RESPIRATORY TRACT

REVIEW OF NORMAL

I. **GROSS 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 *acinus* represents the functional gas exchange area of the lung and is composed of a respiratory bronchiole and its branching structures. The larger *lobule* is the smallest discrete portion of lung bounded by fibrous septa and consists of a terminal bronchiole and its branching structures. A lobule may contain 25-30 acini. The pulmonary arteries follow the airways while the pulmonary veins course through the connective tissue septa. Lymphatic channels are present along the bronchovascular structures but are also found in the pleura and connective tissue septa.

II. **MICRO ANATOMY** - 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 (Kulchitsky) cells. Mucus-secreting glands lie beneath the epithelial surface, and cartilagenous plates help 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 (squamous/membranous) pneumocytes which are interspersed with the surfactant-producing Type II (cuboidal/granular) pneumocytes. In the alveolar septal wall, the alveolar capillary basement membrane fuses with the basement membrane of the alveolar epithelial cells on one side (the "thin" side) and is separated from the basement membrane of the alveolar epithelial cells by the pulmonary interstitium on the other side (the "thick" side). The interstitium contains collagen, elastin, mast cells, occasional inflammatory cells, and connective tissue cells (primarily smooth muscle and fibroblasts). Alveolar macrophages, derived from blood monocytes, are loosely attached to the alveolar wall or lie free within the alveolar space.

III. **DEFENSE MECHANISMS** - Large particulate matter > 10μ in size is filtered by nasal hairs or trapped in the oropharynx. Smaller particles are trapped in the bronchial mucous blanket or the bronchiolar watery secretions rich in lysozyme and secretory IgA. Particles that are 1-5μ in size are accessible to the terminal airways and alveoli where they are phagocytized by the alveolar macrophages.

IV. **GAS EXCHANGE** - *Ventilation* refers to the movement and distribution of air within the tracheobronchial system; *diffusion* is the movement of O_2 and CO_2 between the alveolar space and the capillary blood; and *perfusion* refers to the flow and distribution of blood within the pulmonary vascular bed. Therefore,

alterations in the airways, the alveoli, the blood vessels, or any combination of the three will lead to a decreased O_2 delivery to the tissues.

UPPER RESPIRATORY TRACT

I. **INFLAMMATORY DISORDERS** - These are generally due to a wide variety of viruses and produce various clinical syndromes. In addition to the local effects, systemic effects generally include chills, malaise, myalgias, headache and fever.

A. **ACUTE RHINITIS** (common cold) - This is characterized by increased nasal discharge, sneezing, nasal obstruction and sometimes watering of the eyes and slight conjunctivitis. Fever is relatively uncommon. Principal viruses include rhinoviruses, parainfluenza 1 and 2, echo 28, coxsackie a, and respiratory syncytial virus. The viruses infect the mucosal epithelial cells which are shed in a thin mucoid nasal discharge resulting from the increased vascular permeability and mucus production. These secretions may become superinfected with bacteria and become mucopurulent in nature.

B. **SINUSITIS** - This refers to inflammation of the sinus mucosa and can develop whenever there is interference with drainage from or aeration of the sinuses. Acute sinusitis is usually the result of extension of a neighboring infection into the sinuses. Incomplete resolution or repeated infections may lead to chronic sinusitis. Sinusitis may be complicated by osteomyelitis, meningitis, intra and extracranial abscesses, etc.

C. **EPIGLOTTITIS** - Most commonly seen in children <2 years old, acute epiglottisis is due most commonly to infection by the bacteria *H. Influenzae* and is considered a medical emergency. The inflammatory edema of the epiglottis obstructs the opening to the larynx and produces severe dyspnea. An inspiratory stridor is usually evident.

D. **NASAL POLYPS** - These are inflammatory in nature and consist of polypoid protrusions of edematous mucosa containing a variable number of inflammatory cells. Most polyps are the result of chronic allergies, but may also be found in patients with chronic rhinitis or sinusitis, cystic fibrosis, and sensitivity to aspirin. The polyps are frequently multiple and may cause symptoms of airway obstruction.

E. **VOCAL CORD POLYPS (SINGER'S NODE)** - These are also inflammatory in nature and are usually the result of trauma to the cords or, less commonly, allergies.

III. **NEOPLASIA**

A. **SQUAMOUS PAPILLOMA** - This occurs in the nasal vestibule or larynx. Histologically similar to cutaneous warts, they can seed in the same manner and most are probably related to HPV infection.

B. **INVERTED PAPILLOMA** - Seen more frequently in men and generally benign, this is an endophytic proliferation of squamous cells which often presents as nasal obstruction but which may cause epistaxis or even erode underlying bone. Without adequate surgical excision they may recur and a small proportion may undergo malignant transformation.

C. **SQUAMOUS CELL CARCINOMA**

1. **NASAL (NON-CUTANEOUS)** - These arise from the nasal mucosa or maxillary sinus. There is a correlation between various environmental (cigarette smoking) and occupational (exposure to nickel ore) hazards and the development of this tumor. Local destruction is common but distant metastases are rare.

2. **NASOPHARYNGEAL** - Difficult to diagnose because of their location, these may either be keratinizing, non-keratinizing, or undifferentiated. The latter two have a strong association with Epstein-Barr virus infection.
3. **LARYNGEAL** - These tumors are also associated with smoking as well as alcohol abuse. If they originate from the true vocal cords, they often produce hoarseness and are therefore discovered early. When they arise in other areas, howeveer, they may not produce symptoms until they are well advanced. Overall, there is a mortality rate of approximately 30%.

D. **LETHAL MIDLINE GRANULOMA** - In some ways similar to Wegener's granulomatosis (see Cardiovascular notes), this relatively rare malignancy represents a peripheral T cell lymphoma which may involve any organ but characteristicaly begins with involvement of midline structures such as the nose, sinuses, upper respiratory tract and GI tract. The initial symptoms are those of a rhinitis/sinusitis. The lymphomatous infiltrate ultimately may destroy midline facial features.

LOWER RESPIRATORY TRACT

I. DEVELOPMENTAL ANOMALIES

A. **HYPOPLASIA** - Any condition that reduces the volume of the thoracic cavity during development will prevent the lungs from reaching full size. This is usually the result of compression (diaphragmatic hernia, polycystic kidney disease) or decreased fetal respiratory movement as the result of amniotic fluid deficiency (renal agenesis, bladder obstruction).

B. **DIAPHRAGMATIC HERNIA** - Partial or total absence of the diaphragm may result in herniation of the abdominal contents into the thoracic cavity. Depending on the size of the defect, this may be asymptomatic or catastrophic. In utero, diaphragmatic defects will result in pulmonary hypoplasia due to compression of the lungs by the herniated viscera. These infants will have respiratory difficulties at birth.

C. **BRONCHOGENIC CYSTS** - These represent accessory buds from the foregut which are lined by bronchial epithelium and often have cartilage in the wall. They usually lie in the mediastinum around the tracheal bifurcation, but they may appear in the substance of the lung. They generally contain mucoid material and may predispose to abscess formation. They may also rupture into the tracheobronchial tree or pleural cavity.

D. **BRONCHOPULMONARY SEQUESTRATION** - This represents the presence of lung tissue that has no connection with the tracheobronchial tree and receives its blood supply usually from the aorta. It may occur within the lung (intralobar) where it may serve as a focus of recurrent infection or it may be external to the lung (extralobar) where it may be associated with other concurrent congenital abnormalities.

II. ATELECTASIS

ATELECTASIS - This refers to a condition of collapse or incomplete expansion of alveoli which create areas of lung parenchyma having reduced aeration.

A. **PRIMARY (ATELECTASIS NEONATORUM)** - This results from the failure of lungs to ventilate at time of birth. This may be due to birth trauma, bronchial obstruction, drugs, immaturity, CNS disorders, etc. When placed in water, the lungs will sink since they have no air in the alveoli.

B. **SECONDARY (ACQUIRED ATELECTASIS)** - This results from atelectasis occurring sometime after initial expansion and may be due to deficiency of surfactant (respiratory distress syndromes), loss

of negative intrapleural pressure (chest trauma, pneumothorax), complete obstruction of an airway (by secretions, exudates, neoplasms, or foreign bodies), direct pressure on lungs (usually by accumulation of material in the pleural cavities), or contraction (parenchymal fibrosis). Depending on the etiology, the distribution may be focal, segmental, or massive. The pleural surface over the area of atelectasis has a purple-blue color and is slightly depressed. Although atelectatic lung is still perfused normally, ventilation is decreases leading to an intrapulmonary shunt. With simple mechanical atelectasis, if the lungs are re-expanded soon after collapse, there is little or no residual damage. Infections, however, may develop in areas of collapse and "*carnification*" (complete organization of tissue) can occur if the lungs remain collapsed for an extended period of time.

III. RESPIRATORY DISTRESS OF THE NEWBORN (*RDS Type I, Hyaline Membrane Disease*)

A. **ETIOLOGY** - Immature development of the lung results in a deficiency of *surfactant*, the lipid material synthesized by the Type II pneumocytes that is needed to lower the surface tension of the alveoli and help maintain their patency during expiration. Infants at risk include those born prematurely, those delivered by Caesarean section, and those whose mothers are diabetic (the anti-glucocorticoid effects of hyperinsulinism in the fetus removes the stimulatory effect of cortisol on the production of surfactant). An amniotic fluid lecithin:sphingomyelin ratio of less than 2:1 or the absence of phosphatidyl glycerol in amniotic fluid indicates a high probability of the fetus developing RDS.

B. **PATHOGENESIS** - Decreased surfactant increases the surface tension of the alveoli allowing them to collapse during expiration. This then requires greater inspiratory effort to expand the atelectatic airways (clinically manifested as nasal flaring and retraction of the ribs and sternum during inspiration). Decreased ventilation of an already immature lung produces hypoxia, cyanosis, and metabolic acidosis which in turn triggers vasoconstriction (decreased perfusion leads to additional hypoxia) resulting in endothelial and epithelial injury. There is exudation of fibrin rich fluid into the interstitium and alveolar space and the subsequent formation of *hyaline membranes* (fibrinous exudate admixed with necrotic epithelial cell debris) along the respiratory bronchioles, alveolar ducts and alveoli. This further interferes with gas exchange, perpetuates the hypoxia, and hinders the ability of the Type II pneumocytes to produce surfactant, initiating a vicious cycle.

VI. CIRCULATORY DISORDERS

A. **PULMONARY EDEMA** - Extravascular fluid, initially in the interstitial space and subsequently spilling over into the alveoli, accumulates in the alveolar space due to disturbances of the normal hemodynamic equilibrium (congestive heart failure, myocardial infarction, hypertensive heart disease, longstanding mitral stenosis, etc.) or microvascular injury (see Hemodynamic Disorders).

B. **CHRONIC PASSIVE CONGESTION** - This is associated with chronic failure of the left side of the heart leading to brown induration of the lung (see Hemodynamic Disorders).

C. **PULMONARY EMBOLUS** - This relates to the impaction of a free floating mass (usually thrombus) in the pulmonary arterial bed. The etiology includes multiple entities which would predispose to venous thrombosis or stasis (such as surgery, immobility/immobilization, congestive heart failure, pregnancy, obesity, muscular weakness, cancer, and use of oral contraceptive or exogenous estrogens). The pathologic change and the clinical manifestations of pulmonary emboli are dependent on the size of the vessels in which the embolus impacts and also on the preexistent cardiovascular status of the lung.

1. **CLINICAL** - Small emboli lodge in peripheral pulmonary vessels causing local congestion, edema, and hemorrhage but produce no clinical symptoms. Recurrent showers of small

emboli, however, will result in progressive reduction of the perfusable pulmonary vascular bed and give rise to pulmonary hypertension manifested by dyspnea on exertion, anginal pain, syncope, and venous distention of the neck veins. Occlusion of medium size pulmonary arteries may produce a sudden onset of dyspnea, hyperventilation, and tachycardia. Other related symptoms would be anxiety, syncope, and anterior chest pain. Massive embolization, particularly of the saddle type, may induce the immediate catastrophic syndrome of acute cor pulmonale (perhaps related to release of serotonin and thromboxane A_2 from platelets in the embolus mediating a sudden increase in pulmonary artery resistance) and sudden death (perhaps related to neural reflexes that produce cardiac arrhythmias). If not immediately fatal, these may result in shock with central chest pain, severe dyspnea, cyanosis, tachycardia and diaphoresis (occasionally mimicking myocardial infarct). Most clinically significant emboli, therefore, are the larger ones that originate from thrombi in the femoral/iliac veins and not the deep calf veins.

2. **DIAGNOSIS** - When pulmonary emboli are clinically suspected, the best primary screening tool is a ventilation-perfusion scan of the lung (chest x-rays are frequently normal). Pulmonary arteriography has the best diagnostic sensitivity and specificity but is costly. Blood gases on room air usually reveal a decreased pCO_2 (< 40 mm Hg) secondary to hyperventilation (respiratory alkalosis) and a decreased pO_2 (< 80 mm Hg). There may be a nonspecific elevation of LDH_3.
3. **TREATMENT** - Most patients receive heparin anticoagulation to raise the aPTT to 1.5-2.5 times normal values. In some patients, thrombolytic therapy may be appropriate. Long term oral anticoagulation (3-6 months or longer) is also recommended.
4. **PREVENTION** - This is easier and less expensive than diagnosis and treatment. In clinical situations where venous thrombosis is likely (post-surgery, immobilization, etc), graduated compression stockings and intermittent pneumatic compression boots may be used. Anticoagulation with low molecular weight heparins is also effective. In some circumstances, the placement of inferior vena cava filters may be warranted.

D. **PULMONARY INFARCTION** - This signifies ischemic coagulation necrosis of lung parenchyma and is almost always due to pulmonary emboli. It is not, however, synonymous with pulmonary emboli. Infarcts occur in only 5-10% of pulmonary emboli and generally occur in those patients in whom there is preexisting impairment of the bronchial artery circulation.

1. **MORPHOLOGY** - Grossly, the lesions will vary in size from those barely visible to wedge-shaped involvement of a large part of an entire lobe. Classically, they abut on the visceral pleura with the apex of the wedge-shaped infarct pointing toward the hilus. The majority of infarcts are within the lower lobes, and more frequently seen on the right. Histologically, the infarct shows hemorrhagic coagulation necrosis. A pleural effusion may be present.
2. **CLINICAL** - When symptomatic, a clinical triad indicative of pulmonary infarction includes dyspnea, hemoptysis, and pleuritic chest pain (with possible pleural friction rub). A low grade fever and leukocytosis may be additional findings. Radiologically, a wedge-shaped consolidation along a pleural surface is classic although not that frequently seen. Elevation of the diaphragm may occur.

E. **PULMONARY HYPERTENSION** - This refers to increased pressures within the pulmonary vasculature and is due to increased vascular resistance resulting from vascular obstruction, constriction, obliteration, or increased flow.

1. **PRIMARY** - Mostly a disease of young women, prolonged vasoconstriction of the pulmonary vessels, induced by hypersensitivity to neurohormonal regulators, produces marked thickening of the small arteries and arterioloes with hypertrophy of the media and reduplication of the elastic membranes. Medium sized vessels also show medial hypertrophy and the large arteries may develop uncomplicated atherosclerotic plaques. Insidious development of pulmonary symptomatology (progressive dyspnea, weakness, etc) culminates with death usually due to cor pulmonale.
2. **SECONDARY** - This form is far more common and occurs in patients with known underlying conditions that increase pulmonary vascular pressures or resistance (congestive heart failure, primary pulmonary disease, or recurrent emboli).

F. **ADULT RESPIRATORY DISTRESS SYNDROME** (***ARDS, RDS Type II, Diffuse Alveolar Damage, "Shock" Lung)*** - This disorder is characterized by the acute onset of dyspnea and tachypnea with resulting tachycardia, hypoxemia refractory to therapy, and cyanosis. Mortality approaches 50%.

1. **ETIOLOGY** - Factors triggering this disorder involve a wide variety of mechanisms (high altitude exposure, anaphylaxis, exposure to chemical or physical irritants, fulminating bacterial or viral infection, drugs, oxygen toxicity, trauma, etc.) all of which have the common denominator of widespread diffuse microvascular injury.
2. **PATHOGENESIS** - Diffuse injury to alveolar capillary endothelium may be produced by direct damage to endothelial cells or mediated by leukocyte aggregation and activation. Leukocyte-generated free radicals, lysozymes, and arachidonic acid metabolites may be responsible for further endothelial cell damage, vasoconstriction, destruction of interstitial elastin and collagen, and damage to both Type I and Type II epithelial cells. There is leakage of fibrin rich exudate into alveoli, and the resultant hyaline membrane formation (proteinaceous exudate admixed with necrotic epithelial cell debris) interferes with gas diffusion. The loss of surfactant-producing Type II cells compounds the problem with widespread atelectasis producing a noncompliant "stiff" lung. Enlarged, regenerating Type II cells may become prominent along the alveolar membrane. Ultimately, if the patient survives, interstitial fibrosis develops.

VII. INFLAMMATORY / INFECTIOUS DISEASE

A. **ACUTE BRONCHITIS** - This inflammatory lesion of bronchi may be caused by viruses, irritant gases (smoke, ammonia, sulphur dioxide, etc.), or bacteria (staph, strep. pneumonia, and hemophilus influenza).

B. **MYCOPLASMA/VIRAL PNEUMONIAS** - These pneumonias are caused, respectively, by Mycoplasma pneumoniae (primary atypical pneumonia) and a wide variety of viruses but are morphologically and clinically similar. The pathologic lesions are peribronchiolar and, in general, interstitial (i.e. within the alveolar walls). The alveolar walls are widened by edema and a predominately mononuclear infiltrate. The alveolar spaces are generally free of significant cellular exudate, but focal hyaline membranes may be present reflecting alveolar epithelial damage. When caused by viruses, viral inclusions may be identified. Clinically, there is often a history of recent upper respiratory tract infection, and there may be an irregular fever with myalgia and malaise. Persistent, racking, sparsely productive cough is the hallmark of the disease. There may be a severe frontal headache, worsened during coughing. Chest pain is substernal, pleuritic pain and effusions are infrequent, and dyspnea and cyanosis are rare. X-rays can show nodular, patchy or perihilar infiltrates.

C. **BACTERIAL PNEUMONIA** - Pneumonia can be caused by a wide variety of bacterial agents. The pathologic changes depend in part on the specific agent and the host response to that agent. Streptococcus pneumoniae (pneumococcus) is the most common etiologic agent for both lobar and bronchopneumonias.

1. **MORPHOLOGIC PATTERNS**

a. **Lobar pneumonia** - Lobar refers to an extensive inflammatory consolidation involving an entire lobe or large portion thereof. The lobar distribution tends to reflect the virulence of the organism and/or the decreased effectiveness of the patient's defense mechanisms. Four morphologic stages have classically been described in lobar pneumonia. Antibiotic therapy, however, may abort this natural sequence and well developed lobar pneumonia is encountered less frequently than in the past.

(1) **Congestion** - This stage is characterized by rapid proliferation of bacteria and the early stages of the inflammatory response (vascular hyperemia and serous exudation into alveolar spaces).

(2) **Red hepatization** - Here, the alveolar spaces become packed with neutrophils, extravasated red blood cells, and precipitated fibrin which imparts a gross consistency resembling that of liver. The intense vascular engorgement gives the lung a red appearance. Microscopically, the alveolar infiltrate obscures the intact underlying pulmonary architecture.

(3) **Grey hepatization** - Disintegration of neutrophils and red cells in combination with continued accumulation of fibrin imparts a grayish appearance to the still firm parenchyma. Vascular engorgement is not as prominent.

(4) **Resolution** - In uncomplicated cases, the exudative debris in the alveolar spaces is digested and contraction of the fibrin away from alveolar walls again discloses the preserved native pulmonary architecture. The clumps of intraalveolar debris (*Masson bodies*) are reabsorbed or removed restoring the pulmonary parenchyma to its normal state.

b. **Bronchopneumonia** - This refers to a less extensive, but possibly more destructive, inflammatory consolidation which occurs in patches throughout a lobe (most frequently lower lobes) or lung, typically following tracheobronchial injury by a bronchitis/bronchiolitis or as complications of systemic disorders such as malnutrition, alcoholism, or congestive heart failure with pulmonary edema. The inflammation is centered around the air passages and extends out into surrounding lung parenchyma with tissue destruction, microabscess formation, and subsequent scarring.

2. **CLINICAL PRESENTATION** - The clinical course is typified by a sudden onset, often with shaking chills, followed by high fever. At first, cough is dry or productive of watery sputum. At the stage of red hepatization, the sputum becomes thick, purulent, and hemorrhagic ("rusty" sputum). The associated pleuritis manifests itself by pleuritic pain and a friction rub, and there may be a pleural effusion. Leukocytosis of 15,000 to 40,000 is usually present. Complications include abscesses, empyema, and sepsis.

3. **OTHER ETIOLOGIC AGENTS**

a. **Staphylococcal pneumonia** - This may be a complication of influenza, chronic pulmonary disease, cystic fibrosis, or concurrent staphylococcal infection at other sites. It is also seen more frequently in infants and young children. These organisms tend to produce abscess cavities and pneumatoceles (air-filled pseudocysts) which may progress to empyema or pneumothorax

b. **Gram negative pneumonias** - Most gram negative pneumonias represent hospital acquired infections. They occur in patients who have received previous extended broad spectrum antibiotic therapy or assisted ventilation and those with dissemination to the lungs from another source or site (urinary tract, etc). Mortality rate of gram negative pneumonias is over 50%.

(1) **Klebsiella pneumoniae** - This organism tends to complicate other underlying diseases, chiefly alcoholism. Dyspnea and cyanosis may be quite prominent. The sputum is characteristically thick, gelatinous and "brick red" with blood. Morphologically, abscesses are quite common and chronic lung abscess and pleural empyema are common complications.

(2) **Hemophilus influenzae** - Rare in adults, this is more frequently found in the pediatric age group especially in cases of obstructive pulmonary disease.

(3) **Pseudomonas aeruginosa** - A common cause of nosocomial infection, this organism thrives in the watery environment of humidification devices, and patients who require assisted ventilation are especially prone to infection. Due to involvement of blood vessels, there is often extensive hemorrhage but surprisingly scant neutrophilic reaction.

(4) **Enteric gram negatives** - These organisms are often seeded to the lungs from urinary tract infections. They may colonize in the pulmonary vasculature and may form abscesses.

D. MYCOTIC PNEUMONIAS - In general, the fungi are weak antigens and can cause tissue damage primarily by virtue of the hypersensitivity reaction by the host against the fungal proteins. Most of the deep mycoses (histoplasmosis, coccidioidomycosis, North American blastomycosis, cryptococcosis, etc) induce a chronic granulomatous inflammatory reaction. Candida, mucor, and aspergillus are the major opportunistic fungal organisms and elicit an acute inflammatory response in the debilitated patient. They typically like to invade and obstruct vessels which can result in hemorrhagic infarcts. Pneumocystis carinii is the most common opportunistic agent producing pneumonia in AIDS patients. The organisms proliferate in the alveolar spaces and are associated with a characteristic "frothy-appearing" intraalveolar edema. Nocardia characteristically elicits purulent abscess formation. Actinomycosis invokes both a chronic granulomatous response and a purulent exudation. The fungal colonies *(sulphur granules)* characteristically float in a "sea of pus."

E. PULMONARY TUBERCULOSIS - Worldwide, tuberculosis kills more adults than any other infectious agent. Although the incidence in the U.S. declined dramatically after the introduction of effective anti-tuberculous drugs, the incidence has been steadily rising since 1985, primarily due to the increased numbers of immunosuppressed patients (AIDS, etc.) and the emergence of drug-resistant strains of the mycobacterium

1. **PRIMARY TUBERCULOSIS** - The most common route of infection is through inhalation of contaminated aerosol droplets from an infected individual. The primary focus of infection in the lung parenchyma is usually subpleural, most commonly in the upper portion of lower lobe or the lower portion of the upper lobe. This focus is called the *ghon focus* and typically has central caseous necrosis. The organisms may spread through the lymphatics to produce caseous lymphadenitis in the hilar lymph nodes (which usually show more extensive involvement than the primary focus). The combination of the subpleural lesion and the hilar node involvement is called the *primary ghon complex*. In about 90% of individuals, the only residuum of the primary infection is the presence of a fibrotic or sometimes calcified ghon complex. Occasionally (particularly in pre-school children), a primary infection does not run a benign course and may evolve into a tuberculous pneumonia, erode into a bronchus with resultant bronchogenic dissemination, or disseminate by lymphatic and hematogenous routes to isolated organs (i.e. tuberculous meningitis) or systemically throughout the body.
2. **SECONDARY TUBERCULOSIS** (adult, reactivation, postprimary TB) - Due to the previous exposure and development of hypersensitivity, reexposure to the organism or reactivation of latent organisms produces a prompt granulomatous tissue response often with caseous necrosis. Since mycobacterium organisms prefer areas of high oxygen tension, reactivation is almost invariably localized to the apices of one or both upper lobes. This focus is called the *assmann focus*. Granulomas may coalesce to form larger foci of destruction but most eventually become encapsulated by fibrous tissue and develop areas of dystrophic calcification. In some cases, however, the lesions may remain active, erode into neighboring airways and cavitate. ***Cavitation is considered the anatomic hallmark of secondary tuberculosis.*** Apical cavitary fibrocaseous tuberculosis may heal, spread by direct extension, or be disseminated through the tracheobronchial tree, the lymphatics, or the blood. Local complications may include massive hemoptysis due to erosion of a pulmonary vessel, sufficient fibrosis to result in the loss of ventilating capacity, and infection of the pleura leading to a tuberculous empyema.

F. **CHEMICAL PNEUMONIA**

1. **ASPIRATION PNEUMONIA** - Aspiration occurs most frequently in unconscious patients, those with repeated vomiting episodes, and those with depressed cough reflexes (alcoholic intoxication, central nervous system malfunction, acute drug intoxication, etc). The clinical symptoms are dependent upon the volume and the nature of the aspirate. Aspiration of liquid gastric contents causes extensive acute inflammatory reaction, pulmonary edema, and widespread destruction of epithelium with hemorrhage and hyaline membranes. With extensive involvement, the lung parenchyma may be almost completely destroyed. If sufficient volume with low Ph is aspirated, a distinct clinical picture ensues 2 to 5 hours after aspiration with the onset of cyanosis, dyspnea, tachypnea, tachycardia and shock, bloody frothy sputum, marked pulmonary congestion and edema. X-rays show soft patchy mottling throughout both lung fields, indistinguishable from broncho-pneumonia. Chronic or recurrent aspiration will cause repeated bouts of tracheobronchitis and pneumonia. Symptoms include recurrent cough and sputum production and, with time, chronic fibrosis will ensue with resultant dyspnea and digital clubbing.
2. **LIPID PNEUMONIA**

    a. **Endogenous** (*golden pneumonia, cholesterol pneumonia*) - This is usually seen as a complication of an obstructive lesion of the bronchial tree. Histologically,

there are large numbers of "foamy" macrophages in the alveoli containing surfactant and lipids from degenerating cells.

b. **Exogenous** - This occurs when fatty or oily material is inhaled or aspirated. Clinical symptoms may be relatively few. Occasional cough with sputum production and dyspnea may occur. X-ray appearance may look like an interstitial fibrosis. Occasionally, there may be a large localized mass suggestive of granuloma or carcinoma.

G. **PULMONARY ABSCESS**

1. **PATHOGENESIS** - Aspiration is the most common cause of lung abscess with inoculation of the lower respiratory tract by anaerobic organisms from the oral cavity. These abscesses tend to be solitary and occur most frequently on the right side due to the shallow angle of the right mainstem bronchus. Other causes of abscesses include bacterial pneumonia (especially Staphylococcal and Klebsiella pneumonia), bronchial obstruction, septic emboli, cysts or bullae, and penetrating chest wounds. In some instances, no underlying cause can be identified (primary idiopathic or cryptogenic lung abscess).
2. **PATHOLOGY** - Abscesses consist of localized suppuration and liquefaction necrosis of lung parenchyma, which in chronic cases (> 6 weeks duration) may elicit considerable fibroblastic proliferation in the wall. They may be solitary or multiple and may vary in diameter from a few millimeters to large cavities of 5-15 cm.
3. **CLINICAL SYMPTOMS** - Generally, there is a fever with a prominent cough, often accompanied by copious amounts of foul smelling (esp. anaerobic organisms) or bloody sputum. Chest pain and weight loss may also be present. X-rays may show a homogenous density which, if there is communication with an airway, may reveal an air-fluid level. If the patient does not have putrid sputum, bronchial obstruction should be suspected as the etiology. An infected cavitated infarct could also be suspected. A solitary lung abscess has a fatality rate of 15-20% and with multiple hematogenously spread abscesses, the fatality rate approaches 50%.

VIII. **CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)** - Obstructive disease results from the narrowing/obstruction of the tracheobronchial tree or damage to the pulmonary parenchyma. This results in an increased compliance of the lungs (increased residual volume and total lung capacity) but a decreased elastic recoil (decreased forced expiratory volumes).

A. **CHRONIC BRONCHITIS** ("blue bloaters") - This is a clinical disorder characterized by excessive mucous secretion within the bronchial tree than cannot be explained by either a specific infection or by infiltrative disease. It is defined as a chronic cough with sputum production for at least three months of the year in at least two consecutive years. The major cause is cigarette smoking, but air pollution and occupational irritants may also play a role. The major pathophysiologic disruption is large airway obstruction.

1. **PATHOGENESIS** - As a defense mechanism against chronic irritation of the tracheobronchial mucosa by cigarette smoke and/or other environmental pollutants, there is hypertrophy and hyperplasia of the submucosal mucous glands in the large airways (⇑*Reid Index*) with the resultant hypersecretion of mucus accounting for the increase sputum production. Squamous metaplasia and dysplasia of the surface epithelium may also be present. Goblet cell metaplasia of small bronchi and bronchioles also leads to excessive mucus production, decreases the number of normal ciliated cells (thereby hampering the

normal clearance mechanism of the mucous blanket), and predisposes to obstruction of these airways by mucous plugs. On inspiration, air is able to enter around the mucous plugs, but on expiration as the bronchioles collapse around the plugs, air is trapped and patchy atelectasis develops. This environment is also fertile ground for bacterial growth, and these patients are predisposed to repeated bacterial infection resulting in injury and ultimate fibrosis (*bronchiolitis fibrosa obliterans*) of the bronchiolar walls.

2. **CLINICAL DATA** - The decrease in ventilation produces a major ventilation/perfusion mismatch and as a result, patients tend to be cyanotic. Blood gases generally reveal a chronic hypoxemia (which produces polycythemia) and hypercapnia that causes a respiratory acidosis. The acidosis promotes pulmonary vasoconstriction and, over time, patients develop pulmonary hypertension with ensuing right hear failure. Chest x-rays may be normal in appearance but, with bronchography, bronchial pits or diverticula representing the enlarged bronchial gland ducts are pathognomonic.
3. **COMPLICATIONS** - Repeated infections, cor pulmonale, peptic ulcers, and respiratory failure are the major complications.

B. **EMPHYSEMA** ("pink puffers") - This is defined as an abnormal, permanent, destructive lesion of the pulmonary parenchyma which leads to an increase in the size and volume of the air spaces distal to the terminal bronchiole. The major pathophysiologic disruption is distal airway tissue destruction and with loss of elastic recoil rather than large airway obstruction as is seen with chronic bronchitis. Air moves in on inspiration, but on expiration, without elastic fibers the distal airways collapse upon themselves trapping air behind.

1. **CLASSIFICATION AND PATHOGENESIS**

   a. **Centrilobular** - This pattern is characterized by destructive changes primarily to the respiratory bronchioles. Most striking in the upper lobes, it is seen most frequently in cigarette smokers and for that reason is often also associated with chronic bronchitis. Particles of cigarette smoke impact in the respiratory bronchioles and stimulate macrophages which, among other things, recruit and activate neutrophils. Both macrophage and neutrophilic proteases are released and unless they are inactivated by antiproteases such as alpha-1-antitrypsin, proteolytic digestion of the alveolar walls will ensue. Unfortunately cigarette smoke also inactivates alpha-1-antitrypsin. Additional damage results from free radical release from neutrophils.
   b. **Panlobular** - Most frequently seen in the lower lobes, this pattern is characterized by uniform involvement of the acinus and is seen in patients with inherited or acquired alpha-1-antitrypsin deficiency, especially if they also smoke.
   c. **Paraseptal** - This pattern is characterized by destruction in the distal portion of the acinus directly underlying the pleura or fibrous septa and sparing the respiratory bronchiole. It tends to occur more frequently in the upper lobes, may form large subpleural bullae or pleural blebs, and may be a cause of spontaneous pneumothorax in young adults.
   d. **Irregular (scar) emphysema** - This refers to focal parenchymal loss found in almost all adult lungs, often in areas of old scars from tuberculosis, histoplasmosis, etc.

2. **MORPHOLOGY** - The alveolar walls appear attenuated and broken with fragments of the wall appearing to "float" in large distorted air spaces.

3. **CLINICAL** - Patients usually present with a history of progressive dyspnea and often weight loss. The A-P diameter of the chest is increased (barrel chest) due to the increased lung volume, expiration is prolonged due to the lack of elastic recoil, and patients tend to exhale through pursed lips. Since there is equivalent destruction of airways (ventilation) and vessels (perfusion), the ventilation/perfusion mismatch is less than that of chronic bronchitis. The patients are not cyanotic and blood gas values may even be normal. On chest X-ray, there is increased radiolucency of the lung fields with depression and flattening of the diaphragm.

C. **BRONCHIAL ASTHMA** - This disorder is characterized by an increased sensitivity of the tracheobronchial tree to various stimuli and is manifested by widespread but reversible narrowing of the small airways.

1. **CLASSIFICATION AND PATHOGENESIS**

   a. **Atopic (allergic)** - This form is an IgE mediated hypersensitivity reaction (Type I) and can be triggered by a wide variety of environmental allergens. Onset typically occurs in childhood, and there is often a family history of allergy. Serum IgE levels are usually elevated. Upon contact with an allergen, there is an immediate response of wheezing, edema, and increased mucus secretion due to degranulation of sensitized mast cells and stimulation of submucosal vagal receptors which cause bronchoconstriction. Release of various chemical mediators of inflammation (leukotrienes, prostaglandins, chemotactic factors, etc) potentiate the bronchoconstriction and the interstitial edema reduces overall lung compliance. There is also a delayed response of persistent bronchospasm resulting from the recruitment of inflammatory cells which release additional chemical mediators (including major basic protein).

   b. **Non-atopic** - This form is frequently triggered by upper respiratory infections (primarily viral). The mechanism of action is unknown. IgE levels are usually normal, and a family history is usually lacking.

   c. **Miscellaneous** - Other causes of asthma include various drugs (including aspirin), occupational inhalants, exercise, and emotional stress.

2. **MORPHOLOGY** - Mucous plugs containing desquamated epithelial cells (*Curschmann's spirals*) are present in small bronchi and bronchioles. Submucosal inflammatory infiltrates are composed chiefly of eosinophils, and *Charcot-Leyden crystals* (crystalloids of eosinophil membrane proteins) may be identified in the sputum. Thickened basement membranes and muscular hypertrophy of bronchial walls result from repeated bronchospasm. Goblet cell metaplasia and hyperplasia of submucosal glands may also be present.

3. **COMPLICATIONS** - These include *status asthmaticus*, respiratory failure, pneumothorax or pneumomediastinum, pneumonia, atelectasis, and mucoid impaction.

D. **BRONCHIECTASIS** - This is a permanent dilatation (cylindrical, fusiform, or saccular) of bronchi and bronchioles resulting from inflammatory damage to their walls. It may be due to bronchial obstruction, necrotizing pneumonia, or a variety of congenital or inherited conditions (notably cystic fibrosis). The inflammatory reaction in the bronchial wall ultimately results in weakening, abnormal dilatation, and fibrosis. Clinically, it is usually associated with cough and copious production of purulent sputum. Epithelial necrosis or metaplasia further inhibits normal clearance

of bronchial secretions predisposing to further infection. The lower lobes are usually involved (the left more often than the right), but it may be bilateral in 30-40% of cases.

E. **CYSTIC FIBROSIS** (mucoviscidosis) - This is an inherited autosomal (chromosome 7) recessive disorder of exocrine glands characterized by abnormally viscous secretions and, depending on the severity of the disease, clinically manifested by pancreatic insufficiency, chronic respiratory disease, electrolyte disturbances, infertility, and occasionally cirrhosis of the liver. The submucous glands in the bronchial tree secrete an atypical viscous mucus which is difficult to clear and which predisposes to obstruction and repeated infection. Mucopurulent material is frequently present within the trachea and bronchi, and bronchiectasis is usually present. Most patients usually succumb due to pulmonary complications of the disease.

IX. **RESTRICTIVE LUNG DISEASES** - In contrast to obstructive diseases, this group of disorders is characterized by decreased total lung capacity, reduced oxygen diffusing capacity, decreased lung compliance ("stiff" lung), and increased elasticity. The initiating events are widely varied but all probably result in activation of alveolar macrophages (which release fibroblast stimulating factors) and recruitment and activation of neutrophils (which cause inflammatory or immunologic damage to alveoli and small airways). Early lesions generally show diffuse inflammatory infiltrates within the alveolar walls *(alveolitis)* and peribronchiolar interstitium that ultimately cause vascular and parenchymal destruction with extensive fibrosis.

A. **PNEUMOCONIOSES** - These are primarily occupational diseases caused by the inhalation of inorganic mineral dusts (coal dust, silica, asbestos, talc, kaolin, beryllium, etc). These dusts will elicit, to a variable degree, inflammation and pulmonary fibrosis as a host response. The more soluble particles tend to elicit more of an inflammatory response while the more insoluble materials tend to elicit a fibrotic response. The size, shape, and concentration of the inhaled material also has a bearing on the resultant damage produced. In general, particles less than 2μm in size are able to reach the terminal airways where the alveolar macrophage is the primary defense mechanism. Release of chemical mediators from the macrophages and activation of leukocytes is felt to be the mechanism of injury to the pulmonary parenchyma.

1. **COAL WORKERS LUNG** (*black lung*) - Coal dust is deposited in small airways where it is ingested by macrophages that then migrate into the interstitium and collect around the respiratory bronchioles. The reaction may vary from clinically asymptomatic changes to extensive pulmonary fibrosis and centrilobular emphysema. These patients are also at increased risk of developing tuberculosis.
2. **SILICOSIS** - This is due to the inhalation primarily of quartz dust. The silica particles are ingested by alveolar macrophages which secrete fibroblast stimulating factor and proteases but which are also destroyed by the toxic effects of the silica. The silica is released by the irreversibly injured macrophages only to be reingested by others thereby initiating a repetitive cycle until they become "walled off" by fibrotic nodules of whorled collagen surrounded by lymphocytes and fibroblasts. Hilar lymphadenopathy may develop but does not significantly interfere with pulmonary function. Occasionally, massive fibrosis can occur which does produce symptoms of restrictive disease. Silicosis and tuberculosis are often associated, but there appears to be no increased risk for lung cancer.
3. **ASBESTOSIS** - This results from the inhalation of the long, thin asbestos fibers which cause an alveolitis and interstitial fibrosis. Asbestos fibers cannot be completely engulfed by macrophages and may become encrusted by protein and iron (derived from the hemoglobin released in microhemorrhages). These are called *asbestos or ferruginous bodies* and can be seen around alveolar ducts and distal acinar structures primarily in the

lower lobes. Fibroblast stimulating factors released by macrophages incite fibrosis. These patients have an increased risk of developing primary lung cancer especially if they also smoke. The pleura is also frequently thickened (benign pleural plaques), and there is an increased incidence of malignant mesothelioma of the pleura and peritoneum.

B. **CHRONIC INTERSTITIAL (NON-INFECTIOUS) PNEUMONIAS** - These encompass a group of diseases which have in common an alveolitis with subsequent fibrosis. The end result of each of these is "honeycomb" lung characterized by multiple cystic spaces separated by dense fibrous scars. The cystic spaces represent dilated bronchioles caused by contraction of the fibrous scars and are often filled with mucus and cellular debris.

1. **IDIOPATHIC PULMONARY FIBROSIS** (*Hamman-Rich syndrome, UIP, fibrosing alveolitis*) - By definition, the etiology of this disorder is unknown. It perhaps may be immunologically mediated and may or may not be associated with coexistant collagen vascular disease. Within the lung, there are a variety of changes ranging from slight inflammatory cell infiltrates of the alveolar wall with minimal fibrosis to diffuse alveolar damage with extensive fibrosis and alveolar collapse. It tends to occur in middle aged males and generally is slowly progressive over a number of years.
2. **DESQUAMATIVE INTERSTITIAL PNEUMONITIS** (*DIP*) - This is characterized by the accumulation of macrophages and desquamated epithelial cells (Type II) within the alveolar spaces. This possibly represents an early stage of idiopathic pulmonary fibrosis, however, these patients are more likely to benefit from steroid therapy. Mononuclear cells infiltrate the alveolar walls. but there is little fibrosis. Progressive dyspnea may lead to respiratory failure.
3. **LYMPHOID INTERSTITIAL PNEUMONIA** - This is characterized by lymphocytic infiltrates confined to the alveolar septa. It tends to be an indolent or slowly progressive disease, but the incidence of pulmonary lymphoma is increased in these patients.
4. **PULMONARY ALVEOLAR PROTEINOSIS** - This is characterized by the presence of a proteinaceous PAS positive fluid in alveolar spaces along with necrotic Type II pneumocytes and alveolar macrophages.
5. **HYPERSENSITIVITY PNEUMONITIS** (*extrinsic allergic alveolitis*) - These are primarily occupational diseases resulting from immune-mediated alveolar damage caused by inhalation of environmental organic dusts contaminated by various antigens (animal protein, bacterial products, fungi, thermophilic bacteria, etc). These include moldy hay (*farmer's lung*), cotton dust (*byssinosis*), sugar cane dust (*bagassosis*), maple bark dust (*maple bark stripper's lung*), etc. Acute attacks of dyspnea and cough follow exposure in sensitized individuals and continued exposure may lead to progressive respiratory failure. Treatment is therefore identification and elimination of the allergen.
6. **BRONCHIOLITIS OBLITERANS AND ORGANIZING PNEUMONIA** - This is characterized by loose granulation filling the respiratory bronchioles, alveolar ducts, and alveolar spaces and is associated with diffuse alveolar damage and mild interstitial fibrosis. The disease can have a fulminant course, but patients may benefit from steroid therapy.

C. **SARCOIDOSIS** - This is a systemic disease of unknown etiology. The most widely accepted hypothesis is that it represents an abnormal immunologic response to a variety of non-specific agents or antigens. The incidence is higher in young adults, females, and Blacks. The classical syndrome includes bilateral hilar lymphadenopathy, uveoparotitis, osseous lesions in the short bones of the hands and feet, erythema nodosum, hypergamma-globulinemia, hypercalcemia and hypercalciuria. The lung is the most frequently affected organ, involving approximately 90% of all

cases, but the manifestations are variable and may include hilar lymphadenopathy (enlargement of the lymph nodes may be so great that the designation "potato nodes" has been applied), miliary sarcoidosis (giving a reticulonodular "snow storm" appearance by x-ray due to the multiple miliary sarcoid lesions throughout the lung parenchyma), diffuse fibrosis (leading to symptoms of restrictive lung disease), or "honeycombing" (end stage pulmonary disease). Microscopically, the histology shows granulomas without central caseation, so called "hard granulomas". No organisms are present on acid-fast stains nor can organisms be cultured from the fresh tissue. *Schaumann bodies* and *asteroid bodies* are characteristic but not pathognomonic. In general, the presenting symptoms in thoracic sarcoidosis include cough, dyspnea, chest pain, loss of weight, malaise or excessive fatigue.

X. NEOPLASIA

A. **BRONCHOGENIC CARCINOMA** - Overall, bronchogenic carcinoma is the leading cause of cancer deaths in the U.S. Although there is a greater incidence in men, the incidence in women is increasing rapidly and has replaced breast cancer as the most frequent cause of cancer deaths among women. With the exception of small cell undifferentiated carcinoma, if discovered early, surgery may be effective but the overall 5-year survival is only about 13%. Smoking is probably the single most important etiologic factor and is most closely associated with squamous cell carcinomas and small cell carcinomas. The risk is proportional to the number of cigarettes smoked daily, the duration of the habit, and the tendency to inhale. Environmental/occupational exposure (uranium, asbestos, chromates, nickel, coal, iron, arsenic, radiation, etc) also plays a role in some cancers.

1. **CLASSIFICATION** - Bronchogenic carcinomas are felt to arise from the basal cells of the bronchial epithelium and subsequently differentiate into a variety of recognizable patterns. It is not uncommon, however, for more than one histologic pattern to be present in the same tumor.

   a. **Squamous cell carcinoma** (35%) - This is primarily a central lesion and is the cancer most closely associated with smoking, evolving from preceding dysplastic squamous metaplasia of the bronchial epithelium. It may vary from well-differentiated to poorly differentiated and tends to infiltrate locally before metastasizing. The majority of patients present with signs and symptoms attributable to bronchial obstruction: atelectasis, pneumonia and abscess formation. Infrequently, some tumors may cavitate and simulate the appearance of tuberculosis or infectious lung abscess.

   b. **Adenocarcinoma** (35%) - Although central lesions do occur, the majority of adenocarcinomas are peripheral lesions that tend to spread through submucosal lymphatics to the hilar lymph nodes. They may remain clinically silent until signs and symptoms of definite metastases appear. Occasionally they are associated with focal lung scars and fibrosis.They occur in equal frequency in men and women and are not as closely related to cigarette smoking. The histologic patterns vary but most can be demonstrated to contain mucus-secreting cells. A relatively rare variant of adenocarcinoma, ***bronchioloalveolar carcinoma***, apparently arises from bronchiolar epithelium (Type II pneumocytes, Clara cells) and characteristically grows as cuboidal or columnar cells spreading along alveolar septa. It may present as a peripheral mass lesion, or it may present as irregular nodules scattered throughout one or both lungs simulating diffuse interstitial pneumonia. These

patients may present with cough and chest pain and are often hypoxemic. Although metastases are late occurrences, the overall survival is about 25%.

c. **Small cell undifferentiated (oat cell) carcinoma** (20%) - Almost always a central lesion, this type of cancer occurs predominantly in men, is associated with smoking, and progresses rapidly with wide dissemination. The cells are relatively small with little cytoplasm, and there is no distinctive architectural growth pattern. Thought to arise from the neuroendocrine Kulchitsky cells, these tumors are notorious for producing hormone-like substances (ADH, ACTH, gonadotropins, etc). Radiation and chemotherapy is more effective than surgery, but the overall prognosis is poor.

d. **Large cell undifferentiated carcinoma** (10%) - This tumor is comprised of large pleomorphic undifferentiated cells and may represent undifferentiated squamous cell carcinomas or adenocarcinomas.

2. **CLINICAL PRESENTATION** - In the course of a routine physical examination, patients with a lung nodule may be free of symptoms. The chance for cure by surgical excision would be greatest in these patients. When symptomatic, the usual presentation consists of chronic cough (often with hemoptysis), chest pain, anorexia and weight loss, and dyspnea. X-ray almost always shows an abnormal mass. Intrathoracic manifestations may include endobronchial obstruction with secondary atelectasis, pneumonia, abscess, or bronchiectasis; superior vena cava obstruction; extension to the pleura with or without effusion; extension to hilar and mediastinal lymph nodes; and mediastinal extension with involvement of the phrenic and recurrent laryngeal nerves causing a paralyzed diaphragm and paralyzed vocal cord. Extrathoracic manifestations are generally the result of widespread metastases or systemic syndromes resulting from ectopic hormone production by the tumors.

B. **BRONCHIAL TUMOR** - These tend to occur at a younger age than other malignant neoplasms of the lung and, like small cell undifferentiated carcinomas, arise from the neuroendocrine Kulchitsky cells. They resemble intestinal carcinoid tumors (see GI section) and, like those tumors, can secrete serotonin. Though originally called adenomas, they are not truly benign, but are slow growing and locally invasive. Occurring centrally, they tend to extend into both the lumen and the bronchial wall in a dumbbell shape. Presenting symptoms may be related to the secretion of vasoactive amines or to bronchial obstruction due to the occluding mass. Distant metastases are unusual and the overall prognosis is good.

C. **HAMARTOMA** - These lesions represent local overgrowth of normal tissue and are not true neoplasms. They generally appear as 1-4 cm spherical or ovoid lesions in the lung periphery. The most frequent histologic component present is hyaline cartilage.

D. **METASTATIC TUMORS** - ***Metastatic neoplasms are more common than primary neoplasms*** and tend to present as multiple nodules usually in the lung periphery.

PLEURA AND PLEURAL CAVITY

I. **PNEUMOTHORAX** - This refers to the presence of air within the pleural cavity. It may occur spontaneously as a complication of other pulmonary disease (emphysema, abscess, tuberculosis, carcinoma) or as a result of traumatic damage to the lung or chest wall. Depending on the volume of air

and the degree of atelectasis that it causes, a pneumothorax may be clinically asymptomatic or it may present as sudden onset of unilateral pleuritic pain, dyspnea, and tachypnea.

A. **CLOSED PNEUMOTHORAX** - This occurs when there is no free movement of air into or out of the pleural cavity during respiration. The air in the cavity will gradually be absorbed and the lung will re-expand.

B. **OPEN PNEUMOTHORAX** - This occurs when air is able to move freely into and out of the pleural space during respiration. The lung will remain collapsed until a negative pressure can again be established in the pleural cavity.

C. **TENSION PNEUMOTHORAX** - This occurs when air enters the pleural space during inspiration but does not escape during expiration. As a result, the pressure in the pleural cavity builds up and will force the mediastinal structures toward the opposite side. This will cause distortion and kinking of the great veins resulting in cardiac and respiratory dysfunction. The patient will show increasing anxiety, restlessness, and respiratory distress. This can rapidly lead to death unless the increased pressure is released, usually by sticking a needle through the chest wall into the pleural cavity.

XIII. **PLEURAL EFFUSIONS** - Predisposing factors include any general condition with sodium or protein imbalance (congestive heart failure, nephrotic syndrome), increased pressure in pulmonary capillaries (acute left ventricular failure, pulmonary venous thrombosis), increased permeability of pleural capillaries (inflammatory lesions), and decreased pleural lymphatic drainage (inflammation of parietal pleura, tumor infiltration of lymphatics, etc.). The major cause of a transudative effusion is congestive heart failure, and the major causes of an exudative effusion include pneumonia, malignant disease, tuberculosis, and pulmonary infarction. In a patient over the age of 40 (with no history of febrile illness, no pain, and negative tuberculin test), the most common cause is cancer, and in a patient under the age of 40, the most common cause is tuberculosis.

XIV. **MALIGNANT MESOTHELIOMA** - This may be a late complication of asbestos exposure and arises as a thick pleural mass which tends to encase the lung and invade into surrounding thoracic tissues. Patients often develop recurrent pleural effusions and complain of dyspnea and chest pain. Histologically, the malignant cells may have an epithelial appearance, a spindle cell appearance, or a mixture of the two. Although the tumor usually does not metastasize until later in the disease process, the overall 5-year survival is extremely poor.