

Pathology of Lung

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Classification of Lung Diseases

- Congenital anomalies
- Diseases of vascular origin
- Chronic obstructive pulmonary diseases
- Pulmonary infection
- Diffuse interstitial pulmonary diseases
- Complication of therapy
- Tumours

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Congenital Anomalies:

- Agenesis or hypoplasia of lungs, one lung or single lobe.
- Tracheal and bronchial anomalies
- Vascular anomalies
- Congenital lobar overinflation (congenital emphysema)
- Congenital cysts
- Intralobar and extralobar pulmonary sequestration.

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Atelectasis

Atelectasis refers either to incomplete expansion of the lungs or to the collapse of previously inflated lung substance, producing areas of relatively airless pulmonary parenchyma.

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Types of Atelectasis:

- Obstructive Atelectasis (Absorptive atelectasis)
- Compressive atelectasis
- Patchy atelectasis

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• Obstructive Atelectasis:

- It is the sequence of complete obstruction of an airway, which in time leads to absorption of oxygen trapped in the dependent alveoli.
- Caused by excessive secretion or exudates within smaller bronchi.
- Most often found in bronchial asthma, chronic bronchitis, bronchiectasis, postoperative states and aspiration of foreign bodies.

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Compressive Atelectasis:

- Results when the pleural cavity is partially or completely filled by fluid exudate, tumour, blood or air.
- Found in pleural effusion, abnormal elevation of diaphragm etc.

Patchy Atelectasis:

- Caused by loss of pulmonary surfactant.
- Found in neonatal and adult respiratory distress syndrome.

Pulmonary Oedema

- | | |
|--|---|
| <ul style="list-style-type: none"> • Causes: • Haemodynamic oedema <ul style="list-style-type: none"> - Increased hydrostatic pressure <ul style="list-style-type: none"> • Left sided heart failure • Mitral stenosis • Volume overload • Pulmonary vein obstruction - Decreased oncotic pressure <ul style="list-style-type: none"> • Hypoalbuminaemia - Lymphatic obstruction | <ul style="list-style-type: none"> • Oedema due to Microvascular injury <ul style="list-style-type: none"> - Infective agents <ul style="list-style-type: none"> • Virus, Mycoplasma - Inhaled gas <ul style="list-style-type: none"> • Oxygen, sulphur-di-oxide, cyanate, smoke - Liquid aspiration <ul style="list-style-type: none"> • Gastric contents, near drowning - Drug and chemicals - Shock, trauma and sepsis - Radiation - Miscellaneous • Oedema of unknown origin <ul style="list-style-type: none"> - High altitude - Neurogenic |
|--|---|

Adult Respiratory Distress Syndrome (ARDS)

- **Synonyms:** Adult respiratory failure, shock lung, diffuses alveolar damage, acute alveolar injury, and traumatic wet lung.
- **Definition:** Adult respiratory distress syndrome is a descriptive term for a syndrome caused by diffuse alveolar capillary damage, characterised by rapid onset of severe life threatening respiratory insufficiency, cyanosis and severe arterial hypoxemia that is refractory to oxygen therapy that frequently progress to extreme pulmonary multisystem organ failure.

Conditions Associated with ARDS:

- | | |
|--|--|
| <ol style="list-style-type: none"> 1. Infection <ul style="list-style-type: none"> • Sepsis • Diffuse pulmonary infections • Gastric aspiration 2. Physical/Injury <ul style="list-style-type: none"> • Mechanical trauma • Pulmonary contusions • Near drowning • Fracture with fat embolism • Burns • Ionising radiation 3. Inhaled Irritants <ul style="list-style-type: none"> • Oxygen toxicity • Smoke • Irritant gases and chemicals | <ol style="list-style-type: none"> 4. Chemical Injury <ul style="list-style-type: none"> • Heroin or methadone overdose • Acetylsalicylic acid • Barbiturate overdose • Paraquat 5. Haematological Conditions <ul style="list-style-type: none"> • Multiple transfusion • DIC 6. Pancreatitis 7. Uraemia 8. Cardiopulmonary Bypass |
|--|--|

Morphology:

- The lung become heavy, firm, red and boggy.
- Exhibits congestion, oedema, inflammation and fibrin deposition.
- Alveolar wall become lined with waxy hyaline membrane.

Respiratory Distress Syndrome in Newborn:

Causes:

- Excessive sedation of mother with consequent depression of respiration in the infant.
- Brain injury with failure of the central respiratory centre.
- Feeble respiratory effort secondary to immaturity of lungs and skeletal muscle.
- Aspiration of blood clot and amniotic fluid during birth.
- Asphyxiating coils of umbilical cord about the neck of infant.
- Idiopathic.

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Chronic Obstructive Pulmonary Diseases (COPD)

Def: COPD refers to a group of conditions that share a major symptom – dyspnoea and are accompanied by chronic or recurrent obstruction to air flow within the lung.

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Clinical Conditions Associated with COPD:

- Chronic Bronchitis
- Bronchiectasis
- Bronchial asthma
- Emphysema

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Chronic Bronchitis:

- **Def:** Persistent cough with sputum production for at least 3 months in at least 2 consecutive years.
- Common among habitual smokers and inhabitants of smog-laden cities.
- Ten to 20% of the urban adult population have chronic bronchitis.
- Country dwellers have lower incidence

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Pathogenesis:

- Two factors are important in the genesis of chronic bronchitis:
- Chronic irritation by inhaled substance
- Microbiologic infection
- Smoking is the major influence on chronic bronchitis. The hallmark of chronic bronchitis is the hypersecretion of mucous in the large airways, which is associated with hypertrophy of submucous glands in the trachea and bronchi. There is marked increased in goblet cells of small airways leading to excess mucous production that contributes to airway obstruction. Both submucous gland hypertrophy and increased in goblet cells are caused by tobacco smoke or other pollutants.

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- The role of infection appears to be secondary. Cigarette smoke predisposes the infection in the following ways:
 - It interferes with ciliary action of the respiratory epithelium
 - May cause direct damage to airway epithelium
 - Inhibits the ability of bronchial and alveolar leucocytes to clear bacteria

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Morphology:**Gross:**

- Hyperaemia, swelling and bogginess of the mucous membrane.
- Epithelial surface is covered by mucopurulent secretion
- Heavy cast of secretion and pus may fill the bronchi and bronchioles.

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Microscopic:

- Enlargement of the mucous secreting glands of the trachea and bronchi.
- Increase in goblet cell number.
- Bronchial epithelium may exhibit squamous metaplasia and dysplasia.
- Marked narrowing of bronchioles caused by goblet cell metaplasia, mucous plugging, inflammation and infection.

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- **Complications:** Cor pulmonale with cardiac failure
- **Death:** May result from impairment of respiratory function due to undercurrent bacterial infection.

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Bronchiectasis:

- **Def:** Bronchiectasis is a chronic necrotising infection of the bronchi and bronchioles leading to or associated with abnormal dilatation of airways.

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Associated with:

- Bronchial obstruction due to tumour, foreign body, mucous impaction etc.
- Congenital or hereditary conditions such as congenital bronchiectasis, cystic fibrosis, intralobar sequestration of lung, immunodeficiency states, immotile cilia and kartegener's syndrome.
- Necrotising pneumonia caused by tubercle bacilli, staphylococci, or mixed infection.

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Pathogenesis:

- After bronchial obstruction, air is resorbed from the airways distal to the obstruction, with resultant atelectasis. These changes are reversible. The change become irreversible if;
 - The obstruction persists or
 - There is added infection

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Infection plays a role in the pathogenesis of bronchiectasis in two ways:

- Produces bronchial wall inflammation with weakening and further dilatation and
- Extensive bronchial and bronchiolar damage causes endobronchial obliteration with atelectasis distal to the obliteration and subsequent bronchiectasis around atelectatic areas.

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- In cystic fibrosis, there is squamous metaplasia of respiratory epithelium with necrosis of the bronchial and bronchiolar walls and subsequent bronchiectasis.
- In Kartegener's syndrome (bronchiectasis, sinusitis and situs inversus) there is a defect in ciliary motility, associated with structural abnormality of the cilia. The lack of ciliary activity interferes with bacterial clearance, predisposes the sinuses and bronchi to infection and also affects all motility during embryogenesis, resulting in situs inversus.

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Morphology:

Gross:

- The airways are dilated, some times up to four times of normal size.
- This dilatation may produce cylindrical, fusiform or secular bronchiectasis.

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Histologic:

- In active case, there is an intense acute and chronic inflammatory exudation within the walls of the bronchi and bronchioles, associated with sequestration of the lining epithelium and extensive areas of necrotising ulceration. There may be pseudostratification of columnar cells or squamous metaplasia of remaining epithelium.
- In the chronic case, bronchial and bronchiolar wall and peribronchial area develop fibrosis.

Complications: Cor pulmonale, metastatic brain abscess and amyloidosis.

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Emphysema:

Def: Emphysema is a condition of the lung characterised by abnormal permanent enlargement of the airspaces distal to the terminal bronchiole, accompanied by fibrosis.

Types of Emphysema:

- Centriacinar
- Panacinar
- Paraseptal
- Irregular

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• Centriacinar:

- Central or proximal parts of acini are affected, whereas distal alveoli are spared.
- Occurs in heavy smoker associated with chronic bronchitis.

• Panacinar:

- Acini are uniformly enlarged from the level of the respiratory bronchioles to the terminal blind alveoli.
- Associated with α 1-antitrypsin deficiency.

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- **Paraseptal:**

- Proximal portion of acini is normal but the distal part is dominantly involved.
- Occurs adjacent to areas of fibrosis, scarring or atelectasis.

- **Irregular:**

- The acinus is irregularly involved.
- Associated with scarring.

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Pathogenesis of Emphysema:

- Emphysema results from the destructive effects of high protease activity in subjects with low antiprotease activity.
- Both increased elastase availability and decreased antielastase activity occurs in smokers. It is postulated that impaction of smoke particle in the small bronchi and bronchioles with the resultant influx of neutrophils and macrophages and increased elastase and decreased α -1antitrypsin activity causes the centriacinar emphysema seen in smoker.

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Morphology of emphysema:

- **Gross:** The lung is voluminous and large. Blebs or bulla may be seen.

- **Histology:**

- Abnormal fenestration in the wall of alveoli.
- Complete destruction of septal wall.
- In advanced stage, blebs and bulla formed due to fusion of adjacent alveoli.
- Often, respiratory bronchioles and vasculature of the lungs are deformed and compressed by emphysematous distortion of the air spaces.

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- **Complication:** Corpulmonale

- **Causes of death:** Respiratory acidosis and coma, right sided heart failure and massive collapse of lungs secondary to pneumonia.

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Other Types of emphysema:

- Compensatory emphysema
- Senile emphysema
- Obstructive overinflation
- Bullous emphysema
- Interstitial emphysema

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- **Compensatory Emphysema:** Dilatation of alveoli but destruction of septal walls in response to loss of lung substance elsewhere.
- **Senile Emphysema:** Is due to age-related alterations of the larger alveolar ducts and smaller alveoli.
- **Obstructive over-inflation:** Lung expands because air is trapped within it.

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- **Bullous emphysema:** any form of emphysema that produces large subpleural blebs or bullae.
- **Interstitial emphysema:** The entrance of air into the connective tissue stroma of lung, mediastinum or subcutaneous tissue.

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Bronchial Asthma:

- **Def:** Asthma is a disease characterised by hyper-reactive airways, leading to episode, reversible bronchoconstriction, owing to increased responsiveness of the tracheobronchial tree to various stimuli.

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Types of Asthma:

Types	Precipitating factor	Mechanism or immunologic reaction
Extrinsic:		
•Atopic (allergic)	Specific allergens	Type I (IgE) immune reaction
•Occupational	Chemical challenge	Type I immune reaction
•Allergic bronchopulmonary aspergillosis	Antigens (spore) challenge	Type I and III immune reaction
Intrinsic:		
•Non-organic	Respiratory tract infection	Unknown, hyperactive airways.
•Pharmacological (e.g. aspirin sensitive)	Aspirin	Decreased prostaglandin, increased leukotrienes.

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Morphology of Asthma:

Gross:

- Lungs are overdistended.
- Occlusion of bronchial and bronchi and bronchioles by thick, tenacious mucous plug

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Histologically:

- The mucous plug contains whorls of shed epithelium, which give rise to Curshmann's spirals.
- Numerous eosinophils and Charcot – layden crystals are present.
- Other histological features are
 - Thickening of basement membrane of bronchial epithelium;
 - Oedema and an inflammatory infiltrate in the bronchial walls with prominence of eosinophils
 - An increase in size of the submucosal glands
 - Hypertrophy of the bronchial wall cell muscle.

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Pulmonary Infection

Bacterial Pneumonia:

- Bacterial invasion of the lung parenchyma producing exudative solidification (consolidation) of the pulmonary tissue known as bacterial pneumonia.

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Classification:

- According to etiologic agents
 - Pneumococcal pneumonia
 - Streptococcal pneumonia
- According to nature of host reaction
 - Suppurative
 - Fibrinous
- According to gross anatomical distribution of the disease
 - Lobular bronchopneumonia
 - Lobar pneumonia

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Bronchopneumonia:

- Patchy consolidation
- Parenchymal infection, usually represent an extension of a pre-existing bronchitis or bronchiolitis
- Occurs in infancy and old age.

Lobar Pneumonia:

- Is an acute bacterial infection of large portion of a lobe or of an entire lobe.
- Produces total lobar consolidation.

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Pathogenesis:

- Respiratory airways and alveoli are exposed to air containing hazardous dusts, chemicals and microorganisms. The fate of inhaled particles depends on their sizes. The particles larger than 10 µm are deposited largely in the turbulent air flow of the nose and upper airways. Particles of 3 to 10 µm lodges in the trachea and bronchi by impaction. Smaller particle < 1 µm may remain suspended in the inspired air and can be exhaled.
- The normal lung is free from bacteria with the help of some defence mechanism such as nasal clearance, tracheobronchial clearance, alveolar clearance etc.

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- Pneumonia can result whenever these defence mechanisms are impaired or whenever the resistance of the host in general is lowered.
- Factor that affect resistance in general indicate chronic diseases, immune deficiency, and treatment with immunosuppressive agents, leucopenia, and unusually virulent infection.

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- The clearing mechanisms can be interfered by many factors such as
 - Loss or suppression of cough reflex
 - Injury to the mucocilliary apparatus
 - Interference with phagocytic or bactericidal action of alveolar macrophages
 - Pulmonary congestion and oedema
 - Accumulation of secretion

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Aetiology

<ul style="list-style-type: none"> • Bronchopneumonia <ul style="list-style-type: none"> • Staphylococci • Streptococci • Pneumococci • Haemophilous influenza • Pseudomonous aeriginosa • Coliform bacilli 	<ul style="list-style-type: none"> • Lobar Pneumonia <ul style="list-style-type: none"> • Pneumococci (90-95%) • Klebsiella pneumoniae • Staphylococci • Streptococci • Haemophilous influenza • Some Gram-negative organism
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Morphology:**Lobar pneumonia:**

- There is widespread fibrinosuppurative consolidation of large areas and even whole lobes of the lungs. There are four stages of inflammatory response
 - Stages of congestion
 - Stage of red hepatisation
 - Stage of grey hepatisation
 - Stage of resolution

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- **Stage of congestion:** The lung is heavy, boggy and red. Vascular engorgement and intra-alveolar fluid with few neutrophils and often presence of numerous bacteria.
- **Stage of red hepatisation:** Massive confluent exudation with red cells and neutrophils and fibrin-filling alveolar spaces. The lobe appears red, firm and airless with a liver-like consistency.

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- **Stage of grey hepatisation:** The lung lobes are greyish-brown with dry surface due to progressive disintegration of red cells and persistence of fibrinosuppurative exudates.
- **Stage of resolution:** Consolidated exudates within the alveolar spaces undergo progressive enzymatic digestion to produce granular, semifluid debris that is resorbed; ingested by macrophages or coughed up.

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Bronchopneumonia:

- These are foci of consolidated areas, usually of 3 to 4 cm diameter, slightly elevated, dry, granular, grey-red to yellow and poorly delimited at their margin. Histologically the inflammatory reaction usually comprises suppurative neutrophil-rich exudates that fill the bronchi, bronchioles, and adjacent alveolar spaces.

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Complication of pneumonia:

1. Abscess formation,
2. Emphysema,
3. Organization of exudate and
4. Bacteraemic dissemination.

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Lung Abscess:

- **Def:** A local suppurative process within the lung characterised by necrosis of lung tissue.
- **Causative agents:** Streptococci, staphylococcus aureas and a host of gram-negative organism.

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The causative agents are introduced by the following mechanism

- aspiration of infective material
- antecedent primary bacterial infection
- septic embolism
- other misc. mechanism.

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Morphology:

- Lung abscess vary in diameter from few mm to large cavity of 5 to 6 cm. The cavity may or may not be filled with suppurative debris.
- Cardinal histologic change is suppurative destruction of the lung parenchyma within the central area of cavitations. In chronic case fibroblastic proliferation produces a fibrous wall.

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Pulmonary Tuberculosis:

Primary Pulmonary Tuberculosis:

- Lungs are the usual location of primary infection
- The initial focus of primary infection is the Ghon complex.
- Ghon Complex consists of:
 - A parenchymal subpleural lesion
 - Enlarged caseous lymph nodes draining the parenchymal focus.

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- The course and fate of this initial infection are variable. Most cases are asymptomatic and the undergo fibrosis and calcification.
- In infants and in children or immunodeficient adults progressive spread with cavitation, tuberculous pneumonia or miliarry tuberculosis may follow primary infection.

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Secondary (Reactivation) Pulmonary Tuberculosis:

- Secondary PT represents reactivation of an old, possibly subclinical infection. It occurs in 5-10% of primary tuberculosis.

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Morphology:

- Located in the apex of one or both lungs
- Begins as a small focus of consolidation, usually less than 3 cm in diameter.
- Regional lymph nodes develop foci of tuberculous activity.
- The initial parenchymal focus develops a small area of caseation necrosis.
- Progressively develop fibrocalcific scar.

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Histology:

- Coalescent granulomas are present, composed of epithelioid cells, surrounded by a zone of fibroblasts and lymphocytes that usually contains Langhan’s type giant cells.
- Some cases have caseation necrosis in the centre of the lesion.

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Progressive Pulmonary Tuberculosis:

- A variable number of lesions continue to progress over a period of months or years, causing further pulmonary and even distant organ involvement.
- The resultant clinicopathologic consequences include
 - Cavitory fibrocaceous tuberculosis
 - Miliary tuberculosis and
 - Tuberculous bronchopneumonia.

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Cavitory Fibrocaceous Tuberculosis:

- Drainage of the caseous focus by erosion into a bronchiole the lesion transforms into a cavity. The cavity is lined by a yellow-grey caseous material and is more or less walled off by fibrous tissue.

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Miliary Tuberculosis:

- Lymphohaematogenous dissemination may give rise to Miliary tuberculosis, confined only to the lungs or involving other organs also.
- Individual lesions vary from one to several mm in diameter and distinct, yellow-white, firm areas of consolidation that usually do not have grossly visible central caseation necrosis or cavitation.
- Histologically, present characteristic pattern of individual or multiple confluent tubercles having microscopic central caseation.

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Tuberculous Bronchopneumonia:

- In the highly susceptible, highly sensitised individual, the tuberculous infection may spread rapidly throughout large areas of lung parenchyma and produces a diffuse bronchopneumonia or lobar exudative consolidation.

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Pneumoconiosis:

Non-neoplastic lung reaction to inhalation of mineral dusts.

Examples:

Mineral Dusts	Diseases
Coal dust	Anthracosis
Silica	Silicosis
Asbestose	Asbestosis
Beryllium	Beriliosis

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Bronchogenic Carcinoma:

- Most common visceral malignancy in male
- Accounts for one-third of all cancer death in male and even 7% of all death in both sexes.
- Occurs most often between ages 40 and 70 years with peak incidence in the sixth to seventh decades.
- 2% appears before the age of 40 years.

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Aetiological factors:

- Tobacco smoking
- Industrial hazards
 - Radiation
 - Uranium exposure
 - Exposure with nickel, chromium, coal, mustard gas, arsenic, beryllium, iron etc.
- Air pollution
- Genetic factors
- Scarring

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Histologic Classification of Bronchogenic carcinoma:

1. Squamous cell carcinoma
2. Adenocarcinoma
 - Bronchial derived
 - Acinar
 - Papillary
 - Solid
 - Bronchioloalveolar adenocarcinoma
3. Small cell carcinoma
 - Oat cell carcinoma (lymphocyte-like)
 - Intermediate cell carcinoma (polygonal)
4. Combined (usually with squamous)
5. Large cell carcinoma
 - Undifferentiated
 - Giant cell
 - Clear cells
6. Combined squamous cell carcinoma and adenocarcinoma

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Morphology:

- Arises most often in and around hilus of the lung.
- Begins as an area of in situ cytologic atypia, which yields a small area of thickening or piling up of bronchial mucosa.
- With progression, appears as an irregular, warty excrescence that elevates or erodes the lining epithelium.
- May fungate into bronchial lumen or may penetrate the wall of the bronchus to infiltrate along the peribronchial tissue into the adjacent region of the carina or mediastinum.
- Is grey-white and firm to hard.
- Focal areas of haemorrhage or necrosis may appear to produce yellow-white mottling and softening.

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Metastatic Tumours:

- Both carcinoma and sarcoma arising anywhere in the body may spread to the lungs via the blood or lymphatic or by direct continuity.

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Pleural Tumour:

- Primary
 - Pleural fibroma (benign mesothelioma)
 - Malignant mesothelioma
- Secondary tumour

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Benign Mesothelioma:

- Localised growth that is often attached to the pleural surface by pedicle.
- May be small or large.
- Always remain confined to the surface of the lung.
- Do not produce pleural effusion.
- Consists of dense fibrous tissue with occasional cysts filled with viscid fluid.
- Histologically shows whorls of reticulin and collagen fibres along which interspersed spindle cells resembling fibroblasts.
- Has no relationship to asbestose exposure

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Malignant Mesothelioma:

- Arise from either the visceral or the parietal pleura.
- Increased incidence among persons with heavy exposure to asbestose.
- Is a diffuse lesion that spreads widely in the pleural space and associated with pleural effusion and direct invasion of thoracic structures.
- Consists of a mixture of two types of cells, Mesenchymal stromal cells or epithelial like cells.

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