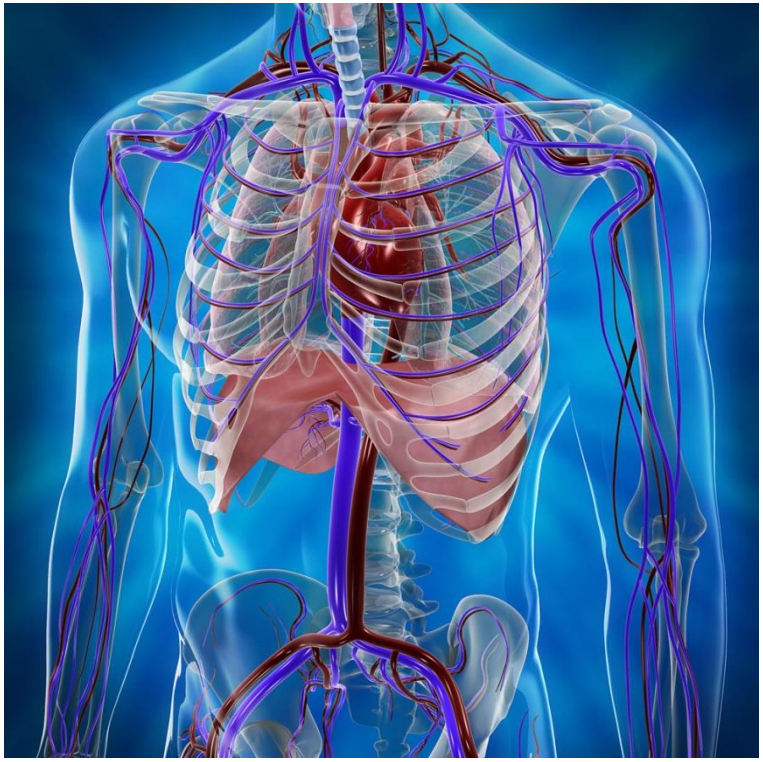
ECE 370
Introduction to Biomedical Engineering

Cardiovascular Physiology

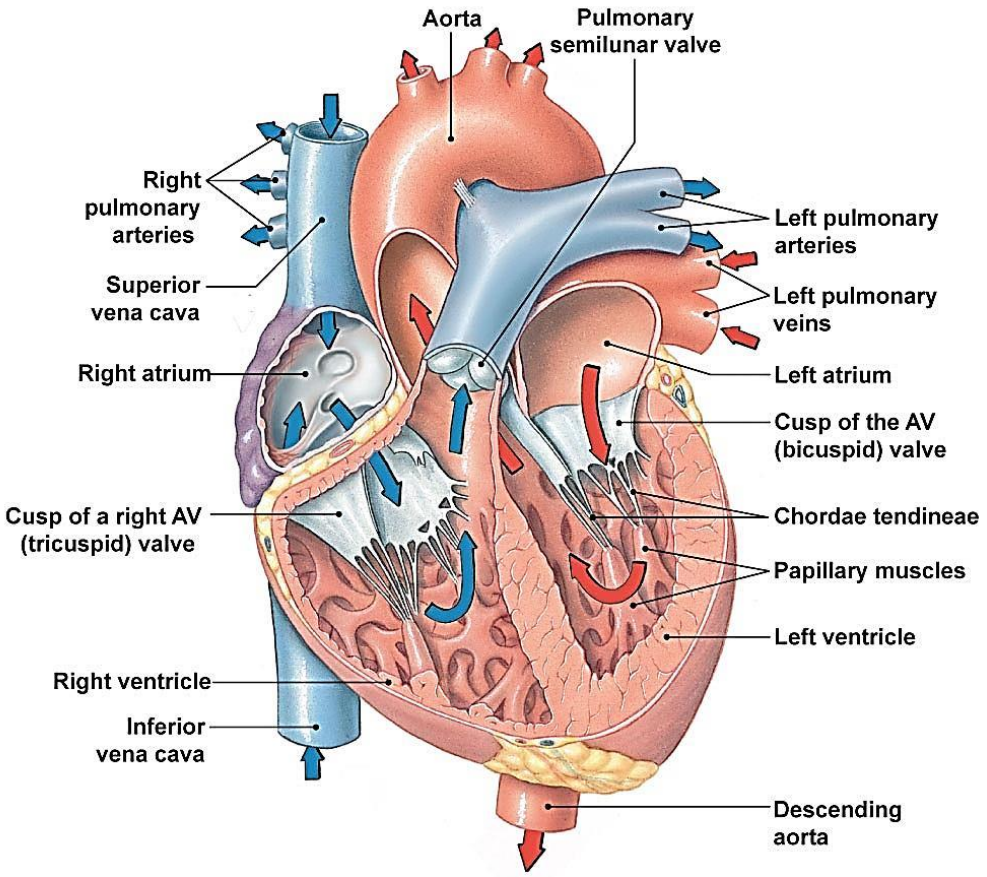
Cardiovascular System Function

- **Functional components of the cardiovascular system:**
  - Heart – “pump”
  - Blood Vessels – “tubing”
  - Blood – “fluid”
- **General functions these provide**
  - Transportation
    - Everything transported by the blood
  - Regulation
    - Of the cardiovascular system
      - Intrinsic v extrinsic
  - Protection
    - Against blood loss
    - Immune
  - Production/Synthesis
    - Of blood

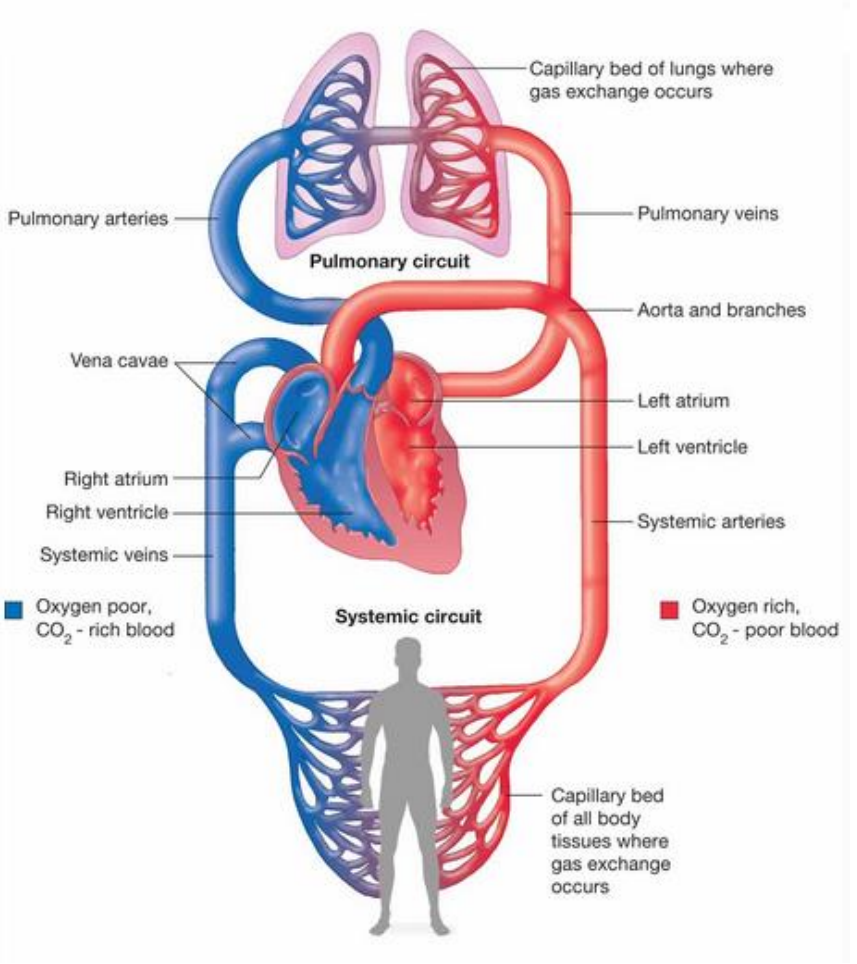


Anatomy

- 4 chambers (2 Atria - 2 Ventricles)
- 4 valves (2 Atrioventricular - 2 Semilunar Valves)

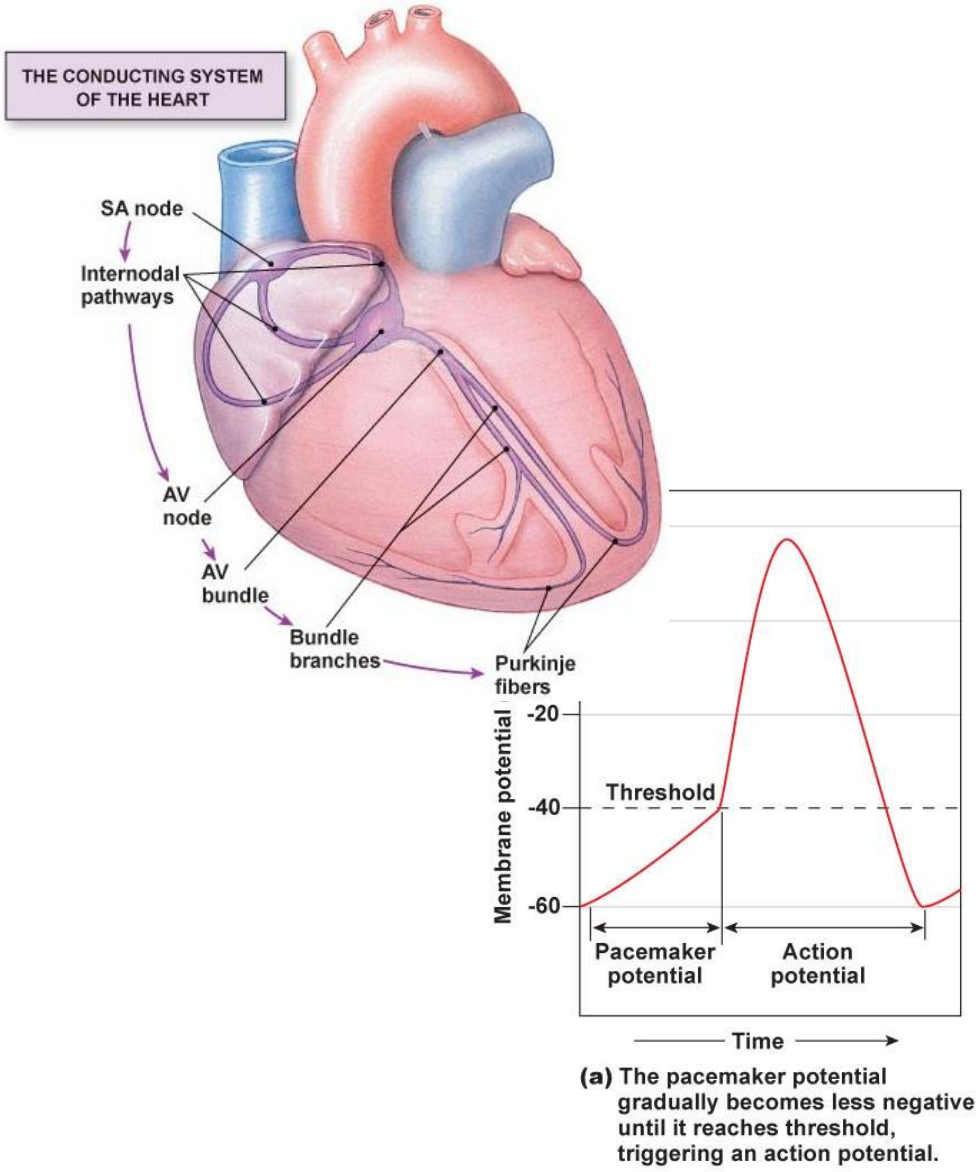


- 2 systems (Pulmonary – Systemic)



Intrinsic Conduction System

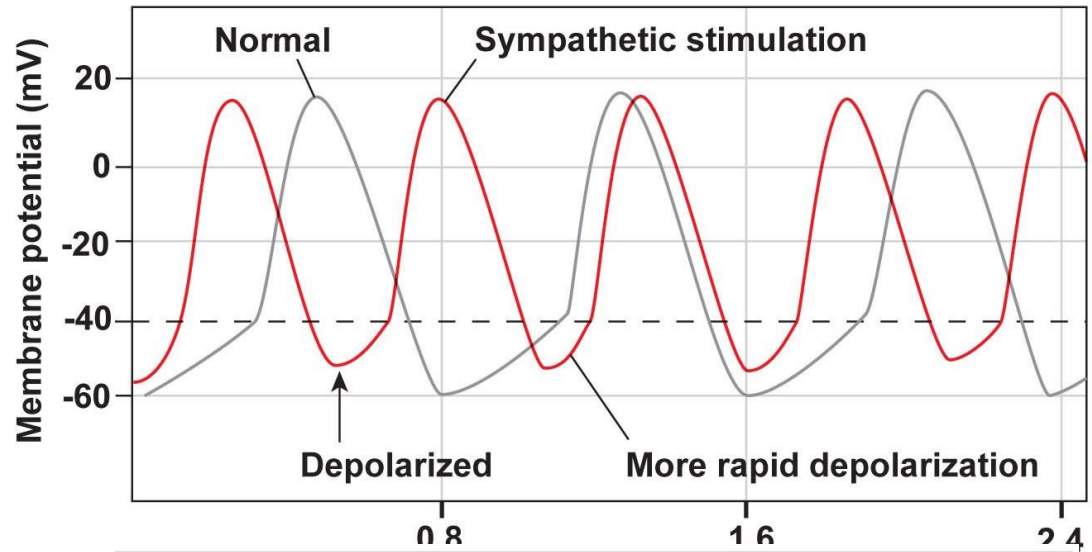
- **Consists of "pacemaker" cells and conduction pathways**
  - Coordinate the contraction of the atria and ventricles
- **Characteristics of Pacemaker Cells**
  - Do not contain many myofibrils
    - Do not contribute to the contractile force of the heart
  - Generate rhythmic APs
    - Leakage channels

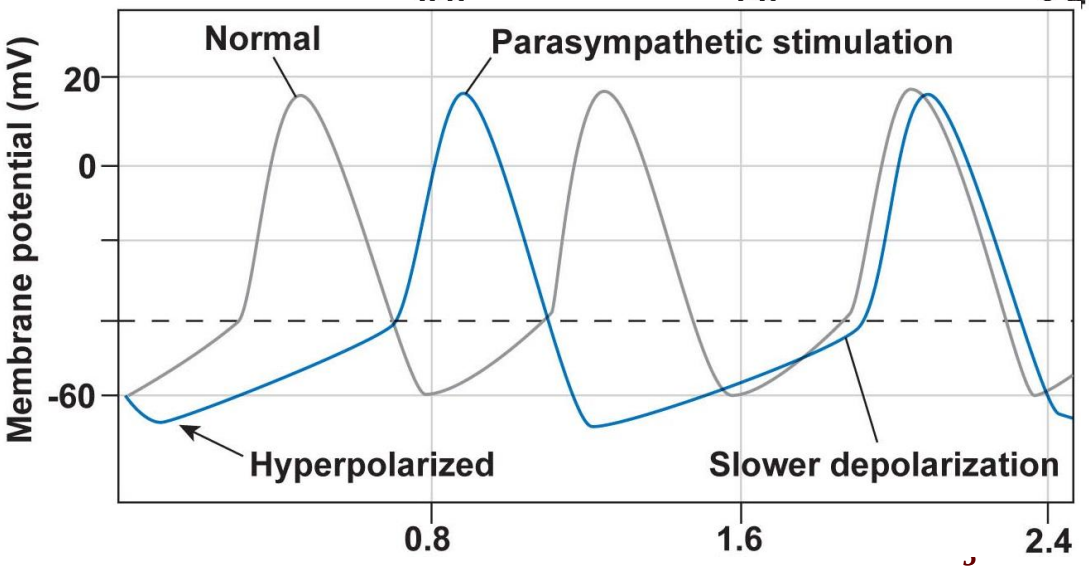


(a) The pacemaker potential gradually becomes less negative until it reaches threshold, triggering an action potential.

Intrinsic Conduction System

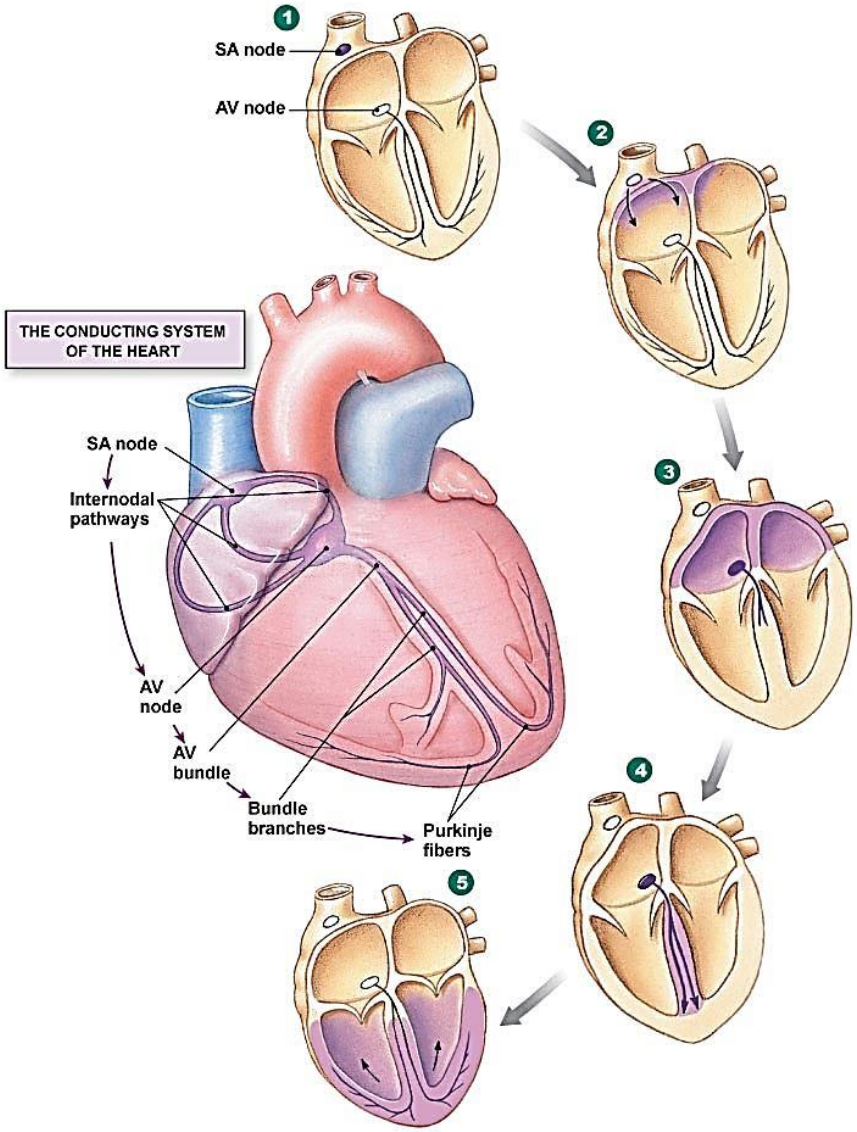
- **Sympathetic Activity Effect:**
  - ↑ heart rate
  - ↑ conduction of APs
  - ↑ contractility
- **Parasympathetic Activity Effect:**
  - ↓ heart rate
  - ↓ conduction of APs
  - ↓ contractility





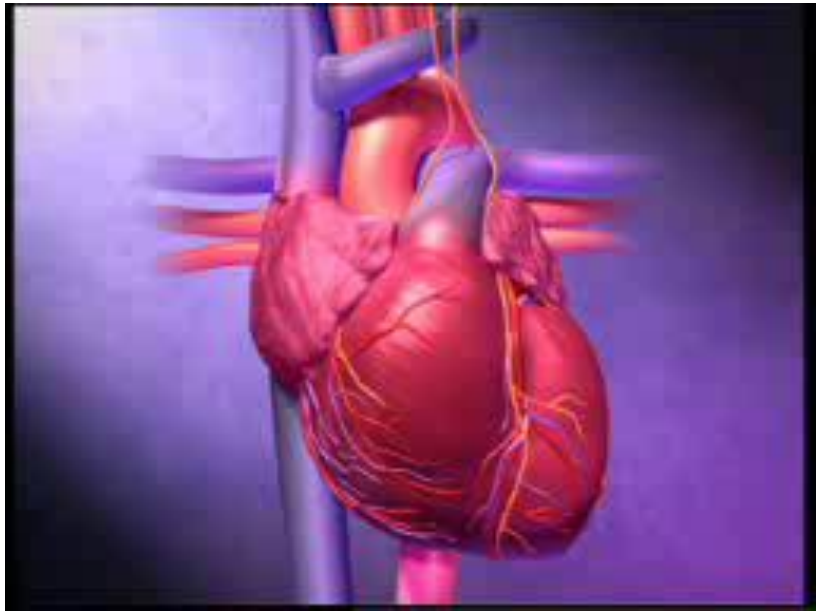
Intrinsic Conduction System

- **Electrical Conduction Pathway**
  - Initiated by Sino-Atrial node (SA node) depolarization
    - Pacemaker → 70-80 APs/minute
  - Depolarization is spread through the atria
  - Atrio-Ventricular node (AV node)
    - Prevents further spread of APs to the ventricles
    - A slight delay at the AV node occurs
      - Allows further emptying of the atria
    - If SA node fails, AV node pacemaker → 40-50 Aps/min
  - Depolarization spreads rapidly through atrioventricular bundle and Bundle of His
    - Splits into left and right bundles and then into conduction myofibers (Purkinje)
  - Purkinje fibers
    - Larger in diameter → conduct impulse very rapidly
    - Depolarization spreads rapidly to the entire ventricles
    - Causes the cells to contract nearly simultaneously
      - Good for ventricular ejection

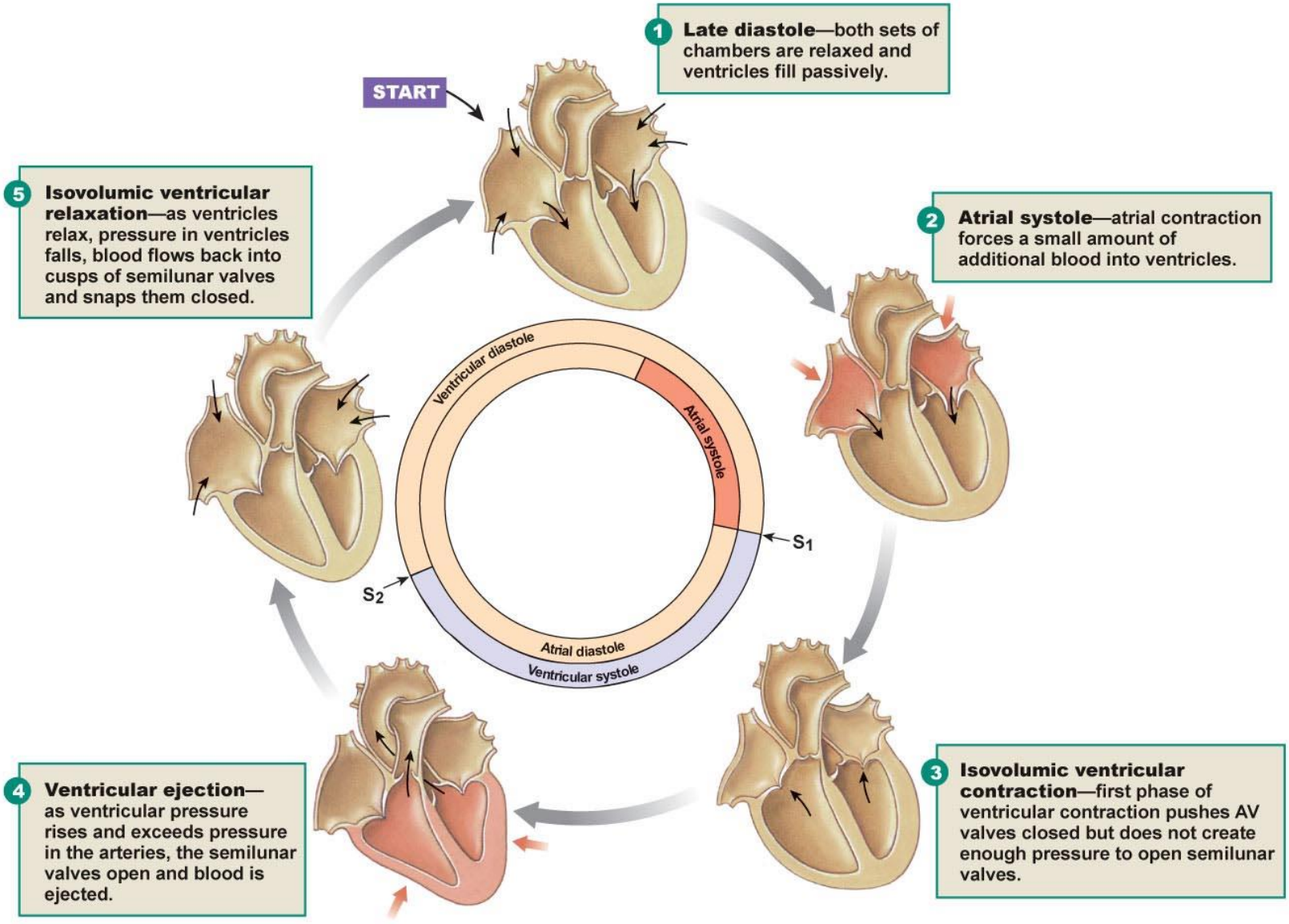


Cardiac Cycle

- **Cardiac cycle**
  - Sequence of events
  - Blood enters the atria → leaves the ventricles → starts over
- **Synchronization**
  - Intrinsic Electrical Conduction System
- **Influencing the rate**
  - Sympathetic and parasympathetic divisions of the ANS
- **Phases**
  - Alternating periods of systole and diastole
    - Systole = period of contraction
    - Diastole = period of relaxation

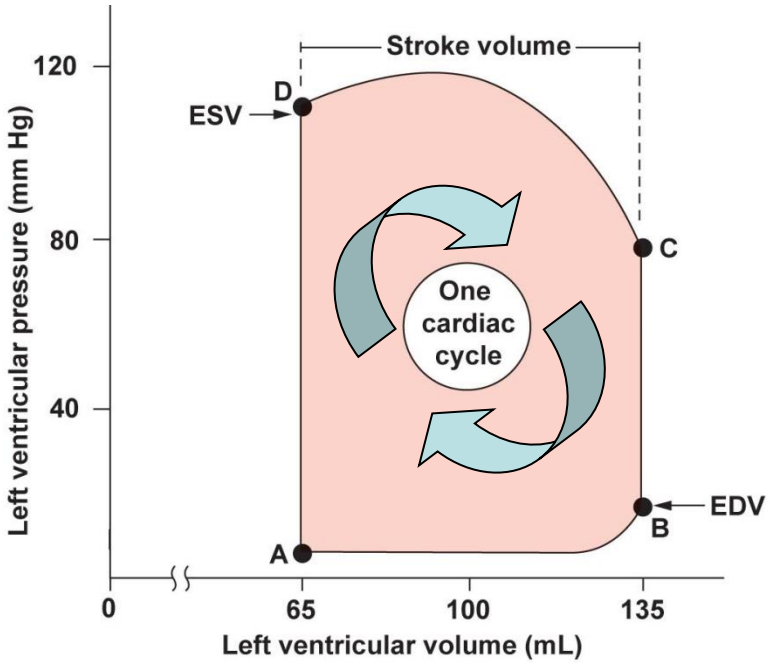


Cardiac Cycle



Cardiac Output (CO)

- **Cardiac Output (CO) = the volume pumped by the left ventricle each minute**
  - Influenced by
    - Stroke Volume (SV)
      - SV = EDV – ESV
      - 135ml – 65ml = 70ml
    - Heart Rate (HR) bpm
      - 80 bmp
  - CO = SV x HR
    = 70 ml/beat x 72bpm = 5040 ml/min
    = 5.04 L/min
- **How is this controlled to account for changing conditions? (exercise, disease, stress…)**
  - Autonomic Nervous System
  - Extrinsic factors (other than ANS) include
    - blood vessels & blood pressure
    - blood volume & viscosity
    - capillary exchange & the lymphatic return
    - cardiovascular disease



ESV: End Systolic Volume
EDV: End Diastolic Volume

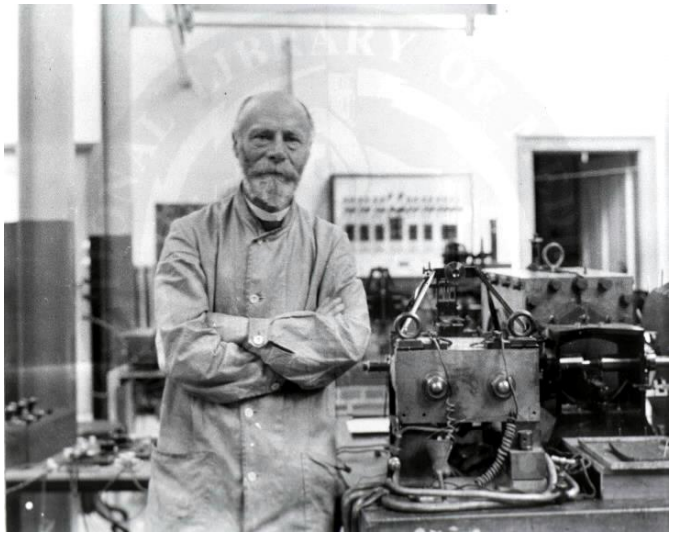
Electrocardiogram (ECG)

- **Electrocardiogram**
  - Paper or digital recording of the electric current produced by the heart which reaches the skin
  - Simple and safe exam
  - Determines further work-up with more specific and expensive exams (e.g. stress-test, ultrasound, etc.)

Electrocardiogram (ECG)

History of the ECG

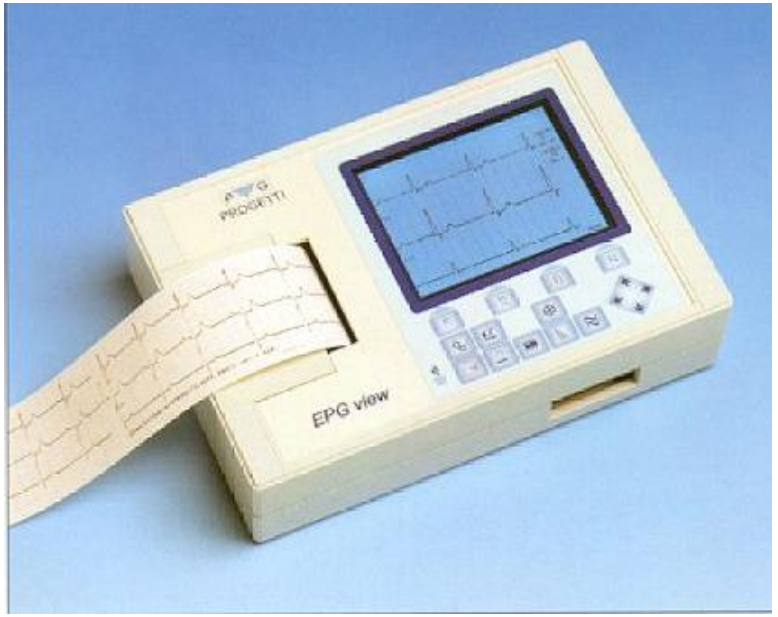
- **ECG from the hospital to Eindhoven's lab, 1.5 km away, via telephone cable.**
- **March 22, 1905 the first "tele-cardiogram" was recorded**
  - A healthy young man
  - Displayed large R waves probably because he had to bike from the lab to the hospital
- **Nobel Prize (1924)**
- **That initial research remains the basis of electrocardiography**

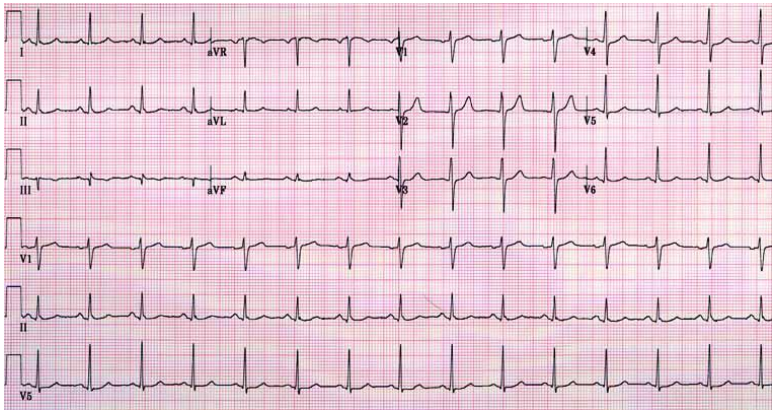


- **Eindhoven's terminology is still used today**
  - "electrocardiogram"
  - P, Q, R, S, T waves

Electrocardiogram (ECG)

- **Performed for many reasons**
  - Precautionary (over 40 year olds)
  - Chest pain
  - Tachycardia
  - Drugs active on the heart
  - Pacemaker (to check for the correct pacing)
- **Anomalies can lead to at least 12 different pathologies that need further investigation**
- **ECG - applications**
  - Diagnostics
  - Functional analysis
  - Implants (pace maker)
  - Biofeedback (Heartrate variability, HRV)
  - Peak Performance Training, Monitoring

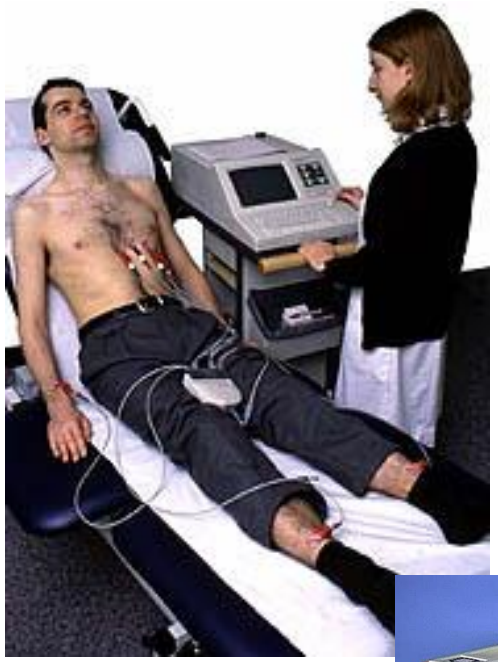


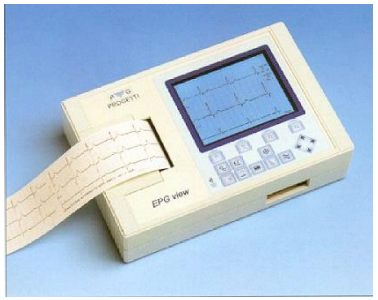


Electrocardiogram (ECG)

Electrocardiograph

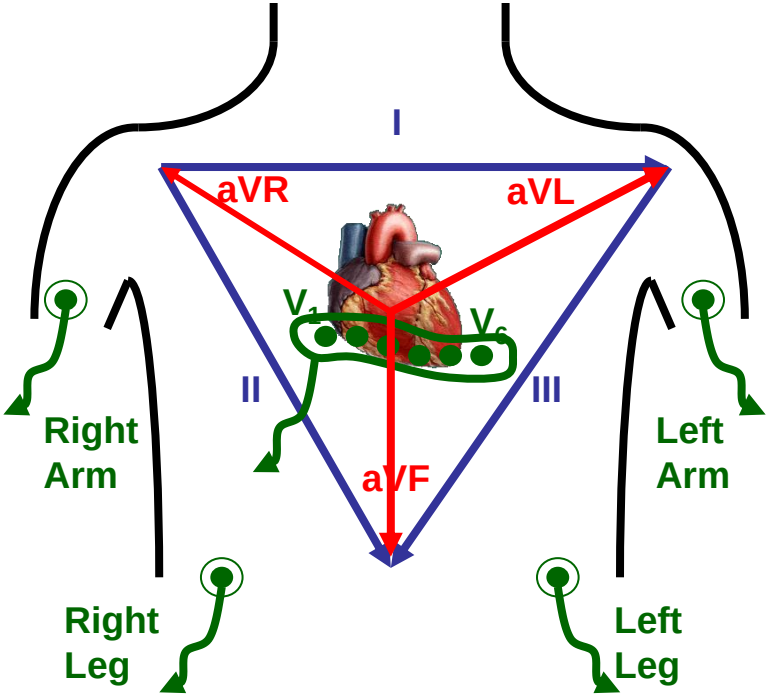
- **A sensitive voltmeter**
  - Records, via electrodes, the potential differences on the surface of the body which are a result of cardiac activity
- **Consists of**
  - A central unit
  - 10 electrodes connected on the patient's body
    - 4 connected on the limbs
    - 6 on the front of the thorax
- **The ECG is recorded digitally and often printed**
  - The horizontal axis corresponds to time and the vertical to potential



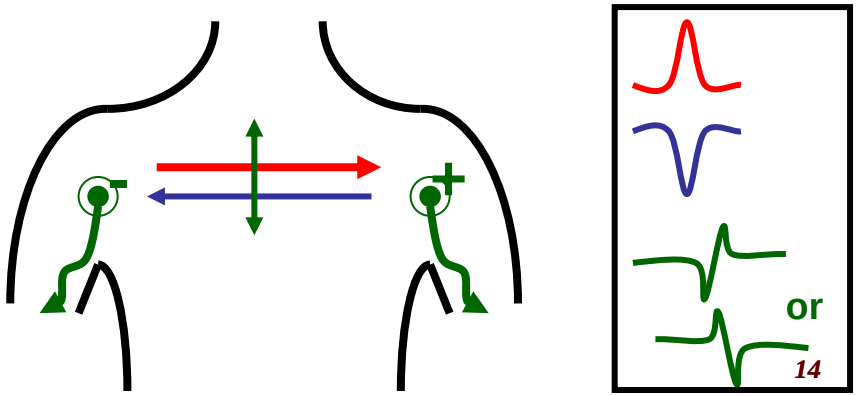


Electrocardiogram (ECG)

- **Leads**
  - 12 leads from 10 electrode
    - Summing of signals from particular electrodes
  - 6 leads from the limbs (classic)
    - Electric potentials which reach the limbs
    - I, II, III, aVR, aVL, aVF
  - 6 precordial leads
    - Electric potential from the front surface of the chest
    - V1, V2, V3, V4, V5, V6
  - 12 leads are now considered obsolete
    - Three leads are usually more than enough

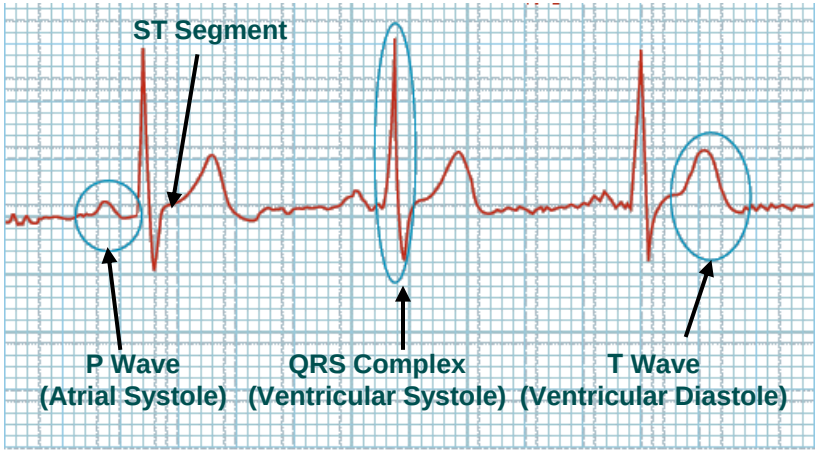


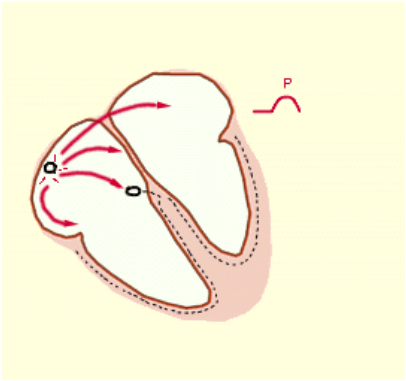
- **Depolarization Wave**
  - From the negative to the positive electrode → positive deflection
  - From the positive to the negative electrode → negative deflection
  - Vertical to the lead → biphasic deflection



Electrocardiogram (ECG)

- **Parts of the ECG**
  - Depolarization of the sinoventricular node and the atria → P wave
  - His bundle and depolarization of the ventricles → QRS complex
  - Repolarization of the ventricles → T wave
  - Between the depolarization and repolarization of the ventricles → isoelectric line, the ST segment

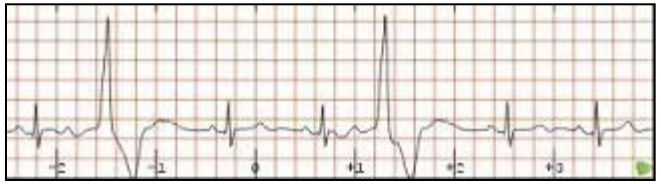




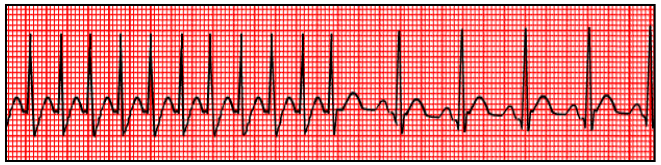
Electrocardiogram (ECG)

Abnormal Rhythms

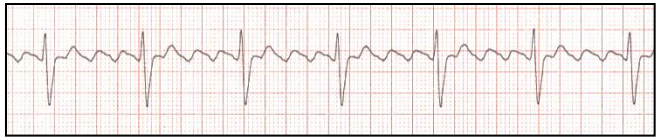
- **Ectopic beat**
  - The ventricular myocardium becomes hyper-excitable and contracts on its own



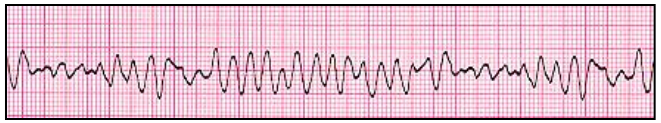
- **Tachycardia**
  - The heart beats too fast



- **Atrial flutter**
  - The atria contact too fast (faster than the ventricles can follow)



- **Ventricular fibrillation**
  - The ventricles contract too fast and unorganized (syncope)

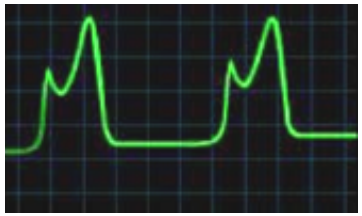


Electrocardiogram (ECG)

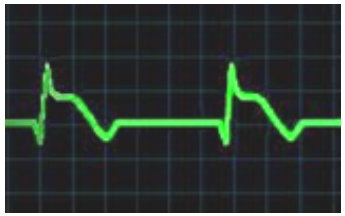
Myocardial Infraction (Heart Attack)

- **MI Diagnosis**
  - ECG
  - Blood enzymes
- **ECG**
  - ST segment elevation the first hours which subsides over time and is followed by T wave inversion
- **Region localization**
  - MI of the lower wall
    - Changes in: II, III and AVF
  - Frontal MI
    - Changes in: V1-V6
  - Side MI
    - Changes in: I, AVL,V5,V6
  - Rear MI
    - Changes in: V1-V3

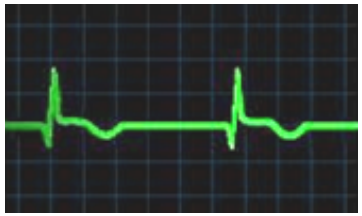
Hyperacute Phase



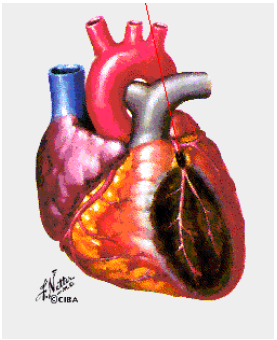
Acute Phase

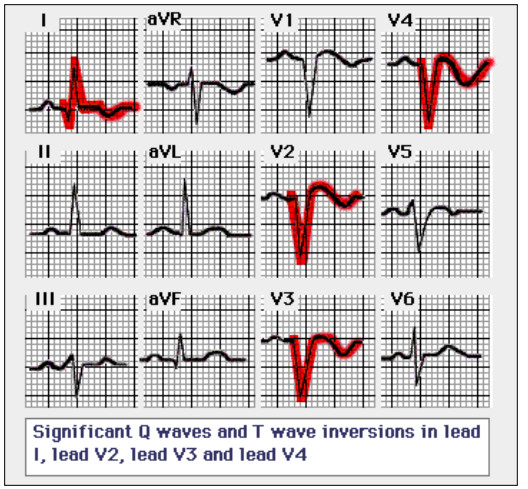


Recovery Phase



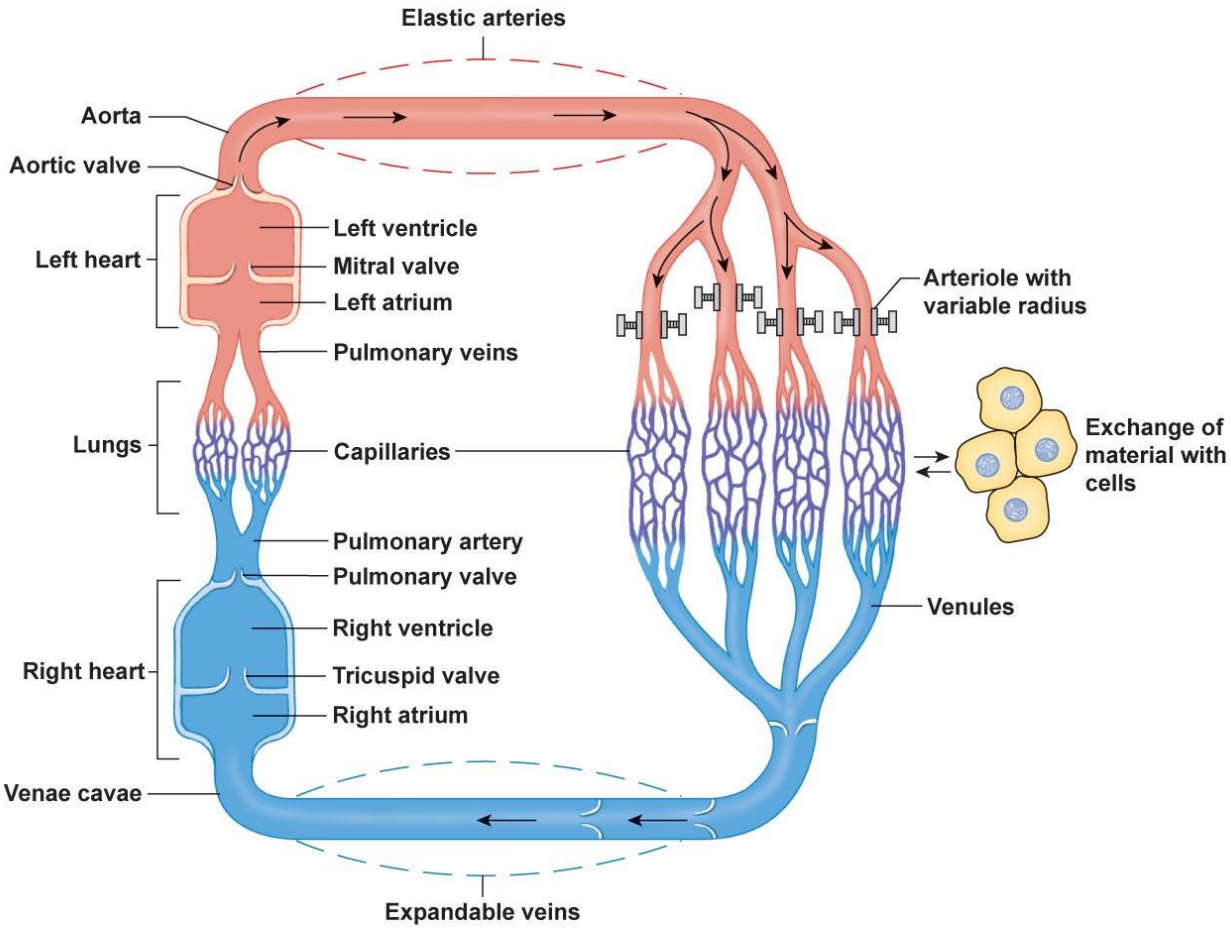
Chronic Phase





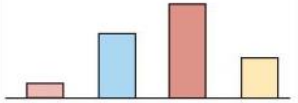
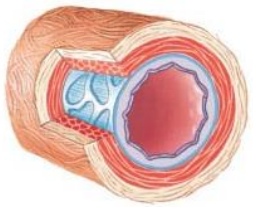
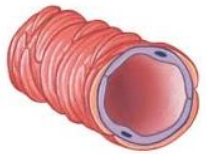
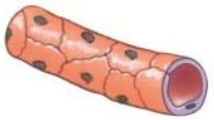
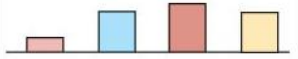
Blood Flow & Pressure Controls

- **Blood Vessels Function to**
  - Provide route (arteries – away, veins – return)
  - Allow for exchange (capillaries)
  - Control & regulate blood pressure



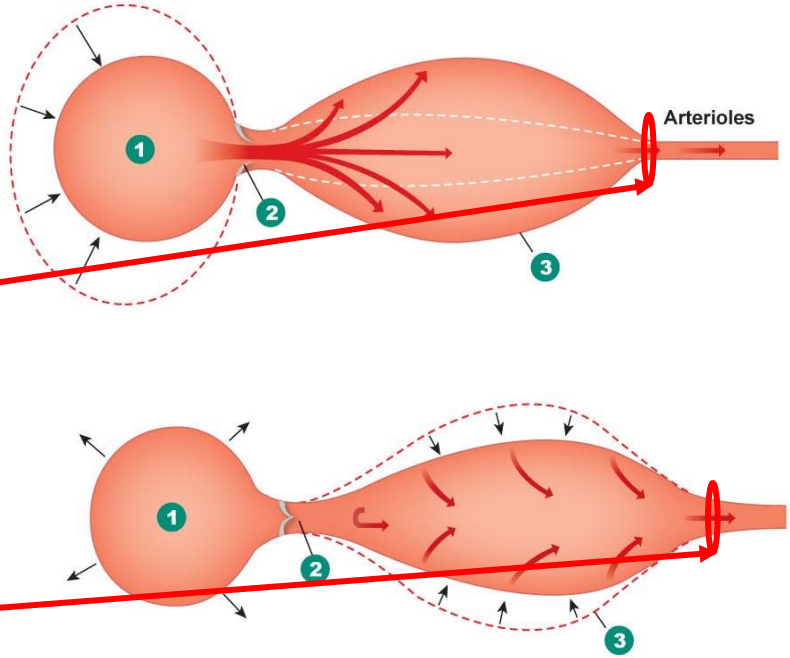
Blood Flow & Blood Pressure Controls

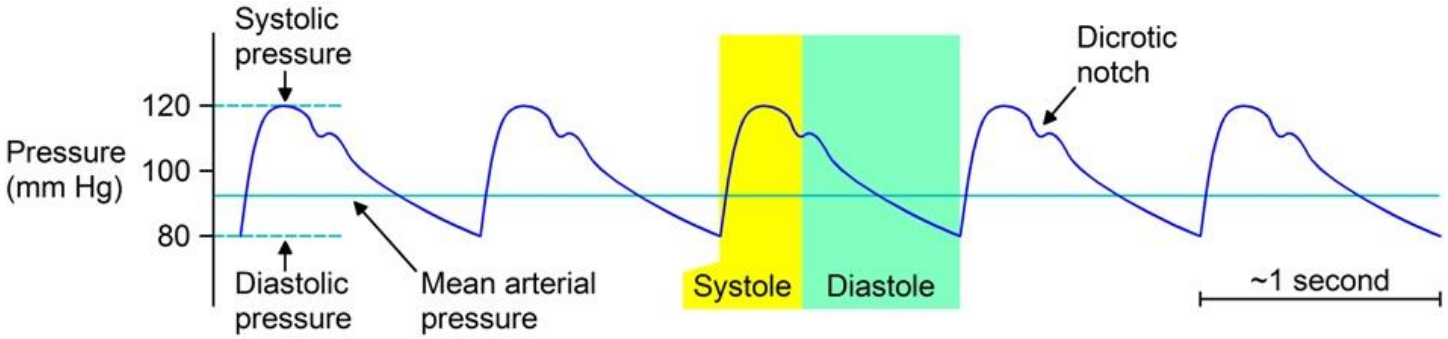
- **Blood Vessel Structure enables specific functions**
  - Aorta
    - absorb pulse pressure (systolic pressure – diastolic pressure) and release energy
  - Large arteries
    - conduct and distribute blood to regional areas
  - Arterioles
    - Regulate flow to tissues
  - Capillaries
    - Allow for exchange
  - Venules
    - Collect and direct blood to the veins
  - Veins
    - Return blood to heart and act as a blood reservoir

	Mean diameter	Mean wall thickness	Endothelium / Elastic tissue / Smooth muscle / Fibrous tissue	
Artery	4.0 mm	1.0 mm		
Arteriole	30.0 μm	6.0 μm		
Capillary	8.0 μm	0.5 μm		
Venule	20.0 μm	1.0 μm		
Vein	5.0 mm	0.5 mm		

Blood Flow & Blood Pressure Controls

- **Blood Vessels & Blood Pressure**
  - Systolic Pressure
    - The pressure that is created when the ventricles contract
    - Usually around 120 mm Hg
  - Diastolic Pressure
    - The pressure that is created by the recoil of the aorta AND the closure of the aortic semilunar valve
    - Usually around 80 mm Hg



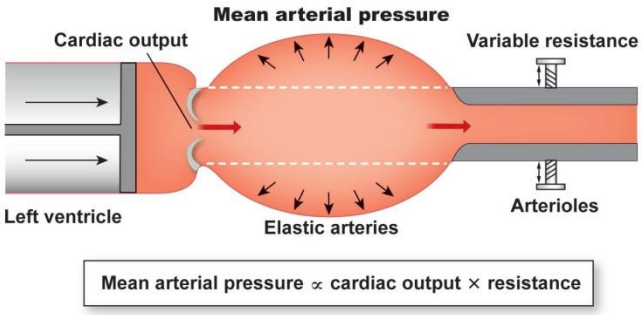


Blood Flow & Pressure Controls

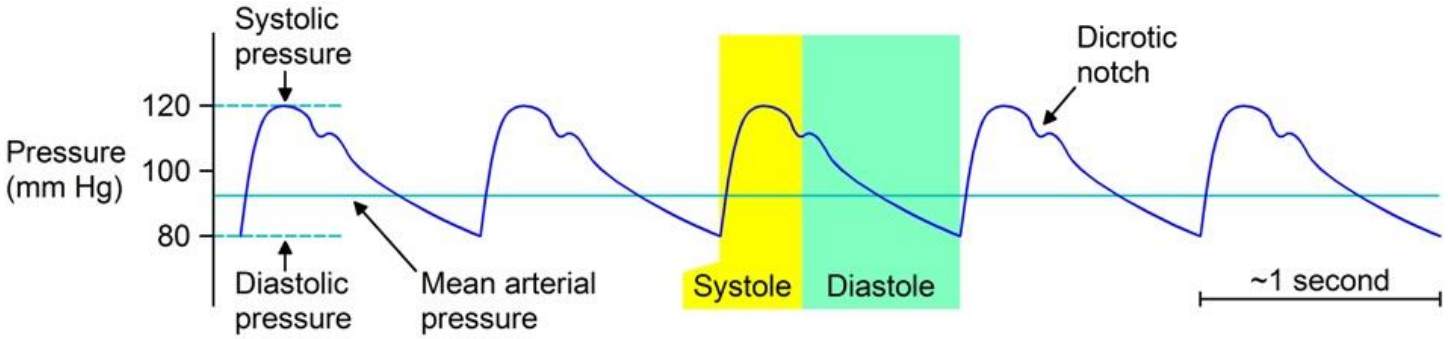
- **Blood Vessels & Blood Pressure**
  - Pulse Pressure
    - The difference between the systolic and diastolic pressures
      - Usually 40 mm Hg (120 mm Hg – 80 mm Hg)
    - Only applies to arteries
  - Mean Arterial Pressure (MAP) = the average pressure within the arterial system
    - MAP = diastolic Pressure + 1/3 Pulse Pressure
    - MAP = 80 mm Hg + 1/3(120 mm Hg – 80 mm Hg) = 93 mm Hg
    - Proportional to the cardiac output and the amount of peripheral resistance
      - Resistance = the opposition to blood flow in the arterioles

$$R \propto L\,\eta/r^4 \propto 1/r^4 \quad (L \text{ and } \eta \text{ relatively constant})$$

L = length of the vessel, η = viscosity of the blood, r = vessel radius

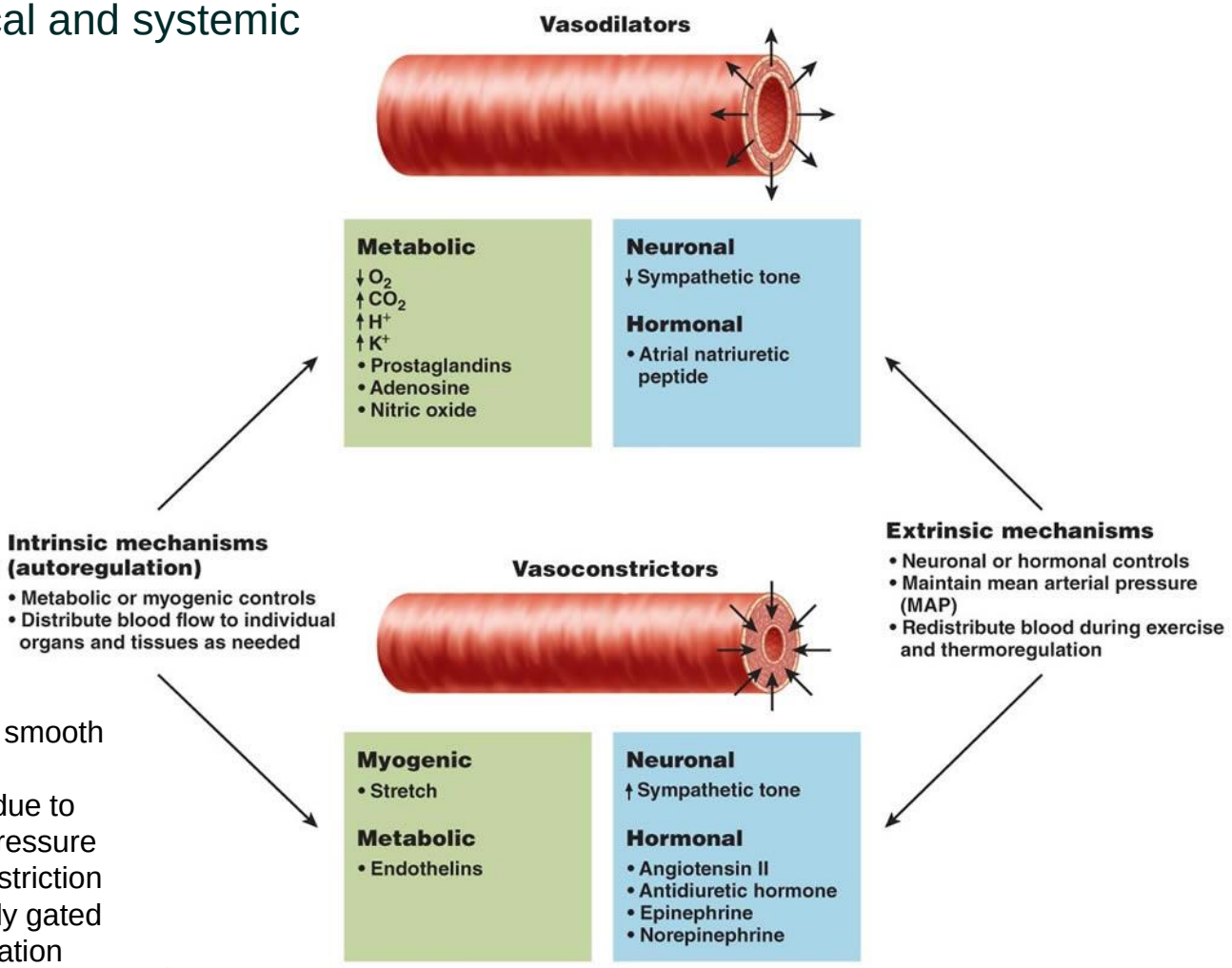


  - Why do we care about systolic, diastolic, and pulse pressures?
    - Then we can determine general health of the cardiovascular system



Blood Flow & Pressure Controls

- **The controls of vessel diameter enables tissues to control their own blood flow**
  - Both local and systemic

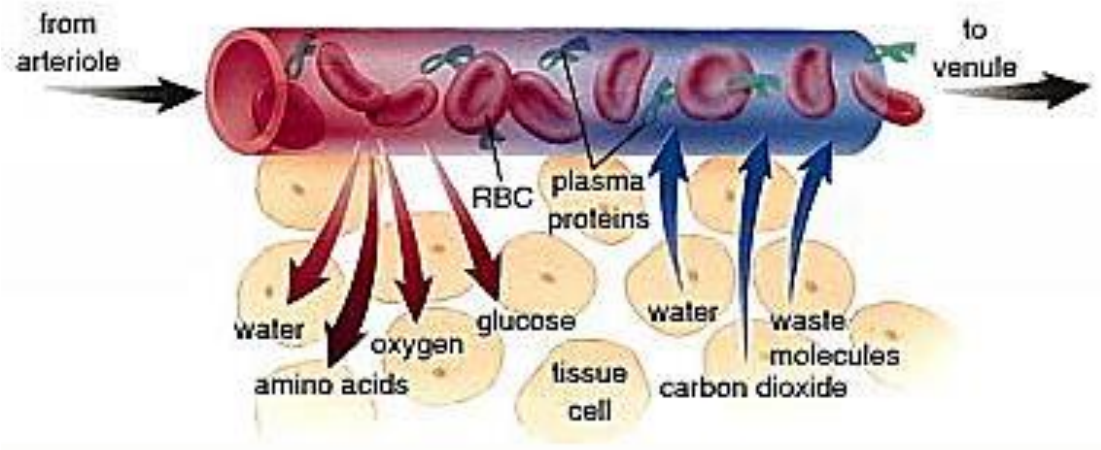


Myogenic response by smooth muscle of arterioles

- Increased stretch due to increasing blood pressure causes vessel constriction due to mechanically gated Ca^{2+} channel activation

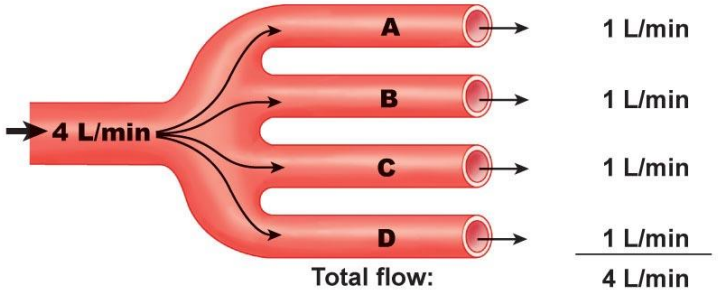
Capillary Exchange

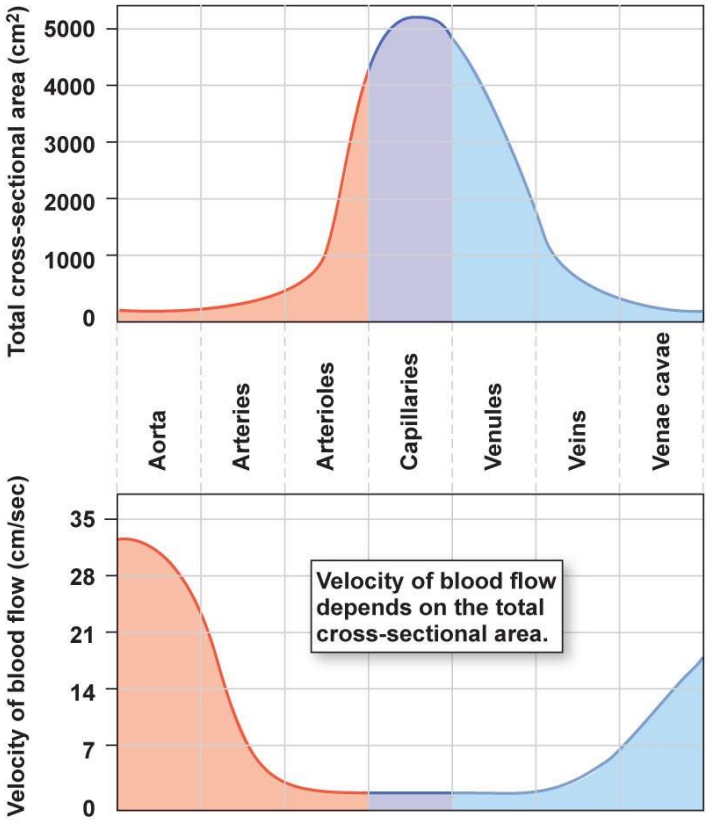
- **Exchange of material**
  - Blood ↔ tissue
  - Takes place at the level of the capillaries
  - Factors affecting the exchange of material
    - Velocity
    - Exchange Processes
    - Pressure



Capillary Exchange

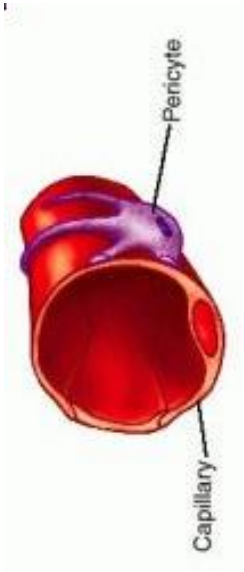
- **Velocity of blood flow**
  - Influenced by volume and diameter
  - Velocity drops in the capillaries (increased number of vessels, increased total cross-sectional area)
  - ↓ velocity → ↑ exchange

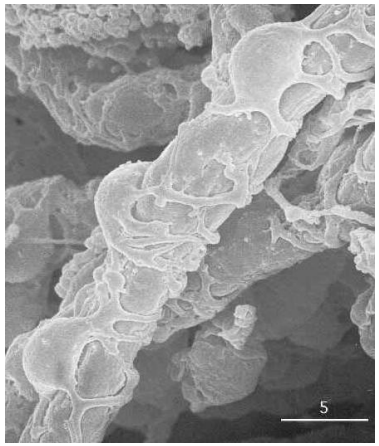


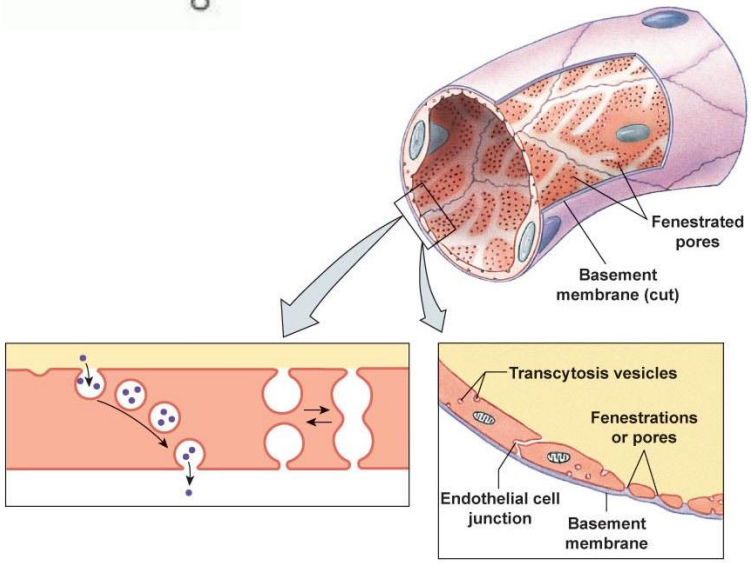


Capillary Exchange

- **Exchange Processes**
  - Diffusion is affected by
    - Surface area for diffusion
      - 6300 m^2 (two football field surfaces)
      - Result of the large cross-sectional area and length of capillaries (~50,000 miles)
    - Membrane permeability
      - Different capillaries have differing permeability's
        - Continuous vs. Fenestrated
        - Also influenced by surrounding cells
  - Diffusion of smaller molecules between the cells
    - paracellular pathway
  - Diffusion of larger molecules through the cells via
    - endothelial transport (transcytosis)

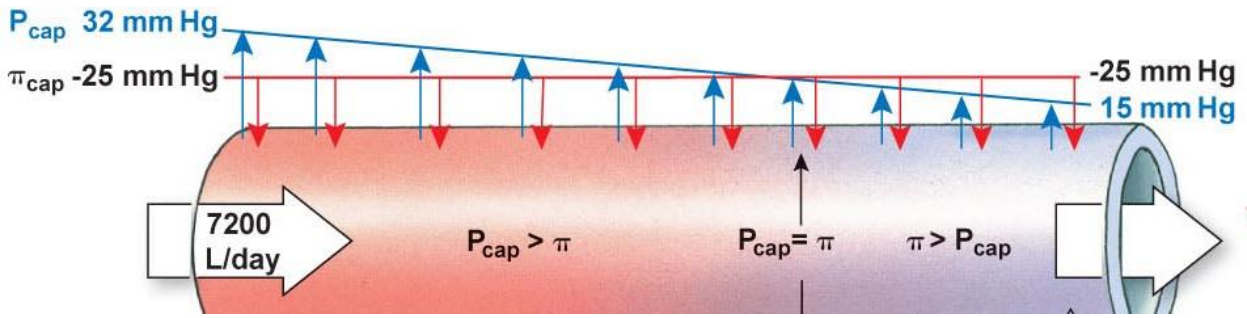






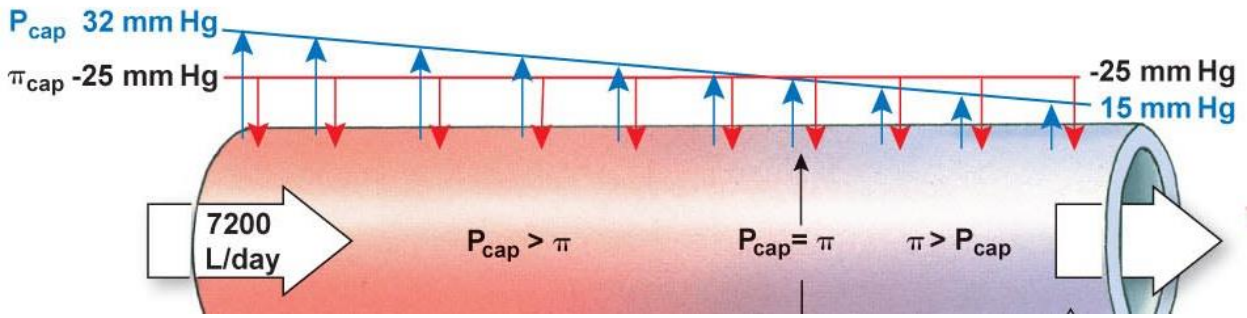
Capillary Exchange

- **Pressures**
  - Capillary hydrostatic pressure (P_{cap})
    - Created by the fluid pressure of blood entering the capillaries
    - Variable throughout the length of the capillary
      - highest on arteriole end (32 mm Hg)
      - lowest on venule end (15 mm Hg)
    - Filtration Force → Moving fluid out of the capillary
    - Interstitial fluid hydrostatic pressure (P_{IF}) is 0 mm Hg
      - No filtration pressure moving fluid back into the capillary
    - The capillary hydrostatic pressure (P_{cap}) is the outward filtration pressure



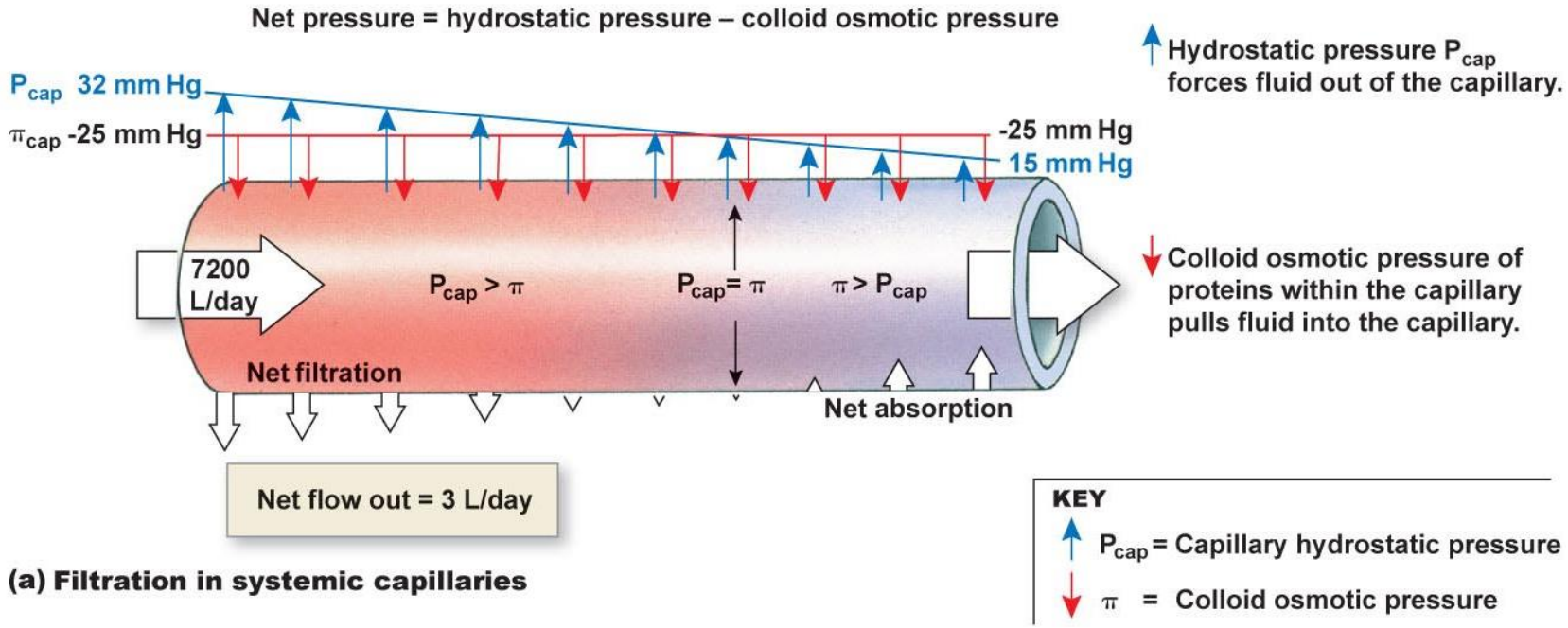
Capillary Exchange

- **Pressures**
  - Colloidal osmotic pressures (π)
    - Created by the "solids" in the blood that are not capable of crossing through the capillary.
    - π_{cap} remains constant
    - Absorption → Moves fluid back into the capillary
    - The interstitial colloid osmotic pressure (π_{IF}) should be 0 mm Hg
    - This makes colloidal osmotic pressure in the capillary a reabsorption pressure



Capillary Exchange

- **All the major factors**
  - Filtration Pressure (ΔP_{out}) is equal to the change in capillary hydrostatic pressure $\Delta P_{out} = (P_{cap} - P_{IF})$
  - Absorption Pressure ($\Delta \pi_{in}$) is equal to the change in colloid osmotic pressure $\Delta \pi_{in} = (\pi_{IF} - \pi_{cap})$
- **Coming together to create**
  - Net Pressure = ΔP_{out} - $\Delta \pi_{in}$



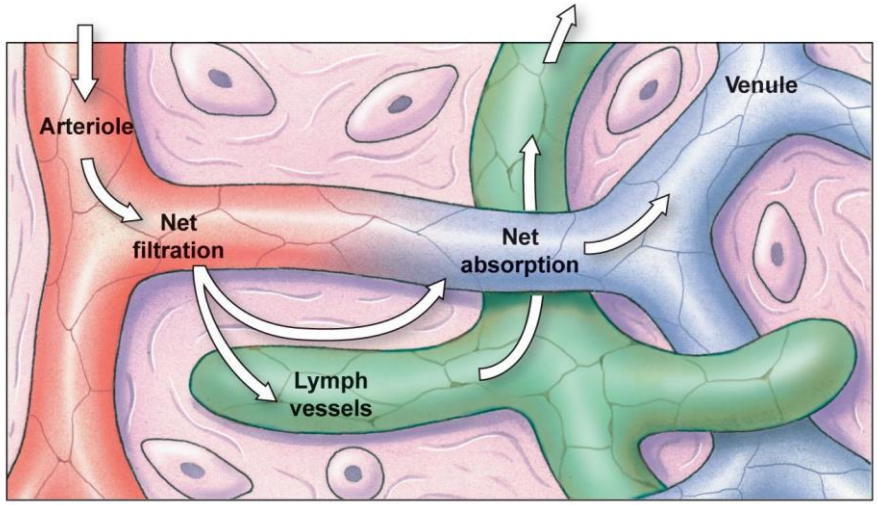
(a) Filtration in systemic capillaries

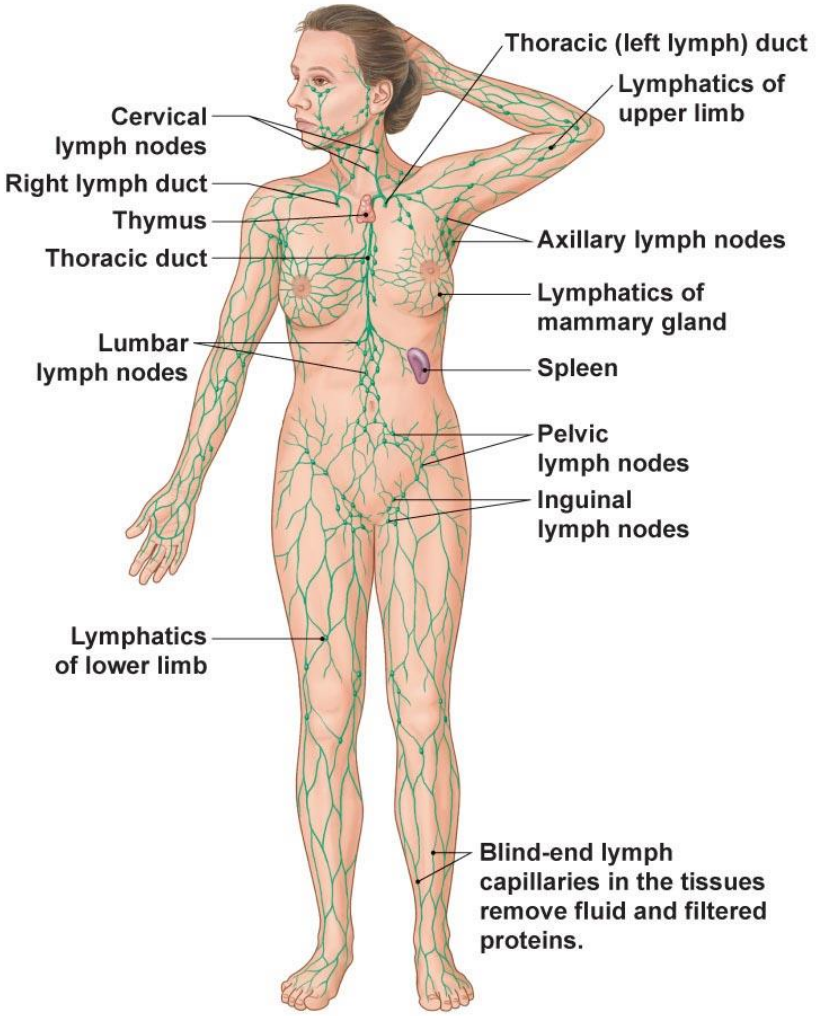
Capillary Exchange

- **The Net Pressure will change in a gradient along the length of the capillary.**
  - Net Pressure $_{\text{arterial end}}$
    $= (P_{cap} - P_{IF}) + (\pi_{cap} - \pi_{IF})$
    $= (32 \text{ mm Hg} - 0 \text{ mm Hg}) + (0 \text{ mm Hg} - 25 \text{ mm Hg}) =$
    $= (32 \text{ mm Hg} + -25 \text{ mm Hg}) = 7 \text{ mm Hg}$
    - This is a filtration pressure
  - Net Pressure $_{\text{venous end}}$
    $= (P_{cap} - P_{IF}) + (\pi_{cap} - \pi_{IF})$
    $= (15 \text{ mm Hg} - 0 \text{ mm Hg}) + (0 \text{ mm Hg} - 25 \text{ mm Hg}) =$
    $= (15 \text{ mm Hg} + -25 \text{ mm Hg}) = -10 \text{ mm Hg}$
    - This is a reabsorption pressure
- **Net pressure at the two ends is not the same!**
  - This means there is a net loss of capillary fluid to the interstitial fluid on a constant basis
  - Where does the excess fluid of 3 L/day go?

The Lymphatic System

- **Fluid gained in the interstitial space**
  - Filtration force > reabsorption force
  - Returned by the lymphatic system
    - Collects the excess fluid “lymph” and returns it to venous circulation
- **Other functions of the lymphatic system**
  - Absorbs and transports fats from the GI tract
  - Filters the returning fluid for purposes protection
    - Immune cells at the lymph nodes



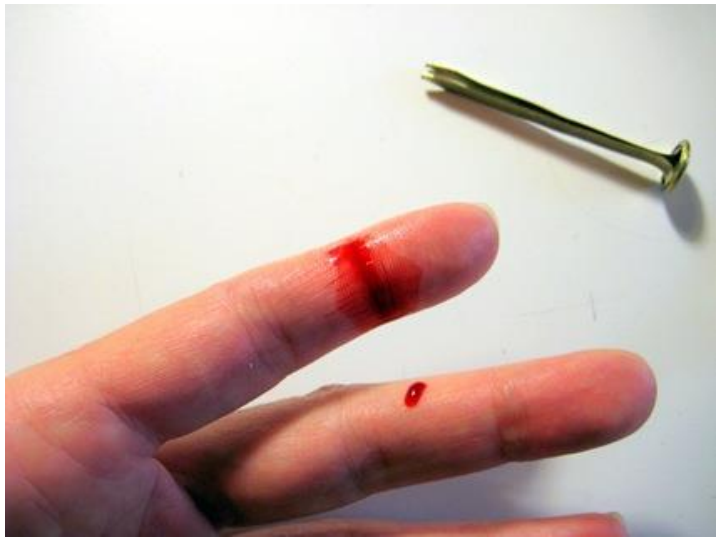


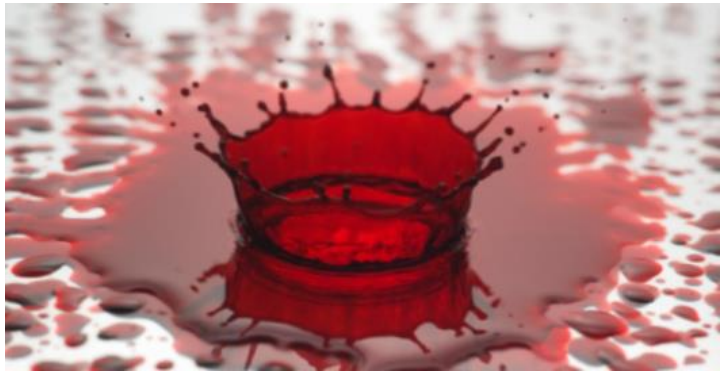
Blood


www.johnshakespeare.com.au
GIVE
BLOOD
NOW!
ASK ME HOW!
SHAKESPEARE

General Functions

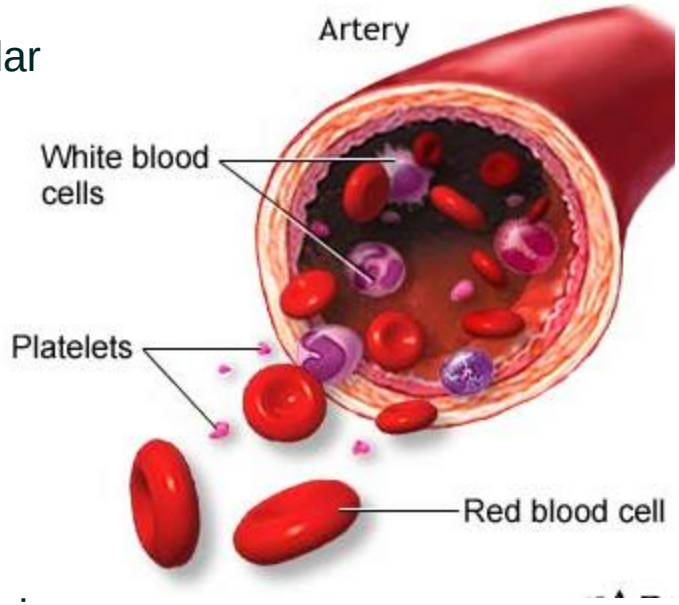
- **Functions as:**
  - a transport medium
    - Gases
    - Nutrients
    - Chemical messengers
    - Heat
    - Wastes
  - a protective medium
    - Platelet activation
    - Coagulation
    - Adaptive Immunity
    - Non-specific defenses
  - a regulatory medium
    - pH
    - Temperature
    - Volume/Cell Count
  - a hydraulic medium
    - Movement of tissues
    - Filtration force

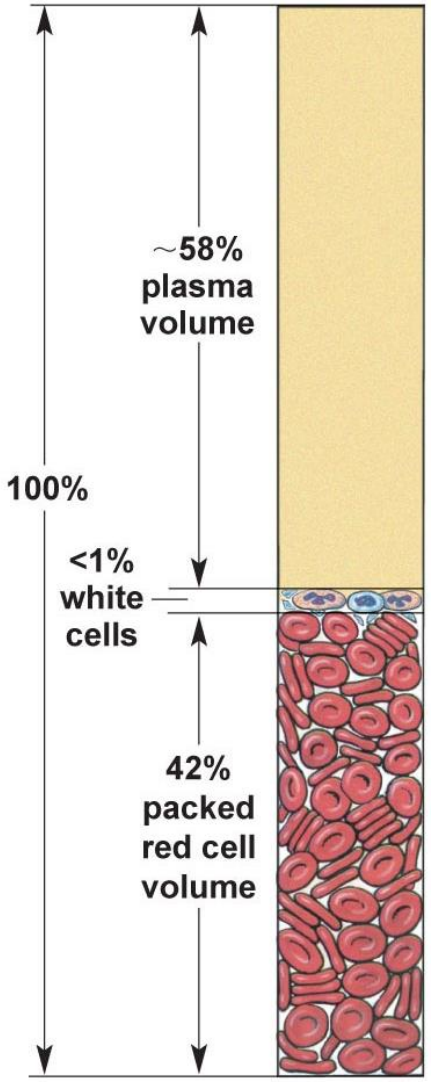




Components

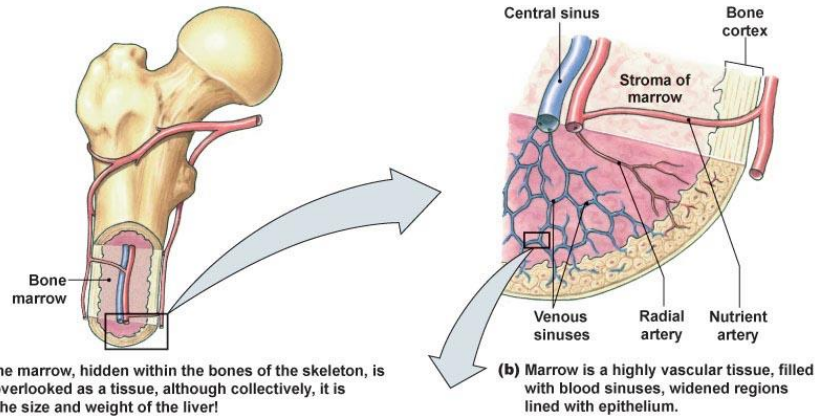
- **Whole blood is divided into**
  - Formed elements (45%)
    - Erythrocytes
    - Leukocytes
    - Platelets
  - Plasma (55%) - Extracellular matrix composed of
    - Water
    - Ions
    - Organic molecules
      - Amino acids
      - Proteins
        - Albumins
        - Globulins
        - fibrinogens
      - Glucose
      - Lipids
      - Nitrogenous wastes
    - Trace elements and vitamins
    - Gases
      - CO_2
      - O_2





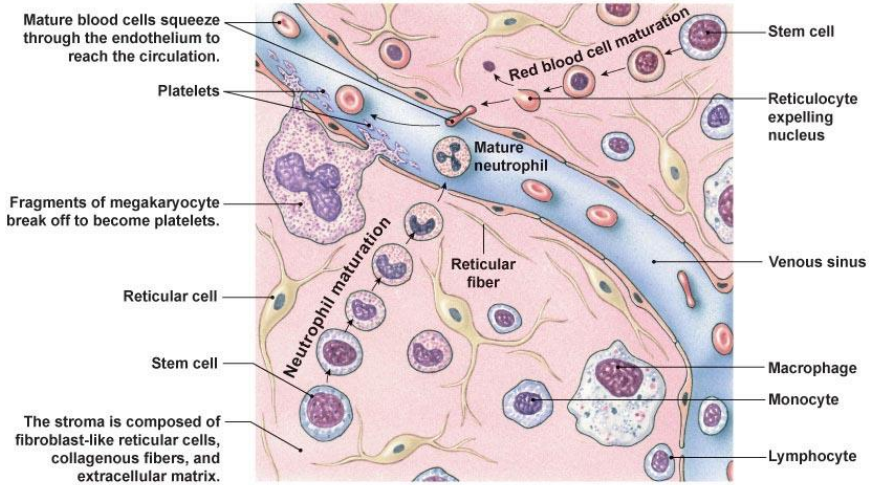
Production & Function of Blood Cells

- **Production of blood cells is called hematopoiesis**
- **All blood cells differentiate from a pluripotent stem cell**
  - Pluripotent = already partially differentiated = produces blood cell types
  - This process occurs in bone marrow
    - Mainly in the epiphyses (ends) of long bones and in the flat bones (sternum, ribs, ilium)
- **Rate is influenced by hormones**
  - EPO (erythropoietin)
    - Produced in the kidney
    - Increases production of erythrocytes
  - TPO (thrombopoietin)
    - Produced in the liver
    - Increases production of blood clotting cells



(a) The bone marrow, hidden within the bones of the skeleton, is easily overlooked as a tissue, although collectively, it is nearly the size and weight of the liver!

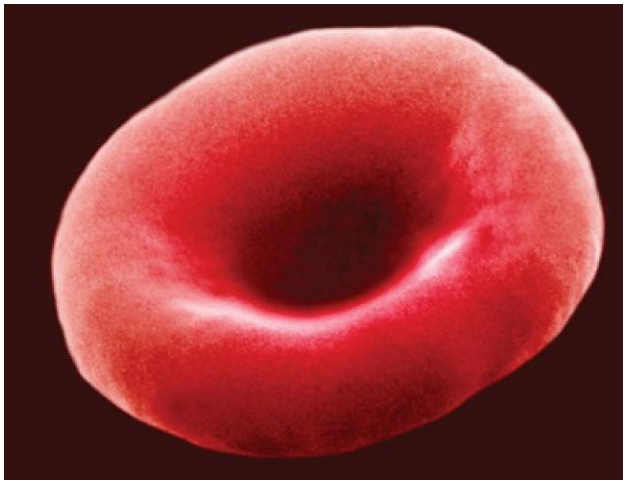
(b) Marrow is a highly vascular tissue, filled with blood sinuses, widened regions lined with epithelium.

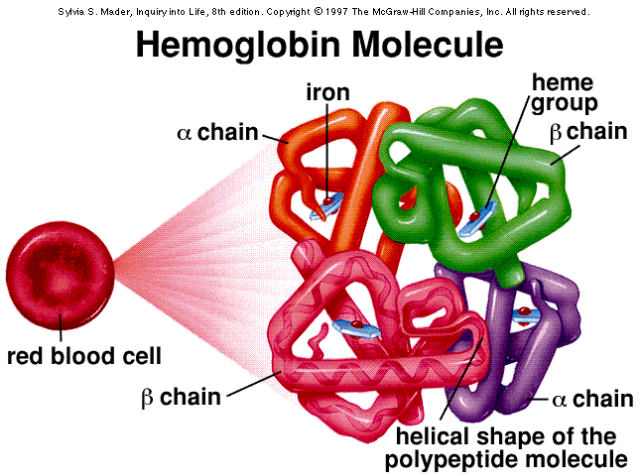


(c) Bone marrow consists of blood cells in different stages of development and supporting tissue known as the **stroma** [mattress].

Red Blood Cells

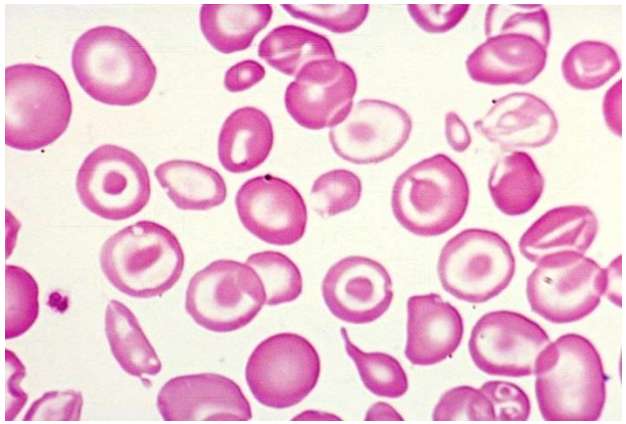
- **Specialized aspects:**
  - Biconcave shape
    - ~8 μm diameter
    - Due to cytoskeletal structure
    - Aids in movement through capillaries and allows them to maintain integrity even as osmotic pressures vary
      - Swelling vs. shrinking
  - Contain and transport hemoglobin (Hb)
    - 97% of the content of a mature RBC
    - 280 million hemoglobin molecules/cell
    - Each Hb molecule carries 4 oxygen molecules
    - Increases the O_2 carrying capacity of blood by about 70 times!
  - Life and death
    - RBCs live for 120 days and are recycled in the liver and spleen

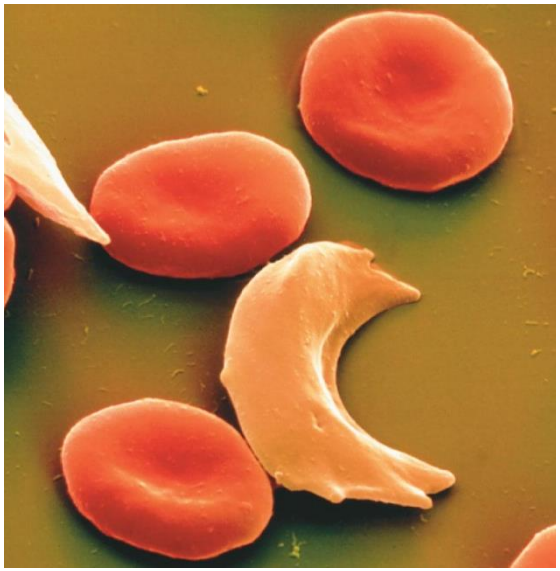




Anemia

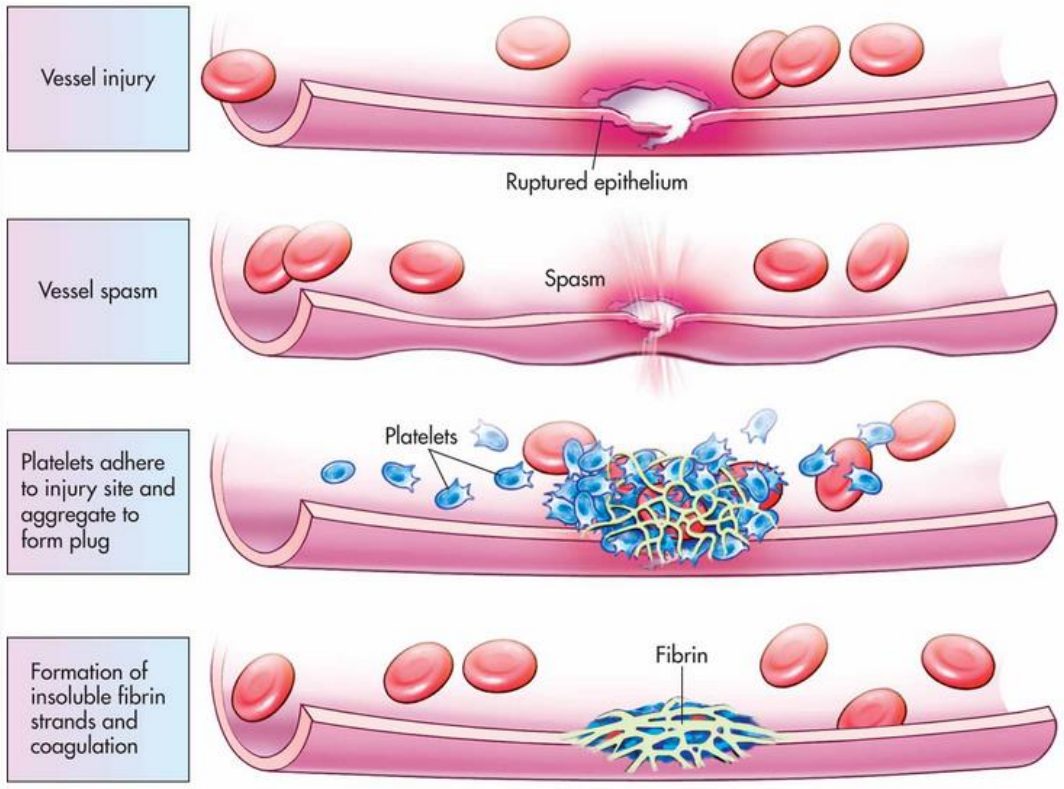
- **Reduction in O_2 carrying capacity in blood because of low Hb content.**
- **RBC damage and loss from**
  - Blood loss
  - Thalassemia
    - Ineffective production of Hb
  - Hemolytic anemia – cells bursting, may be
    - Hereditary such as
      - Sickle cell anemia
      - Spherocytosis
    - Acquired
      - Parasitic issue – malaria, dengue fever
      - Drugs
      - Autoimmune
  - Destruction of RBCs → excess Fe
- **Reduced capacity for RBC production**
  - Aplastic anemia – cells don't form correctly
  - Loss/lack of iron (needed for Hb synthesis)
  - Deficiency in folic acid (needed for DNA production)
  - Deficiency of Vit B12 (needed for DNA production)
    - May be a result of lack of intrinsic factor – needed for B12 absorption
  - Low EPO production





Hemostasis

- **Preventing blood loss occurs in a few steps**
  - Vasoconstriction
    - Reduces blood flow and pressure in damaged vessel
      - Damage releases paracrines that cause immediate constriction of smooth muscle
  - Platelet Plug Formation
    - The process of forming a physical plug to stop blood loss
  - Clot formation (coagulation cascade)
    - Forms a clot (fibrin polymer)

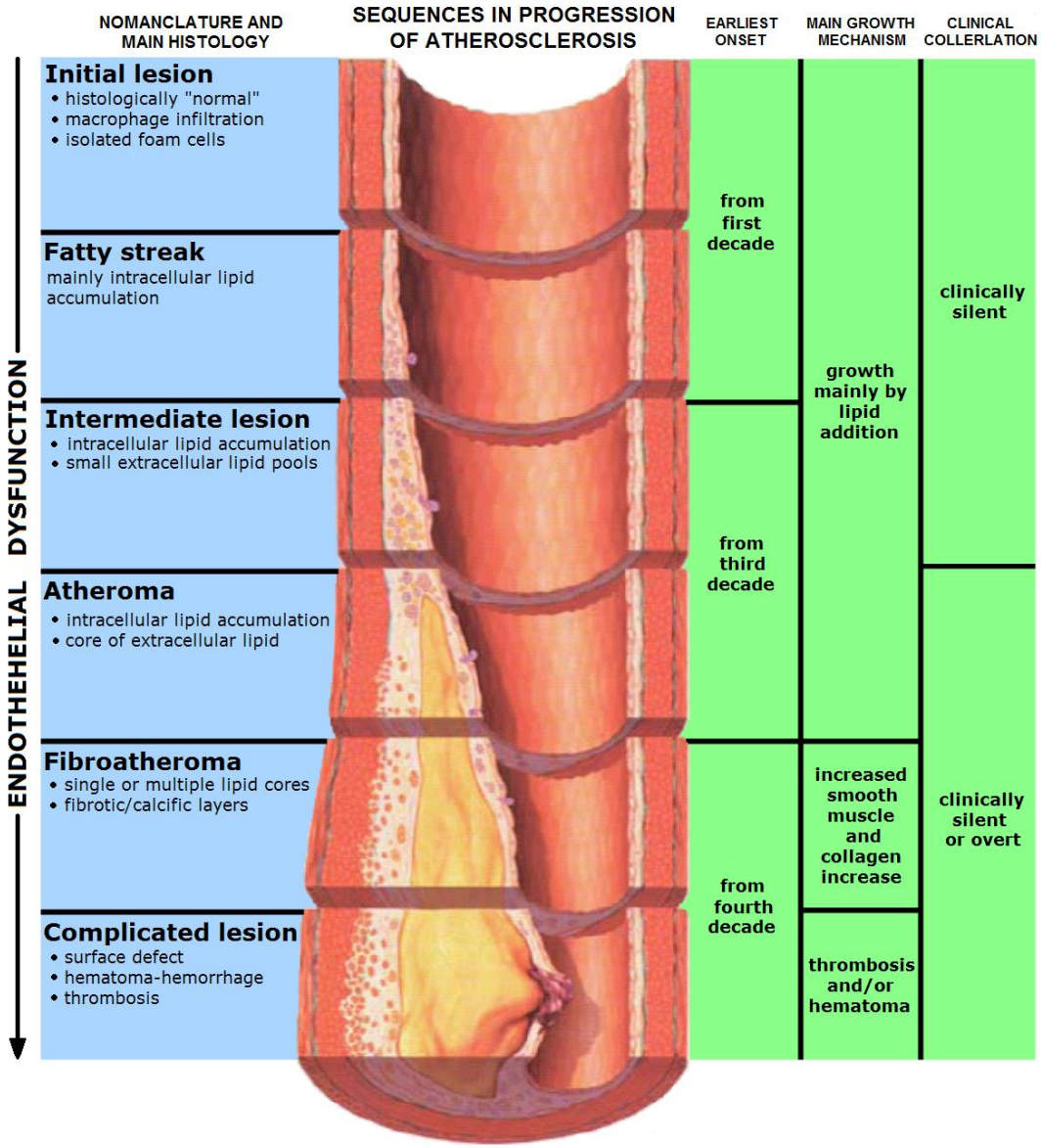


Diseases & Disorders

- **Greater than 50% of the deaths in the U.S. have links to cardiovascular disease!**
  - Net cost is around $450 billion
- **What are the risk factors for CVD?**
  - Controllable
    - Smoking & Obesity
    - Activity level
    - Untreated hypertension
  - Uncontrollable
    - Familial history (genetics)
    - Age & Gender
      - early on males in more danger later in life it equalizes

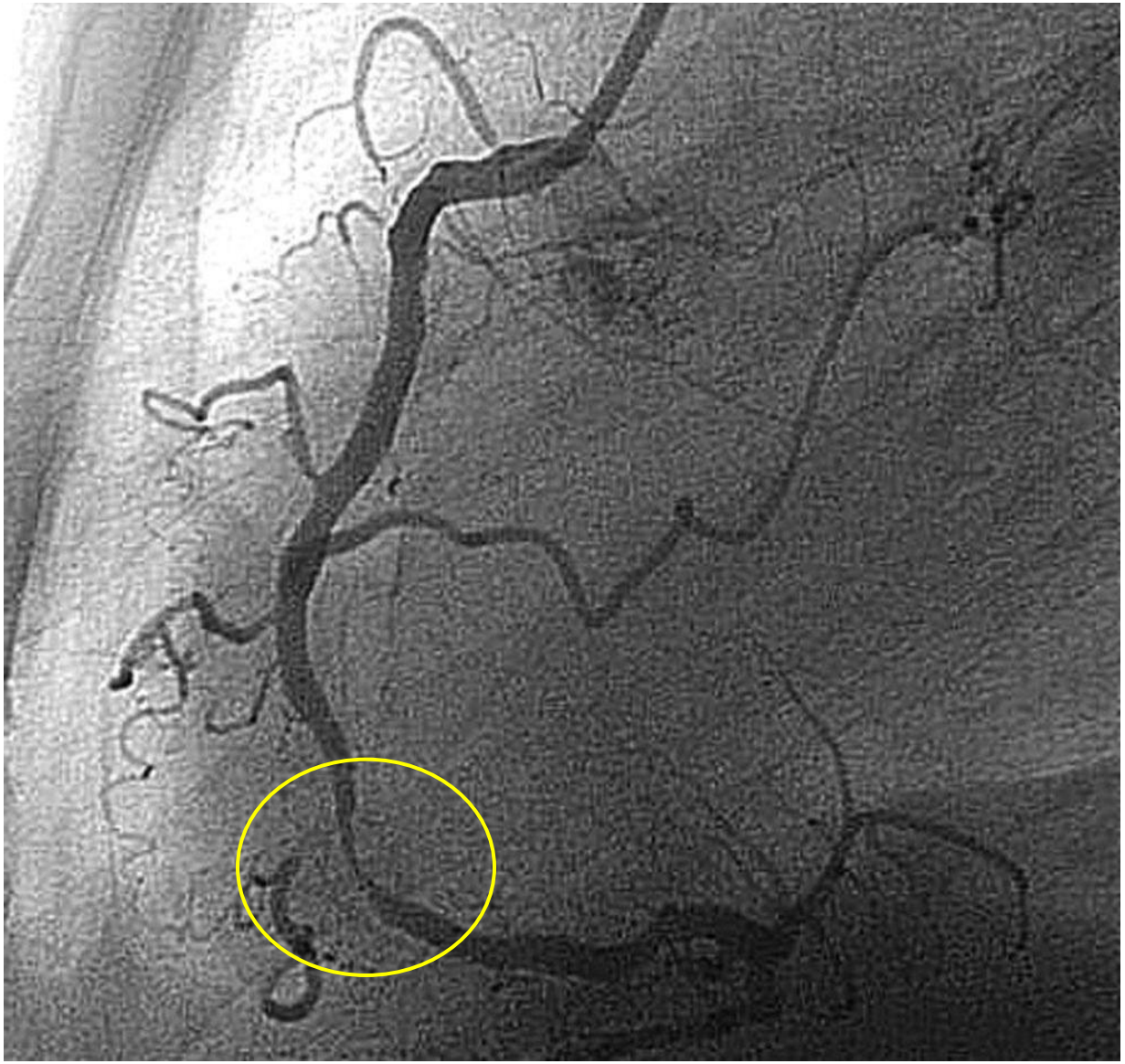
Diseases & Disorders

- **Atherosclerosis**
  - Artery wall thickens as a result of the accumulation of calcium and fatty materials such as cholesterol and triglyceride.
- **Fatty streak**
  - Smooth muscle cells, which are filled with cholesterol, and macrophages
  - Fatty streaks alone does not cause any symptoms but, over time, can develop into a more advanced form
  - First evidence of atherosclerosis in children 10 to 14 years of age
- **Fibrous plaque**
  - A large numbers of smooth muscle cells, macrophages, and lymphocytes all filled with cholesterol
  - Plaque grows and projects into the space inside the artery
- **Complicated lesion**
  - The last stage of atherosclerosis
  - The fibrous plaque breaks open, exposing the cholesterol and connective tissue underneath
  - Provokes a strong clotting reaction
  - The combination of fibrous plaque and the blood clot closes the vessel



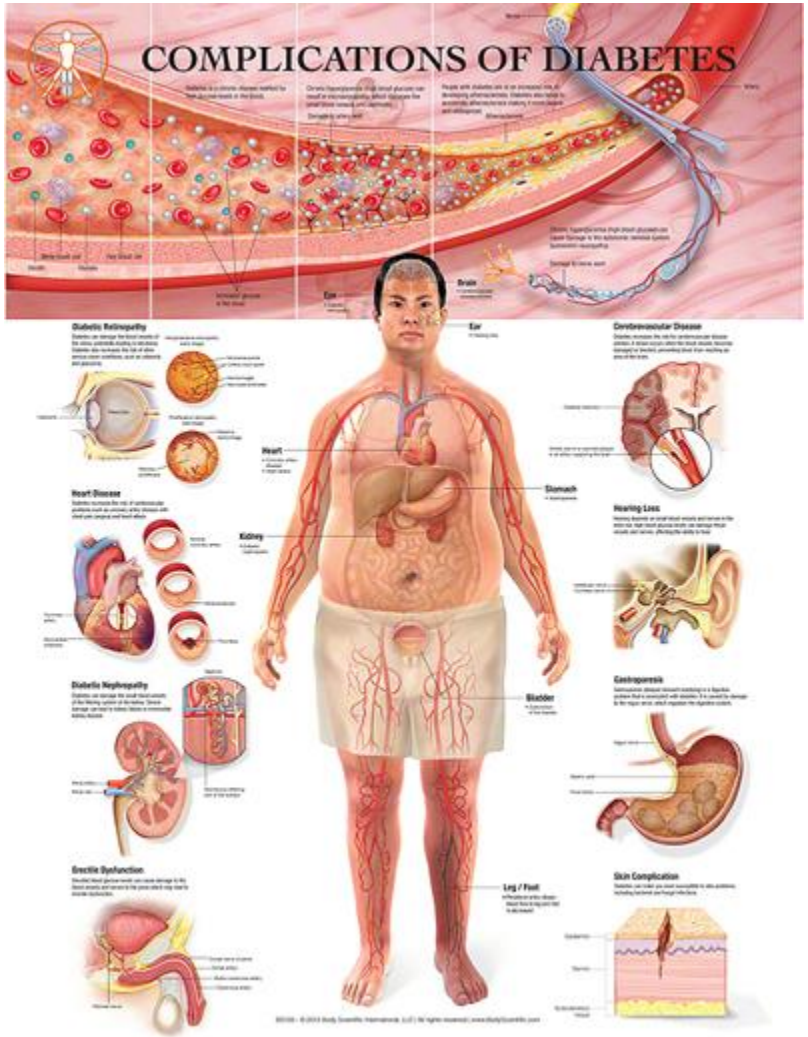
Diseases & Disorders

Notice the narrowing of the lumen within the artery (circle)



Diseases & Disorders

- **Diabetes**
  - What does diabetes have to do with CVD?
    - 2/3 of people with diabetes will die as a result of cardiovascular problems
  - Why?
    - Blood glucose that is normally available for cellular metabolism is not
    - Fats and proteins are metabolized instead and fatty acids are released into the blood
    - LDL-cholesterol levels rise
    - Leads to atherosclerosis and its progression



Diseases & Disorders

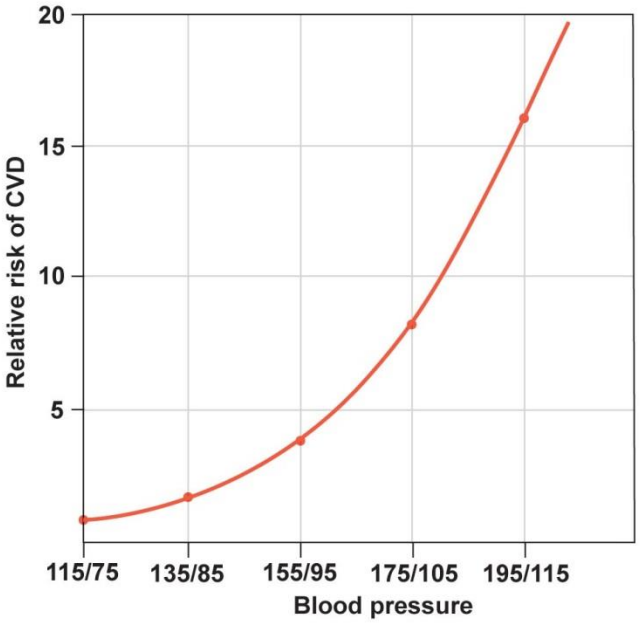
- **Cholesterol**
  - Cell membrane
  - Precursor (steroids)
  - Carried by LDL and HDL (low and high density lipoprotein)
- **So what is good cholesterol?**
  - HDL-C (HDL-cholesterol)
  - Should carry about 30% of your total cholesterol
- **Why is it "healthy"?**
  - Associated with a lower risk of heart attack
  - Hypothesis: picks up cholesterol from plaques and transports it away
  - Involved in reducing inflammation and platelet activation/aggregation

Level mg/dl	**Level** mmol/L	**Interpretation**
<100	<2.6	Optimal LDL cholesterol, corresponding to reduced, but not zero, risk for heart disease
100 to 129	2.6 to 3.3	Near optimal LDL level
130 to 159	3.3 to 4.1	Borderline high LDL level
160 to 189	4.1 to 4.9	High LDL level
>190	>4.9	Very high LDL level, corresponding to highest increased risk of heart disease

Level mg/dL	**Level** mmol/L	**Interpretation**
<40 for men, <50 for women	<1.03	Low HDL cholesterol, heightened risk for heart disease
40–59	1.03–1.55	Medium HDL level
>60	>1.55	High HDL level, optimal condition considered protective against heart disease

Diseases & Disorders

- **High Blood Pressure**
  - Over a period of time, the receptors in the carotid and aortic bodies “reset” or down-regulate their activity → the elevated BP becomes the norm!
- **What is the relationship between elevated BP and CVD?**
  - Prolonged high pressure will cause the heart to fatigue leading to heart failure
  - Usually starts with the left side weakening leading to pulmonary edema and lack of O_2
  - Further weakening occurs and congestive heart failure occurs



Diseases & Disorders

- **How do we fix it?**
  - Prevention!!!
  - Healthy lifestyle is number one
  - If it is uncontrollable (genetic, age…) then
    - Pharmacology is the ticket!