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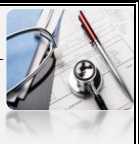

THE DISEASES OF THE RESPIRATORY SYSTEM

(Updated for Academic Year: 2011-2012G/1432-1433H)

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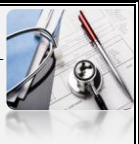


1 - lecture

NORMAL ANATOMY

The air conducting passages consist of the nasal cavities, paranasal sinuses, nasopharynx, oropharynx, hypopharynx (epiglottis and larynx), and tracheobronchial tree. At the carina, the trachea branches into the mainstem bronchi which branch into lobar bronchi which branch into segmental bronchi which supply the intralobar bronchopulmonary segments. Further branching produces subsegmental bronchi, bronchioles, terminal bronchioles, respiratory bronchioles, alveolar ducts and alveolar sacs. The pulmonary arteries follow the airways while the pulmonary veins run through the connective tissue septa. Lymphatic channels are present along the bronchovascular structures but are also found in the pleura and connective tissue septa.

Histology

With the exception of the oropharynx and portions of the nasopharynx and hypopharynx (which are lined by squamous epithelium), the upper respiratory tract and the large airways are lined by **pseudostratified ciliated columnar epithelium interspersed with mucus-secreting goblet cells and neuroendocrine cells.** Mucus-secreting glands lie beneath the epithelial surface and the cartilaginous plates help to maintain patency. Cartilage, submucosal glands and goblet cells are **lost at the level of the bronchioles** which are lined by ciliated cuboidal epithelium and Clara cells (which secrete a non-mucoid watery substance that contains lysozyme and immunoglobulins). The majority of the alveolar surface is lined by the Type I pneumocytes which are interspersed with the surfactant-

producing Type II (cuboidal/granular) pneumocytes. The interstitium contains collagen, elastin, mast cells, occasional inflammatory cells and connective tissue cells (primarily smooth muscle and fibroblasts). Alveolar macrophages that are derived from blood monocytes are loosely attached to the alveolar wall or lie free within the alveolar space.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

A] General considerations

(1) COPD is a group of disorders characterized by **airflow obstruction**.

(2) Characteristics include a marked decrease in the forced expiratory volume (FEV_1).

(3) COPD is often contrasted with restrictive pulmonary disease, a group of disorders characterized by reduced lung capacity due either to chest wall or skeletal abnormalities such as kyphoscoliosis or to interstitial and infiltrative parenchymal fibrotic disease.

Share a major symptom: dyspnea(Difficulty in breathing) with chronic or recurrent obstruction to airflow • within the lung.The incidence of COPD has increased dramatically in the past few decades.

Pathologic Findings in Chronic Obstructive Pulmonary Disease

Name of Disorders	Pathologic findings
Bronchial asthma	**Bronchial smooth muscle hypertrophy.** **Hyperplasia of bronchial submucosal glands and goblet cells.** **Airways plugged by viscid mucus containing Curschmann spirals, eosinophils and Charcot-leyden crystals.**
Chronic bronchitis	**Hyperplasia of bronchial submucosal glands leading to increased Reid index: ratio of the thickness of the gland layer to that of the bronchial wall.**
Pulmonary emphysema	**Abnormal dilation of air spaces with destruction of alveolar walls.** **Reduced lung elasticity.**
Bronchiectasis	**Abnormally dilated bronchi which are filled with mucus and neutrophils.** **Inflamamtion and necrosis of bronchial walls and alveolar fibrosis.**

A group of conditions characterized by limitation of airflow ➢

Emphysema and chronic bronchitis often co-exist. ➢

Due two main reasons:
- Cardiac problems.
- Respiratory prob.

Respiratory disease symptoms :

1-cough (dry or productive)
2-dyspnea
3-wheezing (because the air passages in narrowed duct)
4-chest pain

*investigations of lung disorder

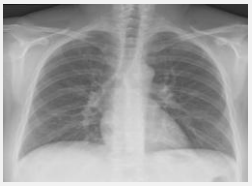
a bronchoscope is passed through the mouth or nose into the lungs.and fluid is squirted into a small part of the lung and then recollected for examination.

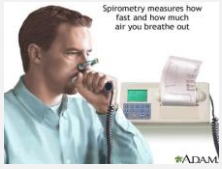
1) RADIOLOGY
X-ray C.T scan

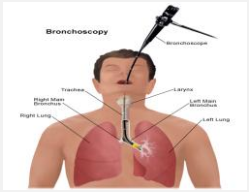
2) LABORATORY
(Sputum cytology and culture)

3) SPIROMETRY

4) BRONCHOSCOPY







5) BRONCHIAL BRUSH BIOPSY

7) Bronchoalveolar lavage

Bronchial Asthma

An inflammatory chronic obstructive airway disease caused by abnormal irritation of bronchial tree to various stimuli

Reversible disease (Mean: we can reverse it's affect by using bronchodilators

Bronchial Asthma

Chronic relapsing inflammatory disorder characterized by:

Hyperactive airways leading to episodic, reversible bronchoconstriction

Due to increased responsiveness of the tracheobronchial tree to various stimuli.

- *Primarily targets:*
  - *the bronchi and terminal bronchioles*
- *Most common chronic respiratory disease in children*
  - *More common in children than adults*
  - *Majority (50-80%) develop symptoms before 5 years of age*

1] Types include **extrinsic** and **intrinsic asthma**

(a) Extrinsic (immune) asthma is mediated by a **type I hypersensitivity response** involving IgE bound to mast cells. The disease begins in **childhood** and usually in patients with a family history of allergy.

- Subtypes include:

1-atopic (allergic) asthma. 2-occupational asthma. 3-allergic bronchopulmonary aspergillosis.

- Develop early in life
- **Other allergic manifestation: allergic rhinitis, urticaria, eczema.**
- Skin test with antigen result in an immediate wheel and flare reaction

(c) Intrinsic (non-immune) asthma includes asthma associated with **chronic bronchitis** as well as other asthma variants such as **exercise-or cold-induced asthma**. It usually begins in adult life and is not associated with a history of allergy

* pathogenesis of bronchial asthma :

Extrinsic (atopic)	**Intrinsic (non-atopic)**
Type I hypersensitivity (IgE) (http://highered.mcgraw-hill.com/olcweb/cgi/pluginpop.cgi?it=swf::535::535::/sites/dl/free/0072437316/120110/micro38.swf::IgE%20Mediated%20Hypersensitivity) . -The causative agents maybe are dust, domestic pets and pollens . More common in children and young . They MAY have another allergic condition such as Eczema . Symptoms come in EPISODIC . (at night or morning) . In this type if you do not know the allergen you can use (SKIN TEST http://www.medicinenet.com/skin_test_for_allergy/article.htm)	Serum IgE levels are usually normal . The causative agent is unknown Non specific allergen . More in adult . Negative skin tests May come with exercise Called: Exercise induce asthma. , aspirin , obesity . Patient has no history of allergy .

1) antigen enters the bronchial tree .

2) antigen presenting cell (APC) engulf it and present it on the surface.

3) The T helper 2 cells will activated and release cytokines which are IL-4 .IL-5,-IL-13 .

4) B cells will produce IgE (extrinsic)

5) IgE will attach to mast cell .

6) When antigen bind to IgE on mast cells the mast cell will produce Histamine that makes the bronchioles constriction

Interleukins	Action
IL 4	**Production of IgE by B cells**
IL 5	**induces an increase in eosinophil production**
IL 13	**Stimulates mucus hyper-secretion**

Pathogenesis :

EXAGGERATED BROCHOCONTRICTION

- Two components:

1-Chronic airway inflammation. 2-Bronchial hyperresponsiveness.

The mechanisms have been best studied in atopic asthma.

A classic example of type 1 IgE-mediated hypersensitivity reaction.

In the airway – initial sensitization to antigen (allergen) with stimulation of TH2 type T cells and production of cytokines (IL-4, IL- 5, and IL-13).

Type I hypersensitivity reaction with exposure to extrinsic allergens

Typically develops in children with an atopic family history to allergies

(1) Initial sensitization to an inhaled allergen

(a) Stimulate induction of subset 2 helper T cells (CD4 TH2) that release interleukin (IL) 4 and IL-5

(b) IL-4 stimulates isotype switching to IgE production.

(c) IL-5 stimulates production and activation of eosinophils.

(2) Inhaled antigens cross-link IgE antibodies on mast cells on mucosal surfaces.

(a) Release of histamine and other preformed mediators

(b) Functions of mediators:

Stimulate bronchoconstriction, mucus production, influx of leukocytes

(3) Late phase reaction (4-8 hours later)

(a) Eotaxin is produced.

Chemotactic for eosinophils and activates eosinophils

(b) Eosinophils release major basic protein and cationic protein.

Damage epithelial cells and produce airway constriction

Other mediators involved

Non-Atopic Asthma

Non immune

Positive family history is uncommon.

Serum IgE – normal.

No other associated allergies.

Skin test – negative.

Hyperirritability of bronchial tree (Stress, exercise, cigarette smoke)

Triggered by respiratory tract infection including

viruses (Examples-rhinovirus, parainfluenza virus, respiratory syncytial virus)

inhaled air pollutants (e.g. sulfur dioxide, ozone)

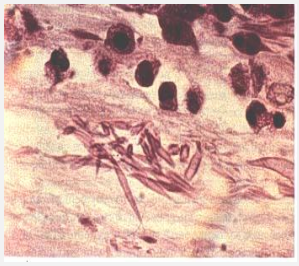
Subtypes:

Drug-induced asthma (Aspirin or nonsteroidal drug sensitivity)

Occupational asthma (fumes, dusts, gases)

2] Clinical presentation. There is marked episodic dyspnea and wheezing expiration caused by narrowing of the airways. Bronchial asthma is related to increased sensitivity of air passages to stimuli which leads to spasm in the bronchial muscular wall.

3] Pathological changes. Morphologic manifestations include bronchial smooth muscle hypertrophy, hyperplasia of goblet cells, thickening and hyalinization of basement membranes, proliferation of eosiniophils and intrabronchial mucous plugs with whorl-like accumulations of epithelial cells (Curschmann spirals) and crystalloids of eosinophil-derived proteins (Charcot-Leyden crystals).



***Curschmann spirals** : (mucus +epithelium)

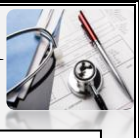
refers to a finding in the sputum of spiral shaped mucus plugs seen in biopsies from asthmatic patients

***Charcot-leyden crystals** : (are formed from the breakdown of eosinophils)

Microscopic crystals slender and pointed at both ends found in people who have asthma and it increases FEV.

Curschmann spirals and Charcot-leyden crystals are found in the asthmatic sputum .

Complications include **superimposed infection, chronic bronchitis, and pulmonary emphysema.** Bronchial asthma may also lead to **status asthmaticus** which is a prolonged bout of bronchial asthma that can last for days and responds poorly to therapy. Death can result from status asthmatics and for this reason this condition is regarded as an acute medical emergency.



* Complications :

1) superimposed infection .

2) chronic bronchitis .

3) pulmonary emphysema .

4) status asthmaticus

* (status asthmaticus) :

a prolonged bout of bronchial asthma that can last for days and responds poorly to therapy (Bronchodilator) ,Death can result from status asthmatics and for this reason this condition is regarded as an acute medical emergency.

Obstructive and Restrictive Pulmonary Diseases

Diffuse pulmonary diseases are divided into:

Obstructive disease: characterized by limitation of airflow owing to partial or complete obstruction at any level from trachea to respiratory bronchioles. Pulmonary function test: limitation of maximal, airflow rate during forced expiration 1 (FEVI).

Restrictive disease: characterized by reduced expansion of lung parenchyma with decreased total lung capacity while the expiratory flow rate is near normal. Occur 1. Chest wall disorder. 2. Acute or chronic, interstitial and infiltrative diseases, e.g. ARDS and pneumoconiosis.

pneumoconiosis / deposition of large amounts of dust or other particulate matter in the lungs, causing a tissue reaction, usually in workers in certain occupations and in residents of areas with excessive particulates in the air

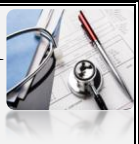
Status asthmaticus

- Severe cyanosis and persistent dyspnea for days and weeks
- Does not respond to therapy
- Hypercapnia, acidosis, sever hypoxia
- May be fatal

	Obstructive	Restrictive
Characteristics	1) Airway Disease. 2) characterized by limitation of air flow. 3) Increase in resistance. 4) Total lung capacity and FVC are either normal or increased (mainly normal) 5) Decrease of expiratory flow rate 7)Decrease of FEV1 8) Difficulty in EXPIRATION.	1) Reduced expansion of lung. 2) Decrease of Total lung capacity. 3) FVC is reduced. 4) Expiratory flow rate is normal or reduced. 5) Difficulty in INSPIRATION.
Causes	4) Anatomic airway narrowing (like what happen in Asthma) 5) Loss of elastic recoli (like what happen in emphysema)	1) Chest wall disorders (with normal lung) 2) Skeletal abnormalities . (Kyphoscoliosis) 3) interstitial and infiltrative parenchymal fibrotic diseases.
Examples	4) Asthma 5) Emphysema 6) Chronic bronchitis 7) Brochiectasis	* Acute : ARDS * Chronic : 1) Pneumoconioses 2) Interstitial fibrosis of unknown etiology 3) Infiltrative condition (Sarcoidosis)

Clinical Term	Anatomic Site	Major Pathologic Changes	Etiology	Signs/Symptoms
Chronic bronchitis	Bronchus	Mucus gland hyperplasia, hypersecretion	Tobacco smoke, air pollutants	Cough, sputum production
Bronchiectasis	Bronchus	Airway dilation and scarring	Persistent or severe infections	Cough, purulent sputum, fever
Asthma	Bronchus	Smooth muscle hyperplasia, excessive mucus, inflammation	Immunologic or undefined causes	Episodic wheezing, cough, dyspnea
Emphysema	Acinus	Airspace enlargement, wall destruction	Tobacco smoke	Dyspnea

= Respiratory bronchiole



2 - lecture

Chronic bronchitis

1] Clinical presentation.

The clinical definition is of chronic bronchitis is a productive cough that occurs during at least 3 consecutive months over at least 2 consecutive years.

- The patient has a prominent cough and produces mucus, the mucus is purulent (greenish, foul smelling)
- he may suffer from dyspnea in variable degrees
- He may presents as a cyanosis "blue bloater" , why blue ? Because in advance stages he suffers from high Pco2 (amount of oxygenated blood is low) ,bloating means he has a lot of air trapped in the lungs because of accumulation of mucus in bronchial tree.

Chronic bronchitis is clearly linked to **cigarette smoking** and is also associated with air pollution, infection and genetic factors ALSO urban dwellers, age 40 to 65. It may lead to **cor pulmonale** (Heart failure induced by pulmonary diseases).

- Patients with chronic bronchitis may suffer from an acute phase called exacerbation (increase in the severity of the disease), this happens when they have a bacterial or viral infection (cold, flu).

Clinical Course : Prominent cough and the production of sputum.

COPD with hypercapnia, hypoxemia and cyanosis. •

Cardiac failure. •

Can occur in several forms:

1-Simple chronic bronchitis.2-Chronic mucopurulent bronchitis 3-Chronic asthmatic bronchitis.

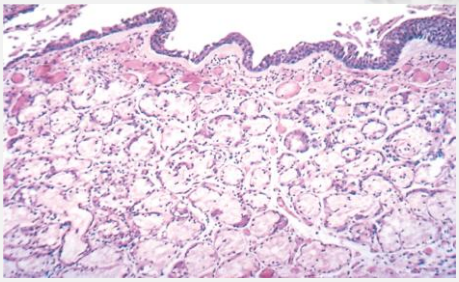
4-Chronic obstructive bronchitis.

2] Pathological changes.

Typical characteristics include hypersecretion of mucus that starts in the large airways due to marked **hyperplasia of mucus-secreting submucosal glands** .Causative factor are cigarette smoking and pollutant

- The magnitude of the increase in size is assessed by (Reid index): It is defined as the ratio between the thickness of the submucosal glands and the thickness of the bronchial wall. It is not used in living patients, as it requires dissection of the airway tube.
- No smooth muscle hypertrophy.

Morphology



- **Enlargement of the mucus-secreting glands, increased number of goblet cells, loss of ciliated epithelial cells, squamous metaplasia, dysplastic changes and bronchogenic carcinoma.**
- **Inflammation, fibrosis and resultant narrowing of bronchioles.**
- **Coexistent emphysema.**

In brief, histology demonstrates enlargement of mucus secreting glands, goblet cell metaplasia, and bronchiolar wall fibrosis.

Diagnosis:

- no need for biopsy
- sputum culture
- pulmonary function test , usually normal may be affected in severe cases
- chest x-ray (shows increase in bronchial markings)
- sputum cytology

to make sure sputum sample is adequate, we look for anthracotic macrophages or respiratory epithelial cells.

Emphysema (*http://www.youtube.com/watch?v=5b6f1LH9WH8&feature=related*)

1] General considerations, definitions and clinical features.

(a) Emphysema is **dilation or dilatation of air spaces** from and beyond the respiratory bronchioles with destruction of alveolar walls.(without inflammation or fibrosis).

(b) The disease is strongly associated with cigarette smoking.

- Is characterized by permanent enlargement of the airspaces distal to the terminal bronchioles accompanied by destruction of their walls, without obvious fibrosis.

2] Clinical characteristics.

Include increased anteroposterior diameter of the chest (Barrell chest); increased total vital capacity; hypoxia, cyanosis and respiratory acidosis.

Incidence: Emphysema is present in approximately 50% of adults who come to autopsy.

Pulmonary disease was considered to be responsible for death in 6.5% of these patients. •

Emphysema: Clinical course

Cough and wheezing - Weight loss & Pulmonary function tests reveal reduced FEV1.

- Classic presentation : the patient is barrel-chested with prolonged expiration , sitting forward in a hunched-over position, attempting to squeeze the air out of the lungs.
- uses accessory muscles of respiration
- Wight loos in advance cases (the patient is thin)
- Patients sometimes are called "pink puffers" because of prominent dyspnea and adequate oxygenation of hemoglobin (normal Po2)
- There is not a lot of coughing

3] Types of emphysema

(a) **Centrilobular (Centriacinar) emphysema**. Dilatation of the respiratory bronchioles is most often localized to the upper part of the pulmonary lobes.

-Occur in heavy smoker in association with chronic bronchitis

-The central or proximal parts of the acini are affected, while distal alveoli are spared

-More common and severe in upper lobes (apical segments)

-The walls of the emphysematous space contain black pigment

(b) **Panacinar (panlobular) emphysema.**

(1) Dilatation of the entire respiratory acinus, including the alveoli, alveolar ducts, respiratory bronchioles and terminal bronchioles. The disease is most often distributed uniformly throughout the lung.

(2) It is associated with loss of elasticity and sometimes with genetically determined **deficiency of alpha 1-antitrypsin** (alpha 1 – protease inhibitor).

More commonly in the lower lung zones. •

(c) **Paraseptal (distal)emphysema.**

(1) Dilatation involves mainly the distal part of the acinus, including the alveoli and to a lesser extent, the alveolar ducts. It tends to localize subjacent to the pleura and interlobar septa.

(2) It is associated occasionally with large subpleural bullae or blebs and its rupture leads to pneumothorax.

-The proximal portion of the acinus is normal but the distal part is dominantly involved.

-Occurs adjacent to areas of fibrosis, scarring or atelectasis.

-More severe in the upper half of the lungs.

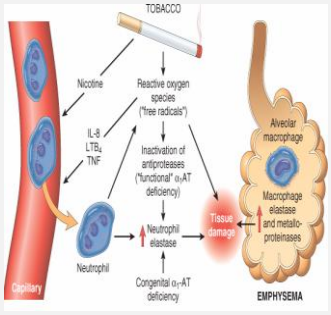
-Sometimes forming multiple cyst-like structures with spontaneous pneumothorax.

(d) **Irregular emphysema**: Is the most common subtype and characterized by irregular involvement of the acinus with scarring within the walls of enlarged air spaces. This type is usually a complication of various inflammatory processes **including chronic pulmonary tuberculosis**.

Pathogenesis of Emphysema

- Is not completely understood.
- Alveolar wall destruction and airspace enlargement invokes excess protease or elastase activity unopposed by appropriate antiprotease regulation (protease-antiprotease hypothesis)
- 2 key mechanisms:
  - 1. excess cellular proteases with low antiprotease level
  - 2. excess ROS from inflammation
- Protease-antiprotease imbalance occur in 1% of emphysema
- α1-antitrypsin, normally present in serum, tissue fluids and macrophages, is a major inhibitor of proteases secreted by neutrophils during inflammation.
- Encoded by codominantly expressed genes on the proteinase inhibitor (Pi) locus on chromosome 14.
- Pi locus is extremely pleomorphic (M , Z)
- Any stimulus that increase neutrophil or macrophages in the lung with release of protease lead to elastic tissue damage. The protease-antiprotease hypothesis explains the effect of cigarette smoking in the production of centriacinar emphysema .

Smokers have accumulation of neutrophils in their alveoli.



-Smoking stimulates release of elastase.

-Smoking enhances elastase activity in macrophages, macrophage elastase is not inhibited by α1-antitrypsin.

-Tobaco smoke contains reactive oxygen species with inactivation of proteases.

3] Complications.

(a) Emphysema is often complicated by or coexistent with **chronic bronchitis.**

(b) **Interstitial emphysema**, in which air spaces may enter into the interstitial tissues of the chest from a tear in the airways may sometimes occur.

(c) Other complications of emphysema may include rupture of a surface bleb (markedly dilated and emphysematous alveolus) with resultant **pneumothorax.**

(is an abnormal collection of air in the pleural space).

4] Postulated causes**.**

Emphysema may result from action of proteolytic enzymes such as elastase on the alveolar wall. Elastase can induce destruction of elastin unless neutralized by the antiproteinase-antielastase activities of alpha 1-antitrypsin which can be deficient in cases of emphysema.

(a) **Cigarette smoking** attracts neutrophils and macrophages, which are sources of elastase (an enzyme which destroys elastic fibers from the wall of alveoli).

(b) **Hereditary alpha 1 antitrypsin deficiency** accounts for a small subgroup of cases of **panacinar emphysema**. It is caused by variants in the *pi* (proteinase inhibitor) gene, localized to chromosome 14.

Death from emphysema is related to: .

Pulmonary failure with respiratory acidosis, hypoxia and coma. .

Right-sided heart failure. .

Morphology

The diagnosis depend largely on the macroscopic appearance of the lung.The lungs are pale, voluminous.

Histologically, thinning and destruction of alveolar walls creating large airspaces.

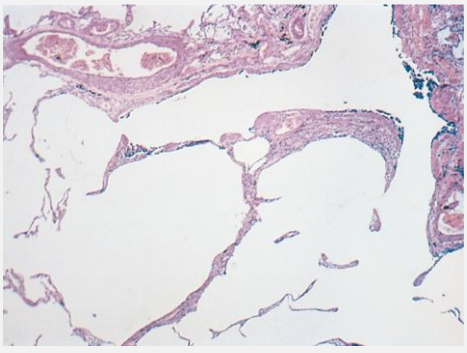
Loss of elastic tissue.

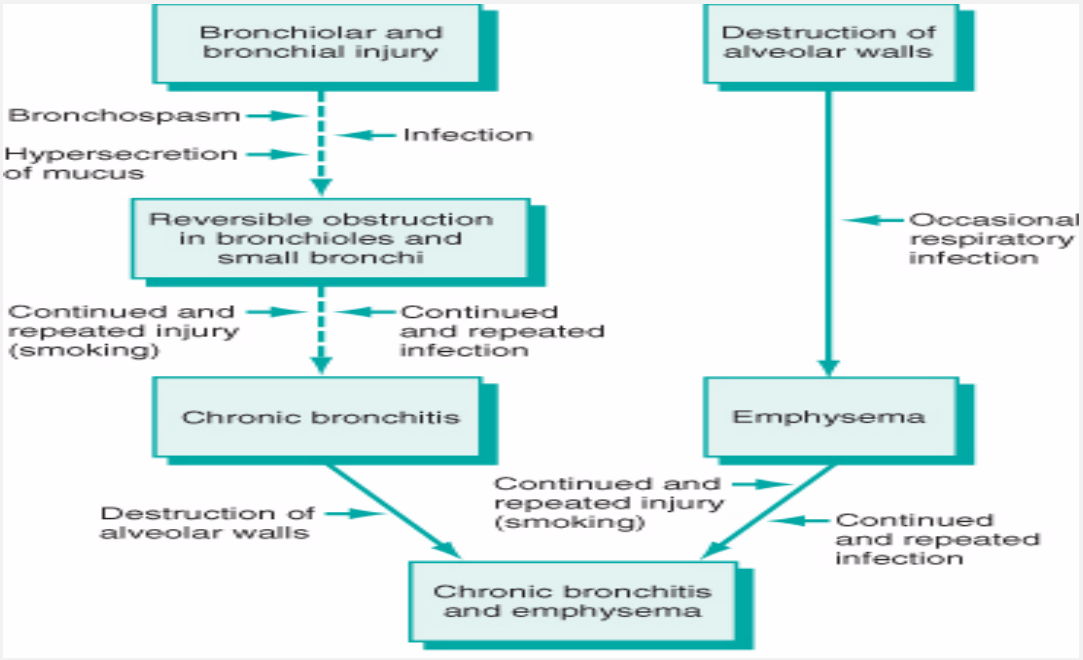
Reduced radial traction on the small airways.

Alveolar capillaries is diminished.

Fibrosis of respiratory bronchioles.

Accompanying bronchitis and bronchiolitis.

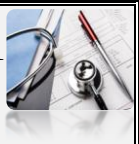




Emphysema and Chronic Bronchitis

http://www.youtube.com/watch?v=9EqCq_8J8vg&feature=related

	Predominant Bronchitis	*Predominant Emphysema*
Appearance	*"Blue bloaters"*	*"Pink Puffers"*
Age	*40-45*	*50-75*
Dyspnea	*Mild, late*	*Severe, early*
Cough	*Early, copious sputum*	*Late, scanty sputum*
Infection	*Common*	*Occasional*
Respiratory Insufficiency	*Repeated*	*Terminal*
Cor pulmonale	*Common*	*Rare, terminal*
Airway resistance	*Increased*	*Normal or slightly increased*
Elastic recoil	*Normal*	*Low*
Chest radiography	*Prominent vessels, large hear*	*Hyperinflation, small heart*



Bronchiectasis (http://www.youtube.com/watch?v=vxoA8FddG7k) •

1] **Definition:** This condition is characterized by **permanent and abnormal bronchial dilatation** which is caused by chronic infection with inflammation and necrosis of the bronchial wall.

it is not primary but rather secondary to persisting infection and inflamation caused by a variety of conditions.

Bronchial dilatation should be permanent.

Conditions associated with Bronchiectasis

1-bronchio obstruction : Localized :tumor, foreign bodies or mucous impaction

Generalized: bronchial asthma & chronic bronchitis

2- Congenital or hereditary conditions:

Congenital bronchiactasis :Cystic fibrosis- Intralobar sequestration of the lung-Immunodeficiency status & Immotile cilia and kartagner syndrome

- 3 Necrotizing pneumonia: Caused by TB, staphylococci or mixed infection.

2] Predisposing factors: include **bronchial obstruction**, most often by tumor.

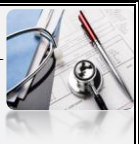
Other predisposing factors include **chronic sinusitis** accompanied by postnasal drip. The disease is rarely a manifestation of **Kartagener-syndrome (sinusitis, bronchiectasis and situs inversus** sometimes with hearing loss and male infertility), caused by a defect in the motility of respiratory, auditory and sperm cilia that is referred to as **primary ciliary dyskinesia,** an ucommon autosomal recessive syndrome. In this condition, there is a structural defect in dynein arms of the cilia which can be seen by electron microscopy. Impaired ciliary activity predisposes to infection in the sinuses and bronchi and disturbs embryogenesis, sometimes resulting in situs inversus. **Male infertility** is an important manifestation of ciliary dyskinesia.

Kartagener Syndrome

- Inherited as autosomal recessive trait.
- Patient develop bronchiactasis, sinusitis and situs invertus.
- Defect in ciliary motility due to absent or irregular dynein arms.
- Lack of ciliary activity interferers with bronchial clearance.
- Males have infertility

3] **Pathological features**: Bronchiectasis most often involves the lower lobes of both lungs. Characteristics include production of copious purulent sputum, hemoptysis and recurrent pulmonary infection that may lead to lung abscesses

- A chest x-ray show "tram tracks" (parallel lines outlining dilated bronchi due to peribronchial inflammation and fibrosis).



Complications :include lung abscesses, metastatic brain abscesses, and amyloidosis

Etiology and pathogenesis

- Obstruction and infection.

  Bronchial obstruction (athelectasis of airway distal to obstruction) – bronchial wall inflammation.

- These changes become irreversible: 1-If obstruction persist.2- If there is added infection.

Morphology of Bronchiectasis

- Usually affects lower lobes bilaterally (vertical airways).
- Dilated airways up to four times of normal, reaching the pleura.
- Tube-like enlargement (cylindroid) or fusiform (saccular).
- Acute and chronic inflammation, extensive ulceration of lining epithelium with fibrosis.

from robbins: clinical course:

- persistent cough with exepectoration of mucopurulent, sometimes fetid, sputum. The sputum may contain flecks of blood.
- Clubbing of finger may development.

3 - lecture

RESTRICTIVE PULMONARY DISEASES

General considerations, definition and causes:

(1) Restrictive pulmonary disease is a group of disorders characterized by reduced expansion of the lung and reduction in total lung capacity.

Characterized by:

- Stiff lung — The lung cannot expand normally due to collagen fibers that overload the elastic fibers
- reduced compliance of the lung
- reduction in total lung capacity

Sign and Symptoms:

- Dyspnea
- Hypoxia
- With progressive severe hypoxia, respiratory failure and cor pulmonale

Cor pulmonale: hypertrophy and dilatation of the right ventricle of heart failure secondary

(2) Examples include abnormalities of the chest wall

1- from bony abnormalities or neuromuscular disease that restrict lung expansion.

It's related to musculoskeletal abnormalities

1-in the thoracic cage and the vertebral column (aren,t so many they are summarized by malformations and deformaties of the vertebral colum (thoracic part)(inhibits the thoracic cage during respiratory act))

2-the intercostals muscles (a lot of these patients may die with respiratory failure although they have the manifestation of muscle disease(they must be severe enough to cause restriction in the movement of the thoracic cage))

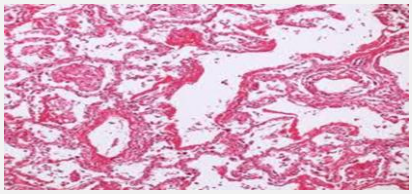
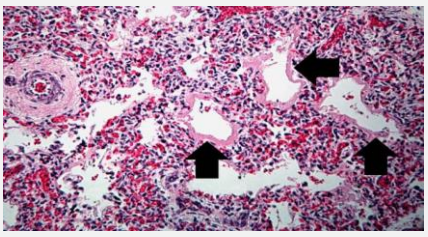
(3) Also included are the interstitial lung disease, a heterogenous group of disorders, characterized by interstitial accumulations of cells or non cellular material within the alveolar walls and the interstitial (connective tissue) of the lung that restrict expansion and often interfere with gaseous exchange. Prominent examples are acute conditions such as **the adult and neonatal respiratory distress syndromes**; **pneumoconioses** such as coal worker's pneumoconiosis, silicosis and asbestosis; **diseases of unknown etiology** such as **sarcoidosis** and **idiopathic pulmonary fibrosis,** various other conditions such as eosinophilic granuloma, hypersensitivity.

pneumonitis and chemical or drug associated disorders such as berylliosis or the **pulmonary fibrosis associated with bleomyxin toxicity**; and **immune disorders** such as systemic lupus erythematosus, systemic sclerosis (scleroderma), Wegener granulomatosis and Goodpasture syndrome.

Compliments:-

1-The main compliment of paitents with RLD is Dypnea (and many time they need oxegen). we can help the symptoms and stop it from worsening but we cannot revisit completely.RLD percentage of happening is less than COPD

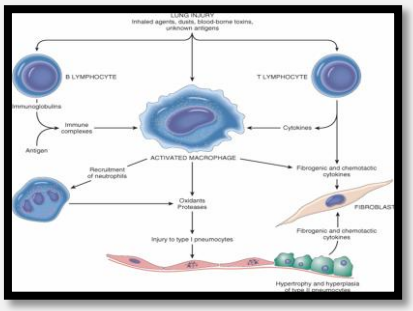
2- cough (most of the time dry cough)

Acute conditions	Causes	Characteristics
adult respiratory distress syndrome (ARDS)	• Initiated by damage to alveolar capillary endothelium and alveolar epithelium and is influenced by the following pathogenetic factors: a) Neutrophils release substances toxic to the alveolar wall. b) Activation of the coagulation cascade is suggested by the presence of microemboli. c) Oxygen toxicity is mediated by the formation of oxygen-derived free radicals. • produced by diffuse alveolar damage with resultant increase in alveolar capillary permeability, causing leakage of protein-rich fluid into alveoli (exudative phase). the alveoli filled with protein instead of air. • Causes include indirect lung injury by: shock, sepsis, uremia, acute pancreatitis, overdose with street drugs such as heroin or therapeutic drugs such as bleomycin. *Direct lung injury by: trauma, aspiration of gastric contents, inhalation of chemical irritants such as chlorine and oxygen toxicity.	• formation of an intra-alveolar hyaline membrane composed of fibrin and cellular debris.  • The result is severe impairment of respiratory gas exchange with consequent severe hypoxia. • ARDS can be a manifestation of the severe acute respiratory syndrome (SARS). The SARS virus is a coronavirus that destroys the type II pneumocytes and causes diffuse alveolar damage. ○ Mortality was 100% ○ Now 30 -40% with good ICU support ○ Poor prognosis: old age, multisystem failure, high level of IL-1.
neonatal respiratory distress syndrome (hyaline membrane disease)	• deficiency of surfactant, most often as a result of immaturity. • Predisposing factors: – Prematurity. – Maternal diabetes mellitus and delivery by cesarean section.	• the most common cause of respiratory failure in the newborn and is the most common cause of death in premature infants.  • Marked by: – Dyspnea – Cyanosis – Tachypnea shortly after birth

Chronic restrictive lung diseases:

- Are a heterogenous group with little uniformity regarding terminology and classification.
- Similar clinical signs, symptoms, radiographic alterations and pathophysiologic changes.
- Account for about 15% of non-infectious lung diseases.
- End-stage: diffuse interstitial pulmonary fibrosis.

Pathogenesis of interstitial lung diseases:



- Influx of inflammatory cells into the alveoli and alveolar walls
- Distortion of the normal structure of alveoli
- Release of chemical mediators
- Promotion of fibrosis

ADULT RESPIRATORY DISTRESS SYNDROME (ARDS)

1] ARDS is produced by **diffuse alveolar damage** with resultant increase in alveolar capillary permeability, causing leakage of protein-rich fluid into alveoli.

2] Characteristics include the formation of an **intra-alveolar hyaline membrane** composed of fibrin and cellular debris.

3] The result is severe impairment of respiratory gas exchange with consequent severe hypoxia.

Causes include a wide variety of mechanisms and toxic agents, including **shock, sepsis** **if a person has septicemia he suddenly may develop ARDS**, **trauma** **a person have an accident he broke his hand and rupture of the spleen and liver ….. he may develop ARDS**, **uremia, aspiration of gastric contents** **happens to a person that has stroke , cerebrovascular accident or anesthesia**, acute pancreatitis, inhalation of chemical irritants such as chlorine, **oxygen toxicity** or overdose with street drugs such as **heroin** or therapeutic drugs such as **bleomycin** **treatment with large amount of oxygen over a long period of time the oxygen will give rise to free radical** 4]

(ARDS)the white lung syndrome:- (may happen after major surgeries).

5] ARDS can be a manifestation of the severe acute respiratory syndrome (SARS). The SARS virus is a coronavirus that destroys the type II pneumocytes and causes diffuse alveolar damage.

6] ARDS is initiated by damage to alveolar capillary endothelium and alveolar epithelium and is influenced by the following pathogenetic factors:

(a) Neutrophils release substances toxic to the alveolar wall.

(b) Activation of the coagulation cascade is suggested by the presence of microemboli.

(c) Oxygen toxicity is mediated by the formation of oxygen-derived free radicals.

NEONATAL RESPIRATORY DISTRESS SYNDROME

(HYALINE MEMBRANE DISEASE)

General considerations:

- Neonatal respiratory distress syndrome is the most common cause of respiratory failure in the newborn and is the most common cause of death in premature infants. This syndrome is marked by dyspnea, cyanosis and tachypnea shortly after birth. This syndrome results from a deficiency of surfactant, most often as a result of immaturity.

Predisposing factors:

- **Prematurity. (less than 36 weeks). (a women that has multiple pregnancies)**
- **Maternal diabetes mellitus and delivery by cesarean section.**
  amniotic fluid aspiration (when the child may aspirate his own amniotic fluid)
  (because of the immaturity of the lung the baby will have damage of type ii pnmoucytes and therefore they cannot secrete surfactant and therefore there will be alveolar collapse)

Pneumoconioses. These environmental diseases are caused by **inhalation of inorganic duct particles.** They are exemplified by the following conditions:

(1) **Acanthracosis** is caused by inhalation of **carbon dust;** it is endemic in urban areas and causes no harm. Characterized by **carbon-carrying macrophages**, it results in irregular black patches visible on gross inspection.

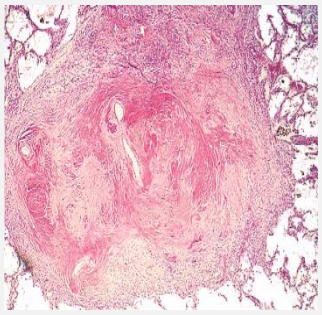
(2) **Coal worker's pneumoconiosis** is caused by inhalation of **coal dust,** which contains both carbon and silica.

(a) **Simple coal worker's pneumoconiosis** is marked by **coal macules** around the bronchioles, formed by ingestion of coal dust particles by macrophages. In most cases, it is inconsequential and produces no disability.

(b) **Progressive massive fibrosis** is marked by fibrotic nodules filled **with necrotic black fluid**. It can result in **bronchiectasis, pulmonary hypertension,** or death from respiratory failure or right-sided heart failure.

if the practicals where small then it will be sacattared in the air and if its 7 micron or more it will be stopped by the cilia and if the dimension is in between it may be inhaled and it will cause damge to type ii pnmoucytes leads to inflammation lead to fibrosis.

3] **Silicosis** is a chronic occupational lung disease caused by **exposure to free silica dust** **specially in coal mine**; it is seen in miners, glass manufacturers and stone cutters. In the Gulf region and in "desert climate", it could be due to inhalation of sand.

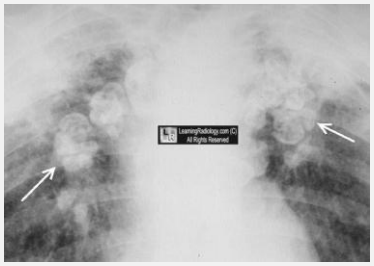


(a) This disease is initiated by **ingestion of silica dust by alveolar macrophages; damage to macrophages initiates an inflammatory response** mediated by lysosomal enzymes and various chemical mediators.

(b) **Silicotic nodules** that enlarge and eventually obstruct the airways and blood vessels are characteristics.

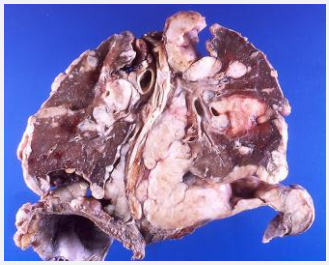
(c) Silicosis is associated with **increased susceptibility to tuberculosis**; the frequent concurrence is referred to as **silicotuberculosis.**

Pathogenesis:



- Crystalline silica is highly fibrogenic.
- Scattered lymphocytes and macrophages are drawn rapidly with fibrosis.
- Some particles are transported to lymph nodes.

4] **Asbestosis** is caused by **inhalation of asbestos fibers.**



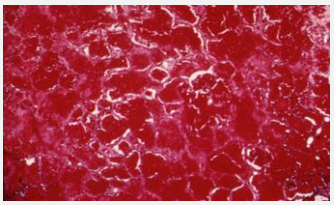
(a) This disease is initiated by uptake or asbestos fibers by alveolar macrophages. A fibroblastic response occurs, probably from release of fibroblast-stimulation growth factors by macrophages and leads to **diffuse interstitial fibrosis** mainly in the lower lobes.

because the **asbestos fibers** can damage the tissue there will be injury and if there is injury there is bleeding and if there is bleeding there is blood and if there is blood there is **haemosiderin that's why they look brown**

(c) It is characterized by the presence of **ferruginous bodies** which are yellow-brown, rod-shaped bodies with clubbed ends that stain positively with Prussian blue; these arise from iron andprotein coating on asbestos fibers. Dense **hyalinized fibrocalcific plaques of the parietal pleura** are also present.

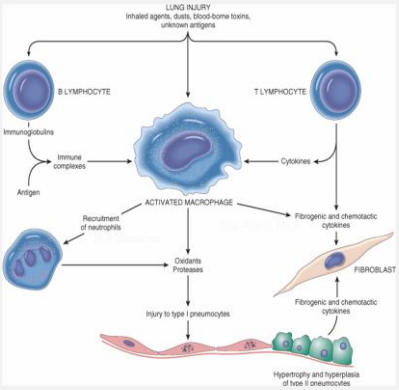
(c) Asbestosis results in marked predisposition to **bronchogenic carcinoma** and to **malignant mesothelioma** of the pleura or peritoneum. Cigarette smoking further increases the risk of bronchogenic carcinoma.

Selected Examples of Interstitial Lung Diseas

Disorder	Description
I. Hypersensitivity pneumonitis (extrinsic allergic alveolitis)	• An immunologically mediated inflammatory lung disease (type III and IV) • primarily affects the alveoli and is therefore often called allergic alveolitis. • caused by inhalation of various antigenic substances exemplified by inhalation of spores of thermophilic actinomycetes from moldy hay causing "farmer's lung". (occupational) **very common in penguin breeders (an old women always clean her window from penguin dropping each morning she will develop** Hypersensitivity pneumonitis (extrinsic allergic alveolitis **)** **A person like to breed birds he will have** Bird Fancier's Lung (BFL) • May present either as an acute reaction with fever, cough, dypsnea and constitutional complains 4 to 8 hours after exposure **or as** • a chronic disease with insidious onset of cough, dyspnea, malaise and weight loss
II. Goodpastures dynrome	• Hemorrhagic pneumonitis and glomerulonephritis caused by antibodies directed against glomerular basement membranes. • Male sex, Age: 20 to 30 years or 60 to 70 years • Pulmonary complaints consist of hemoptysis and dyspnea. • Hematuria, proteinuria, red cell casts and renal failure are results of glomerulonephritis. • Antiglomerular basement membrane antibody can be detected in serum. 
III. Eosinophilic granuloma	• Proliferationa of histiocytic cells related to Langerhan's cells of the skin.
IV. Sarcoidosis	Granulomatous disorder of unknown etiology. **Here in Saudi Arabia the most common cause of granuloma is T.B (which has caseous necrosis) whereas** Sarcoidosis doesn't have caseous necrosis) Sarcoidosis doesn't have caseous necrosis – affect the lymph nodes causing lymph nodes enlargement- affect black people more than others.

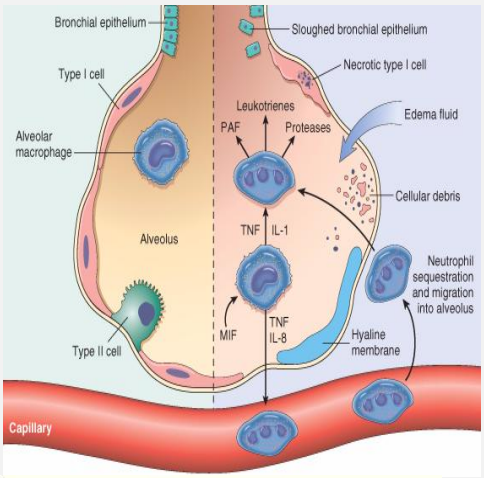
Idiopathic pulmonary fibrosis:

- Male > Female
- Immune complex disease with progressive fibrosis of the alveolar wall.
- pathogenesis:
  - Some form of alveolar wall injury result in interstitial edema and alveolitis.
  - Type I pneumocyte is more susceptible to injury.
  - Type II pneumocyte hyperplasia (regenerate).
  - Fibroblast proliferation with progressive fibrosis of intra-alveolar exudate and interalveolar septa.
  - IgG deposits are seen in alveolar wall



Clinical features of IPF:

- Males are affected more often than females.
- Most patients are between 40 &70 years old.
- Gradual onset of dyspnea with respiratory difficulty.
- Hypoxemia and cyanosis.
- Cor pulmonale and cardiac failure may result.
- The progression in individual cases is unpredictable.
- The median survival is about 3 to 5 years.



Sarcoidosis

An inflammatory condition of the tissues, most noted for originating in the lymph nodes or the lungs

affecting all races

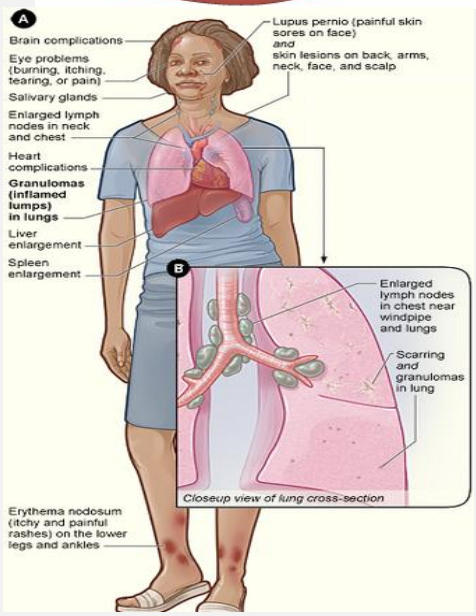
affecting both sexes equally

Non- casaeting granuloma

Bilaterl hilar LN

Lung nodules

Other organs



In the clinic:- if a patient have mild dyspnea with chronic dry persistent cough you should investigate him rediologicaly (by C.T scan and by X-ray

In the clinic:- (in the intensive care unit we have blood gas analyzer) when you do blood gas analyses you take the arterial blood than measure the PO2 and PCO2 in these patient they will have accumulation of PCO2 and PO2 will be reduced and as the disease advance they wil have respiratory acidosis and respiratory failure.

In the clinic:- to know the sputum is a good sample (its coming from the deep part of the bronchiole)(in the people that live in cities because they have anthracotec macrophage) or a bad sample in people that live in the dessert