

- [The Blood Vessels](#)
- [The Heart](#)
- [The Lung](#)

BLOOD VESSELS

HEMOSTASIS and THROMBOSIS:

- **Hemostasis:** The arrest of hemorrhage as a response to vascular injury.
- BLOOD COAGULATION
 - **Intrinsic Pathway:** Factor XII -----> Factor XI -----> Factor IX
 - **Extrinsic Pathway:** **Tissue Factor (Thromboplastin)** -----> Factor VII + Ca⁺²
 - **Common Pathway:** Factor X -----> (Prothrombin -----> Thrombin) -----> (Fibrinogen -----> Fibrin)
- PLATELET AGGREGATION:
 - **Von Willebrand Factor** from endothelial cells enhances aggregation.
 - **Thromboxane A₂ (TXA₂)** enhances aggregation.
- ENDOTHELIAL FACTORS: Injury to the endothelium is the most important precipitating event of thrombosis.
 - Function of endothelial cells:
 - Permeability barrier
 - Vasoactive factors: **NO**
 - Anti-thrombotic factors: **Prostacyclin (PGI₂)**
 - Clotting Factors:
 - **Factor VIII**
 - **Von Willebrand Factor**
 - Anti-Coagulant Factors: **Thrombomodulin**
 - Fibrinolytic Agents: **TPA**
 - **Plasminogen Activator Inhibitor (PAI)** inhibits fibrinolysis
 - Inflammatory Mediators: IL-1, Cell adhesion molecules
 - Growth Factors: CSF, FGF, PDGF
- CLOT LYSIS: (Plasminogen -----> Plasmin) -----> (Fibrin -----> Fibrin split products)
 - Thrombosis itself results in production of TPA, which converts plasminogen to plasmin to effect fibrinolysis.

ATHEROSCLEROSIS: Progressive accumulation within the intima of smooth muscle cells and lipids.

- PATHOGENESIS and PATHOLOGY:
 - Progression:
 - Early on: Proliferation of smooth muscle cells and accumulation of lipid.
 - *Smooth muscle cells* as well as lipid is required for the atheroma to form.
 - Later: Infiltration of macrophages, lymphocytes, and connective tissue.
 - Later: Organized thrombus formed, with canals (*vaso plaquorum*) going through the lesion.
 - ELEMENTS of ATHEROSCLEROTIC PLAQUE:
 - Vascular Endothelium
 - Arterial Smooth Muscle Cell
 - Mononuclear Phagocyte
 - Lymphocytes and Neutrophils
- ATHEROGENIC PROCESSES: The overall process of atherogenesis is a combination of the theories below.
 - **Insudation Hypothesis:** Lipids in the atheroma are derived from plasma lipoproteins (LDL) in the blood.
 - **Encrustation Hypothesis:** Says that small mural thrombi represent the initial event in atherosclerosis.
 - We now know that this isn't true. Mural thrombi are not the initial event, but they are critical to the later progression of the atheroma, i.e. toward thrombosis.
 - **Reaction to Injury Hypothesis:** Smooth muscle cells accumulate as a response to injury, *as a result of release of PDGF and other growth factors.*
 - This theory explains smooth muscle proliferation but not lipid accumulation.
 - **Monoclonal Hypothesis:** Points to the fact that many plaques contain cells that are mostly monoclonal. Perhaps their proliferation was due to a virus or cell-specific mutagen.

- **Intimal Cell Mass Hypothesis:** This is the initial lesion. Accumulation of smooth muscle cells at junctions and branching points of arteries.
- **Hemodynamic Hypothesis:** Atheromas tend to occur at locations of turbulence, pressure, and shear forces. Hypertension predisposes to atheromatous formation.
- **UNIFYING HYPOTHESIS:** Likely order of events in Atherogenesis
 - Intimal cell mass predisposes at branch points.
 - Lipid accumulation occurs.
 - Lipid Insudation results in cellular injury, leading to accumulation of macrophages and platelets
 - Macrophages and platelets release growth factors
 - Smooth muscle proliferation and endothelial injury may result in loss of anticoagulant properties of endothelia, and a thrombus results.
- **MORPHOLOGY:**
 - **INITIAL LESION of ATHEROSCLEROSIS**
 - **FATTY STREAKS:** Can be found in young children as well as adults, and not necessarily at branch points.
 - **INTIMAL CELL MASSES:** At branch points, may also be the initial lesion.
 - **CHARACTERISTIC LESION of ATHEROSCLEROSIS: Fibrous Fatty Plaque**
 - **FIBROUS CAP:** Layer of fibrous connective tissue overlying the atheroma. Contains foam cells (macrophages) and smooth muscle cells, as well as fibroblasts.
 - **ATHEROMA:** Necrotic, lipid-laden center of the lesion. Term can also be used to describe the whole lesion.
- **COMPLICATIONS**
 - **COMPLICATED LESIONS:** Changes in structure of vessel itself.
 - **Thrombosis:** Damage to endothelial cells leads to loss of anti-coagulant properties (clotting inhibitors), leading to Thrombosis.
 - **Neovascularization:** Organization of the thrombus
 - **Thinning of the Media:** Can lead to aneurysm.
 - **Calcification**
 - **Ulceration**
 - **COMPLICATIONS:**
 - Acute occlusion leading to **Myocardial Infarct**. Usually due to hemorrhage into a plaque, or thrombosis.
 - Chronic narrowing of vascular lumen, causing chronic ischemia and sometimes atrophy to kidney.
 - **Aneurysm** formation
 - **Cholesterol Embolism:** Embolism of atheromatous material
- **RISK FACTORS:** Any factor with a doubling in the incidence of ischemic heart disease. *Atherosclerosis is the most common cause of heart disease in the Western Hemisphere.*
 - hypertension
 - blood cholesterol level
 - cigarette smoking
 - diabetes
 - increasing age
 - male sex
 - physical inactivity
 - stressful life patterns.
- **MECHANISMS of LESION PROGRESSION:**
 - Cytokines
 - **PDGF and FGF** cause proliferation of smooth muscle and endothelial cells.
 - **IFN and TGF-beta** inhibit cell proliferation and thus could account for endothelial cell discontinuities.
 - **IL-1 and TNF** stimulate activation of PAF, Tissue Factor, and PAI (plasminogen activator inhibitor) in endothelial cells.
 - T-Lymphocytes
 - Endothelium: Loss of continuity of endothelial layer
 - Increase permeability to lipoproteins
 - Permit platelet interaction with vessel wall, and subsequent release of growth factors
 - Blood may enter the wall, allowing interaction, either through an organized thrombus or through a tear or discontinuity in the endothelial surface.

- Thrombosis
- HEREDITARY DISORDERS OF LIPID METABOLISM AND ATHEROSCLEROSIS
 - **FAMILIAL HYPERCHOLESTEROLEMIA**: Defect in LDL receptors.
 - APO-E
 - HDL:
 - LIPOPROTEIN(A)

HYPERTENSIVE VASCULAR DISEASE:

- **HYPERTENSION**: Defined as systolic blood pressure greater than 160mm, or diastolic blood pressure greater than 90mm, or both.
 - Subtypes:
 - **BENIGN HYPERTENSION**: Asymptomatic
 - **MALIGNANT HYPERTENSION**: Rapidly progressing to end-organ failure.
 - MORPHOLOGY: Blood vessels show **fibrinoid necrosis** or concentric hyperplasia of smooth muscle-cells -- **onion-skin** changes).
 - **PATHOGENESIS**:
 - **ESSENTIAL HYPERTENSION**: Primary hypertension in which there is no single identifiable cause. The majority of cases
 - **Renin** from kidney is a major player.
 - Renin converts Angiotensinogen -----> Angiotensin I
 - ACE converts Angiotensin I -----> Angiotensin II
 - Angiotensin II effects:
 - Vasoconstriction.
 - Stimulate secrete of **aldosterone** from adrenal glands -----> K^+ excretion and Na^+ retention, fluid retention in kidney -----> higher blood volume.
 - **SECONDARY HYPERTENSION**: Hypertension secondary to a disease. Minority of cases.
 - **Renal Ischemia**: Anything causing ischemia to the kidney (vascular stenosis or atherosclerosis of Renal Artery or arterioles) will release renin and probably result in hypertension.
 - **Fibromuscular Dysplasia** of Renal Artery is a congenital disorder, with progressive concentric thickening of the Renal Artery. Occurs in young females.
 - **Cushing's Syndrome**: Primary hypersecretion of cortisol.
 - **Conn's Syndrome**: Primary hypersecretion of aldosterone.
 - **Pheochromocytoma**: Adrenal medullary tumor.
 - Norepinephrine is secreted in spurts, so patient will have wildly fluctuating, paroxysmal elevations in blood pressure.
 - **Thyrotoxicosis**
 - **RISK FACTORS**: Similar as those for atherosclerosis and CAD.
 - Genetics: often found to be familial
 - Diet
 - Stressful lifestyle
 - Obesity
 - **CLINICAL MANIFESTATIONS**: Often asymptomatic
 - Early on: Headache, nosebleeds, tinnitus, dizziness, fainting, visual impairment.
 - Later: End-stage hypertension results in stroke, heart failure (from compensatory hypertrophy), renal failure
- **ARTERIOSCLEROSIS**: Arterial vascular changes characterized by thickening and loss of elasticity of arterial walls. It may be seen in patients with chronic hypertension, and, to a lesser degree, as part of the aging process.
 - **BENIGN (HYALINE) ARTERIOSCLEROSIS**: Particularly occurs in kidneys. The blood vessel walls take on a glassy, "hyaline" appearance. This change reflects mild or "benign" hypertension and are particularly seen in kidneys.
 - **MALIGNANT (HYPERPLASTIC) ARTERIOSCLEROSIS**: This change refers to the concentric rings of increased connective tissue and smooth muscle giving the arteries an onion-skin appearance. Such changes signify acceleration of the hypertension.
 - **ARTERIOLOSCLEROSIS**: Smooth muscle proliferation, thickening, and loss of elasticity of walls occurring in the arterioles.

- **MONCKEBERG MEDIAL SCLEROSIS:** Degenerative calcification of the media of large and medium arteries in old people.
 - Usually vessels in the extremities.
 - Usually is benign and subclinical.

VASCULITIS:

- **GENERAL PROPERTIES:** Inflammation and necrosis of blood vessels, including arteries, veins and capillaries. The damage may be due to infectious agents, mechanical trauma, radiation or toxins; often no specific etiologic factor is identified. The pathogenesis is thought to involve immune mechanisms such as deposition of immune complexes, direct attack by circulating antibodies etc.
- **POLYARTERITIS NODOSA:** Systemic vasculitis affecting medium and small muscular arteries.
 - **PATHOLOGY:** Multiple organs involved, but the lungs are characteristically not involved. If lung involvement is present, suspect Wegener's Granulomatosis.
 - **CLINICAL FEATURES:**
 - Condition is associated with Hepatitis-B in about 30% of cases.
 - Treatment: steroids, cyclophosphamide.
- **HYPERSENSITIVITY ANGIITIS:**
 - **PATHOGENESIS:** Maybe hypersensitivity to a drug, a bacterial product, or maybe secondary to an autoimmune disease like SLE.
 - **PATHOLOGY:** Affects mainly the small vessels -- arterioles and capillaries. Will see fibrinoid necrosis.
 - As opposed to Polyarteritis Nodosa, this disease affects small arteries. Otherwise its similar.
 - As opposed to Malignant Hypertension (which can also show petechiae), this disease is associated with inflammation whereas malignant hypertension is not.
 - **CLINICAL:** **Petechiae** will be present from capillary hemorrhage.
 - **LEUCO CYTOCLASTIC VASCULITIS:** Confined predominantly to the skin and presenting as purpuric lesions.
 - **PATHOLOGY:** Fibrinoid necrosis of small vessels, extravasated red cells.
 - **CLINICAL:** Clinically presents as purpura.
- **CHURG-STRAUSS SYNDROME, ALLERGIC GRANULOMATOSIS and ANGIITIS:**
 - **PATHOLOGY:** Mainly affects the lungs, it is found in young people, and it is associated with asthma.
 - Will find Eosinophilia in the blood.
- **GIANT CELL ARTERITIS, TEMPORAL ARTERITIS:**
 - **PATHOLOGY:** Giant cells present in the wall of any of the cranial arteries, usually the Temporal Artery.
 - Thrombus found in lumen of the artery. A granulomatous infiltrate will be found in the artery.
 - **Giant Cells** will be present in the artery, hence the name./=
 - **CLINICAL FEATURES:**
 - Occurs in older population, at least 50 yrs old.
 - Patient presents with headache and temporal pain. Visual symptoms are common, and blindness is a complication in 50% of cases.
 - Temporal Artery will feel firm and nodular.
 - Treatment: responds well to steroids.
- **WEGENER'S GRANULOMATOSIS:**
 - **PATHOLOGY:**
 - Two key pathological findings
 - *Systemic vasculitis* of small arteries and veins.
 - *Granulomatous inflammation of **nose, sinuses, and lung**.*
 - **Anti Cytoplasmic Nuclear Antibodies (ANCA)** are found in serum.
 - **CLINICAL FEATURES:** Patient may have persistent sinusitis, pneumonitis, hematuria, proteinuria.
- **TAKAYASU ARTERITIS:** An inflammatory disorder of the aortic arch and its major branches, with localized stenosis or occlusion
 - **PATHOLOGY:** Also known as **PULSELESS DISEASE**, as the obliteration and thickening of the Aortic Arch may result in no pulse in the wrist.
 - **PATHOGENESIS:** An auto-immune basis has been proposed.
 - **CLINICAL FEATURES:** It is most common in young women, similar to other auto-immune disorders.
- **KAWASAKI DISEASE (MUCOCUTANEOUS LYMPH NODE SYNDROME):**
 - **PATHOGENESIS:** Thought to be viral etiology.
 - **PATHOLOGY:** Acute necrotizing vasculitis.

- **Coronary Aneurysms** are found in 70% of patients -- an unusual finding.
 - CLINICAL:
 - Infancy and early childhood
 - Fever, rash, conjunctival and oral lesions
 - Lymphadenitis
- **THROMBOANGIITIS OBLITERANS (BUERGER'S DISEASE):** An occlusive, inflammatory disease of the medium-sized and small arteries in the distal arms and legs.
 - PATHOLOGY: Microscopically, there is acute inflammation of arteries with thrombosis and obliteration of lumen.
 - CLINICAL FEATURES:
 - **Intermittent Claudication** (weakness relieved by rest) is seen in legs.
 - Strongly associated with smoking. Young or middle-aged males.

RAYNAUD'S PHENOMENON: Intermittent attacks of ischemia of fingers or toes due to intense arterial vasospasm, often precipitated by cold or emotional stimuli.

ANEURYSMS:

- SHAPES OF ANEURYSMS:
 - **Fusiform:** Most common form.
 - **Saccular:** Most common form.
 - **Dissecting:** Actually a hematoma, splitting apart of media.
 - **Arteriovenous Fistula:** Direct connection of arterioles to venules, bypassing the tissue and causing necrosis.
- **ATHEROSCLEROTIC ANEURYSMS:** Most common type of aneurysm.
 - PATHOLOGY: Usually found in **abdominal aorta**. Lumen may only be slightly enlarged, but you will see lots of atherosclerosis and thrombosis.
 - CLINICAL FEATURES: May be asymptomatic, or may be found coincident to some other X-ray, surgery, or medical procedure.
 - **Ruptured Aneurysm** is the most dramatic presentation, surgical emergency.
 - **TREATMENT:** Put a synthetic graft over the aneurysm.
- **CONGENITAL (BERRY) ANEURYSMS:** Usually occurs at a main branching point of the basilar artery.
 - PATHOLOGY: Fairly small aneurysm, saccular in shape.
- **DISSECTING ANEURYSMS:** Not really an aneurysm, actually it's a hematoma in the muscular media of the Aorta.
 - PATHOGENESIS: Results from Marfan's Syndrome or from longstanding hypertension in elderly males.
 - Dissection splits the aortic wall in two. Multiple types have been described.
 - **TYPE-A:** Start at Aortic Arch and extend proximally to include the Aortic valves, resulting in hemopericardium. Grave prognosis.
 - **TYPE-B:** Start Aortic Arch and extend distally, down through the abdominal Aorta.
 - **Double-Barrel Aorta:** Dissection penetrates back into the true Aortic lumen, temporarily relieving the pressure and biding some time.
 - PATHOLOGY: **Cystic Medial Necrosis** is the characteristic finding -- cystic changes in media of aorta.
 - Stains positive for mucopolysaccharide.
 - CLINICAL FEATURES: Patient describes a severe **tearing** type of pain.
- **SYPHILITIC ANEURYSMS:** Aneurysms in **Thoracic Aorta** resulting from **Obliterative Endarteritis** of the *vaso vasorum* supplying the Aorta.
 - PATHOLOGY: Characteristic **Tree-Bark Appearance** of linear and patchy scars is seen on the luminal aspect of the aorta.
 - CLINICAL: Aortic calcification, **Aortic Insufficiency**, and **hemopericardium** are frequent complications.
- **MYCOTIC ANEURYSMS:** These lesions are caused by significant weakening of the blood vessel wall by infection.

VEINS:

- **VARICOSE VEINS:** Enlarged and tortuous blood vessels. Occurs most commonly in the legs.
 - **RISK-FACTORS:**
 - older age
 - female sex
 - heredity
 - posture
 - obesity.
 - **PATHOLOGY:** Dilation and elongation of the veins, incompetence of venous valves.
 - **SITES:**
 - **Varicose Veins of Legs** is most common.
 - **Hemorrhoids**
 - **Esophageal Varices**
 - **Varicocele:** Varicose veins of pampiniform plexus of scrotum.
- **DEEP VENOUS THROMBOSIS:** Associated with prolonged bed-rest, blood stasis, and reduced cardiac output. Risk for pulmonary embolism.
 - **Thrombophlebitis:** Inflammation, commonly from a bacterial infection, with secondary thrombosis of deep leg veins.
 - **Phlebothrombosis:** Thrombosis of deep leg veins without initial inflammation.

LYMPHATIC VESSELS:

- **LYMPHANGITIS:**
- **LYMPHATIC OBSTRUCTION**
 - **Lymphedema:**
 - **Lymphangiectasia:**
 - **Elephantiasis:**
 - **Milroy Disease:** Inherited form of lymphedema present at birth.

BENIGN BLOOD-VESSEL TUMORS:

- **HEMANGIOMAS:** Benign tumors of blood vessels. They don't know whether it's a true neoplasia or just a hamartoma.
 - **Types:**
 - **CAPILLARY HEMANGIOMA:** Containing capillaries.
 - Juvenile Hemangioma:
 - **CAVERNOUS HEMANGIOMA:** Containing open vascular spaces.
 - Multiple Hemangiomatous Syndromes:
 - **CLINICAL:** Truly benign and not important, unless they are a problem cosmetically.
- **GRANULOMA PYOGENICUM:** Mass of granulation tissue resembling a hemangioma. They are truly benign and occur after some injury
- **VASCULAR ECTASIA:** Local Dilatation and growth of blood vessels, not a tumor.
 - **Spider Angiomata** is an example.
- **GLOMUS TUMOR (GLOMANGIOMA):** A benign, painful tumor of the **glomus body** -- neuromyoarterial receptor which is sensitive to temperature and regulates arterial flow.
 - **PATHOLOGY:** Small, reddish blue spots occur most commonly in the distal fingers and toes.
 - Histologically, there is a mixture of branching vascular channels and nests of glomus cells.
- **HEMANGIOENDOTHELIOMA:** A vascular tumor composed of endothelial cells, considered to be intermediate between benign hemangiomas and frankly malignant angiosarcomas. Histologically, several variants are described, based on the predominant cell type - spindle cell, epithelioid etc.
 - **Epithelioid Hemangioendothelioma**
 - **Spindle-Cell Hemangioendothelioma**
 - **CLINICAL:** In general, surgical excision is curative. Rarely do these tumors metastasize.
- **MULTIPLE HEMANGIOMATOUS SYNDROMES:** Angiomatous lesions present in two or more tissues.
 - **Von Hippel-Lindau Syndrome:** Hemangiomas in brain and retina.
 - **Sturge-Weber Syndrome:** Vascular lesions in brain and skin.

MALIGNANT BLOOD-VESSEL TUMORS:

- **ANGIOSARCOMA:** Malignant neoplasm arising from blood vessels.
 - CARCINOGENS have implicated as causes:
 - **Thorotrast** -- radio-opaque dye.
 - **PVC**
 - **Arsenic.**
 - PATHOLOGY: Most commonly found on scalp, breast, other soft tissues, or liver.
 - Resembles hemangiomas, except the lining endothelial cells are malignant.
 - CLINICAL: Variable prognosis, from indolent to high malignant.
 - **LYMPHEDEMA-ASSOCIATED ANGIOSARCOMA:** Occurs in 1% of cases, some 20 years after an axillary-node dissection for breast cancer. Occurs in associated with lymphedema of the upper extremity.
 - Also known Stewart-Treves Syndrome.
- **HEMANGIOPERICYTOMA:** Rare malignant neoplasm thought to arise from pericytes, smooth muscle cells external to the walls of capillaries and arterioles.
- **KAPOSI SARCOMA:**
 - PATHOGENESIS: In AIDS patients, caused by infection of **HHV-8**
 - FOUR TYPES
 - **Classical / European:** Found in older men of Poland, Italy. Chronic course and rarely fatal.
 - **African:** Also chronic, more malignant than above, but still not usually fatal.
 - **Transplant-associated:** Immunosuppression, particularly with renal transplants.
 - **AIDS-ASSOCIATED:** Immunosuppression.
 - Found in highest incidence in **homosexual at-risk group**, as compared to other groups, perhaps because of sexual transmission of HHV-8 virus.
 - PATHOLOGY: Two stages
 - **Patch Stage:** Early on.
 - **Plaque, Nodular Stage:** Later progression.
- **BACILLARY ANGIOMATOSIS:** Vascular infection appearing like Kaposi Sarcoma, and caused by *Bartonella Henselae* (same causal agent as Cat Scratch Fever).
 - AIDS patients may also have this, so this infection should be ruled out before settling on Kaposi Sarcoma.

THE HEART

CORONARY VESSELS:

- **LEFT ANTERIOR DESCENDING (LAD) CORONARY ARTERY:** Most common artery to occlude. Results in an **anterior infarct**:
 - Anterior wall.
 - Anterior two thirds of septum.
 - Entire apex of heart, circumferentially.
- **LEFT CIRCUMFLEX CORONARY ARTERY:** Occlusion gives you a **posterolateral infarct** -- posterior, lateral left aspect of heart.
- **RIGHT CORONARY ARTERY:** Results in a **posterior septal infarct** -- posterior one third of septum, inferior aspect, and posterior wall of heart.
 - *Infarction of the Right Ventricle is rare*, because the right side has far less demand for oxygen. Right Ventricular infarcts are usually extensions of posterior septal infarcts caused by occlusion of the Right Coronary Artery.

MYOCARDIAL HYPERTROPHY and CONGESTIVE HEART FAILURE:

- CAUSES of HEART FAILURE
 - **Pump Failure:** Failure that is intrinsic to the myocardium.
 - Two types:
 - **Systolic Failure:** Failure to pump blood out of heart. Low ejection fraction.
 - **Diastolic Failure:** Failure to distend the heart to fill the ventricles, as in **constrictive pericarditis**.
 - Most common reason for pump failure is from **myocardial hypertrophy**, usually secondary to hypertension.
 - Myocarditis
 - Cardiomyopathy
 - **Conduction System Failure:** Secondary to MI
 - Valvular Failure: Inflammatory (endocarditis), autoimmune, or congenital.
 - **Cardiac Malformations:** Congenital
 - **Blood Loss / Obstruction of Blood Flow:** Extracardiac causes. Pulmonary emboli or bleeding.
- HEART'S RESPONSE TO INJURY
 - **HYPERTROPHY:** Normal heart is 250-350g. myocardial cells can hypertrophy to about 3X size, or about 900g.
 - **Box Car Nuclei** are the characteristic histological appearance of hypertrophied cells.
 - **DILATATION:** Could be caused by pump failure (filled ventricles that can't empty), Aortic Insufficiency, or many other causes.
 - **NECROSIS:**
 - Ischemic Necrosis
 - Contraction Band Necrosis.
 - DEGENERATION
 - INFLAMMATION
 - RESOLUTION
 - FIBROSIS
 - CALCIFICATION: Dystrophic calcification
- PATHOGENESIS
 - HUMORAL RESPONSES
 - CELLULAR HYPERTROPHY
 - ABNORMAL PROTEIN ISOFORMS
 - ALTERATIONS in CALCIUM HOMEOSTASIS
 - PROTO-ONCOGENES
 - EXTRACELLULAR MATRIX
 - ADRENERGIC DESENSITIZATION
- PATHOLOGY
- CLINICAL FEATURES

CONGENITAL HEART DISEASE:

- **HEART EMBRYOLOGY:**
 - Openings generally allow blood to pass from right heart to left heart, bypassing the lungs.
 - **FORAMEN OVALE:** An opening at the midpoint of the interatrial septum. It is open during fetal life allowing the passage of blood from the right to the left atrium. This natural fetal shunt allows the blood to bypass the fetal lungs.
 - **DUCTUS ARTERIOSUS:** Fetal blood vessel that connects the pulmonary artery with the aorta allowing the oxygenated blood from the fetal pulmonary artery to bypass the lungs and enter directly into the aorta.
- **INITIAL LEFT-to-RIGHT SHUNT (Late Cyanotic or Non-Cyanotic)**
 - **PATHOGENESIS:** LATE CYANOSIS is Initial left-to-right shunt will lead to Pulmonary Congestion -----> Right Ventricular Hypertrophy plus **pulmonary hypertension**. In the baby, the pulmonary hypertension eventually (over months or years) get so bad as to surpass systemic blood pressure yielding a **late Right-to-Left shunt -----> cyanosis**.
 - **VENTRICULAR SEPTAL DEFECT (ROGER DISEASE):** Most commonly diagnosed congenital heart disease.
 - **PATHOGENESIS:** Maybe membranous or muscular, depending on where it occurs.
 - **MEMBRANOUS VSD:** Most common, 85% of cases.
 - **MUSCULAR VSD:** Less common.
 - **MURMUR:** **Holosystolic Murmur** can be heard.
 - **CLINICAL:** Most commonly diagnosed disorder, and often associated with other defects, like Tetralogy of Fallot.
 - **ATRIAL SEPTAL DEFECTS:**
 - **PATENT FORAMEN OVALE:** Most common locale of atrial septal defect.
 - **OSTIUM SECONDUM DEFECT:**
 - **OSTIUM PRIMUM DEFECT:**
 - **CLINICAL:** Small defects are usually asymptomatic, whereas the larger ones may cause shunting of the blood from left to right.
 - **PATENT DUCTUS ARTERIOSUS:** Incomplete involution of the ductus arteriosus.
 - **TREATMENT:** Sometimes the ductus will close naturally. Otherwise, two ways to get a patent ductus arteriosus to close:
 - **Indomethacin:** Inhibits prostaglandin synthesis in ductus, which forces its closing. The opening is mediated by prostaglandins (PGE₂).
 - Surgically tie it off.
 - **PERSISTENT TRUNCUS ARTERIOSUS:** Pulmonary artery and aorta are not separated one from another but remain a common vessel.
- **INITIAL RIGHT-to-LEFT SHUNT (Cyanotic)**
 - **TETRALOGY OF FALLOT**
 - **Classical Diagnostic Symptoms:**
 - **Pulmonary Artery Stenosis:** The principle etiology responsible for the pulmonary hypertension and right-to-left shunt.
 - **Ventricular Septal Defect**
 - **Dextroposition of Aorta (overriding):** Aorta originates from the septal area, such that it receives blood originating from both right and left ventricle.
 - **Right Ventricular Hypertrophy**
 - **Patent Ductus Arteriosus** often co-occurs with Tetralogy, although it isn't part of the syndrome. It is helpful in Tetralogy, as it provides a channel for shunted blood to get back into the pulmonary circulation where it belongs.
 - (Right Atrium -----> Right Ventricle -----> VSD -----> Left Ventricle -----> Aorta -----> through the Ductus Arteriosus -----> Pulmonary Arteries)
- **NO SHUNT**
 - **TRANSPOSITION of the GREAT ARTERIES (Cyanotic):** Aorta and the pulmonary artery are transposed. The aorta arises from the right ventricle and the pulmonary artery from the left ventricle. It presents with cyanosis of early onset.
 - **COARCTATION of the AORTA:** Congenital constriction of the aorta.
 - **PATHOGENESIS:** Occurs usually just proximal or distal to the ductus arteriosus (connection of aorta and pulmonary artery).

- **PRE-DUCTAL COARCTATION:** Occurs in infants. Considered to be incompatible with life.
- **POST-DUCTAL COARCTATION:** Occurs in adults. Post-ductal coarctation is associated with a discrepancy in blood pressure between upper and lower extremities -- arms much higher than legs, as arms get all the blood.
 - Such patients also develop extensive arterial anastomoses between the subclavian artery and the aorta distal to the constriction.
 - **Internal Mammary Artery**
 - **Intercostal Arteries** -- notching on chest wall
 - Cerebral hemorrhage is common because of high blood pressure in brain.
- **PULMONARY STENOSIS**
- **CONGENITAL AORTIC STENOSIS**
- **DEXTROCARDIA:** Characterized by inversion of the cardiac chambers. In this condition the left atrium and ventricle are on the right side and the right atrium and ventricle on the left. It may be associated with *situs inversus*.
- **EBSTEIN MALFORMATION:** Congenital Tricuspid Valve Insufficiency.
 - Congenital heart disease characterized by downward displacement of abnormal tricuspid valve into an underdeveloped right ventricle.
- **ENDOCARDIAL FIBROELASTOSIS (EFE):** Thickening of the endocardium of the heart chambers and valves most prominent in the left ventricle.
 - **PRIMARY EFE:** Congenital disease of unknown etiology.
 - **SECONDARY EFE:** Complication of various other cardiac disease characterized by interventricular hypertension or turbulent blood flow.

ISCHEMIC HEART DISEASE:

- **ANGINA PECTORIS:** Pain originating in chest and radiating to left shoulder, typically. But there are variants.
 - **STABLE ANGINA:** Exertional angina.
 - **UNSTABLE ANGINA:** Late angina carrying poor prognosis. Angina even at rest.
 - **VARIANT (PRINZMETAL) ANGINA:** Episodic angina occurring at rest, and due to coronary artery spasm.
- **LAB INDICATORS:**
 - **TROPONIN-T:** Most recent blood protein has been shown to have very good predictive value for an early MI. Very specific to MI.
 - Cardiac troponin is its own isotype and is different from troponin of the skeletal muscle.
 - **CAL (Coronary Artery Lesion):** Mnemonic indicates the time course of elevated blood enzymes.
 - **CPK (Creatine Phosphokinase)** will go up first (around same time as Troponin). Again, it's the cardiac isoform that does up. Peaks a few hours after the event.
 - **AST (Aspartate aminotransferase)** goes up next. Peaks next.
 - **LDH (Lactate Dehydrogenase)** is the third enzyme to peak, and lasts the longest.
 - **LDH-1** becomes elevated in 6-12 hrs. There is no proportional increase in LDH-2, so the LDH-1:LDH-2 ratio goes up.
- **PATHOGENESIS / PATHOLOGY:** Coronary atherosclerosis, thrombosis, and coronary artery spasm.
 - Two types of infarcts
 - **TRANSMURAL INFARCT:** Infarct going from epicardium to endocardium, caused by coronary artery occlusion.
 - **Stunned Myocardium** is present in the periphery of an infarct zone -- edematous and dysfunctional muscle that is not yet dead and may be recovered.
 - **SUBENDOCARDIAL INFARCT:** Diffuse, circumferential infarct, around the *subendocardium* (just inside the endocardial layer). Caused by shock, CHF, hypotension, or anything that results in inadequate blood supply to the coronary arteries.
 - Arteries perfuse the myocardium from the outside in. Thus with inadequate blood, the outer layers of muscle will get the blood first, and the inner layers may become ischemic.
 - The endocardium can get its blood from the heart chambers itself -- hence the lesion is described as subendocardial.
 - **GRADES:** Coronary atherosclerosis or stenosis is graded as follows.
 - **GRADE 1:** 0-25% OCCLUSION -- asymptomatic and common
 - **GRADE 2:** 25-50% OCCLUSION -- possible stable angina

- GRADE 3: 50-75% OCCLUSION -- stable angina
 - GRADE 4: 75%+ OCCLUSION -- unstable angina, impending MI and thrombosis.
 - **ENDOTHELIAL INJURY:** Early grade atherosclerosis may show paroxysmal coronary artery contractions resulting from endothelial injury.
 - The substances that were supposed to stimulate release of NO leading to vasodilatation, instead wind up stimulating vasoconstriction, because there are no endothelial cells present to release the NO.
 - This vasoconstriction can occur with Grades 1 and 2
 - Can also cause thrombosis in more advanced lesions.
 - **TIME COURSE of CHANGE:** Time after infarct. *The myocardium can survive up to one hour of absolute ischemia (center of the infarct) and up to four hours of relative ischemia (periphery of the infarcted area).*
 - **1-5 min:** Swelling of mitochondria and ER; reversible changes. Glycogen depletion and depletion of ATP are noticeable, but no morphological changes grossly.
 - **20-40 min:** Irreversible changes microscopically. Cell necrosis, nuclear changes, plasma membrane rupture.
 - **4-12 hrs:** Onset of irreversible coagulative necrosis. Myocardial cells lose striations. Thrombus is still present.
 - **18-24 hrs:** Pyknosis, karyolysis, karyohexis. **Myocytolysis** occurs -- loss of cytoplasm.
 - **1-3 days:** Widespread necrosis. Infiltration of PMN's begins. Thrombus has often been lysed naturally by now. Infarct can be recognized on gross examination -- tissue is mottled, red, and congested.
 - **4-10 days:** PMN's move out, and macrophages take over to clean up the debris. *Period of greatest weakness*, during which **rupture** and cardiac tamponade may occur. 50% of ruptures occur within first 5 days and 87% within 14 days. Grossly, necrotic tissue is yellow, soft, and pus-like.
 - **1 month:** Granulation tissue has developed. The infarct heals from the outside in, with the central area of necrosis being the last to fibrose.
 - **3 months:** Scar formation is complete.
 - **CONTRACTION BAND NECROSIS:** Hyper contraction of myofilaments. Typically found at the margins of infarcts or in reperfusion injury.
- **CLINICAL:**
 - **SYMPTOMS:** Either excessive sympathetic or parasympathetic symptoms may be seen.
 - Sympathetic Symptoms: tachycardia, sweating, pallor
 - Parasympathetic Symptoms (Vagal discharge): bradycardia, vomiting.
 - **Fever** may be seen. Myocardial cells may release endogenous pyrogens such as IL-1 when they rupture.
 - **Cardiogenic Shock:** Oliguria, hypotension, pulmonary edema, pale and cold extremities.
 - Leukocytosis with left shift will be seen.
 - Arrhythmias and other EKG changes may be seen.
- **COMPLICATIONS**
 - **ARRHYTHMIAS:** 85% of cases. Most important cause of death from MI, and can occur at any time, either acute or chronic, after the MI.
 - The arrhythmias are often reversible -- they go away when edema and inflammation disappear.
 - **CARDIOGENIC SHOCK:** 15% of cases, relatively rare. Systemic hypotension due to pump failure.
 - **EXTENSION of the INFARCT**
 - **RUPTURE, CARDIAC TAMPONADE:** 1-2% of cases. Rare.
 - **ANEURYSM**
 - **MURAL THROMBOSIS and EMBOLISM:** Arterial embolism may go to distal artery and cause tissue necrosis (kidney), petechiae, or gangrene.
 - **PERICARDITIS: DRESSLER SYNDROME** is a delayed pericarditis that occurs following cardiac surgery or myocardial infarction.

COR PULMONALE: Right ventricular failure.

- **ACUTE COR PULMONALE:** May occur from a saddle pulmonary embolus.
- **CHRONIC COR PULMONALE:** From COPD or from left ventricular failure.
- **CLINICAL:** High central venous pressure, jugular venous distension.

ACQUIRED VALVULAR and ENDOCARDIAL DISEASES:

- **RHEUMATIC HEART DISEASE:**
 - **ACUTE RHEUMATIC FEVER:** A hypersensitivity disease typically caused by an abnormal immune response to Strep-A antigens.
 - **PATHOGENESIS:** Immune mechanism involves both B and T cells.
 - **CLINICAL:** Patient must have at least one of the major symptoms, and two of the minor symptoms of the **JONES'S CRITERIA:**
 - **MAJOR JONES'S SYMPTOMS:**
 - **Carditis:** Found in 35% of patients.
 - **Polyarthritis:** found in 75% of patients.
 - **Chorea:** Rapid jerky, dyskinetic involuntary movements.
 - **Erythema Marginatum**
 - **Subcutaneous nodules**
 - **MINOR JONES'S SYMPTOMS:**
 - Fever
 - Arthralgia
 - History of Rheumatic Fever or Rheumatic Heart Disease
 - Acute-Phase Reactants: high sed-rate, or positive C-Reactive Protein, which are evidence of inflammation.
 - Prolonged PR interval by ECG.
 - **RISK-FACTORS:** The more severe the initial Streptococcal infection, the more likely it is for patients to develop Rheumatic Fever.
 - **CHRONIC RHEUMATIC HEART DISEASE:**
 - **PANCARDITIS:** Rheumatic heart disease is typically a pancarditis, affecting all three layers of the heart.
 - **VALVULITIS:** Endocarditis affecting Mitral and Aortic Valves.
 - **MITRAL VALVE** is most common: Chordae Tendineae get fused together, resulting in **MITRAL STENOSIS**. *Rheumatic Fever is the most common cause of mitral stenosis.*
 - Stenosis has a fishmouth appearance.
 - You may also at the same time see **mitral insufficiency** in the same patient.
 - **AORTIC VALVE** is second most common, which can lead to **AORTIC STENOSIS**.
 - **PERICARDITIS:** Often seen, but described as **Bread-and-Butter Pericarditis**. This is an inflammatory process, but it is *not Constrictive Pericarditis*.
 - **HISTOPATHOLOGY:** It is aseptic so no bacteria are present.
 - **ASCHOFF BODY** is the characteristic finding. A granuloma composed of a central triangular area of fibrinoid necrosis surrounded by histocytes. They heal by scarring.
 - **ANITCHKOFF CELLS:** Found around the perimeter of the Aschoff bodies. They are also called **Caterpillar cells**. Round-to-ovoid nuclei have chromatin disposed in a wavy ribbon resembling a caterpillar.
- **BACTERIAL ENDOCARDITIS:**
 - **CAUSES:**
 - **Congenital Heart Defects** lead to stasis of blood in the heart and therefore predispose to them.
 - **Bicuspid Aortic Valve** predisposes to bacterial endocarditis resulting in Aortic Stenosis.
 - Sepsis
 - **Types:**
 - **ACUTE ENDOCARDITIS**
 - **SUBACUTE ENDOCARDITIS**
 - **CONSEQUENCES**
 - Valvular insufficiency or stenosis
 - **Septic Emboli** are thrombo-emboli plus bacteria, which may be thrown to a distal artery, causing gangrene.
 - Heart Failure secondary to valvular insufficiency.
 - Immune complex glomerulonephritis.
- **MARANTIC (NON-BACTERIAL THROMBOTIC) ENDOCARDITIS:** Occurs in people suffering from malnutrition, marasmus. They cannot repair the little foci of damage that occur with normal wear and tear of the heart (constant contraction and what not).

- Small aggregates of fibrin collect on cardiac valves. It is a form of intravascular thrombosis, and increased coagulability of the blood is seen.
- **CALCIFIC AORTIC STENOSIS:**
 - CLINICAL: Multiple causes:
 - **Idiopathic:** Can occur without any predisposing conditions in the elderly.
 - **Atherosclerotic:** As an extension of atherosclerosis of the aorta into the aortic valve
 - **Rheumatic Heart Disease:** Complication of rheumatic endocarditis.
 - **Bicuspid Aortic Valve:** Congenital malformation predisposing to infection.
 - CLINICAL: Aortic Stenosis can lead to **angina** as it reduces coronary blood flow.
- **MITRAL VALVE PROLAPSE:** Protrusion of the loosened up mitral valve leaflets into the left atrium during systole. It may or may not be associated with mitral regurgitation.
- **CARCINOID HEART DISEASE:** Endocardial fibrosis of the **right** atrium and ventricle, pulmonic and tricuspid valves.
 - PATHOGENESIS: Caused by a carcinoid tumor secreting biogenic amines (**histamine and serotonin**). Usually the tumor is metastatic to the liver.
 - The left side of the heart is not affected because the biogenic amines are neutralized in the lung.
- **COLLAGEN DISEASES**
 - LUPUS ERYTHEMATOSUS: **LIBMAN SACKS ENDOCARDITIS** is a complication of SLE.
 - **PATHOLOGY:** Most often involves the *mitral valve*.
 - RHEUMATOID ARTHRITIS
 - ANKYLOSING SPONDYLITIS
 - SCLERODERMA
 - POLYARTERITIS NODOSA

PRIMARY MYOCARDIAL DISEASE:

- **VIRAL MYOCARDITIS: PANCARDITIS**, where all three layers of myocardium may be involved --endocarditis, myocarditis, and pericarditis.
- **HYPERSENSITIVITY MYOCARDITIS**
- **GIANT CELL MYOCARDITIS**

METABOLIC DISEASES:

- **HYPERTHYROID HEART DISEASE:**
 - Thyroid hormone does not directly affect the Coronary arteries.
 - Increased metabolic rate increases the demand for oxygen systemically, which results in tachycardia, which further increases (exacerbates) the demand for oxygen in the heart. Thus the heart potentially suffers both an increase in oxygen demand and an increased work load.
- **HYPOTHYROID HEART DISEASE**
- **THIAMIN DEFICIENCY (BERIBERI) FAILURE:** High output heart failure.

CARDIOMYOPATHY: Primary idiopathic disease of the myocardium, which is *not* caused by ischemia, valvular dysfunction, infection, inflammatory disorders, or congenital anomalies.

- **IDIOPATHIC DILATED CARDIOMYOPATHY:** Also called congestive cardiomyopathy.
 - **ALCOHOLISM** is a risk-factor for this form of Cardiomyopathy. You may also get Beriberi high-output failure with Alcoholics.
 - **TOXIC CARDIOMYOPATHY**
- **HYPERTROPHIC CARDIOMYOPATHY:**
 - **PATHOLOGY:** Patient will have *asymmetrical* septal hypertrophy and a disarray of muscle fibers.
 - This diminishes volume of left ventricle and causes abnormal myocardial contraction.
 - **CLINICAL:** The disease is inherited as an autosomal dominant trait.
- **RESTRICTIVE CARDIOMYOPATHY**
 - **AMYLOIDOSIS:** Endomyocardial biopsy is required for a definitive diagnosis. Must demonstrate amyloid infiltrates in the heart. Amyloidosis can mimic other forms of restrictive cardiomyopathy.

CARDIAC TUMORS:

- **CARDIAC MYXOMA:** The most common primary benign tumor of the heart. Typically located on the mitral valve.
 - It is a gelatinous polyp connected to the endocardium.
- **RHABDOMYOMA:** Primary benign tumor of the myocardium, typically found in children.
- **PAPILLARY FIBROELASTOMA**

PERICARDIAL DISEASES:

- **PERICARDIAL EFFUSION:** Accumulation of fluid in the pericardial sac in excess of the normal content (50 ml).
 - **PATHOLOGY:** Fluid may be of multiple types
 - Serous effusion
 - Chylous effusion
 - Hemorrhagic effusion
- **CONSTRUCTIVE PERICARDITIS:** Chronic inflammation obliterates the pericardial cavity. Fibrous exudate in pericardium. Results in inability for heart to expand, or **diastolic heart failure**.
 - **PATHOLOGY:** It leads to Pulmonary Hypertension and elevated CVP.
 - **CLINICAL:** It is rare. Rheumatic Heart disease does not lead to constrictive pericarditis.

THE LUNG

LUNG MEASUREMENTS:

- **TIDAL VOLUME (TV):** The volume of air inhaled during a normal inspiration.
- **EXPIRATORY RESERVE VOLUME (ERV):** The maximum volume of air that can be exhaled after a normal expiration.
- **INSPIRATORY RESERVE VOLUME (IRV):** The maximum volume of air that can be inhaled after a normal inspiration.
- **VITAL CAPACITY (VC):** The maximum possible volume of air that one can expire in a single breath, after having taken a maximal inspiration.
 - Or: The sum of the Tidal Volume, Inspiratory Reserve Volume, and Expiratory Reserve Volume.
- **RESIDUAL VOLUME (RV):** The volume of air that remains in the lungs after a maximal expiration. It is the air that remains in the lung basically no matter what you do unless the lungs collapse.
 - This is normally about 20% of Total Lung Capacity.
- **TOTAL LUNG CAPACITY (TLC):** Defined as the Vital Capacity plus the Residual Volume.
 - "Capacity" indicates that it is actually the sum of two separable volumes.

PULMONARY FUNCTION STUDIES:

- **FEV-1: Forced Expiratory Volume** in one second. The maximum volume of air that can be exhaled during the first second of a forced vital capacity (FVC).
 - In a normal individual, the FEV₁ is 80% of the FVC.
 - In COPD the FEV₁ is markedly reduced.
- **FVC: Forced Vital Capacity.** One of many pulmonary function tests. The patient makes a full inspiration, and then exhales as hard and fast as possible into a spirometer. This expired volume is designated as the FVC.

Measurement	Restrictive Lung Disease	Obstructive Lung Disease
FVC: Forced Vital Capacity	Decreased	Normal or Decreased
FEV ₁ / FVC ratio	Decreased	Decreased markedly
RV: Residual Volume	Normal or increased	Increased (barrel chest)
TLC: Total Lung Capacity	Decreased markedly	Normal or increased
Diffusion Capacity	Decreased	Decreased

CONGENITAL DISORDERS:

- **CONGENITAL CYSTIC ADENOMATOID MALFORMATION:** A congenital anomaly in which the lung parenchyma is converted into multiple gland-like spaces lined by bronchiolar epithelium that are separated from each other by loose fibrous tissue, usually affecting one lobe of lung, and occasionally associated with other congenital anomalies
- **EXTRA LOBAR SEQUESTRATION:** A mass of lung tissue that is not connected to the bronchial system and is located outside of the visceral pleura.
 - **INTRALOBAR SEQUESTRATION** (probably acquired, not congenital) is a mass of lung tissue not connected to the bronchial system, within the visceral pleura.

DISEASE of BRONCHI and BRONCHIOLES:

- INFECTIONS
- IRRITANT GASES
- BRONCHIAL OBSTRUCTION and ATELECTASIS:

- **ATELECTASIS:** Collapse of a previously inflated lung, or incomplete expansion of the lung. This reduces oxygenation and predisposes to infection.
- **BRONCHIECTASIS:** *Irreversible dilatation of the bronchi*, which can be caused by many conditions.

BACTERIAL PNEUMONIA: Inflammation and consolidation of the pulmonary parenchyma.

- **TYPES OF PNEUMONIA**
 - By type of infiltrate: This distinction is outdated and not so important anymore
 - **Lobar Pneumonia:** *Streptococcus Pneumoniae*. Consolidation of an entire lobe or most of it.
 - **Bronchopneumonia:** Scattered foci of consolidation. Most other bugs.
 - By where it is acquired:
 - Community-Acquired: *Strep, Staph, H. Flu*
 - Nosocomial: *Pseudomonas*
 - Opportunistic (Immunocompromised)
- Factors that predispose to pneumonia:
 - Loss of cough reflex (coma, anesthesia)
 - Viral Pneumonia (loss of ciliary carpet)
 - Interference with phagocytic function -- smoke and alcohol.
 - Pulmonary edema or congestion
 - Accumulated secretion, Cystic Fibrosis.
- Complications:
 - **ABSCESS FORMATION:** Most common in Gram-negative pneumonias, which you can get from aspiration of bugs from mouth (poor dentition), or comatose state.
 - **Post-Pneumonia Abscess Formation:** commonly occurs from three community-acquired bugs:
 - *Staph Aureus*
 - *Klebsiella*
 - Type-III Pneumococcus
 - **Empyema:** Pus in the pleural space.
 - Organization and residual fibrosis.
 - Dissemination to other organs
 - Pleuritis, pleural effusion
- The bugs
 - PNEUMOCOCCAL PNEUMONIA
 - *KLEBSIELLA* PNEUMONIA
 - STAPHYLOCOCCAL PNEUMONIA
 - STREPTOCOCCAL PNEUMONIA
 - GRAM-NEGATIVE OPPORTUNISTIC PNEUMONIAS
 - *E. COLI*
 - *PSEUDOMONAS AERUGINOSA*
 - **LEGIONELLA PNEUMONIA:** Pneumonia caused by a Gram-negative intracellular bacteria, *Legionella pneumophila*.
 - **CLINICAL:** This bacteria may cause a mild, self-limited fever in otherwise healthy individuals, or a severe pneumonia in smokers, the elderly, or individuals with chronic lung disease.
 - Mortality is high (10-20%) in immunocompromised patients.
 - **PSITTACOSIS: Ornithosis.** A self-limited pneumonic illness transmitted to humans from birds.
 - **CLINICAL:** Characterized by severe systemic symptoms and surprisingly few respiratory symptoms other than cough.
 - **MYCOPLASMA:** Atypical pneumonia or "Walking Pneumonia."
 - **PATHOLOGY:** Characterized by peribronchiolar infiltrates of lymphocytes and plasma cells.
 - **CLINICAL:** It causes an acute self limited lower respiratory tract infection (tracheo-bronchitis and pneumonia), affecting mostly children and young adults.

VIRAL PNEUMONIA:

- **AT-RISK:** Children and immunocompromised patients.
- **HISTOLOGY:** It differs from bacterial pneumonia.
 - You find two things:

- Chronic interstitial pneumonia. Interstitial infiltrates thickened by lymphocytes.
 - Diffuse Alveolar Damage (DAD)
- You must identify **viral inclusions** to prove it is a viral infection.
- **CYTOMEGALOVIRUS (CMV) PNEUMONIA:** A viral infection which, like most viral pneumonias, produces an interstitial pneumonitis or DAD.
 - **HISTOLOGY:** Large cell with both nuclear and cytoplasmic inclusions. Large blue nucleus with halo (**Owl-Eye Cells**) can be seen.
 - **CLINICAL:** Children, or immunocompromised adults. Common in AIDS patients.

TUBERCULOSIS: *MYCOBACTERIUM TUBERCULOSIS*

- **MANIFESTATIONS:**
 - **Primary Tuberculosis:** Initial infection. May be asymptomatic and usually resolves.
 - **Miliary Tuberculosis:** Tuberculosis that has spread through the blood, either through the lung, or disseminated to other places in body.
- **Infection-Immunity:** Once you get Tb, you always have it, and you are then immune to reinfection.
- **Ghon Complex:** Combination of granulomas found in lung, plus **hilar lymphadenopathy**, both identifiable on X-Ray.
- **RESISTANCE: Multiple Drug-Resistant (MDR) Tuberculosis** is a big problem. High mortality rate, and you can go to jail for not taking your drugs.

FUNGAL INFECTIONS

- **HISTOPLASMOSIS: *HISTOPLASMA CAPSULATUM***
 - **GEOGRAPHIC LOCATION:** Midwest, Ohio valley
 - **INFECTION:** *Histoplasma* is found in CHICKEN SHIT.
 - **PATHOPHYSIOLOGY:** Acute Histoplasmosis is most similar to tuberculosis in its histology and pathophysiology.
 - Pulmonary Infection will leave little **caseating granulomas** that can be silent in immunocompetent patients, and that eventually **calcify**.
 - *Histoplasma* live **intracellular**, inside alveolar macrophages. This is their route of dissemination, hence primary sites of dissemination are reticuloendothelial.
 - **HISTOPLASMOMA:** Isolated immunocompetent mass of yeast, often growing in a previously formed cavitation.
- **BLASTOMYCOSIS: *BLASTOMYCES DERMATIDES***
 - **GEOGRAPHIC LOCATION:** The southeast, Tennessee valley.
 - **MORPHOLOGY:** Big yeasts with **broad-based budding**.
 - **PATHOPHYSIOLOGY:** Blasto also has huge conidia, but in yeast form it is primarily **extracellular** rather than intracellular.
 - It forms **uncalcified granulomas** in the lungs in immunocompetent people. These granulomas are similar to the cutaneous ones formed by *Sporothrix*.
 - Response can be both suppurative and granulomatous, even in the same infection, in the lung.
- **COCCIDIOMYCOSIS: *COCCIDIODES IMMITIS***
 - **INFECTION:** Initial infection is also pulmonary, and calcified granulomas are formed.
 - **PATHOPHYSIOLOGY:**
 - **VALLEY FEVER:** It forms valley fever and is found in the desert southwest. This is usually self-limiting.
 - Usually infects the lung, but it can also infect the skin.
 - **MORPHOLOGY:** Forms a **tissue cyst** similar to *Toxoplasma Gondii*. Little spherules filled with yeast.
 - Spherules usually do not provoke an inflammatory response until the cyst ruptures.
- **CRYPTOCOCCOSIS:** Opportunistic yeast present in the soil and in pigeon droppings.
 - **CLINICAL:** Varies from an asymptomatic infection to a severe life-threatening illness.
 - **PATHOLOGY:** Histologic features vary depending on the patient's immune status; a granulomatous reaction is usually seen in cases with an intact immune system.
 - Yeast is unique in that the thick capsule stains bright red with **mucin** stains, a feature that makes morphologic identification of the organism quite reliable.
- **ASPERGILLOSIS:**

- CLINICAL: Three different clinical presentations
 - **INVASIVE PULMONARY ASPERGILLOSIS:** Occurs in immunocompromised folks. Invades blood vessels.
 - **ASPERGILLOMA:** Isolated immunocompetent cluster of mold. Often grows in a previously formed cavitation.
 - **ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS:** Occurs in Asthmatics, characterized by transient pulmonary infiltrates and eosinophilia.

PNEUMOCYSTIC CARINII PNEUMONIA:

- CLINICAL: Typically occurs in immunocompromised patients.
 - Symptoms range from asymptomatic to severe.
- HISTOLOGY: Histologically there is a prominent frothy **foamy intra-alveolar exudate**, containing the organisms.
 - The exudate is *distinctive* --*acellular* proteinaceous material in the airspaces. It is "bubbly."
 - Use silver stains to demonstrate the organisms themselves.

ACUTE INTERSTITIAL LUNG DISEASES:

- **DIFFUSE ALVEOLAR DAMAGE (DAD, ARDS):** Also known as Shock Lung.
 - PATHOGENESIS: Injury to lung resulting in diffuse alveolar capillary damage. Characterized by *interstitial inflammation* and the accumulation of alveolar exudate.
 - PATHOLOGY:
 - **EXUDATIVE PHASE:** First week following the injury. Acute injury to epithelia and endothelia cause necrosis and capillary leakage.
 - **Hyaline Membranes** are prominent along the alveolar walls, consisting of fibrin, plasma proteins and cell debris.
 - Edema thickens the membranes. Edema peaks 1 day post injury.
 - The air spaces are still apparent, but membranes are thickened.
 - Interstitial inflammation begins.
 - **ORGANIZING PHASE:** Proliferation of fibroblasts, and filling of airspaces with fibrous debris.
 - **Interstitial inflammation** peaks in the organizing phase: lymphocytes primarily, with plasma cells and some histiocytes.
 - Epithelial regeneration occurs: Type II Pneumocytes proliferate -----> Type-I pneumocyte, in order to replace the damaged ones.
 - CLINICAL FEATURES: Rapid onset of severe life-threatening respiratory insufficiency, cyanosis, and severe arterial hypoxemia.
 - RADIOLOGY: Early on, bilateral lung infiltrates, later progressing to complete white-out.
 - MORTALITY: 50% on average. Frequently progress to Multisystem organ failure. But it varies and depends on the cause.
 - Multiple Causes: DAD is the common end to many etiologies.
 - **OXYGEN:** Oxygen damage is an important causes of DAD. Oxygen toxicity.
 - SHOCK
 - DRUG-INDUCED: **Bleomycin**, chemotherapeutic agent, can cause DAD
 - **Heroin** also does it.
 - RADIATION PNEUMONITIS
 - PARAQUAT
 - RDS of the NEWBORN
- **BRONCHIOLITIS-OBLITERANS ORGANIZING PNEUMONIA (BOOP):**
 - PATHOLOGY: Polypoid plugs fill bronchiolar and alveolar airspaces. Distinct in that it involves the airspaces.
 - CAUSES:
 - Infections (viral and bacterial)
 - Inhaled toxins and drugs
 - Idiopathic
 - Associated with collagen vascular disease
 - CLINICAL FEATURES: Patients improve gradually. Steroids help.

- **ACUTE INTERSTITIAL PNEUMONIA (HAMMAN-RICH SYNDROME):** Idiopathic fulminant pulmonary fibrosis.
 - **PATHOLOGY:** Resembles the Organizing Stage of DAD histologically.
 - Differs from UIP in that it is acute and rapidly progressive. Should not be characterized with UIP.
 - **CLINICAL:**
 - Affects young adults who present with flu-like symptoms of rapid onset
 - Prognosis is grave.

PULMONARY HEMORRHAGE SYNDROMES: Mostly rare diseases

- **GOODPASTURE SYNDROME:**
 - **PATHOGENESIS:** It is caused by a circulating cytotoxic autoantibody to basement membranes. It affects the *lungs* and *kidneys*:
 - Proliferative, rapidly aggressive glomerulonephritis. **Type-II** cytotoxic antibody hypersensitivity.
 - DAD and massive hemorrhage in lungs.
 - **CLINICAL:** This disease typically occurs in young men and is treated by administration of corticosteroids, cytotoxic drugs, and plasmapheresis (plasma exchange to remove antibodies)
 - Alveolar hemorrhage leads to hemoptysis, which can be life-threatening.
 - Prognosis is correlated with the degree of involvement of the kidney.
- **IDIOPATHIC PULMONARY HEMOSIDEROSIS:** Similar to Goodpasture Syndrome, but no renal disease or anti-BM antibodies.
 - **CLINICAL:** Occurs in children younger than 16 years.
 - **PATHOLOGY:** Characterized by diffuse alveolar hemorrhage similar to Goodpasture Syndrome.
- **WEGENER'S GRANULOMATOSIS:** Systemic necrotizing vasculitis.
 - **PATHOGENESIS:** Unknown etiology.
 - **PATHOLOGY:** Characterized by granulomatous lesions of the upper and lower respiratory tract (*nose, sinuses, and lungs*) and renal glomerular disease.
 - **Acute, necrotizing granulomas** of nose, sinuses, and lungs.
 - **Necrotizing Vasculitis** of small and medium arteries.
 - Focal or diffuse necrotizing glomerulonephritis.
 - **Anti-Neutrophilic Cytoplasmic Antibodies (ANCA)** are almost always found in the blood.
 - **HISTOLOGY:** Geographic, irregular outline of necrotic area is characteristic.
 - **CLINICAL:** Most prevalent in age 50's.
 - **TREATMENT:** Immunosuppressant cyclophosphamide. It produces improvement in prognosis and both complete remission and substantial disease free intervals are induced in most patients.
- **ALLERGIC ANGIITIS and GRANULOMATOSIS (CHURG-STRAUSS SYNDROME):**
 - **PATHOGENESIS:** Systemic vasculitis involving both systemic and pulmonary circulation.
 - **CLINICAL:** Occurs almost exclusively in people with asthma.
 - Peripheral blood eosinophilia is seen, so this could also be considered a form of pulmonary eosinophilia.
 - **DRUG-INDUCED REACTIONS:** Drugs can cause a variety of pulmonary problems -- almost all of the eosinophilic, acute and chronic interstitial, and even obstructive diseases can be precipitated by drug reactions.

Other Rare Pulmonary Syndromes:

- **BRONCHOCENTRIC GRANULOMATOSIS:**
 - **PATHOLOGY:** Granulomatous and necrotizing lesions of the bronchioles. Eosinophilia is found.
- **LIPID PNEUMONIA**
 - **ENDOGENOUS:** Due to bronchial obstruction.
 - **EXOGENOUS:** Due to aspiration of oils like mineral oil.
- **PULMONARY ALVEOLAR PROTEINOSIS:**
 - **PATHOLOGY:**
 - Characterized radiographically by diffuse pulmonary opacification
 - Characterized histologically by accumulation of intra-alveolar dense granular material that contains abundant lipid and PAS positive material.

- **CLINICAL:** Patients present with nonspecific respiratory difficulty and may have a variable clinical course.

PULMONARY EOSINOPHILIAS: Patchy infiltrates occurring with Eosinophilia of blood and/or sputum.

- **EOSINOPHILIC PNEUMONIA:** Divided into three main groups, all having the same histology.
 - **SIMPLE EOSINOPHILIC PNEUMONIA (LOEFFLER SYNDROME):** Usually mild self-limited disease that resolves spontaneously.
 - Lung Biopsy is usually unnecessary.
 - **TROPICAL EOSINOPHILIC PNEUMONIA:** Pneumonia caused by filarial infections. Responds well to antifilarial drugs.
 - Lung biopsy is usually unnecessary.
 - **CHRONIC EOSINOPHILIC PNEUMONIA:**
 - **PATHOGENESIS:** Usually associated with chronic asthma, peripheral blood eosinophilia and elevated IgE.
 - **CLINICAL FEATURES:** Variable, ranging from mild to severe.
 - Steroids work well, but recurrences may occur.
 - **CAUSES:**
 - Drugs
 - Fungal hypersensitivity
 - Parasites
 - Inhalents
 - Idiopathic
- **PULMONARY EOSINOPHILIC GRANULOMA (HISTIOCYTOSIS X):**
 - **PATHOLOGY:** *There is no blood or sputum eosinophilia.*
 - Histiocytes proliferate to form patchy nodular interstitial lesions. The infiltrate is composed of a variable mixture of histiocytes (Langerhans cells) and eosinophils, as well as occasional plasma cells and lymphocytes.
 - **LANGERHANS CELL** is the characteristic cell, a histiocyte. It contains a bland, folded or indented nucleus, an inconspicuous nucleolus, and abundant eosinophilic cytoplasm with indistinct cell borders.
 - In active lesions, Langerhans cells are numerous and occur in clusters.
 - Electron microscopy of Langerhans cells demonstrates the characteristic **Birbeck granules**.
 - These cells stain positively with **S100 protein stain** (an immunoperoxidase stain).
 - **LANGHANS GIANT CELL** is a horse-shoe like pattern of giant-cells seen in granulomas -- not the same as langerhans giant cells.
 - **CLINICAL:** Patients may present with cough and dyspnea, or they may be asymptomatic.
 - **EPIDEMIOLOGY:** Presents in young (age 30) individuals, and associated with heavy smoking.
 - Radiographically, there are multiple nodules distributed throughout both lungs.
 - Prognosis for the disease is quite good.
- **ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS:** Hypersensitivity to Aspergillus as well as other molds.
 - Type I (IgE) and III (immune complex) hypersensitivity are included. Some think Type IV (CMI) hypersensitivity also occurs.
 - Responds well to steroid therapy.
- **ALLERGIC ANGIITIS and GRANULOMATOSIS (CHURG-STRAUSS SYNDROME)**
- **BRONCHOCENTRIC GRANULOMATOSIS**
- **MUCOID IMPACTION of the BRONCHI**

OBSTRUCTIVE PULMONARY DISEASES:

- **CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD):** Characterized by *decreased expiratory flow in the airways of the lung*.
 - **CLINICAL:** This is a physiological definition, diagnosed on the basis of pulmonary function studies.
 - **Diseases:**
 - Emphysema and chronic bronchitis are always included.

- Asthma and bronchiectasis are often included in the definition.
 - **SMALL AIRWAYS DISEASE:** Alterations in the distal small airways are probably the earliest abnormalities in COPD. This can result in early chronic airway obstruction.
- **CHRONIC BRONCHITIS:** *Presence of a chronic productive cough without a discernible cause for at least 3 months out of the year, for 2 successive years.*
 - **CLINICAL:** *The disease is diagnosed based on clinical criteria, as opp. to Emphysema which is an anatomic diagnosis.*
 - **RISK-FACTORS:**
 - Cigarette smoking is most important cause
 - Air pollution, SO₂, NO₂ are also factors.
 - **COMPLICATIONS:** Bacterial (*H. Influenzae* and *Strep. Pneumoniae*) and viral (RSV, Adenovirus) exacerbations can occur.
 - Chronic Bronchitis can lead to pulmonary hypertension -----> Cor Pulmonale.
 - **PATHOLOGY:** Hypersecretion of mucus in response to chronic injury.
 - Hypertrophy and Hyperplasia of submucosal glands.
 - Mucous and goblet cell metaplasia and hyperplasia. Goblet cells are normally 1:20 cells of bronchial epithelium, but they can become as prevalent as 1:1.
 - Can also serous -----> mucous metaplasia, indicative of chronic inflammation.
 - **REID INDEX** can be used to quantify the degree of hypertrophy seen in bronchitis.
 - It is the ratio of the *thickness of the submucosal glands divided by the thickness of the bronchial wall*
 - The Reid index normally is less than 0.4, but in chronic bronchitis the Reid index is increased to 0.6 or 0.7.
- **EMPHYSEMA:**
 - **PATHOGENESIS:** *Abnormal permanent enlargement of the air spaces distal to the terminal bronchiole, accompanied by destruction of their walls.*
 - Destruction of alveolar walls is a necessary finding to diagnose emphysema, otherwise the condition is called **Hyperinflation**.
 - **PROTEASE-ANTIPROTEASE HYPOTHESIS:** A theory that emphysema results from an imbalance between proteases (mainly elastase) and antiproteases in the lung.
 - In the lung, elastases are released from *neutrophils* and *alveolar macrophages*, thus any inflammatory process is likely to offset the Protease:Antiprotease balance.
 - **SUBTYPES:**
 - **CENTRIOBULAR EMPHYSEMA:** Enlargement and destruction of the respiratory bronchioles, center part of the lobe, sparing of the distal parenchyma (furthest away from the bronchiole and closer to septum).
 - Most common type, related to smoking, and frequently involving upper lung zones.
 - Centrilobular may progress to Panacinar Emphysema in chronic cases.
 - **PANACINAR (PANLOBULAR) EMPHYSEMA:** The entire acinus is uniformly involved, primarily in the lower zones of the lung, with destruction of alveolar septa from the center to the periphery.
 - **CLINICAL:** Typically occurs in lower lung zones. Associated with alpha1-Antitrypsin Deficiency, rarely, or more commonly as a complication of Centrilobular Emphysema.
 - **LOCALIZED (PARASEPTAL) EMPHYSEMA:** Localized right next to the septum. Usually asymptomatic.
 - Complications: Can present as spontaneous pneumothorax or bullous disease of the lung in young adults.
 - **IRREGULAR (PARACICATRICIAL) EMPHYSEMA:** Emphysema forming around localized areas of previous scarring (cicatrix).
 - **PATHOLOGY:** Characterized by enlarged airspaces containing anthracotic pigment.
 - **BULLA:** Large subpleural airspaces of air measuring 1-2 cm in diameter.
 - **CLINICAL:** Most prevalent in male smokers.
 - May be asymptomatic early on, and often does not become disabling until 50's - 80's.
 - **alpha1-ANTITRYPSIN DEFICIENCY:**
 - **PATHOGENESIS:** Genetic defect, product of two alleles on Chrom #14. Dominant phenotypic expression.
 - **alpha1-Antitrypsin** inhibits the proteolytic actions of trypsin, elastase in the lung, and collagenase.

- Deficiency results in **panlobular emphysema** due to the unchecked action of elastase in the lung.
 - PHENOTYPES: **Protease Inhibitor (PI)**, same as alpha-Antitrypsin) has three:
 - **PI-MM**: Normal wild-type 95%
 - **PI-MZ**: Heterozygote (deficient PI) 3-5%
 - **PI-ZZ**: Homozygote (no PI) <1%
 - PI-MZ is associated with an increased risk for emphysema, and at a younger age, *only if the patient is a smoker*. Non-smokers who are PI-MZ are not at increased risk.
 - ASTHMA
 - PATHOGENESIS: Tracheo-bronchial hyperreactivity, leading to paroxysmal airway narrowing.
 - HISTOPATHOLOGY:
 - Thickening of basement membranes
 - Eosinophilic inflammation, and edema in the walls of the bronchi.
 - Smooth muscle hypertrophy
 - Prominent mucous plugs.
 - Desquamation of bronchial epithelium and metaplasia may occur.
 - CLINICAL FEATURES: Wheezing, dyspnea, cough.
 - EPIDEMIOLOGY: 10% of children are effected, 5% of adults.
 - TREATMENT:
 - beta-Adrenergics
 - Corticosteroids, either inhaled (common) or systemic (only in severe cases)
 - Methylxanthine
 - Anti-Cholinergics
 - SUBTYPES:
 - Traditional Categorization:
 - **Extrinsic Asthma**: Allergic, associated with increased IgE and Eosinophilia.
 - **Intrinsic Asthma**: Non-allergic.
 - New Categorization, by cause:
 - **ALLERGIC** (IgE Type-I hypersensitivity)
 - INFECTIONS
 - EXERCISE-INDUCED
 - OCCUPATIONAL
 - DRUG-INDUCED
 - AIR POLLUTION
 - EMOTIONAL FACTORS
 - **STATUS ASTHMATICUS**: Severe acute asthma which does not respond to treatment and persists (for days or weeks). In rare instances, acute episodes can result in death.

PNEUMOCONIOSES: Lung diseases caused by exposure to particulate matter (dust particles)

- PATHOGENESIS: Inhaled dust particles are able to *stimulate fibrosis* in the lung, resulting in damage.
 - RISK-FACTORS: Particle-size, length of exposure, and individual susceptibility also play a role.
 - Disease has characteristics that are both interstitial and obstructive -- fibrosis in the interstitium, and inflammation in the airspaces.
- **SILICOSIS**: A pneumoconiosis caused by the inhalation of silicon dioxide (silica), usually in crystalline form as quartz. Two forms of silicosis exist:
 - **Simple nodular silicosis**.
 - **Progressive massive fibrosis**.
- **CAPLAN SYNDROME**: Coexistence of rheumatoid arthritis and a pneumoconiosis.
- **COAL WORKERS' PNEUMOCONIOSIS**: Exposure to coal dust.
 - CLINICAL OUTCOME / PATHOGENESIS: Multiple types, from asymptomatic to complicated.
 - **Asymptomatic Anthracosis**: "Anthracosis" specifically refers to an asymptomatic pneumoconiosis.
 - **Simple coal-workers pneumoconiosis**. Characterized by coal macules and nodules containing carbon-laden macrophages, with little or no pulmonary dysfunction
 - **Complicated coal-workers pneumoconiosis**: Progressive massive fibrosis, which is black scars in the lungs causing compromised pulmonary function.
- ASBESTOS-RELATED DISEASES

- PLEURAL PLAQUE
- PLEURAL EFFUSION
- **ASBESTOSIS (PULMONARY PARENCHYMAL INTERSTITIAL FIBROSIS)**
 - **PATHOLOGY:** Interstitial fibrosis of varying severity.
 - **Asbestos Bodies** can be seen -- asbestos fibers coated by iron, containing proteinaceous materials.
- BRONCHOGENIC CARCINOMA
- MALIGNANT MESOTHELIOMA: See Pleura section. Only malignant mesothelioma is related to asbestos -- not benign mesothelioma.
- **BERYLLIOSIS:** Lung disease from inhalation of Beryllium
 - ACUTE EXPOSURE: Acute pneumonitis
 - CHRONIC EXPOSURE: Cell-mediated immunity -----> non-caseating granulomas in lungs, hilar lymph nodes, and sometimes RES organs.
 - Maybe asymptomatic for years.
- TALCOSIS

INTERSTITIAL LUNG DISEASES: Those diseases which occur primarily in the interstitium (alveolar walls), rather than the alveolar spaces (which is predominantly obstructive lung diseases).

- **HYPERSENSITIVITY PNEUMONITIS:**
 - **PATHOGENESIS:** Immunologic lung disease. Type III and IV hypersensitivity. Three categories of allergens are responsible.
 - Thermophilic actinomyces
 - Molds
 - Animal proteins
 - **CLINICAL:** May be acute or chronic. Individual diseases are given names reflecting circumstances of exposure.
 - Usually there is an associated allergen, which is obvious to the patient.
 - **PATHOLOGY:** Similar to chronic interstitial pneumonitis.
 - Non-necrotizing granulomas in the interstitium.
 - Macrophages.
 - **FARMER'S LUNG:** Hypersensitivity pneumonitis caused by exposure to moldy hay, typically occurring in farmers.
- **SARCOIDOSIS:** Chronic systemic granulomatous disease.
 - **PATHOGENESIS:** Unknown etiology.
 - **PATHOLOGY:** **Non-caseating granulomas** occur in almost any organ of the body.
 - The lung is the most frequently involved organ, and histologically one may see multiple non-caseating granulomas scattered in the interstitium of the lung.
 - Tends to show a peribronchiolar distribution, following lymphatic pathways.
 - **CLINICAL:** Clinical presentation is variable. Often presents with pulmonary problems but not always.
 - **EPIDEMIOLOGY:**
 - Peak age 20-40 years old.
 - More common in blacks than whites (15:1), and more common in women.
 - **DIAGNOSIS**
 - Radiograph: Bilateral infiltrates with hilar lymphadenopathy (**Ghon's Complex**), which may imitate Tuberculosis.
 - **Angiotensin Converting Enzyme (ACE)** is elevated in Sarcoidosis patients.
 - Tissue biopsy is often needed.
 - **NECROTIZING SARCOID GRANULOMATOSIS:** A rare variant of sarcoidosis, that has vasculitis and focal parenchymal necrosis, as well as the characteristic sarcoid granulomas.
 - **CLINICAL:** This disease responds well to steroids and has an excellent prognosis.
- **USUAL INTERSTITIAL PNEUMONIA (UIP):** Pathologically, UIP is an
 - **PATHOGENESIS:** Thought to be immunological basis.
 - High comorbidity with autoimmune disorders like RA, SLE, Scleroderma, Hashimoto's Thyroiditis.
 - **PATHOLOGY:** Interstitial inflammation and fibrosis.

- The single most important histologic finding that separates UIP from other interstitial pneumonias is the **marked variation from field to field in degree of lung involvement and also in the nature and appearance of the cellular infiltrate.**
 - Predominant cell type is the lymphocyte.
 - CLINICAL FEATURES: Progressive respiratory insufficiency. Begins insidiously with gradual onset of dyspnea and cough.
 - Chest X-Ray will show bilateral infiltrates, which may progress to white-out.
- **DESQUAMATIVE INTERSTITIAL PNEUMONIA (DIP):** Second-most common chronic interstitial pneumonitis.
 - PATHOGENESIS: Unknown etiology.
 - PATHOLOGY: Characterized histologically by the accumulation of numerous macrophages in alveolar spaces, as well as interstitial abnormalities.
 - As compared to UIP, DIP has a more uniform appearance.
 - CLINICAL: Patients usually present with slow onset of cough and dyspnea.
 - Patients generally of a younger age group and have better prognosis.
 - Radiographic findings include bilateral lower lobe **ground glass** infiltrates.
 - Patients often respond to steroid therapy, and DIP has a more favorable prognosis and better response to steroid therapy than UIP.
 - DIP is milder than UIP and may represent a very early stage of UIP
- **LYMPHOID INTERSTITIAL PNEUMONIA (LIP):** Rare.
 - PATHOLOGY: Characterized by a dense and diffuse interstitial infiltrate of lymphocytes, plasma cells and histocytes, that are histologically benign, polymorphous and polyclonal.
 - CLINICAL: LIP may be difficult to distinguish from a well-differentiated lymphocytic lymphoma.
- **HONEYCOMB LUNG:** End-stage fibrotic lung, found in many different interstitial lung diseases.
 - PATHOLOGY: This is the final common pathway for most interstitial lung diseases, both acute and chronic.
 - The lungs become solid with alternating areas of fibrosis and cysts. The cysts occurs from restructuring of the distal airspaces.
- **RESTRICTIVE LUNG DISEASE:** General term referring to a group of diffuse pulmonary diseases characterized by inability for the lung to expand, yielding decreased total lung capacity.
 - **Kyphoscoliosis:** Chest wall disorders in the presence of normal lungs can result in this condition.
 - Any of the acute or chronic interstitial/infiltrative lung diseases, such as DAD, pneumoconiosis, UIP, etc., can result in this disorder.

PULMONARY HYPERTENSION:

- **PRIMARY HYPERTENSION:** Rare condition, typically occurring in young women.
- **SECONDARY HYPERTENSION:** Secondary to other conditions such as COPD, congenital or acquired heart disease, etc.

BENIGN LUNG TUMORS:

- **CARCINOID TUMOR:** Neuroendocrine tumor secreting serotonin. Low-grade malignancy.
 - PATHOLOGY: *Carcinoid is on the benign end of the neuroendocrine tumors.*
 - THREE TYPES:
 - CENTRAL: 90% of cases
 - Peripheral
 - Atypical
 - Gross Appearance: It looks distinctively yellow, rather than white (as in most other tumors).
 - HISTOLOGY: Uniform, monotonous-looking cells.
 - CLINICAL: Good prognosis. 90% 5-yr survival.
 - Generally occurs in younger age group (avg age 45 years) than bronchogenic carcinoma
 - Symptoms: skin flush, cyanosis, diarrhea.
- **PULMONARY HAMARTOMA:** Usually Peripheral in location.
 - PATHOLOGY: A benign localized proliferation of normal tissue components -- hyaline cartilage containing cleft like spaces lined by respiratory epithelium
 - Occasionally there may also be fibrous tissue, fat, and blood vessels.

- **CLINICAL:** Pulmonary hamartomas are relatively common lesions which usually are discovered as an incidental finding on routine chest x-ray.
- **THYMOMA:** A mediastinal tumor (of thymus) most frequently occurring in the anterior mediastinum.
 - **CLINICAL:** Peak incidence in the 5th decade of life.
 - Associated diseases include myasthenia gravis, red cell hypoplasia and hypogammaglobulinemia.
 - Most thymomas are slow growing with a relatively benign clinical behavior, unless they are invading or impinging on surrounding structures.
- **BRONCHOGENIC CYST:**
 - **PATHOLOGY:** A benign cyst, most frequently located in the middle or anterior mediastinum, or in the lung.
 - The cyst is lined by respiratory epithelium and the wall of the cyst contains muscle and cartilage.
 - **CLINICAL:** It may present in childhood with respiratory distress due to compression and atelectasis, or recurrent infections; it rarely may be an incidental finding in adults.

MALIGNANT LUNG TUMORS:

- **EPIDEMIOLOGY:** General clinical properties of lung cancer
 - **PROGNOSIS:** **Overall 5-yr survival is 8-10%.** Bad prognosis!
 - **TREATMENT:** Surgical resection where possible, but the patient must qualify as a good candidate for surgery.
 - **QUALIFICATIONS:** Only 20-30% of patients wind up being viable candidates for surgery.
 - Patient must be able to withstand cardiopulmonary stress.
 - No metastases can be present.
 - **EXCEPTION:** Small Cell Carcinoma is not treated with surgery. It's treated with chemotherapy.
- **TUMOR CATEGORIES:**
 - **CENTRAL:** Originating from bronchioles greater than 1mm in diameter, and associated with smoking.
 - **PERIPHERAL:** Originating from lung parenchyma, airspaces less than 1mm in diameter, and not associated with smoking.
- **SQUAMOUS CELL CARCINOMA: CENTRAL**
 - **PATHOGENESIS:** Smoking leads to **squamous metaplasia** of broncho-alveolar cells, which can then become transformed to squamous-cell cancer.
 - Usually occurs in the **upper lobe**.
 - **PATHOLOGY:** Four diagnostic histological features
 - **Keratin pearls** and individual cell keratinization can be seen, with inter-cellular bridges.
 - **Individual Keratinization** of cells.
 - **Intracellular Bridges**
 - **CLINICAL FEATURES:** Closely associated with cigarette smoking.
 - **Hypercalcemia** is a common paraneoplastic syndrome, resulting from tumor-secretion of **PTHrP** (PTH-Related Peptide).
 - **Hemoptysis** is unique to this tumor among the lung cancers.
 - Used to be the most common cancer, now on the decline.
 - **COMPLICATIONS:**
 - **SUPERIOR VENA CAVA SYNDROME** occurs if the tumor obstructs the SVC, leading to engorgement of head and neck.
 - **PANCOAST TUMOR / SYNDROME:** Apical lung tumor impinges on 8th cervical or 1st or 2nd thoracic nerves, causing neuralgias.
 - This results in shoulder pain radiating in an ulnar distribution down the arm (Pancoast syndrome).
 - A Pancoast tumor may also involve the cervical sympathetic nerves and cause **Horner syndrome** (enophthalmos, ptosis and miosis).
- **ADENOCARCINOMA: PERIPHERAL** -- and not closely associated with smoking.
 - **EPIDEMIOLOGY:** Becoming more common, and may surpass Squamous Cell Carcinoma as the most common lung cancer.
 - **PATHOLOGY:**
 - **FOUR TYPES** of Adenocarcinoma based on histology: *all four types stain positive for mucin.*
 - **ACINAR:** Well differentiated "back-to-back" acinar glands.
 - **SOLID:** Poorly differentiated. This is also a type of **LARGE CELL CARCINOMA**.
 - **PAPILLARY:** Rare, finger-like projections.

- **BRONCHO-ALVEOLAR:** Originating from the bronchioles. Also see BRONCHO-ALVEOLAR CARCINOMA
 - Stains positive for **mucin**, indicating the neuroendocrine secretions.
 - **Scar Carcinoma:** Outdated term. Adenocarcinomas are associated with pleural scarring. The tumor actually probably originates from a desmoplastic reaction at the scar borders.
- **CLINICAL:** It is rapidly becoming the most common cancer. Prognosis depends on the stage.
- **BRONCHIOLO-ALVEOLAR CARCINOMA:** Subtype of adenocarcinoma, arising in terminal bronchioles or alveoli on the walls.
 - **PATHOLOGY:** Solitary mass, multiple lobules, or diffuse infiltrate resembling pneumonia.
 - Underlying pulmonary architecture is preserved.
 - **Tumor cells** (cuboidal and columnar epithelium) grow along bronchiolar walls.
 - **CLINICAL:** Occurs equally in males and females.
 - 1:1 Male:Female ratio.
- **ADENOSQUAMOUS CARCINOMA:** Rare tumor, has features of both adeno and squamous cell carcinoma.
 - **PATHOLOGY:** Large bulky peripheral tumors.
 - **CLINICAL:** Studies indicate that this mixed tumor is more aggressive than either of the other pure carcinomas.
- **SMALL CELL CARCINOMA: CENTRAL.** *Small cell carcinomas are on the malignant end of the neuroendocrine tumors, i.e. a malignant Carcinoid tumor. The tumor is fast-growing and highly malignant.*
 - **THREE TYPES** based on histological classification:
 - **Oat Cell:** Smallest cells.
 - **Intermediate:** Large cells.
 - **Combined:** Small cell carcinoma, combined in the same tumor with adenocarcinoma or squamous carcinoma.
 - **PATHOLOGY:** Characterized by sheets of small blue tumor cells, with virtually no cytoplasm.
 - To diagnose, you can also look for **neurosecretory granules** on EM.
 - **CLINICAL FEATURES:** Traditionally has male predominance. Females are catching up, but males still predominate by 5:1.
 - Most patients already have metastatic disease at the time of diagnosis; hence, chemotherapy is the usual treatment for this tumor (rather than surgical resection).
 - **PARANEOPLASTIC SYNDROMES** are very frequently found along with the primary cancer.
 - Tumors often secrete **ACTH**, leading to **Cushing's Disease**
 - Tumors can secrete **ADH**, leading to **Syndrome of Inappropriate ADH-secretion (SIADH)**.
 - **TREATMENT: Chemotherapy.** This tumor grows too fast for surgery. Most of the others are treated with surgery.
- **LARGE CELL UNDIFFERENTIATED CARCINOMA:** Wastebasket group. Tumor lacks the histological features of any of the other categories.
 - **PATHOLOGY:** They usually have a solid pattern and are composed of large malignant cells having a moderate amount of cytoplasm. No evidence of squamous or glandular differentiation.
- **RARE PULMONARY TUMORS**
 - **CARCINOSARCOMA**
 - **PULMONARY BLASTOMA**
- **METASTATIC TUMORS:** Metastases to the lungs. *It is the most common type of tumor to be found in the lung.*
 - The metastatic tumors commonly originate from the liver or stomach.
 - Often there is also **lymphangiitis**, or metastases that reached the lung through the lymphatic system.
 - Tumors usually have sharp borders.

PLEURA:

- **PNEUMOTHORAX:** Air in the pleural spaces.
 - **SPONTANEOUS PNEUMOTHORAX**
 - **TRAUMATIC PNEUMOTHORAX**
 - **IATROGENIC PNEUMOTHORAX**
- **PLEURAL EFFUSION**
 - **HYDROTHORAX:** Refers to a pleural effusion that resembles water (transudate).
- **PLEURITIS**
- **SOLITARY FIBROUS TUMOR** of the PLEURA

- **MESOTHELIOMA**
 - **BENIGN MESOTHELIOMA: Pleural Fibroma**, does not produce a pleural effusion.
 - **MALIGNANT MESOTHELIOMA**: Related to asbestos exposure.
 - **PATHOGENESIS**: May arise from visceral or parietal pleura. Diffuse tumor invading lung and spreading widely in the pleural space.
 - **CLINICAL**: Associated with pleural effusion.
 - Poor prognosis.
- **EMPYEMA**: A variant of pyothorax in which thick pus accumulates within the pleural cavity, often with loculation and fibrosis.

PULMONARY EMBOLISM:

- **PREDISPOSING CAUSES**: Occurs only when the circulation is already inadequate
 - Pre-existent heart or lung disease.
 - Cancer
 - Immobilization
 - Hypercoagulable states.
- **EFFECTS**: Pulmonary emboli lead to 2 main effects
 - Respiratory compromise due to under perfusion.
 - Hemodynamic compromise due to increased resistance to pulmonary blood flow.
- **CLINICAL**: Patient will present with sudden onset of unexplained dyspnea.
 - Hemoptysis and pleuritic chest pain will be present -- only if the embolus resulted in a lung infarct.