Cardiovascular Physiology

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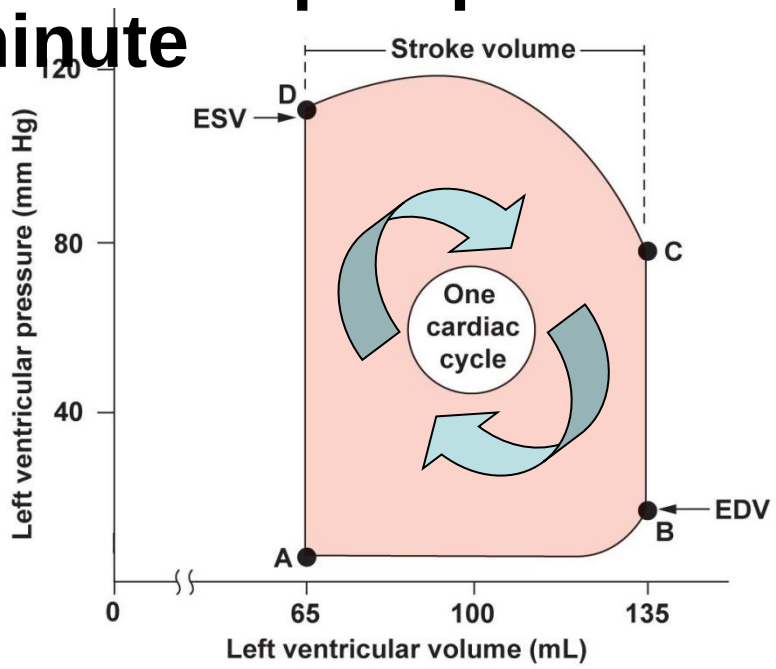
Lecture Outline

- Cardiac Output & Control Systems
- Blood Flow & Blood Pressure Controls
- Medullary Center for Cardiovascular Control & the Baroreceptor Reflex

Cardiac Output

- **Cardiac Output (CO) is the volume pumped by the left ventricle each minute**
  - **influenced by**
    - **Stroke Volume (SV)**
      EDV – ESV = SV
      135ml – 65ml = 70ml
    - **Heart Rate (HR) bpm**
      80 bmp
  - **CO = SV x HR**
    70ml/b x 72bpm = 5040 ml/min
    =5.04L/min
  - **How is this controlled to account for changing conditions? (exercise, disease, stress…)**
    - **What influences SV?**
    - **What influences HR?**

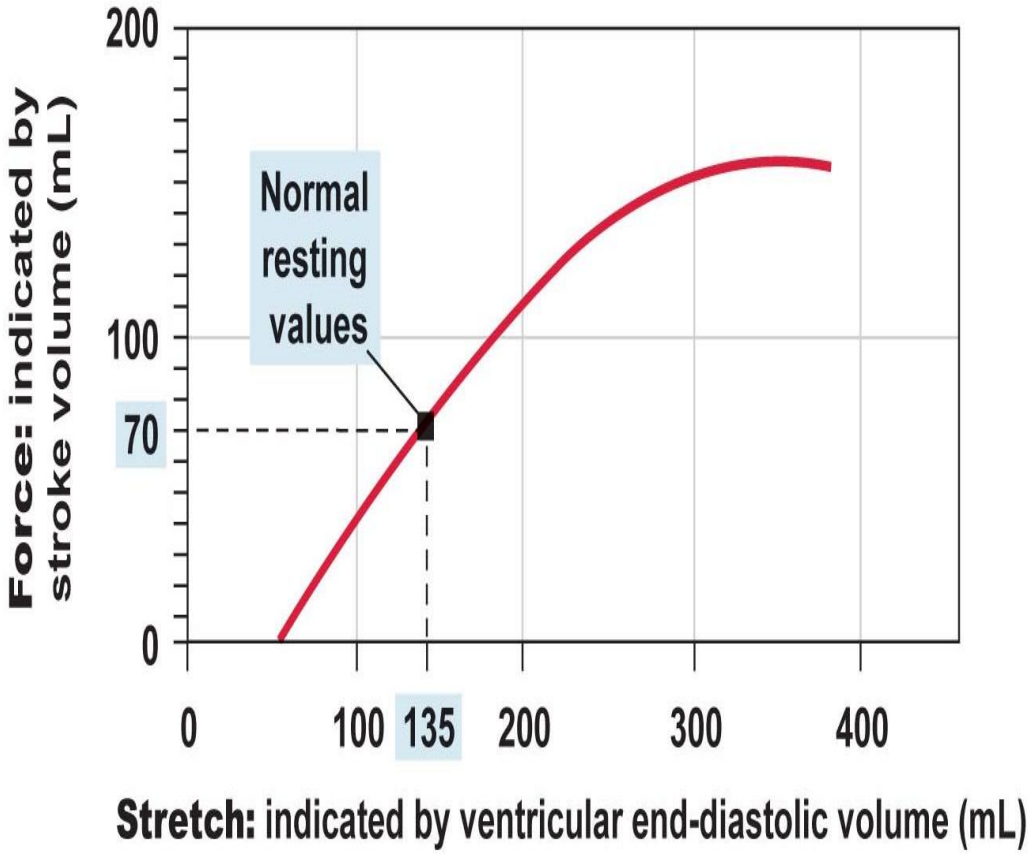


- **Influencing stroke volume**

– **Pre Load**

- **The amount of stretch within the contractile myocardial fibers**
- **Represents the "load" placed on the muscle fibers before they contract**
- **They respond according to length-tension patterns observed in muscle tissue by Frank, then by Starling**

Relationship between **Stretch** and **Force** within the left ventricle



– **Became known as the Frank-Starling Law of the Heart**

– **"The heart will pump** all the blood that is returned to it"

Influencing stroke volume

- Pre Load
  - operates under Frank-Starling Law of the Heart
  - What then influences the stretch applied to cardiac muscle tissue prior to contraction?
    - Venous return, driven by
      - » Skeletal muscle pump
      - » Respiratory pump
      - » Atrial Suction

Cardiac Output

- Influencing stroke volume
  - Contractility
    - Stronger contraction = larger stroke volume
    - Due to inotropic agents
      - Epinephrine, Norepinephrine, Digitalis* are (+) inotropic agents
      - ACh is a (-) inotropic agent
      - How do they work?

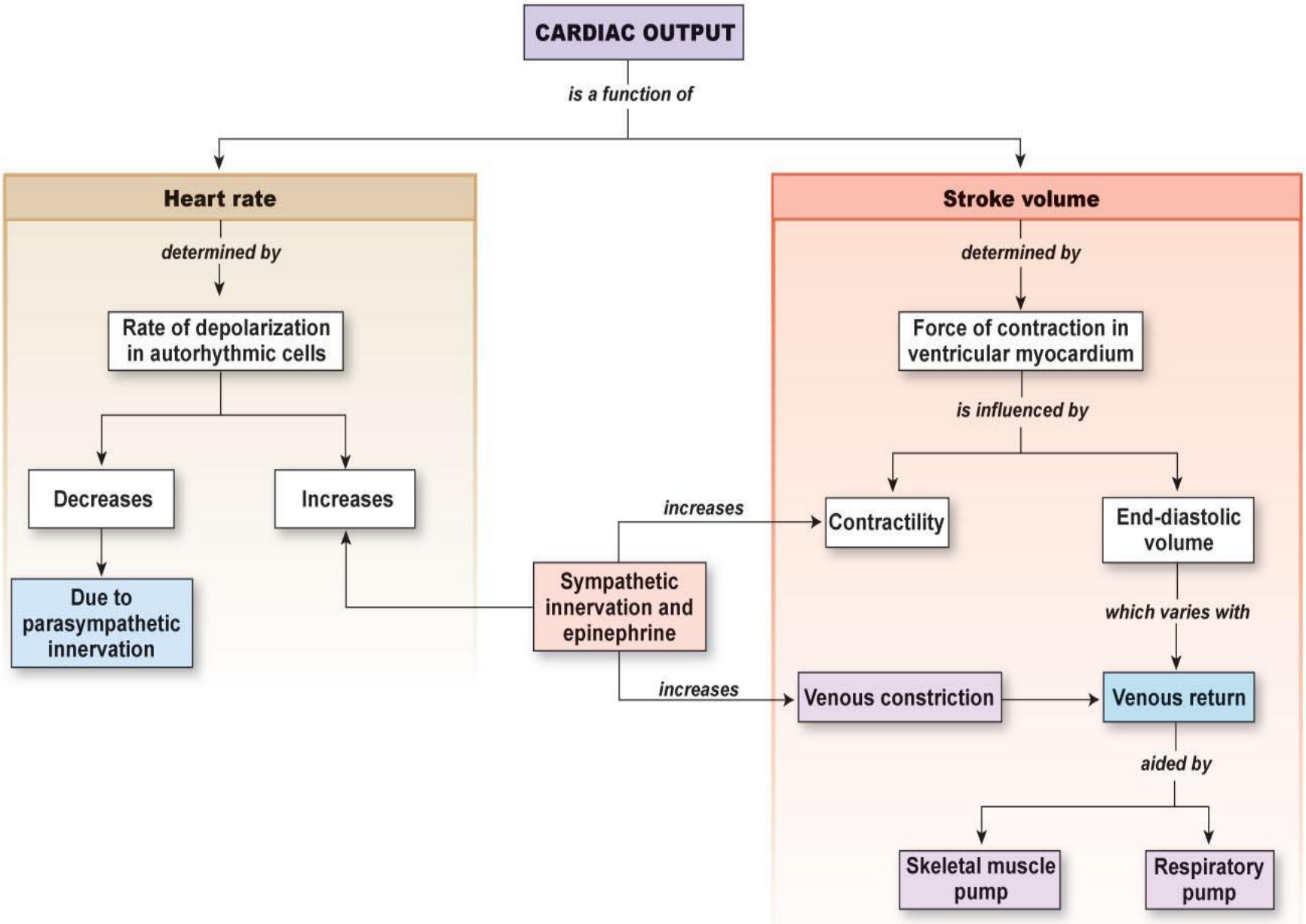
* A group of medicines extracted from a plant called foxglove(digitalis purpurea, yüksük otu) are called digitalis – a cardiac glycoside drug that lowers Na^+/K^+ ATPase activity and therefore the NCX transporter activity, resulting in elevated ICF Ca^{2+} which creates a stronger graded contraction.

Cardiac Output

- Influencing stroke volume
  - **Afterload**
    - This is the amount of pressure that is sitting on the semilunar valves that must be overcome before ventricular ejection can occur
    - The more pressure that must be built up during Isovolumetric ventricular contraction reduces the time that ejection can occur
      - Reduces the ejection fraction (SV/EDV)
        - » Normal 70ml/135ml = 52%
        - » Elevated aortic pressure causes the reduction from normal
        - » 60ml/135ml = 44%
    - indirect relationship
      - Higher aortic pressure = lower stroke volume
    - Causes?
      - Elevated blood pressure
      - Loss of compliance in aorta (loss of elasticity)

- **Influencing Heart Rate**
  - **Rate is set by pacemaker cells rate of depolarization**
    - **Chronotropic effects may be excitatory**
      - **Sympathetic activity**
    - **Or inhibitory**
      - **Parasympathetic activity**

Cardiac Output Overview of Influences

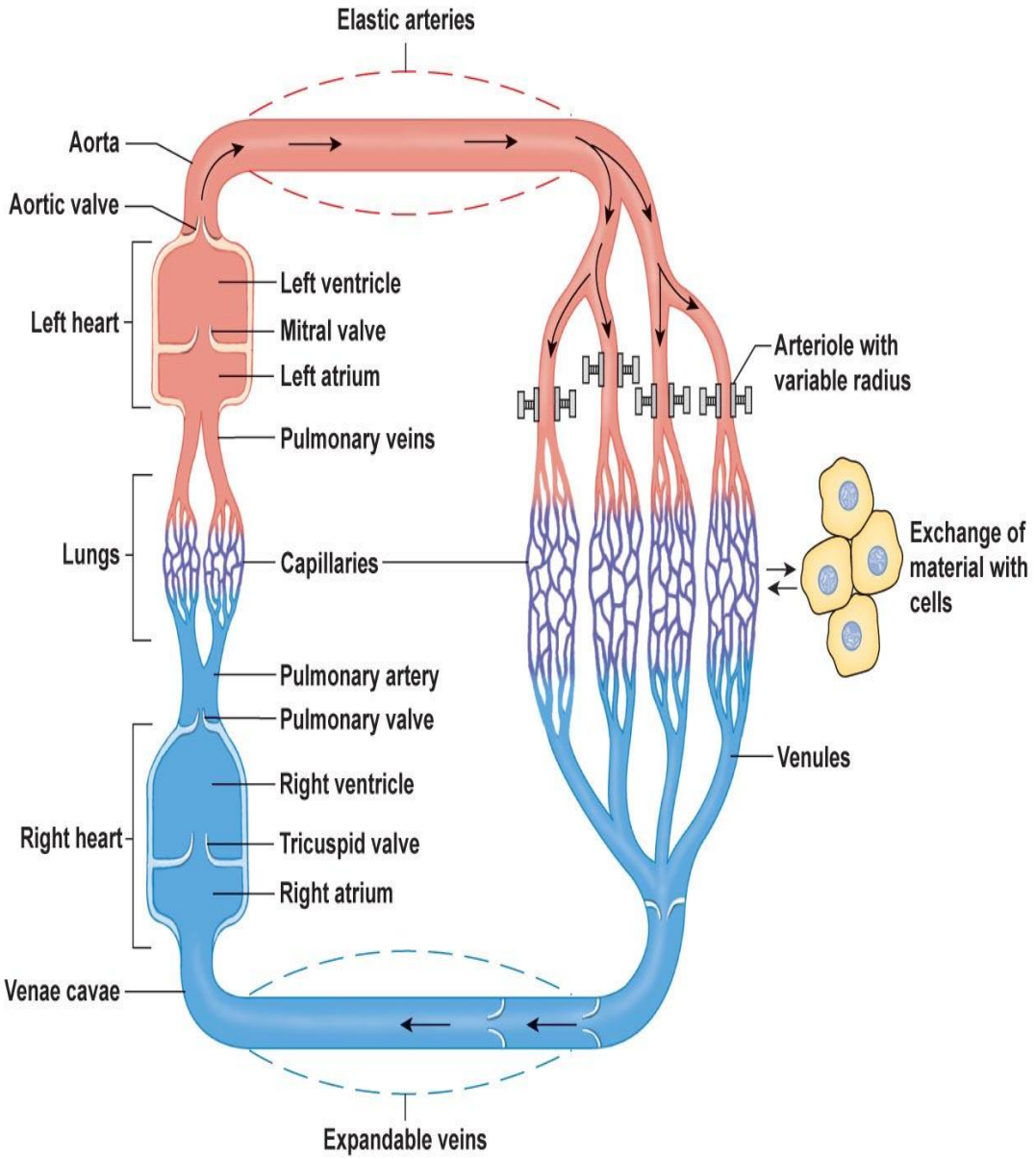


Blood Flow & Blood Pressure Controls

- CO tells us how much blood is ejected per minute and is influence by both intrinsic & extrinsic factors
- Extrinsic factors (besides ANS) include
  - blood vessels & blood pressure
  - blood volume & viscosity
  - capillary exchange & the lymphatic return
  - cardiovascular disease

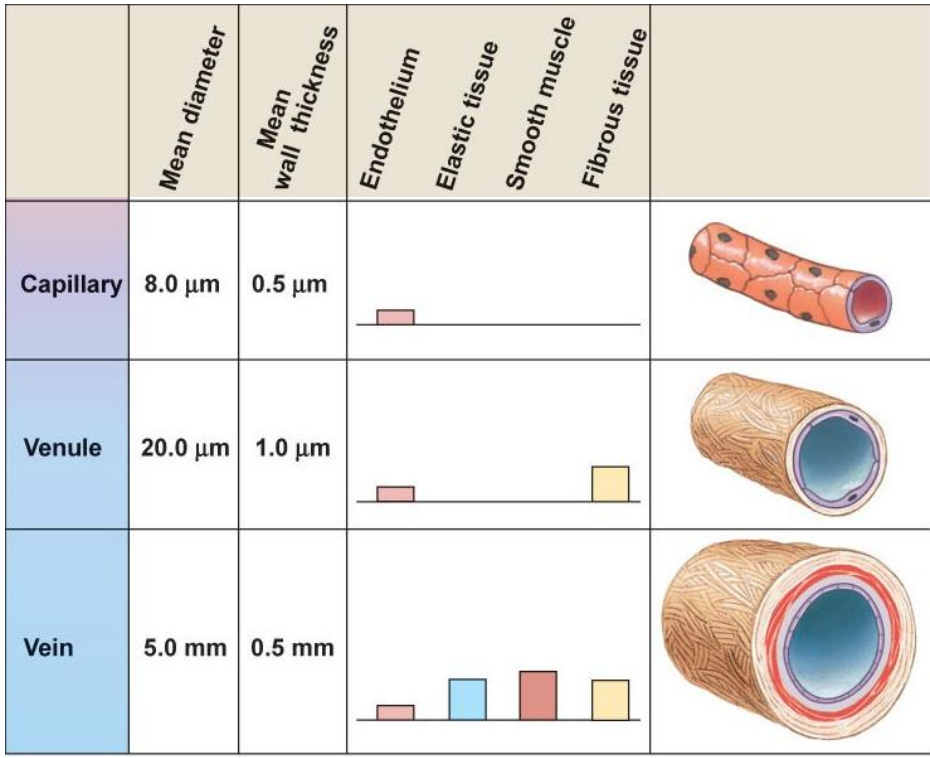
Blood Flow & Blood Pressure Controls

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



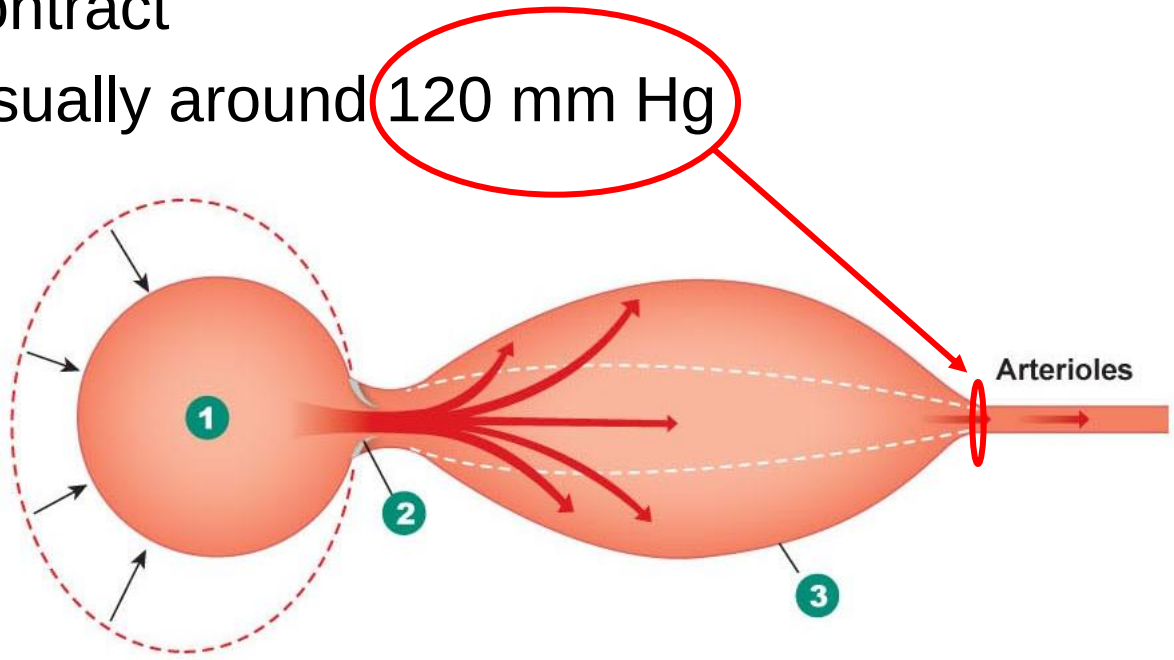
Blood Flow & Blood Pressure Controls

- Capillaries
  - Allow for exchange
- Venules
  - Collect and direct blood to the veins
- Veins
  - Return blood to heart and act as a blood reservoir



Blood Flow & Blood Pressure Controls

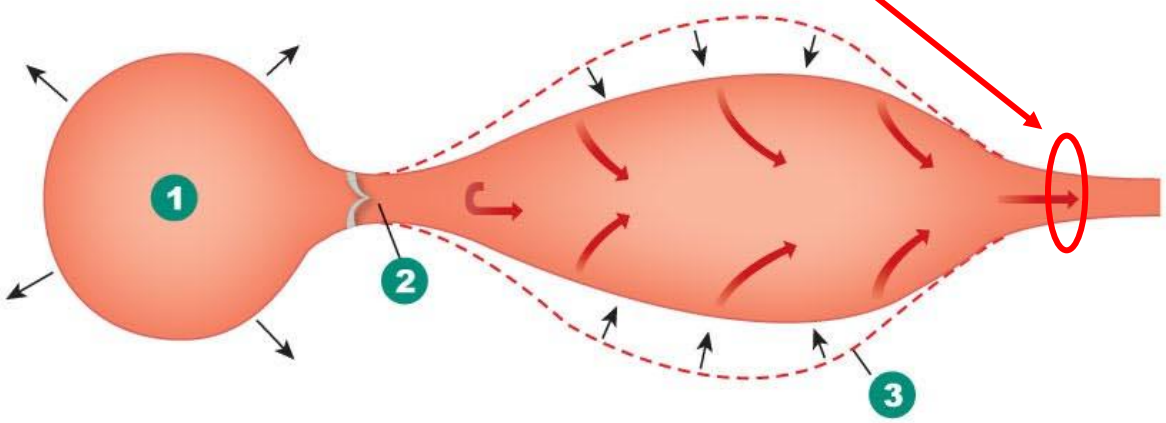
- Blood Vessels & Blood Pressure
  - Systolic Pressure
    - The pressure that is created when the ventricles contract
    - Usually around 120 mm Hg



Cardiac Physiology

Blood Flow & Blood Pressure Controls

- Blood Vessels & Blood Pressure
  - 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 & Blood 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**
  - **Why do we care about systolic, diastolic and pulse pressures?**
    - **We can determine the average pressure within the arterial system = Mean Arterial Pressure (MAP)**

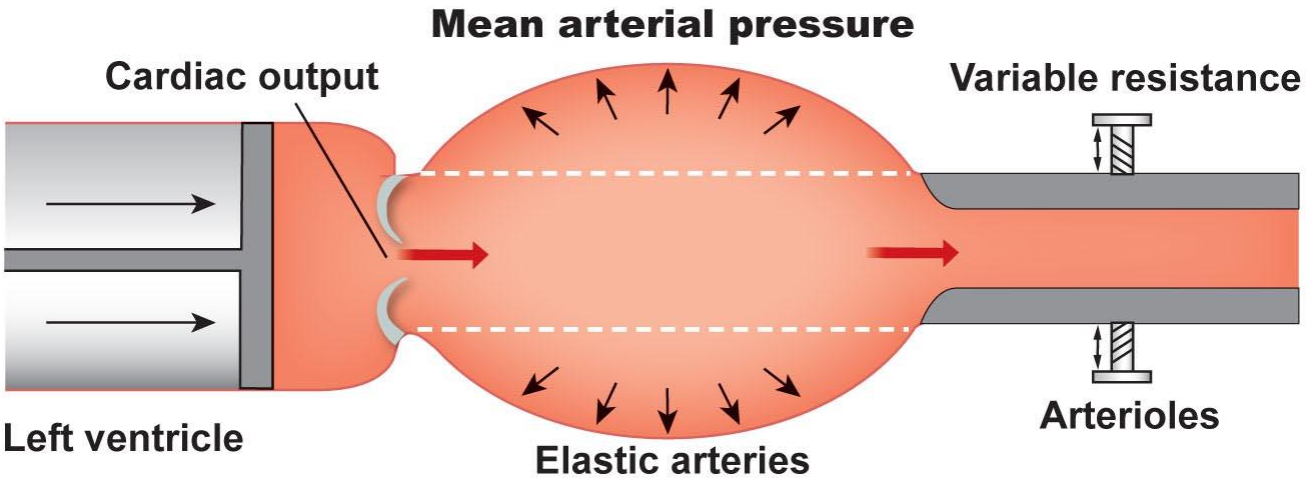
      MAP = diastolic Pressure + 1/3 Pulse Pressure

      MAP = 80 mm Hg + 1/3(120 mm Hg – 80 mm Hg)

      MAP = 93 mm Hg
    - **Then we can determine general health of the cardiovascular system**

Blood Flow & Blood Pressure Controls

- MAP is proportionate to the cardiac output and the amount of peripheral resistance
  - If CO increases but resistance to the outflow does not change
    - Then more blood is flowing into the system than out and arterial pressure must go up to allow inflows to equal outflows



Mean arterial pressure $\propto$ cardiac output $\times$ resistance

Blood Flow & Blood Pressure Controls

- **MAP is proportionate to the cardiac output and the amount of peripheral resistance**
  - **The opposition to blood flow in the arterioles**
    - **Resistance is directly proportional to the length (L) of the vessel, and the viscosity(η) (thickness) of the blood and inversely proportional (to the 4^{th} power) of the vessel radius, so….**

$$R \propto L\,\eta/r^4$$

However as the L and η should remain relatively constant, we can determine that peripheral resistance is mainly a factor of the vessel diameter

$$R \propto 1/r^4$$

- **The controls of vessel diameter are both local and systemic**
  - **Enables tissues to control their own blood flow**
  - **Local controlling mechanisms include**
    - **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**
    - **Paracrines – local substances which alter smooth muscle activity**

vasoconstrictors

      - **Serotonin**
        - » **Secreted by activated platelets**
      - **Endothelin**
        - » **secreted by vascular endothelium, Endothelins are the most potent vasoconstrictors known.**

vasodilators

      - **NO secreted by vascular endothelium**
      - **Bradykinin – from various sources**
      - **Histamine – from mast cells in connective tissues**
      - **Adenosine secreted by cells in low O_2 (hypoxic) conditions**
      - **$\downarrow O_2$, $\uparrow CO_2$, $\uparrow K^+$, $\uparrow H^+$, $\uparrow$temp**

- **The controls of vessel diameter are both local (intrinsic) and systemic (extrinsic)**
  - **Systemic controlling mechanisms for vasoconstriction include**
    - **NE – sympathetic postganglionic neurons**
    - **Serotonin – neurons**
    - **Vasopressin (ADH) – posterior pituitary**
    - **Angiotensin II – part of renin-antiogensin pathway**
  - **Systemic controls for vasodilation include**
    - **Beta-2 epinephrine – from adrenal medulla**
    - **ACH – parasympathetic postganglionic neurons**
    - **ANP (atrial natriuretic peptide) – from atrial myocaridum and brain**
    - **VIPs (vasoactive intestinal peptides) – from neurons**

Neural Regulation of Blood Pressure

- **CNS contains the Medullary Cardiovascular Control Center**
  - **Receives inputs from carotid and aortic baroreceptors**
  - **Creates outflow to sympathetic and parasympathetic pathways**
    - **Sympathetic to SA & AV nodes and myocardium as well as to arterioles and veins**
    - **Parasympathetic to the SA Node**
  - **Baroreceptors initiate the <u>baroreceptor reflex</u>**

Capillary Exchange

- Cardiovascular process involving
  - all three functional systems
    - heart, blood & blood vessels
  - and physics
    - velocity of blood flow
    - cross-sectional area of capillaries
    - Exchange processes
      - diffusion & transcytosis
    - Pressures
      - Filtration
        - » Influenced by capillary hydrostatic pressure
      - colloid osmotic pressures (oncotic pressure)
        - » Influence bulk flow

Capillary Exchange

- The physics involved: Pressures
  - Capillary hydrostatic pressure (P_{out})
    - The filtration force in the capillaries
    - 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**)
    - Direct relationship between capillary hydrostatic pressure (CHP) and movement of fluids across the capillary membrane
    - There should be no filtration pressure moving fluid back into the capillary (interstitial fluid hydrostatic pressure)

      P_{IF} = 0 mm Hg

      …So the outward filtration pressure (P_{out}) is attributable to the capillary hydrostatic pressure (P_{cap})

Capillary Exchange

- The physics involved:
  - colloidal osmotic pressures **[Oncotic** (π)]
    - Created by the “solids” in the blood that are not capable of crossing through the capillary.
    - Inverse relationship between fluid movement and colloid osmotic pressure or *oncotic pressure*
      - π_{cap} remains constant
        - » However the effect of this is variable again from ateriolar end to venule end as the filtration pressure is reduced due to the length of the capillary and the loss of fluid
      - π_{IF}
        - » The interstitial colloid osmotic pressure should be 0 mm Hg
        - » This is what makes colloidal osmotic pressure in the capillary a reabsorption pressure

        $\pi_{in} = (\pi_{IF} - \pi_{cap}) = (0 \text{ mm Hg} - 25 \text{ mm Hg}) =$ **-25 mm Hg**

Capillary Exchange

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

Capillary Exchange

- The Net Pressure will change in a gradient along the length of the capillary.
  - Net Pressure $_{arterial\ end} = (P_{cap} - P_{IF}) + (\pi_{cap} - \pi_{IF})$
    (32 mm Hg – 0 mm Hg) + (0 mm Hg – 25 mm Hg) =
    (32 mm Hg + -25 mm Hg) = **7 mm Hg**
    - **This is a filtration pressure**
  - Net Pressure $_{venous\ end} = (P_{cap} - P_{IF}) + (\pi_{cap} - \pi_{IF})$
    (15 mm Hg – 0 mm Hg) + (0 mm Hg – 25 mm Hg) =
    (15 mm Hg + -25 mm Hg) = **-10 mm Hg**
    - **This is a reabsorption pressure**
- filtration pressure is greater than the reabsorption pressure ($P_{out} > \pi_{in}$)
- This means there is a net loss of capillary fluid to the interstitial fluid on a constant basis

Heart

Heart Valves: Heart has several valves made of connective tissue, that prevent backflow of blood as it circulates.

- **Atrioventricular (AV) Valves: Close between atria and ventricles**
  - **Right AV Valve: Connects right atrium to the right ventricle.**
  - **Left AV Valve: Connects left atrium to the left ventricle.**
- **Semilunar Valves: Close as blood leaves the ventricles and enters the arteries.**

Heart murmur: Rushing, gurgling sound created by backflow of blood due to damaged or imperfect heart valves. Fairly common (10% of healthy population). Most are asymptomatic.

Heart Beat

- **Average 70 beats per minute.**
- **100,000 beats every day.**
- ***Cardiac cycle* about every 0.8 sec.**
  - **Diastole: Heart relaxes and blood flows into chambers (0.4 sec).**
  - **Systole: Heart contracts.**
    - **First atria (0.1 sec)**
    - **Then ventricles (0.3 sec)**
- **Pumps about 8000 liters of blood/day.**
- **Pacemaker (Sinoatrial node): Controls heart rate.**
  - **Regulated by nervous and endocrine systems.**
- **Two heart beat sounds ("Lub-dupp"):**
  - **First sound: Ventricles contract, AV valves close.**
  - **Second sound: Heart relaxes, semilunar valves are *closing*.**
- **Pulse: Arteries expand and contract with each heartbeat.**