improvement (FEV1/FVC becomes normal), whereas other diseases (such as COPD) have no (or very little) improvement.

**Transfer factor*

- Another important PFT is the transfer factor. This test asks the following question: "How well can this lung exchange gas?"
    - Carbon monoxide (CO) is used to measure this
    - The result is given as DL_{CO} (Davidson calls it TL_{CO})[5]
- Let us walk through the journey of CO through the respiratory tree and see how could this test be affected in pathological states:[6]
    - When we say there is increased DL_{CO} we mean that there is increased gas exchange in this lung
    - When we say decreased DL_{CO} → decreased gas exchange in this lung
    1) CO enters the respiratory tract through the bronchi until it reaches the alveoli
    2) CO crosses the alveolar capillaries→ goes into RBC → attaches to hemoglobin
        a) In case of alveolar destruction (**emphysema) → ↓** DL_{CO}
        b) In case of increased blood in the lungs (pulmonary hemorrhage - Goodpasture syndrome) there will be more Hb available for CO to bind to → ↑ DL_{CO}

Bottom line: in emphysema, we get a decrease in DL_{CO} (aka TL_{CO})

**Lung volumes in obstructive pulmonary diseases:*

Note that when talking about FEV1/FVC ratios we never talked about total lung volume. Total lung volume can't be easily measured because no matter how much we expire the air out of our lungs, there will always be some air present inside (known as residual volume). Therefore we need special tests to measure total lung volume (helium or body plethysmography)

Bottom line: the only important thing here is that if total lung capacity (TLC) was measured in lung diseases, it would be increased in obstructive diseases (because there is obstruction to air leaving the lung which leads to an increase in the amount of air present in the lungs) and decreased in case of pulmonary fibrosis.

A summary for pulmonary function tests[7]:

	Asthma	Chronic bronchitis	Emphysema	Pulmonary fibrosis
FEV_1	↓↓	↓↓	↓↓	↓
VC	↓	↓	↓	↓↓
FEV_1/VC	↓	↓	↓	→/↑
TL_{CO}	→	→	↓↓	↓↓
K_{CO}	→/↑	→	↓	→/↓
TLC	→/↑	↑	↑↑	↓
RV	→/↑	↑	↑↑	↓

(RV = residual volume; see text for other abbreviations)

[5] 22nd edition page 653

[6] This might be a little bit too detailed, just know that emphysema causes decreased DL_{CO}

[7] Taken from Davidson 22nd edition page 653

2. Spirometry → gives FEV1/FVC
    a. which should be decreased and do not improve with bronchodilators (vs. asthma)
3. Lung volumes might be measured
    a. Expect them to be increased (Increased total lung capacity TLC)
4. Gas transfer value (DL_{CO})
    a. Suspect emphysema if it is decreased
5. Pulse oximetry
    a. Less than 93% → patient might need oxygen therapy
6. Measure alpha 1 antitrypsin levels in patients with premature emphysema (< 50 years) especially if the patient has coexisting hepatic disease (cirrhosis)
    a. Alpha 1 antitrypsin fights trypsin and other enzymes that damage the parynchema therefore emphysema develops early in case of deficinecy
    b. The liver problems arise because there is a problem in the synthesis of alpha 1 antitrypsin (which is normally done in the liver) which leads to its accumulation in the liver leading to raised LFTs.
7. ABG

Management

1. Best thing to do is to *stop smoking.*
2. Bronchodilators
    a. <u>Short acting</u> bronchodilators for mild disease
        i. Beta 2 agonists: *Salbutamol, Terbutaline*
    b. <u>Long acting</u> bronchodilators for moderate to severe disease
        i. Beta 2 agonists: *Salmeterol, Formoterol, Indacaterol*
        ii. Anticholinergics (muscarinic antagonists) are more appropriate for patients with moderate to severe disease. This is because it is believed that beta agonists might cause CVS side effects (tachycardia, etc.): *Tiotropium bromide*
    c. Oral bronchodilators can be given to patients who cannot inhale efficiently
        i. *Theophylline*: not commonly used because it has lots of side effects and drug interactions
3. Corticosteroids
    a. Inhaled corticosteroids do not alter the natural history of the FEV1 decline (meaning that it doesn't make the diseases any better)
        i. Usually given in combination with long acting beta agonists
    b. Oral corticosteroids are useful in acute exacerbations (discussed later)
        i. Remember steroids have many side effects such as osteoporosis and Cushing's syndrome
4. Pulmonary rehabilitation
    a. Encourage patients to exercise
5. Oxygen therapy
    a. Improves survival and quality of life in patients

6. Vaccinations
    a. Influenza vaccine yearly
    b. Strep pneumoniae vaccine every 5-6 years

Smoking cessation & home **Oxygen** therapy are the only intervention shown to lower mortality

Complications of COPD:

- Cor pulmonale
- Pulmonary HTN
- Secondary polycythemia
- Acute exacerbations (mostly due to infections or noncompliance)

Acute exacerbation of COPD

Definition

- There are many definitions: any deterioration necessitating a change in management
- Increase in symptoms and deterioration in lung function and health status
- Patients might be managed at home by increasing the doses of their medications
- If patient has cyanosis, edema, or altered level of consciousness → must go to hospital

Management

1. Don't give 100% O_2 because it might cause respiratory depression and worsens the patient's ventilation and acidosis. (BUT WHY? skip the next part if you are not interested to know)
    a. We have central respiratory centers that are present in the brainstem. Their goal is to keep us breathing. They respond to an increase in $PaCO_2$
        i. This excitation by $PaCO_2$ is greatest in the first two days[8], later it loses its effect; they are "desensitized"
        ii. Patients with COPD have this center desensitized and therefore not working
    b. We also have other peripheral chemoreceptors in the carotid and aortic bodies that are stimulated by O_2 and they are NOT desensitized like the central ones
        i. These are the ones keeping our COPD patients breathing
    c. If we give our COPD exacerbation patient 100% O_2 these peripheral chemoreceptors will not be stimulated anymore→ patient will stop breathing→ this will increase $PaCO_2$ → Decreased pH → **worsens respiratory acidosis**
        i.
    d. <u>Bottom line:</u> don't give 100% O_2 to patients presenting with COPD exacerbations

[8] Look Guyton and Hall Physiology 12 edition page 507

2. Give nebulized[9] short acting beta 2 agonist and an anticholinergic agent (salbutamol and ipratropium)
3. Oral corticosteroids
4. Antibiotics (aminopenicillin or macrolide) if there is increase in sputum color, volume, purulence[10], or breathlessness
    a. Because bacterial infections might be involved in causing acute exacerbations of COPD

Bronchiectasis

Abnormal **permanent** dilation of bronchi of small and medium sized bronchi.

Causes:

- Any condition that causes chronic inflammation, destruction, and scarring
    1. *Cystic fibrosis*: autosomal recessive disease that causes thick mucus secretion
        a. Mucus plugs increase the likelihood of infections→ bronchiectasis
    2. *Ciliary dysfunction*[11] (immotile cilia syndrome)
        a. Cilia not working properly→ increased mucus plugs and infections→ bronchiectasis
        - About 50% of patients with primary ciliary dyskinesia will have situs inversus[12] and sinusitis (kartagener syndrome)
    3. *Foreign body:*
        a. Obstruction→ inflammation→ destruction→ bronchiectasis
    4. Tumor obstructing bronchi
    5. *TB* obstructing bronchi
    6. *Infections* (Fungal, measles, whooping cough,etc.)
    7. *Agammaglobulinemia*
        a. Immunocompromised → infections → bronchiectasis

So it may be caused by many diseases that result in chronic infections and inflammation of the bronchi.

- **Note that bronchiectasis due to cystic fibrosis will be different than foreign body in areas of lung involved..**
    - Systemic diseases such as cystic fibrosis of ciliary dyskinesia would cause bronchiectasis in both lungs
    - A foreign body will cause localized bronchiectasis (distal to the obstructed bronchus)
    - Agammaglobulinemia will cause bronchiectasis in lung bases.

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[9] بُخار

[10] containing or producing pus

[11] For example in Kartagener syndrome

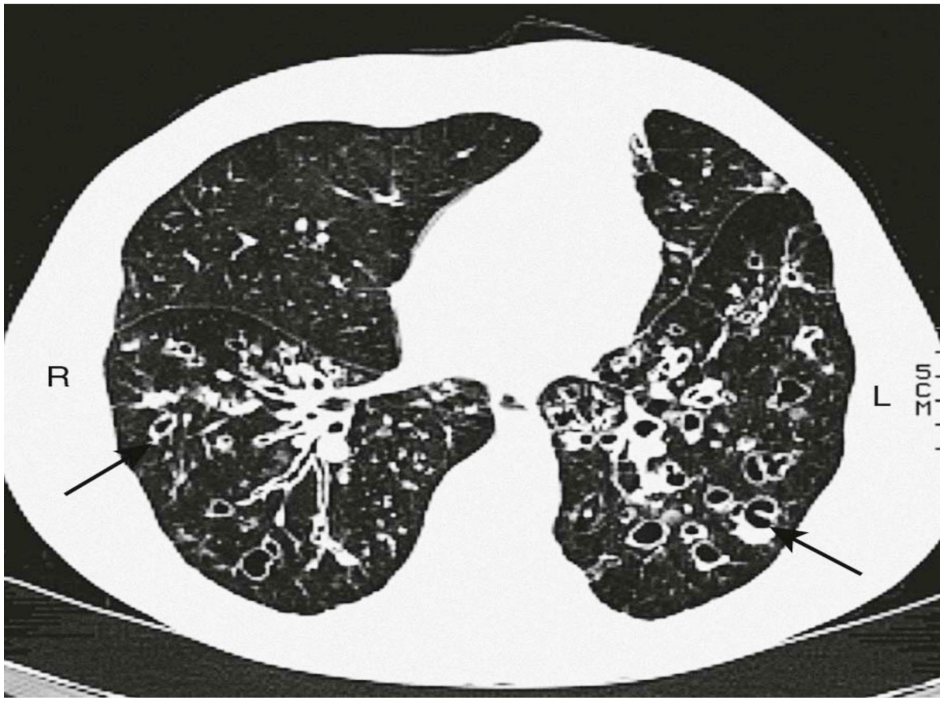
[12] Uncommon condition in which the major visceral organs are reversed or mirrored from their normal positions.

Clinical features

- Mainly similar to COPD. May have increased likelihood for *infections* commonly pneumonias (because the blocked area is an excellent place for bacteria to grow) so patients might have increased *purulent copious sputum* with fever. Their sputum might have a *bad smell* leading to halitosis[13]
- On auscultation: Wheezes or crackles.

Investigation

1. Should culture patient's sputum because they often have special infections (*Pseudomonas aeruginosa*) and we should know their antibiotic sensitivity by culture in order to properly treat it
2. CT scan (the best non-invasive test) shows dilated bronchi



3. Chest x-ray:
   It might be normal BUT in advanced cases it may show 1 to 2 cm cysts and crowding of bonchi (tram tracking)
4. Can also look for diseases that cause this condition
   For example: screen for ciliary dysfunction, CF, etc.

[13] Halitosis means bad breath in the mouth.

Management

1. If the patient has airflow obstruction→ treat that same as COPD patients (inhaled bronchodilators and corticosteroids)
2. Physiotherapy: helps the patient to get rid of all the sputum in the respiratory tract
    a. Video of somone with CF performing respiratory PT https://youtu.be/vE-ozzjkPY8?t=6m44s
3. Antibiotics: usually same as COPD (aminopenicillin or macrolide) but usually for longer durations and higher doses
    a. If culture shows *Pseudomonas or Staph aureus*, antibiotic therapy might be more difficult and should use sensitivity to guide antibiotic therapy

Prevention

- Treat any cause of bronchial obstruction early to avoid the development of bronchiectasis (remove the foreign body early before it progresses to chronic inflammation and bronchiectasis)

MCQ

A 60-year-old male has had a chronic cough for over five years with clear sputum production. He smoked one pack of cigarettes per day for 20 years and continues to do so. X-ray of the chest shows hyperinflation without infiltrates. Arterial blood gases show a pH of 7.38, PCO2 of 40 mm Hg, PO2 of 65 mm Hg. Spirometry shows a FEV1/ FVC of 65%. The most important treatment modality for this patient would be:

A. Oral corticosteroids
B. Home oxygen
C. Broad-spectrum antibiotics
D. Smoking cessation program

The answer is d. This patient's chronic cough, hyperinflated lung fields, abnormal pulmonary function tests, and smoking history are all consistent with chronic bronchitis. A smoking cessation program can decrease the rate of lung deterioration and is successful in as many as 40% of patients, particularly when the physician gives a strong antismoking message and uses both counseling and nicotine replacement. Continuous low-flow oxygen becomes beneficial when arterial oxygen concentration falls below 55 mmHg. Antibiotics are indicated only for acute exacerbations of chronic lung disease, which might present with fever, change in color of sputum, and increasing shortness of breath. Oral corticosteroids are helpful in some patients, but are reserved for those who have failed inhaled bronchodilator treatments.