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THE DISEASES OF THE RESPIRATORY SYSTEM

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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 (FEV₁).
- (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.

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. Inflamantion and necrosis of bronchial walls and alveolar fibrosis.

Bronchial Asthma

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.
- (b) **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.

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 eosinophils and intrabronchial mucous plugs with whorl-like accumulations of epithelial cells (Curschmann spirals) and crystalloids of eosinophil-derived proteins (Charcot-Leyden crystals).

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.

Chronic bronchitis

1] **Clinical presentation.**

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

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

2] **Pathological changes.**

Typical characteristics include hypersecretion of mucus due to marked **hyperplasia of mucus-secreting submucosal glands**.

Emphysema

1] **General considerations, definitions and clinical features.**

- (a) Emphysema is **dilation of air spaces** from and beyond the respiratory bronchioles with destruction of alveolar walls.
- (b) The disease is strongly associated with cigarette smoking.

2] **Clinical characteristics.**

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

3] **Types of emphysema**

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

(c) **Paraseptal 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.

- (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.

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**.

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.

Bronchiectasis

- 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.
- 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 uncommon 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.

- 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

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.
- (2) Examples include abnormalities of the chest wall from bony abnormalities or neuromuscular disease that restrict lung expansion.
- (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 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 bleomycin toxicity**; and **immune disorders** such as systemic lupus erythematosus, systemic sclerosis (scleroderma), Wegener granulomatosis and Goodpasture syndrome.

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.
- 4] **Causes** include a wide variety of mechanisms and toxic agents, including **shock, sepsis, trauma, uremia, aspiration of gastric contents, 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**.
- 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.
- Maternal diabetes mellitus and delivery by cesarean section.

Pneumoconioses. These environmental diseases are caused by **inhalation of inorganic dust 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.

- 3] **Silicosis** is a chronic occupational lung disease caused by **exposure to free silica dust**; 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**.

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

- (a) This disease is initiated by uptake of 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.

- (b) 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 and protein 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 Disease

Disorder	Description
Hypersensitivity pneumonitis (extrinsic allergic alveolitis)	Interstitial pneumonia caused by inhalation of various antigenic substances exemplified by inhalation of spores of thermophilic actinomycetes from moldy hay causing "farmer's lung".
Goodpastures syndrome	Hemorrhagic pneumonitis and glomerulonephritis caused by antibodies directed against glomerular basement membranes.
Eosinophilic granuloma	Proliferation of histiocytic cells related to Langerhan's cells of the skin.
Idiopathic pulmonary fibrosis	Immune complex disease with progressive fibrosis of the alveolar wall.
Sarcoidosis	Granulomatous disorder of unknown etiology.

PULMONARY INFECTION

Pneumonia

1. General considerations and clinical characteristics:

- (a) Pneumonia is an inflammatory process of infectious origin affecting the pulmonary parenchyma.
- (b) It is characterized by **chills and fever**, productive cough, blood tinged or **rusty sputum**, pleuritic pain, hypoxia with shortness of breath and sometimes cyanosis.

- (c) If bacterial, it is most characteristically associated with neutrophilic leukocytosis with an increase in band neutrophils ("shift-to-the-left").
2. **Morphologic types of pneumonia.** There are three morphologic and clinical patterns: **lobar pneumonia, bronchopneumonia and interstitial pneumonia.**
3. **Bacterial pneumonias.**
- (a) **Lobar pneumonia** is most often caused by *Streptococcus pneumoniae* (the pneumococcus). It is characterized by a predominantly **intra-alveolar exudate** and may involve an entire lobe of the lung.
- (b) **Bronchopneumonia** is caused by a wide variety of organisms. It is characterized by a **patchy distribution** involving **one or more lobes**, with an **inflammatory infiltrate extending from the bronchioles into the adjacent alveoli.**
4. **Interstitial (primary atypical) pneumonia** is caused by various infectious agents, most commonly *Mycoplasma pneumoniae* or viruses. It is characterized by **diffuse, patchy inflammation** localized to interstitial areas of alveolar walls.
- (a) **Mycoplasma pneumoniae.**
- (1) This is the **most common form of interstitial pneumonia**; it usually occurs in children and young adults and it **may occur in epidemics.**
- (2) Onset is more insidious compared to bacterial pneumonia and usually follows a mild, self-limited course.

- (3) Characteristics include an inflammatory reaction confined to the interstitium, with no exudate in alveolar spaces and intra-alveolar hyaline membranes.
- (4) **Diagnosis** is by sputum cultures, requiring several weeks of incubation and by complement fixing antibodies.
- (5) *Mycoplasma pneumoniae* may be associated with non specific agglutinins reactive to red cells. This phenomenon is the basis for a quick and easy laboratory test that can provide early diagnostic information.

Morphologic Variants of Pneumonia: Causative Organisms and Characteristics

Variant	Causative Organism	Characteristics
Lobar pneumonia	Most frequently streptococcus pneumoniae (pneumococcus)	Predominantly intra-alveolar exudate resulting in consolidation. May involve the entire lobe . If untreated, may morphologically evolve through four stages ; congestion, red hepatization, gray hepatization and resolution.
Bronchopneumonia	Many organisms including staphylococcus aureus, haemophilus influenza, Klebsiella pneumoniae, and streptococcus pyogenes	Acute inflammatory infiltrates extending from the bronchioles into the adjacent alveoli. Patchy distribution involving one or more lobes.
Interstitial Pneumonia	Most frequently viruses or mycoplasma pneumoniae	Diffuse, patchy inflammation localized to interstitial areas of the alveolar walls. Distribution involving one or more lobes.

- (b) **Viral pneumonias are the most common types of pneumonia in childhood.** They are cause most commonly by influenza viruses, adenoviruses, rhinovirus and respiratory syncytial virus, may also arise after childhood exanthems (viral eruptions) such as rubeola (measles) or varicella (chicken pox); the measles virus produces giant cell

pneumonia, marked by numerous giant cells and often complicated by tracheobronchitis.

- (c) **Rickettsial pneumonias:** **Q fever** is the most common rickettsial pneumonia; it is caused by *Coxiella burnetii*. It may infect persons working with infected cattle or sheep, who inhale dust particles containing the organism, or those who drink **unpasteurized milk** from infected animals.
 - (d) **Ornithosis (psittacosis)** is caused by an organism of the genus *Chlamydia*, which is transmitted by inhalation of dried excreta of infected birds.
5. ***Pneumocystis carinii* pneumonia** is the most common **opportunistic infection in patients with acquired immunodeficiency syndrome (AIDS)**; it also occurs in other forms of immunodeficiency.
- (a) It is caused by *pneumocystis carinii* (recently renamed *Pneumocystis jiroveci*) which is **now classified as a fungus**.
 - (b) Diagnosis is by morphologic demonstration of the organism in biopsy or bronchial washing specimens.
6. **Hospital-acquired gram-negative pneumonias.**
- (a) These pneumonias are often fatal and occur in hospitalized patients, usually those with serious, debilitating diseases.
 - (b) Causes include many **gram-negative organisms**, including *Klebsiella*, *Pseudomonas aeruginosa* and *Escherichia coli*. Endotoxins products by these organisms play an important role in the infection.

Important Features of Selected Bacterial Pneumonias

Organism	Characteristics	Complications
Streptococcus pneumoniae	Most common in ilderly or debilitated patients, especially those with cardiopulmonary disease and malnourished persons	May lead to empyema (pus in the pleural cavity).
Staphylococcus aureus	Often a complication of influenza or viral pneumonias or a result of blood-borne infection in intravenous drug users; seen principally in debilitated hospitalized patients, the elderly, and those with chronic lung disease.	Focal inflammatory exudates or abscess formation frequent; may lead to empyema or to other infectious complications, including bacterial endocarditis and brain and kidney abscesses.
Streptococcus pyogenes	Often a complication of influenza or measles.	Lung abscess.
Klebsiella pneumoniae	Most frequent in debilitated hospitalized patients and diabetic or alcoholic patients, high mortality rate in elderly patients.	Considerable alveolar wall damage; leading to necrosis, sometimes with abscess formation.
Haemophilus influenza	Usually seen in infants and children but may occur in debilitated adults, most often those with chronic obstructive pulmonary disease.	Meningitis and epiglottitis in infants and children.
Legionella pneumophilia	Infection from inhalation of aerosol from contaminated stored water most often in air conditioning systems	

Lung abscess

1. This is a localized area of suppuration within the parenchyma, usually resulting from bronchial obstruction (often by cancer) or from aspiration of gastric contents; may also be a complication of bacterial pneumonia.

2. Patients predisposed to the formation of lung abscesses are those who have aspiration by **loss of consciousness** from alcohol or drug overdose, neurologic disorders, or general anaesthesia.
3. Frequent **causes** include Staphylococcus, pseudomonas, Klebsiella or Proteus, often in combination with anaerobic organisms.
4. **Clinical manifestations** include fever, foul-smelling purulent sputum and radiographic (chest xray) show evidence of a fluid-filled cavity.

CANCERS OF THE LUNG

General consideration. Most lung tumors are malignant; those that arise from metastases from primary tumors elsewhere **occur more frequently** than those that originate in the lung.

Tumors of the Lung

Type	Location	Characteristics
<u>Bronchogenic carcinoma:</u> Squamous cell carcinoma	Central	Appears as a hilar mass and frequently results in cavitation; clearly linked to smoking; incidence greatly increased in smokers; may be marked by inappropriate parathyroid hormone (PTH) like activity with resultant Hypercalcemia.
<u>Adenocarcinoma:</u> Bronchial-derived	Peripheral	Develops on site of prior pulmonary inflammation or injury (scar carcinoma); less clearly linked to smoking.
Bronchioloalveolar	Peripheral	Less clearly related to smoking; columnar to cuboidal tumor cells line alveolar walls; multiple densities on x-ray, mimicking interstitial pneumonia.
Small cell (oat cell) carcinoma	Central	Undifferentiated tumor; most aggressive broncho-genic carcinoma usually already metastatic at diagnosis; is often associated with ectopic production of corticotrophin (ACTH) or antidiuretic hormone (ADH); incidence greatly increased in smokers cannot be treated by surgery.
Large cell carcinoma	Peripheral	Undifferentiated tumor which may show features of squamous cell or adenocarcinoma on electron microscopy.
<u>Other carcinomas of the lung:</u> Carcinoid	Major bronchi	Low malignancy, spreading by direct extension into adjacent tissues, may result in carcinoid syndrome.
Carcinoma, metastatic to the lung.		Higher incidence than primary lung cancer.

Bronchogenic carcinoma

Etiology and epidemiology

- (a) Bronchogenic carcinoma is the leading cause of death from cancer in both men and women. It is increasing in incidence, especially in women, in parallel with cigarette smoking.
- (b) This type of carcinoma is directly proportional in incidence to the number of cigarettes smoked daily and to the number of years of smoking. Various histologic changes, including squamous metaplasia of the respiratory epithelium often with atypical changes ranging from dysplasia to carcinoma in situ precede bronchogenic carcinoma in cigarette smokers.

Other etiopathogenic factors

- (a) Air pollution.
- (b) Radiation: incidence increased in radium and uranium workers.
- (c) Asbestos: increased incidence with asbestos and greater increase with combination of asbestos and cigarette smoking.
- (d) Industrial exposure to nickel and chromates.

Clinical features

- (a) The 5 year survival rate is less than 10%.
- (b) The tumor often spreads by local extension into the pleura, pericardium or ribs.

Clinical manifestations may include cough, hemoptysis and bronchial obstruction, often with atelectasis and pneumonitis. Other *clinical features* include:

- (1) **Superior vena cava syndrome:** compression or invasion of the superior vena cava, resulting in facial swelling and cyanosis along with dilatation of the veins of the head, neck and upper extremities.
- (2) **Pancoast tumor** (superior sulcus tumor): involvement of the apex of the lung, often with Horner syndrome (ptosis, miosis and anhidrosis): due to involvement of the cervical sympathetic plexus.
- (3) **Hoarseness** from recurrent laryngeal nerve paralysis.
- (4) **Pleural effusion:** often bloody (bloody pleural effusion suggests malignancy, tuberculosis or trauma).
- (5) **Paraneoplastic endocrine syndrome:** the most frequent of which is adrenocorticotrophic hormone (ACTH) or ACTH-like activity with small cell carcinoma; also of note are the syndrome of inappropriate diuretic hormone secretion with small cell carcinoma of the lung and parathyroid-like activity with squamous cell carcinoma.

Classification

- (a) Bronchogenic carcinoma is subclassified into squamous cell carcinoma, adenocarcinoma (including bronchioloalveolar carcinoma), small cell carcinoma and large cell carcinoma; it appears that all share a common endodermal origin despite their morphologic differences.
- (b) For therapeutic purposes, the bronchogenic carcinomas are often subclassified into small cell carcinoma, which is not considered amenable to surgery, and non small cell carcinoma, in which surgical intervention may be considered.

DISEASES OF THE PLEURA

- ‡ Can be divided for practical purposes into:
 - A] **Inflammatory conditions** (pleuritis) which can be acute or chronic and is often caused by pyogenic organisms or tuberculosis causing empyema, pleural effusions and adhesions.
 - B] **Neoplastic lesions of the pleura** which can be caused by direct spread of a bronchogenic carcinoma, metastases from other parts of the body (secondaries) or a primary neoplasm called **mesothelioma**.
- ‡ **Primary tumours of the pleura** are rare except after exposure to asbestos. After exposure, there may be a latent period of up to 50 years before development of the tumour. Patients usually present with chest pain and breathlessness and there is commonly a pleural effusion. Histologically, mesotheliomas may have spindle cells (sarcoma like) and glandular patterns. Mesotheliomas are highly malignant tumours that spread to adjacent structures like the pericardium and lung and death usually occur 10 months after diagnosis, although metastases are rare. Exposure to asbestos also causes development of benign collagenous thickening of the pleura termed pleural plaques.
- ‡ **Diagnosis** of pleural diseases in general is made by radiological investigations, cytological and histological assessments (cytological examination of pleural fluid and also pleural biopsies) in addition to bacteriological assessment and culture.