**Pathological basis of**

**respiratory system diseases**

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**Learning Objectives**

**Nose, Nasal sinuses & Nasopharynx**

**-Pathology of inflammatory diseases; rhinitis, sinusitis, and nasopharyngitis**

**-Granulomatous lesions**

**-Benign and malignant tumors and tumor like lesions**

**-Tumors of the larynx**

**Obstructive pulmonary diseases (airway diseases)**

**-Pathological bases of decreased expiratory flow rate**

**-Pathology of bronchial asthma**

**-Pathology of bronchiectasis**

**-Pathology of chronic bronchitis**

**-Pathology of pulmonary emphysema**

**Restrictive pulmonary diseases**

**-Diffuse interstitial lung diseases**

**-Pathology of acute respiratory destress syndrome (ARDS)**

**-Pathology of chronic restrictive pulmonary diseases**

 **-Pneumoconiosis**

 **-Interstitial fibrosis of unknown etiology**

 **-Infiltrative conditions**

**-The outcome of chronic restrictive pulmonary diseases**

 **-Honey comb lung**

**Lung Atelectasis**

**-Definition**

**-Types**

**-Pathology and effects**

**Pneumonia**

**-Definition**

**-Classification**

**-Pathology of bronchopeumonia**

**-Pathology of lobar pneumonia**

**Pulomonary hypertension**

**-Definitiom**

**-Pathogenesis and causes**

**-Pathological changes in pulmonary microcirculation**

**Tumors of the lungs and bronchi**

**-WHO classification of lung carcinoma**

**-The four major histological types**

**- Pancoast’s tumor**

 **-Pancoast’s syndrom**

**Tumors of the pleura**

**-Benign mesothelioma**

**-Malignant mesothelioma**

**Nose, Nasal sinuses & Nasopharynx**

**Acute Rhinitis:**

 Two types:

Infectious rhinitis (common cold); viral (rhinovirus)

Allergic rhinitis (hay fever, atopic rhinitis)

Type 1-(anaphylactic) hypersesitivity reaction to allergens like pollens,

 animal dandruff, house dust

**Acute sinusitis**

Complicates acute infection of the nose and dental sepsis

Pathogenesis includes impairment of drainage of the sinuses due to mucosal

 edema or nasal polyp.

Organisms; Strept.pyogenes, strept. Pneumonia and staph. aureus

**Histopathology of acute rhinitis, sinusitis and nasopharyngitis**

-Edema & hyperemia of mucosa

-Hyperactivity of mucosal glands.-

In Viral infection, there are few neutrophils in mucosa and exudate with

 mucoserous nasal secretion

When secondary bacterial infection occurs, large number of neutrophils migrate

 to the mucosa and exudate Leading to mucopurulent exudate (mucus with pus)

**Chronic rhinitis, sinusitis and nasopharyngitis**

Follows repeated attacks of acute inflammation that fail to resolve.

The most important predisposing factor is inadequate drainage of sinuses

due to nasal obstruction by polyp or hyperplasia of nasopharyngeal lymphoid

tissue (adenoid)

**Chronic granulomatous rhinitis**

 Like tuberculosis (TB.), leprosy, tertiary syphilis and fungal infection

**Necrotizing granulomas** of the nose and upper respiratory tract

 Two types:

1.Wegener’s granulomatosis

2.Malignant (lethal) midline granuloma.

**1.Wegener’s granulomatosis**; consists of:

a.necrotizing granulomas in the lung and upper air ways.

b.necrotizing vasculitis (inflammation of blood vessels wall with necrosis)

c.focal glomerulonephritis (Immune complex disease primarily affects the

 glomeruli)

**2.Malignant (lethal) midline granuloma.**

Progressively spreading ulcerative lesion

Erodes the soft tissues and bone in the midline of face; nose, nasal sinuses

 and nasopharynx.

It represents a type of non-Hodgkin’s lymphoma of T-cell type.

**Tumors of the nose, sinuses & nasopharynx**

**Benign tumors**

**1) Squamous Papilloma.**

 Two types:

-Exophytic (fungating) papilloma.

-Inverted papilloma.

Inverted papilloma:

Is a locally aggressive benign tumor

Recurs if not adequately excised

May change to carcinoma.

3

**2) Angiofibroma**

Occurs in Nasopharynx

In childhood and adolescence.

Almost exclusively in boys.

Highly vascular tumor.

Easily bleed.

Microscopically; admixture of blood vessels & fibrous tissue

**3)Hemangioma**: is the most common benign tumor of the nose.

**Malignant tumors** of the nose and nasal sinuses:

1**-**Squamous cell carcinoma is the most common

 2-Adenocarcinoma

 3-Anaplastic carcinoma.

**Malignant tumour** of the nasopharynx

Is called **Nasopharyngeal carcinoma**

It is of 3 types according to WHO classification:

1-Keratinizing squamous cell carcinoma (WHO type I).

2-Non-keratinizing differentiated carcinoma (WHO type II)

3-Non-keratinizing undifferentiated carcinoma (WHO type III)

 The type III carcinoma is also called "Lymphoepithelioma" due to heavy

infiltration of tumor stroma by non-neoplastic lymphocytes.

 It is closely associated with Epistein-Barr virus

 It is, unfortunately, the most frequent type of nasopharyngeal ca.

**Singer’s nodule (laryngeal nodule):** *it is not tumor*

Inflammatory polyp, arises on the vocal cords, causes hoarseness of voice.

common in heavy smokers and those who use their voice

grossly: small, smooth, round, sessile or pedunculated.

microscopic: fibro-myxoid core covered by normal squamous epithelium

**Benign tumors of the larynx**

**Squamous cell Papilloma**

Is the commonest benign tumor of the larynx.

Occurs usually on vocal cords.

Two types

 1) adult type: usually Solitory, may recurs after excision and rarely

 becomes malignant

 2) in children: they are multiple, of viral etiology, and regress spontaneously

 after adolescence

 They may cause suffocation

Other benign tumors of the larynx: angiomas, lipoma, myxoma and

 granular cell tumor.

**Malignant tumors of the larynx**

**Squamous cell carcinoma**

Is the most common malignant tumor of the larynx

\*Commonly affects males over 50 years.

\*Risk factors; -smoking is the most important.

 -Human papilloma virus (HPV), is another risk factor

Glottic tumors ( in the true vocal cords) are well differentiated with less

 incidence of lymph node metastasis and have better prognosis than the

 supraglottic and infraglottic tumors, which are often less differentiated,

 and tend to be more invasive with early Lymph nodes metastasis.

The tumor is also characterized by ocal extention with destruction of the surrounding tissue with cervical lymph nodes metastasis and distant metastasis.

Erosion of the adjacent vessels particularly the carotid artery may lead to fatal

hemorrhage

**The Bronchi**

**Acute bronchitis**

acute inflammation of large extra-lobular bronchi.

occurs in adults.

usually mild but may aggravate an established chronic bronchitis.

**Acute bronchiolitis**

acute inflammation of small intra-lobular bronchi & bronchioles.

occurs in children, old people & in states of debility.

rare in adults, except as a complication of influenza.

serious condition due to the liability of the organism to spread to the adjacent acini causing broncho-pneumpnia.

**Catarrhal bronchitis.**

inflammation limited to the surface epithelium.

excessive secretion of mucus or mucopurulent.

microscopic: edema & neutrophils infiltration confined to the surface epithelium

in severe cases, the surface epithelium may be shed, called ulcerative bronchitis

**Obstructive versus restrictive pulmonary diseases**

**Obstructive diseases (airway diseases)**

Limitation of airflow usually resulting from an increase in resistance caused

 by partial or complete obstruction at any level

Total lung capacity and Forced vital capacity are normal or increased

The hallmark is **decreased expiratory flow rate** with decreased FEV1 (forced

 expiratory volume at 1 second)

**decreased expiratory flow rate & FEV1** results from either:

1.Anatomic airway narrowing, classically seen in bronchial asthma

2.Loss of elastic recoil of the lungs: characteristic of pulmonary emphysema.

**The Four major diffuse obstructive airway diseases:**

Bronchial Asthma

Chronic bronchitis

Bronchiectasis

Emphysema

**Restrictive lung diseases,**

 Characterized by reduced expansion of the lung parenchyma during

inspiration resulting in decreased total lung capacity.

FVC is reduced and the expiratory flow rate is normal or reduced proportionately

**The restrictive defects**

Are due to chest wall disorders or interstitial lung diseases

**1.chest wall disorders** (in the presence of normal lungs):

a. Severe obesity,

b. Diseases of the pleura

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Pneumothorax

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c. Neuromuscular disorders, such as the Guillain-Barré syndrome (autoimmune

 disease attacks the nerves and affect the respiratory muscles).

**2.interstitial lung diseases**

a) Acute restrictive disease include acute respiratory distress syndrome (ARDS)

b) Chronic restrictive diseases, include Pneumoconiosis, Interstitial fibrosis of

 unknown etiology and infiltrative conditions like sarcoidosis

**Obstructive pulmonary diseases**

**Chronic bronchitis**

It is defined as persistent productive cough (cough with sputum) for at least

 3 consecutive months in at least 2 consecutive years without other apparent

 explanation.

\*It is not an inflammatory disease

\*It consists of metaplastic and hyperplastic changes result from chronic irritation

 of the bronchial epithelium mainly by cigarette smoke & atmospheric pollution.

Microscopical chnges:

hyperplasia + hypertrophy of mucus glands.

increase number of goblet cells.

decrease number of ciliated cells.

hyperplasia and hypertrophy of mucus glands with increase number of goblet cells, leads

to excessive production of mucus.

While decrease number of ciliated cells leads to accumulation of mucus in the bronchi

 leading to bronchial obstruction. With subsequent infection, the mucus secretion is changed

 to mucopurulent secretion.

**Bronchial asthma**

widespread bronchial obstruction, due to

1. paroxysmal spasm of the smooth muscles in the airways

2. edema of the mucosa of the airways

3. presence of thick mucus in the lumen of bronchi and bronchioles.

clinically: tightness in the chest, **difficult *expiration***, wheezing and nonproductive

 cough.

**The major etiologic factors of asthma are:**

1. genetic predisposition to type I hypersensitivity ("atopy"),

2. acute and chronic airway inflammation,

**Two main types of asthma:**

**Extrinsic (atopoic) asthma; (70%)**

 starts in childhood.

 due to type 1-(atopic) hypersensitivity reaction to external allergens like

 pollens, animal dandruff, mites (house dust) or fungi.

The patients have a genetically determined predisposition to develop

 Ig E- antibody

Skin test and provocation inhalation test shows typical type 1 reaction.

**Intrinsic asthma**

Starts later in life.

No individual or family history of atopic diseases.

No responsible allergen can be determined by skin test or provocation

 inhalation test.

Commonly associated with chronic bronchitis and nasal polyp.

**Histopathology in Asthma**

 (Diagnosis of Asthma is clinical, not by biopsy. The understanding of histopathology in asthma is essential for the correlation with the clinical aspects of the disease)

1) Plugging of the bronchi by mucinous secretion, resulting from an increase

 in the number of goblet cells in the mucosa and hypertrophy of submucosal

 mucous glands.

2) Hyaline thickening of the basement membrane.

3) Congestion and edema of the submucosa.

4) Hypertrophy of the smooth muscles of small bronchi and bronchioles.

**Bronchiectasis**

**Definition**

 permanent dilation of the bronchi and bronchioles caused by destruction

of the muscle and elastic supporting tissue, usually resulting from chronic necrotizing infections.

The involved bronchi are easily collapsible, this leads to airflow obstruction and impairment of clearance of secretions with sub sequent infection.

**Etiology**

1) Loss of ventilated lung substance like in lung collapse and bronchial

 obstruction by foreign body or tumor

 The force of the inspired air falls on the bronchial wall and causes bronchial

 dilation.

2) Necrotizing inflammation of the bronchi which leads to destruction of the

 elastic supporting tissue

3) Fibrous band connecting the bronchial wall with a fibrosed adherent pleura.

 Contraction of this fibrous band causes traction of the bronchial wall with

 dilatation

4) In children; bronchiectasis is rare, it may complicates:

bronchopneumonia.

atelectasis.

fibrocystic disease.

5) Less common causes;

Kartagener’s (immotile cilia) syndrome.

Immune deficiency syndrome (frequent infections)

**Pathology of Bronchiectasis**

fibrosis of lung tissue surrounding the *bronchiectatic* *cavities*

at first the cavities are dry. Then secretion accumulates and without effective

 treatment, subsequent infection occurs with purulent secretion.

Then infection with putrefying organism leads to decomposition of the

 secretion with *foul smelling breath & sputum*

Microscopically: the cavities are lined by respiratory columnar epithelium,

 later, ulceration & squamous metaplasia.

**Pulmonary Emphysema**

Abnormal *permanent dilation* of the airspaces ***distal*** *to the terminal*

*bronchioles*, accompanied by *destruction* of their walls *without obvious*

*fibrosis*

Enlargement of airspaces, not accompanied by destruction is called

 overinflation.

Emphysema is classified according to its anatomic distribution within

the lung lobule

Respiratory acinus is the portion of the lung tissue formed by the branches

 of a single terminal bronchiole

Lung lobule is a cluster of three to five acini (i.e. it is supplied by 3-5

 terminal bronchioles)

**There are two major types of pulmonary emphysema:**

1. Centriacinar (centrilobular) emphysema
2. Panacinar emphysema

In Centriacinar (centrilobular) emphysema:

The dilated air spaces are the respiratory bronchioles,

In slices of fixed inflated lung, the dilated air spaces are seen around the

 center of the lobule (centrilobular).

Panacinar emphysema

Is the type of emphysema that occurs in α1-antitrypsin deficiency.

The dilation initially affects the alveolar ducts and alveoli.

Then progress to involve the respiratory bronchioles, thus involving the

 entire acinus (Panacinar).

Pathogenesis of emphysema

Two critical imbalances:

Protease-antiprotease imbalance

Oxidant-antioxidant imbalance

Both are almost always coexist and their effects are additive in producing

 the end result of tissue damage.

**Protease-antiprotease imbalance**

\*Proteases (particularly elastase enzyme) secreted by neutrophils during inflammation

\*α1-Antitrypsin, is a major antiprotease normally present in serum and tissues.

 In patients with α1-Antitrypsin deficiency, any stimulus, like cigarette smoke, which activate neutrophils in the lungs will lead to unopposed elastase activity with tissue damage and emphysema.

 Patients with homozygous deficiency of α1 Anti trypsin, have a markedly decreased

serum level of α1-antitrypsin. They have high incidence of severe panacinar emphysema before the age of 10 yr.

Heterzygotes patients tend to be unaffected, but centrilobular emphysema induced by

 cigarette smoking occurs more rapidly

Oxidant-antioxidant imbalance

Normally, the lung contains antioxidants (superoxide dismutase and glutathione)

 that keep oxidative damage to a minimum.

Tobacco smoke contains abundant oxidants (reactive oxygen species) (free

radicals),which deplete the antioxidant

Oxidants in smoke can inactivate α1 Antitrypsin, resulting in "functional"

 α-1antitrypsin deficiency even in patients without enzyme deficiency.



**Mediastinal (interstitial) emphysema**

entrance of air into the connective tissue stroma of the lung ,mediastinum,

and subcutaneous tissue

Causes:

spontaneous

sudden increase in intra-alveolar pressure (vomiting or coughing) that

causes a tear, with dissection of air into the interstitium.

perforating injury (e.g., a fractured rib).

When the air enters the subcutaneous tissue, the patient may blow up

likea balloon, with marked swelling of the head and neck and crackling

crepitation all over the chest.

In most instances, the air is resorbed spontaneously when the site of entry is sealed.

**Restrictive pulmonary diseases**

**Diffuse interstitial lung diseases**

diffuse and usually chronic involvement of the interstitium in the alveolar walls.

pulmonary interstitium is composed of:

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elastic tissue

occasional mononuclear cells.

**Acute restrictive pulmonary diseases**

**\*Acute Respiratory Distress Syndrome (ARDS)**

ARDS is a clinical syndrome caused by diffuse alveolar capillary and

epithelial damage.

Characterized by rapid onset of respiratory insufficiency, cyanosis and

severe arterial hypoxia that is refractory to oxygen therapy

It may progress to multisystem organ failure with high mortality.

The histologic manifestation of ARDS in the lungs is known as *diffuse alveolar damage (DAD).*

**Causes of ARDS**

 ARDS iss a well-recognized complication of:

major trauma

shock; (hemorrhagic or septic shock)

inhalation of toxic irritants; O2, NO2, Chlorine

DIC (Disseminated Intravascular Coagulopathy)

Extensive burn

Massive pulmonary embolism

**Pathogenesis of ARDS**

diffuse alveolar damage (DAD) with endothelial & epithelial injury causes

increased vascular permeability leading to interstitial and then intra-alveolar

edema with fibrin exudation and formation of hyaline membrane (hence, the old

terminology, *hyaline membrane disease*)

These changes lead to Poor lung aeration

**Chronic restrictive pulmonary diseases.**

Pneumoconiosis

Interstitial fibrosis of unknown etiology,

Infiltrative conditions (sarcoidosis)

The end stage of most chronic restrictive lung diseases, irrespective of etiology,

 is diffuse interstitial pulmonary fibrosis with honeycomb lung

**Honeycomb lung** is non-specific descriptive term used for acquired conditions in which cystic spaces develop in fibrotic lungs, contraction of the fibrous tissue distorts the native architecture, creating enlarged airspaces enclosed within thick fibrous walls.

Pneumoconiosis

Group of lung diseases which result from inhalation of dusts:

1. Inorganic (mineral) dusts

2. Organic (biological) dusts

3. Chemical fumes and vapors

The reaction of the lung to mineral dusts depends on:

Size of the dust particle,

Its shape,

Its chemical composition

Its concentration

Duration of exposure

Coexistence of other lung diseases.

Particles > 5 μ are unlikely to reach distal airways (trapped in the

nasopharynx, trachea& major bronchi).

Particles < 1 μ tend to act like gases and move into and out of alveoli

 (exhaled with expired air)

Particles that are 1-5 μ are the most dangerous, because they get lodged

 at the bifurcation of the distal airways.

Particles < 0.02 μ (Sub-micronic) may penetrate alveolar wall into the

 interstitial.

**Pneumoconiosis caused by Inorganic (mineral) dusts:**

1. Pulmonary anthracosis

2. Coal Workers' Pneumoconiosis

3. Silicosis

4. Asbestosis

**1. Pulmonary anthracosis**

Caused by inhalation of soot particles

Inhaled pigment is engulfed by alveolar macrophages, which then accumulate

in the connective tissue along the lymphatics or in lymph nodes.

It is of a little clinical significance;

pigment accumulates without a appreciable cellular reaction (no fibrosis)

**2. Coal Workers' Pneumoconiosis (CWP)**

Caused by inhalation of coal dust particles

Occurs in two stages:

**A) Simple CWP**

Coal particles are ingested by macrophages, retained in relatively

immobile alveoli adjacent to the respiratory bronchioles

Accumulated dust provokes a local fibrotic reaction

After several years there will be fibrotic obliteration of the peri-

bronchiolar alveoli lead to dilatation of the respiratory bronchioles

forming a centrilobular Emphysema with dust blackening called

Focal dust emphysema

Simple CWP is characterized by formation of:

coal macules consists of dust-laden macrophages

coal nodule: consists of dust-laden macrophages with small amounts of collagen fibers

**B) Complicated CWP (progressive massive fibrosis) (PMF)**

Occurs on a background of simple CWP by coalescence of coal nodules

Requires 10-20 years to develop.

It is characterized by intensely blackened multiple fibrous scars up

to 10 cm in diameter,

Microscopically the lesions consist of dense collagen and pigment.

PMF has a tendency to progress even in the absence of further exposure.

Death may occur due to

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Pulmonary hypertension,

Core pulmonale ( latin term means "pulmonary heart") (RVF)

May become infected by TB.

There is no increased risk of lung carcinoma

**3. Silicosis**

The most prevalent chronic occupational disease in the world.

It is caused by inhalation of Silica

Two forms of Silica; crystalline & amorphous.

crystalline forms (including quartz) are (particularly quartz) the most toxic

 and fibrogenic.

After inhalation, silica particles are Ingested by macrophages. cause

 release of mediators by pulmonary macrophages, including IL-1, TNF,

 fibronectin, fibrogenic cytokines leading to dense fibrous reaction with

 formation of Silicotic nodules in the upper zones of the lungs

Microscopic; Silicotic nodules are composed of silica particles in the center

 of the nodules surrounded by concentric rings of fibrous tissue

As the disease progresses, the individual nodules may coalesce into hard,

 collagenous scars, with eventual progression to PMF which progress to

 honeycomb lung

Most individuals are asymptomatic, they do not develop shortness of

 breath until PMF (progressive pulmonary fibrosis) is present

The disease may be progressive, even if the person is no longer exposed

 to the dust.

Complications:

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associated with an increased susceptibility to tuberculosis

the relationship between silica and lung cancer continues to

 be controversial

**4.Asbestosis**

Results from inhalation of asbestos

Two distinct forms of asbestos:

1) serpentine type

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most of the asbestos used in industry

2) amphibole type

the fibers are straight, needle like, stiff, and brittle

more pathogenic

Serpentine fibers with their more flexible, curled structure, are likely to

become impacted in the upper respiratory passages and removed by the

mucociliary elevator. Those that are trapped in the lungs are gradually

removed from the tissues, because they are more soluble.

While the traight, stiff amphiboles, can align themselves in the air stream and arehence delivered deeper into the lungs, where they may penetrate

epithelial cells and reach the interstitium.

Both types of asbestos can cause "**Asbestos-Related Diseases**" which include:

1. Interstitiallung fibrosis (asbestosis)

2. Localized fibrous plaques or, rarely, diffuse fibrosis in the pleura

3. Pleural effusions

4. Bronchial carcinoma

5. Malignantmesothelioma of the pleura and peritoneum

6. Laryngeal carcinoma.

7. An increased incidence of asbestos-related cancers in family members of

 asbestos workers

 Inhaled asbestos fibers are mostly retained in the respiratory bronchioles

of the lower lobes, then pass into the alveolar ducts & alveoli where the

small fragments are engulfed by macrophages

 Complete fibers are surrounded by macrophages & become coated with

iron & protein derived from phagocyte ferritin forming a drumstick shaped body called **Asbestos body**.

Asbestosis causes diffuse pulmonary interstitial fibrosis, by interacting

with lung macrophages (stimulates macrophages to release fibrogenic

enzymes)

In this way the affected regions become honeycombed. Simultaneously,

the visceral pleura undergoes fibrous thicken (pleural plaques)

The fibrosis may trap and narrow pulmonary arteries and arterioles,

causing "pulmonary hypertension" and "cor pulmonale".

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Caplan's syndrome

Characterized by the presence of multiple nodules up to 5 cm. in diameter

scattered throughout the lungs of workers who are exposed to inhaled dusts

including coal, silica & asbestos

Rheumatoid arthritis is usually present

Rheumatoid factor in the blood is positive

Not all patients with rheumatoid arthritis & Pneumoconiosis develop Caplan’s

syndrome.

**Pneumoconiosis caused by Organic (biological) dusts**

Inhaled organic dusts may affect the Bronchi causing "Byssinosis" or affect the alveoli causing "Extrinsic allergic alveolitis"

**Byssinosis**

Occupational lung disease develops after many years of exposure to dusts in the cotton

Bronchoconstriction induced by inhalation of cotton dust or associated bacteria from cotton bales

**Extrinsic allergic alveolitis**

Induced by type-III hypersensitivity reaction in the alveoli where

circulating antibodies react with inhaled antigens

The most severe form is called **Farmer’s lung** which is characterized by acute episodes of fever, headache, malaise with cough, dyspnea & basal lung crepitations, occur 4-5 hours after exposure to a moldy hay dust and persist for 24 hours.

Microscopically, the alveolar walls are thickened by infiltration of lymphocytes, plasma cells, macrophages & eosinophils with sarcoid like granulomas.

Another example of extrinsic allergic alveolitis is **Bird fancier’s (breeder’s)**

**disease** caused by inhalation of bird droppings dusts

Repeated attacks of Extrinsic allergic alveolitis cause diffuse interstitial lung fibrosis with the end result of Honeycomb lung

**Interstitial Pulmonary Fibrosis (IPF)**

also known as cryptogenic fibrosing alveolitis

Characterized histologically by diffuse pulmonary interstitial fibrosis of

unknown etiology

known causes of fibrosis, such as asbestosis and collagen-vascular diseases

must be ruled out before the designation of “IPF" is used.

The histologic pattern of fibrosis in IPF is referred to as:

**Usual interstitial pneumonia (UIP)**

The histologic hallmark of UIP is patchy interstitial fibrosis which is

progressive leading to honeycomb fibrosis

Complications include respiratory failure, pulmonary hypertension & cor

pulmonale

The mean survival is 3 years or less (poor prognosis).

Lung transplantation is the only definitive therapy available (poor response to steroid)

The other form of interstitial pneumonia is called

**Desquamative interstitial pneumonia (DIP)**

DIP is a smoking-related interstitial lung disease

histologic features are:

accumulation of large number of macrophages containing dusty

 brown pigment (smoker's macrophages) in the alveolar spaces

thickening of the alveolar septa by a sparse inflammatory infiltrate

 (usually lymphocytes), with mild interstitial fibrosis,

Because the interstitial fibrosis is mild, pulmonary function usually show

 mild restrictive abnormality

DIP has a good prognosis with excellent response to steroid therapy and

smoking cessation.

**Atelectasis (collapse)**

Defined as loss of lung volume caused by inadequate expansion of airspaces.

Atelectasis is classified into three forms

Resorption atelectasis

Compression Atelectasis

Contraction Atelectasis

**Resorption atelectasis**

occurs when there is bronchial obstruction

Distal to the obstruction, the air already present is gradually absorbed, and

 alveolar collapse follows

Accumulation of secretions may occur and so liable for infection

This collapse is eversible (by removing the obstruction)

**Compression Atelectasis** (passive or relaxation atelectasis)

associated with accumulations of fluid, blood, or air within the pleural cavity

causing mechanical compression and collapse of the adjacent lung

Infection is unlikely (no accumulation of secretion)

\*This collapse is reversible if the cause is treated early (before the organization of the pleural lesion)

**Contraction Atelectasis** (cicatrization atelectasis)

local or generalized fibrotic changes in the lung or pleura which restrict lung expansion and increase elastic recoil during expiration.

Results from contraction of fibrous tissue

It is irreversible (due to fibrosis)

**Pneumonia**

Inflammation of the lung charecterized by Consolidation (Solidification) due to the presence of inflammatory exudate in the distal air ways spaces.

Can be classified

Etiological classification according to the causative agent

Anatomical classification (used in pathology):

bronchopneumonia

lobar pneumonia

**Bronchopneumonia**

Occurs when the infection initially colonize the bronchi and bronchioles and

 then extend into the adjacent alveoli (through the bronchiolar wall) resulting

 into patchy consolidation which involves more than one lobe

Occurs in infants, elderly & in debilitating dis.

Complete resolution is uncommon, except in mild cases, because there is

 usually damage to the bronchiolar wall

in debilitating diseases with prolonged bed rest, accumulation of secretion

 in the dependent parts with subsequent secondary infection results in a so

 called Hypostatic bronchopneumonia

Grossly

 Most often seen in the lower lobes, as focal dark red areas, about 1 cm.

 diameter which appear to be centered around a bronchiole from which

 pus can be squeezed

Microscopically

 Acute inflammation of the bronchioles with filling of the surrounding alveoli

 by inflammatory exudate rich in neutrophils

**lobar pneumonia**

Watery inflammatory exudate filling the alveoli and flows directly through

the lumen of the bronchioles into the adjacent lobules and segments resulting into diffuse consolidation that is sharply confined to the affected lobe.

There is no significant damage to the bronchiloar wall, Why?

In untreated lobar pneumonia four stages can be recognized

1. Acute congestion

2. Red hepatization

3. Grey hepatization

4. Resolution

**1.Acute congestion**

 1st and 2nd day

Grossly

The affected lobe is heavy, dark red, firm and abundant frothy red fluid can be squeezed

Microscopic

Congestion of the alveolar capillaries

Alveolar spaces are filled with edema fluid contains many neutrophils

**2.Red hepatization**

 2nd – 4th day

Grossly

The affected lobe is covered by greyish fibrin

Cut surface of the lobe is dry, firm, **red** and granular, feels like liver

Microscopic

Congestion of the alveolar capillaries

Alveolar spaces contain fine network of fibrin with large number of

RBC & neutrophils

**3.Grey hepatization**

 4th – 8th day

Grossly

The affected lobe is covered by greyish fibrin

Cut surface of the lobe is dry, firm, **grey** and granular, feels like liver

Microscopic

No more congestion of the alveolar capillaries

Alveolar spaces are filled by dense network of fibrin with neutrophils and few RBC

**4.Resolution**

 On 8th day

 Migration of macrophages from the alveolar septa to the intra-alveolar exudate followed by release of fibrinolytic enzymes from the macrophages leading to liquifaction of the exudate which is absorbed or coughed up.

Complete resolution occurs with re-aeration of the alveoli takes1-3 weeks

**Pulomonary hypertension (PH)**

Systolic blood pressure in the pulmonary circulation exceeding 25 mm Hg at

rest, measured during right heart catheterization

**Causes**

1.Secondary to cardiac conditions

 a. Congenital cardiac shunt

 b. Increased left atrial pressure

 c. left ventricular failure

2. Secondary to hypoxia

 a. Chronic obstructive airways diseases

 b. High altitude

3.Lung fibrosis

 a. pneumoconiosis

 b. Interstitial pulmonary fibrosis

4. Recurrent pulmonary emboli

5. Idiopathic

 a. Primary pulmonary hypertension

 b. Pulmonary veno-occlusive disease

**Congenital cardiac shunt**

Post- tricuspid shunts (left to right shunts)

 VSD

PDA

Persistent truncus arteriosus.

In these cases there is transmission of systemic arterial pressure into

pulmonary circulation, resulting in characteristic pulmonary vascular

changes, these changes are:

**1.** Hypertrophy of the media of the small pulmonary arteries

**2.** Migration of smooth muscle cells from media to the intima forming an

 intimal myofibroblast proliferation in the pulmonary arteries & arterioles

**3.** These changes lead to occlusion of the small pulmonary arteries

**4.** Followed by dilation of small arteries arising proximal to the site of occlusion

 to maintain the blood flow to the pulmonary capillary bed

Clusters of these dilated small pulmonary arteries are called "**Angiomatoid**

 **lesions"**

Proliferation of of myofibroblasts & mesenchymal cells occurs within the

 angiomatoid lesion in a plexiform pattern forming the "**Plexiform lesions**"

 which are characteristic of pulmonary hypertension due to congenital

 cardiac shunt.

When pulmonary blood pressure increases rapidly or severely, there will be wide spread fibrinoid necrosis ( necrotizing arteritis) of the small pulmonary arteries.

**Hypoxia**

In chronic hypoxia the vascular changes include smooth muscle hypertrophy in the media of pulmonary arterioles

This leads to increase pulmonary vascular resistance causing pulmonary

 hypertension

Intimal fibrosis is insignificant, therefore pulmonary hypertension of the

 chronic hypoxia is reversible

In cases of **elevation of left atrial pressure:**

There is medial hypertrophy and intimal fibrosis with muscularization of the pulmonary arterioles and veins leading to pulmonary hypertension.

In **pulmonary fibrosis**:

obliterative fibrosis of pulmonary arteries and arterioles lead to irreversible

increase in the pulmonary resistance & Pulmonary hypertension.

**Tumors of the lungs & bronchi**

**Benign tumors**

**Pulmonary chondroma (adenochondroma)**

It is a Hamartoma (not true tumor)

Discovered by chance on chest imaging as a discrete rounded shadow

Requires surgical intervention to exclude bronchial carcinoma

Microscopically: it is composed of mature cartilage with glands by respiratory

 epithelium

**Carcinoma of the lung**

The number one cause of cancer-related deaths in industrialized countries

95% arise from the bronchial epithelium and called **bronchial carcinoma**

Age 40 – 70 yrs

The most important risk factor is smoking

Macroscopically, bronchial carcinoma is divided into two types

 **1**.Hilar (central) type arise in a main bronchus

  **2**.Peripheral type arise in a peripheral bronchus

**Tumor at the apex of the lung** that extends to the lower cords of brachial

plexus and sympathetic chain with pain and sensory disturbances producing

Pancoast’s syndrome

This tumor is called **Pancoast’s tumor**.

**Four major histologic types of carcinomas of the lung**

1. Adenocarcinoma

2. Squamous cell carcinoma

3. Neuro-endocrine tumors

4. Large-cell carcinoma

combination of histologic patterns (e.g., adenosquamous carcinoma)

For therapeutic purposes, carcinomas of the lung are **previously** classified into two broad groups:

1. Small-cell lung cancer (SCLC) include -Small cell carcinoma

2. Non-small-cell lung cancer (NSCLC). include the Squamous cell carcinoma,

 Adenocarcinoma and Large-cell carcinoma

Small-cell lung cancer (SCLC) has metastasized by the time of diagnosis and so ii is not curable by surgery and best treated by chemotherapy, with or without radiation therapy

NSCLCs

Usually respond poorly to chemotherapy

Better treated by surgery

**The 2015 WHO classification of lung carcinomas**

**1) Adenocarcinoma**

**2) Squamous Cell Carcinoma**

**3) Neuroendocrine tumors**

 **a-Small cell carcinoma**

 **b-Large cell neuroendocrine carcinoma**

 **c -Carcinoid tumors**

 **\***Typical carcinoid tumor

 **\***Atypical carcinoid tumor

**4) Large Cell Carcinoma**

**1) Adenocarcinoma**

Is the most common lung cancer

Mainly of peripheral type

Grow slowly and are smaller in size than other types

Tends to metastasize widely at an early stage

Malignant cells in sputum in 50% of cases

**2) Squamous cell carcinoma**

-Is the second most common lung cancer

-Closely correlated with the smoking

-Usually hilar (central) arising in a large bronchus

- Usually large tumors

-Prone to massive necrosis and cavitation

 -Arises from a bronchial epithelium which has undergone squamous metaplasia

Squamous metaplasia 🡪Dysplasia 🡪Carcinoma in situ 🡪 Invasive carcinoma

-In 2/3 of cases, malignant cells can be identified in sputum

**3) Neuro-endocrine tumors**

-The third most common lung cancer

**-The 2015 World Health Organization classification of the neuro-endocrine tumors of the lung includes:**

 1-**Small cell carcinoma**

 -Combined small cell carcinoma

 2-**Large cell neuroendocrine carcinoma**

 -Combined large cell neuroendocrine carcinoma

 3-**Carcinoid tumors**

 -Typical carcinoid tumor

 -Atypical carcinoid tumor

**Small cell carcinoma**

20-30 %

Commonly Hilar (central)

Arises from the neuro-endocrine cells in the bronchial epithelium called

 Kalchitsky’s cells

Recently the accepted theory is that this tumor arises from the Stem cells

Three variants of small cell carcinoma:

 **1. Classic type (Oat cell carcinoma)**

 composed of cells with small round or oval uniform nuclei with a very

 little cytoplasm.

 **2. Intermediate cell type**

 Composed of cell with nuclei similar to oat cell type but with more

 abundant cytoplasm.

 **3. Combined small cell Ca.**

 Oat cell Ca. mixed with squamous cell carcinoma and / or adenocarcinoma

These three variants have similar behavior and response to treatment

Not to be misdiagnosed as Squamous cell carcinoma. or Adenocarcinoma.

Malignant cells can be detected in sputum in 2/3 of cases

**Bronchial carcinoid**

1% of lung tumor

**\*Typical Carcinoid:**

 -Slowly growing, low grade malignant tumor

 -Male = Female

 -Is composed of nests of polyhedral cells with small nuclei & granular

 cytoplasm

 -Lymph node metastasis in < 10%

**\*Atypical carcinoid**

 -Has histological features of malignancy

 -More aggressive

 -L.N. metastasis in 70%

**4) Large cell carcinoma**

10-15 % of lung cancer

Composed of cells with large nuclei and abundant cytoplasm without

characteristic feature of squamous cell carcinoma, small cell carcinoma or adenocarcinoma.

E.M. exam. Shows that large cell ca. represent poorly differentiated squamous cell carcinoma or adenocarcinoma

Most cases of LCC are now reclassified as

 -Squamous cell carcinoma

 -Adenocarcinoma,

 -Large cell neuroendocrine carcinoma

**Tumors of the pleura**

 **1)** **Benign Mesothelioma (Pleural fibroma**)

 -Rare

 -localized growth

 -No relationship to asbestose exposure

**2) Malignant mesothelioma**

**-**associated with exposure to asbestose with a very long latent period, 20 years

 or more

-The tumor affects both visceral & parietal pleura forming diffuse thickening of the

 pleura that ensheaths and compress the lung

-Severe hemorrhagic pleural effusion