- The major complication of thrombi in any location in the heart is the detachment of fragments and their transport to distant sites (embolization), where they lodge and occlude arterial vessels.

Marantic Endocarditis--> As we get older, our valves don't close properly. Valve develops irregularities on surface (cause turbulance, which encourages clot formation)

Bacterial Endocarditis Involving Aortic Valves→ Leaflets of the heart get infected, blood clots form around bacteria (almost protect them). Bacteria can spread to other parts of the body when embolism occur.

Mural Thrombis of Left Ventricle→ Ventricles dilate, large clots form, and cause massive damage, this is a medical emergency

Venous Thrombus

- The deep veins of the leg are the most common site for thrombosis.
    - Primarily due to sluggish blood flow
        - Most often the result of prolonged immobilization
    - May cause swelling of the leg, or may be completely asymptomatic
    - Pulmonary Embolism may occur

Thombosis- High Risk Patients

- Tissue Damage
- Prolonged Immobilization
- Myocardial Infarction
- Neoplasms—Solid or hematopoetic
    - Trosseu syndrome—pancreatic adenocarcinoma
- Prosthetic heart valve
- DIC (also increased risk of hemorrhage)
- Pregnancy/ postpartum (amniotic fluid can trigger)
- Oral BCPs
- Smokers
- Hyperlipidemia→ high cholesterol
- Sickle Cell disease→ RBCs change shape
- Atrial fibrillation

Case Study #3— A 75 year old man is playing golf on a very hot day and suddenly becomes dizzy and collapses. He is taken to the ER and his BP is 60/40. An IV line is inserted in his arm and intravenous saline is administered. A few hours later, he develops renal failure due to myoglobinuria (damage that occurs when you damage muscle tissue, if he urinates its brown: Myoglobin travels through circulatory system and gets trapped in kidney tubules, which block the flow of urine) with acute tubular necrosis. (death of cells—He is in a shock state) He is placed on dialysis, and his renal function gradually increases over the next few weeks. When his serum creatine level falls to 1.0 mg per dl (most of it is being removed, which is good: If it is higher than One, than there is an indication of a dysfunctional kidney), he is released from the hospital.

vessel. Once they dilate the coronary artery, they place a stent that maintains patency (opening) of the vessel. This allows better blood supply to the heart.

Angina Pectoris or chest pain can indicate many things. In a younger person, it indicates asthma or anxiety. In an older person, it indicates chest pain.

Questions and Answers

1. Why did this man have shortness of breath? **He had blockage of his coronary artery; blockage of left ventricle. Blood doesn't flow out at the same rate; his tissues are not getting enough oxygen, he has to breathe faster.**

2. What caused the occlusion of his left main coronary artery**? Atherosclerosis, Inflammation and injury to blood vessels, which narrows the vessels due to cholesterol deposits that mediate in inflammatory response, which cause fibroblasts to initiate wound healing, which leads to the formation of cholesterol with clusters surrounded by fibrous capsule, which is a lesion of Atherosclerosis, which causes occlusion which can be accelerated by genetics or poor diet.**

3. Why was he treated with an anticoagulant? **To avoid the possibility of a clot forming of the artherosclerotic plaque, which would cause a huge infarction.**

4. Why was a stent inserted into his coronary artery following angioplasty? **To maintain patency (opening) of the area where balloon dilated vessel blood will continue to flow.**

Coronary Artery Stenosis (narrowing) → **If they died of a heart attack, you'll see a clot. If a clot should form here, it would takeout major blood supply.**

Hemostasis (clotting factors are activated) → after initial injury, there is a brief period of arteriolar vasoconstriction (neurogenic reflex augmented by local factors such as endothelin—(substance secreted by endothelial cells, that increase vasoconstriction and help form clots)(releases substances that cause arterioles to contract) (triggered nerves)

→ Endothelial injury exposes the blood to the extracellular matrix (ECM)

-- The ECM is highly thrombogenic (very likely to form clots)

-- Platelets adhere, flatten, and then activate

-- To form hemostatic plug (primary hemostasis) {They form a wall; platelets can stick to one another, but they need molecules for structural support AKA fibrin)

-- Clotting factors get activated

-- Fibrinogen breaks down into fibrin, which is the glue that holds platelets together at site of vessel injury is leaking

Steps of Clot Formation

1. Endothelial Injury causes the extracellular matrix to be exposed and there is reflex vasoconstriction. Endothelin is released, collagen exposed, platelets sit down at the site of injury. (Vasoconstriction)

2. Platelets adhere to collagen and release factors. (Primary hemostasis)

3. Polymerized fibrin and platelets aggregste to form a permanent plug. Platelets and fibrin come together. (Secondary Hemostasis) This is a 12-step process.

4. Anti-Thrombotic Factors (body has means to stop clot formation)→ Tissue plasminogen activator (fibrinolysis which breaks down fibrin)

-- Thrombomodulin→ blocks coagulation cascade (acts on pre-cursors, 10-12 proteins that lead to fibrin formation)

--- Both prevent fibrin from forming

- control size of clot, and blood flow

(Anti-thrombotic counter-regulation)

Disseminated Intravascular Coagulation (DIC)

→ Disseminated Intravasular coagulation is a serious and often fatal acquired disorder (can happen when you inhale toxic substances

-- Platelets and clotting factors are consumed by massive intravascular coagulation, often within capillary beds (when you ingest amniotic fluid)

--- Conversely, this leads to uncontrollable hemorrhage in other areas of the body

{--You get tissue infarction due to blockage of capillaries

-- You use up all your clotting factors}

Pathophysiology of DIC

The central event in the initiation of DIC is the activation if the intrinsic or extrinsic clotting cascades within the vascular compartment by tissue injury, or damage to endothelium, or both. Thromboplastins from amniotic fluid can also intiate the clotting cascade. Endothelial cells release factors that cause clotting, caused by external injury.

Pathology of DIC—Many venules, capillaries, and arterioles contain multiple, small, fibrin/platelet thrombi

-- The meshwork of fibrin may fragment red blood cells, forming schistocytes

-- Widespread ischemic changes in many organs occur, leading to multi-organ failure

Microthrombi in Glomerulus→ clots in glomerulus will cause kidney infection or renal faillre.

Schistocytes→ red cells that become fragmented→ they torn because as blood cells diverge in capillary platelets get torn apart by going against microthrombi which are sharp

Atherosclerosis—Not veins or capillaries

-- A disease of large and medium sized arteries

-- Accumulation within the intima of smooth muscle cells and lipids

-- Produces irregular thickening of the wall and narrowing of the wall

-- Artheroschletotic plaques forming irregular thickening

Complications of Artherosclerosis

- Acute Occulsion→ heart attack or stroke→ clots forming on plaques

--Ischemic necrosis

- Chronic Occlusion

-- Atrophy→ (narrow vessels but it interferes with blood supply)

- Aneuysm formation→ weaken walls of vessel, vessel becomes brittle and It can crack or dilate. You see this more with aortic Atherosclerosis.

- Embolism→ clots form on plaques, then they break off

Environmental and Nutritional Pathology

Case Study #1- A 43 year old woman is seen by her local doctor with a complaint of fatigue and shortness of breath. Blood tests reveal a decreased red blood cell count and an increase in mean corpuscalr volume, consistent with megaloblastic anemia. A bone marrow biopsy is performed to confirm the diagnosis. It shows marked hypercellularity, with numerous immature, enlarged cells (megaloblasts). The woman is treated with injections of b-12 and she eventually resumes her normal activities.

B-12 is appropriate in DNA synthesis in bone marrow. Hypercellularity means there are a lot of cells in bone marrow.

Questions and Answers
1. Why did this woman complain of fatigue and shortness of breath? Because she was anemic.
2. Why did she have a hypercellular bone marrow? Deficency of B12 prevents cells from maturing in bone marrow.
3. Why were her bone marrow cells enlarged and immature? Because the DNA wasn't dividing properly
4. Why was she treated with injections of vitamin B12? Intrinsic Factor brings B12 from gut to circulation—Better if b12 is injected, this woman was missing the intrinsic factor

-----Problem is a genetic deficiency. They are missing intrinsic factor which is a carrier protein that carries B12 from lumen in the gut where food is and you swallowed it to mucosa to blood vessels 7 blood stream. So no matter how much you give, it wont be absorbed.
Give through IV it is directly absorbed into the blood stream ∴ bypass that problem

Numerous neoblastic cells is similar signs as B12 deficiency

If low B12 then megaloblastic anemia

If normal B12 then leukemia

Nicotine→ Mainly responsible for the addictive nature of cigarette smoking (feeling of well being)

Smoking puts you at an increase risk of many diseases.

	MALE	FEMALE
Lung cancer	22	12
Mouth cancer	27	6
Larynx cancer	10	18
Esophageal cancer	8	10
Coronary artery disease (over 35)	3	2
Cerebral vascular disease (over 35)	4	5
COPD	10	10

- Collagen synthesis
- Cancer Prevention

Antioxidant Functions

- donate and accepts hydrogen atoms readily
- Protects cell membranes from damage by free radicals

Deficiency of Vitamin C

- Scurvy
  - Fatigue
  - Bleeding gums, joints

Fat Soluble Vitamins

Case Study #2- A 63 year old woman is seen by her local doctor for back pain. An X-ray of her spine shows several collapsed vertebrae (bone becomes weaker). Blood tests reveal an increse in calcium and a decrease in vitamin D. Levels of parathyroid hormone are also increased. The results of a bone density scan are consistent with the presence of osteoporosis. Expolatory neck surgery reveals a parathyroid adenoma. Following removal of the tumor, her blood values of calcium, vitamin D, and PTH return to normal, and her bone density gradually increases. (looking for enlargement of parathyroid gland)

Questions and Answers

1. Why did this woman have back pain? Collapsed vertebrae
2. What caused the collapse of her vertebrae? Adenoma that was secreting Parathyroid hormone
3. Why was her calcium level increased? Since there were high levels of PTH, calcium was being "leeched" from bones, and was found in the blood.
4. Why was her Vitamin D levels decreased? Vitamin D was inhibited by the PTH
5. What was the cause of her osteoporosis? Reduction of calcium in the bones, leads to weaker more brittle bones

6. Why did removal of her parathyroid adenoma reverse the loss of blood density? Calcium was no longer being leeched from the bones, so density returned to normal This hormone tends to mobilize calcium from bones to blood. Calcium Mineralization of bone is lost, bone gets softer causes collapsed vertebrae. Bones are now more susceptible to fracture