CARDIOVASCULAR PHYSIOLOGY:
THE VASCULAR SYSTEM
In Physiology Today

Diagram:
- To venule
- Systemic capillary: $O_2$, Glucose, $CO_2$
- From arteriole
- Muscle cell: $H_2O$, ATP, $CO_2$, $O_2$, Glucose
Hemodynamics

\[ F = \Delta P / R \]

• Blood flow (F)
  – High to low pressure
  – Rate = L/min

• Pressure (P)
  – Hydrostatic pressure
  – Pressure exerted by blood
  – Generated by contraction of the heart
  – Magnitude varies throughout the system
  – Units of \( \Delta P \) are mmHg

• Resistance to blood flow (R)
  – A measure of the friction that impedes flow
Hemodynamics

\[ F = \Delta P/R \]

- Resistance is due to:
  - Viscosity
    - Variable
    - Friction between molecules of a flowing fluid
    - \( > \) friction = \( > \) viscosity
    - Increases as hematocrit increases
  - Length of the vessel
    - Fixed
  - Radius of the vessel
    - Variable
    - **Most important variable in determining resistance in blood vessels**
Changes in the Radius of a Vessel

- Effect of vessel radius \( (r) \) on resistance \( (R) \)
- Volume of blood is exposed to far more surface friction against the walls of a smaller tube
- Given the same pressure gradient, flow through a tube decreases 16 fold when the radius is halved
### Functions of Endothelial Cells

1. Serve as a physical lining that blood cells do not normally adhere to in heart and blood vessels.

2. Serve as a permeability barrier for the exchange of nutrients, metabolic end products, and fluid between plasma and interstitial fluid; regulate transport of macromolecules and other substances.

3. Secrete paracrine agents that act on adjacent vascular smooth muscle cells; including vasodilators—prostacyclin and nitric oxide (endothelium-derived relaxing factor, EDRF)—and vasoconstrictors—notably endothelin-1.


5. Play a central role in vascular remodeling by detecting signals and releasing paracrine agents that act on adjacent cells in the blood vessel wall.

6. Contribute to the formation and maintenance of extracellular matrix.

7. Produce growth factors in response to damage.

8. Secrete substances that regulate platelet clumping, clotting, and anticoagulation.

9. Synthesize active hormones from inactive precursors (Chapter 14).

10. Extract or degrade hormones and other mediators (Chapters 11, 13).

11. Secrete cytokines during immune responses (Chapter 18).


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**Endothelium**

- All blood vessels and the heart are lined with an endothelium
- Endothelial cells have many functions
Pressures in Systemic and Pulmonary Vessels

- Large arteries serve as low-resistance tubes conducting blood to various organs.
- Act as a pressure reservoir for maintaining blood flow during diastole.
Arterial Blood Pressure

• Factors determining pressure in any elastic tube
  – Volume
  – Compliance
    • How easily the structure stretches
    • Compliance = $\Delta$ volume/$\Delta$ pressure
    • Higher the compliance, the easier it stretches
  – Arteries have low compliance. Why?
    • Arteries are resistance vessels
  – Average pressure nearly 100 mmHg
Arterial Blood Pressure

- 1/3 of the stroke volume leaves the arteries during systole.
- The rest of the volume remains in the arteries during systole:
  - Distending the walls
  - Raising blood pressure
- During diastole, arterial walls passively recoil and blood continues to be driven into the arterioles.
Mean Arteriole Pressure (MAP)

- Systolic pressure (SP)
- Diastolic pressure (DP)
- **Pulse pressure**
  - PP = SP − DP
  - PP = 120 − 80
  - PP = 40 mmHg
- **Mean arteriole pressure**
  - Pressure driving blood into the tissues
  - MAP = DP + \( \frac{1}{3} \) (PP)
  - MAP = 80 + \( \frac{1}{3} \) (40)
  - MAP = 93 mmHg
Arterioles

• 2 Major Roles
  – Determine blood flow to organs
  – Major factor in determining MAP

• Produce the greatest resistance to blood flow
  – Remember flow rate?
    • \( F = \frac{\Delta P}{R} \quad F = \frac{MAP}{R} \)
  – Vasoconstriction/Vasodilation
    • Intrinsic controls
    • Extrinsic controls
  – Intrinsic tone
    • Spontaneous contractile activity
    • Independent of neural, hormonal or paracrine input
Intrinsic Controls

• Organs and tissues alter their own arteriole resistance
  – Self regulate blood flow

• Includes
  – Active hyperemia
    • Increased blood flow when tissue metabolic activity increases
  – Reactive hyperemia
    • Short term increase in blood flow following a brief period of ischemia
  – Local response to injury
Intrinsic Controls

- Endothelial cells secrete paracrine agents that diffuse to adjacent vascular smooth muscle cells
  - Vasodilation/Vasocontriction
  - Nitrous Oxide (NO)
    - Also called endothelium derived relaxing factor (EDRF)
    - Released continuously to maintain vasodilation in the basal state
  - Prostacyclin (PGI$_2$)
    - Eicosanoid
Controls of Arteriole Radius

**Neural controls**
- Vasoconstrictors
  - Sympathetic nerves that release norepinephrine
- Vasodilators
  - Neurons that release nitric oxide

**Hormonal controls**
- Vasoconstrictors
  - Epinephrine
  - Angiotensin II
  - Vasopressin
- Vasodilators
  - Epinephrine
  - Atrial natriuretic peptide

**Local controls**
- Vasoconstrictors
  - Internal blood pressure (myogenic response)
  - Endothelin-1
- Vasodilators
  - ↓ Oxygen
  - $K^+$, $CO_2$, $H^+$
  - Osmolarity
  - Adenosine
  - Eicosanoids
  - Bradykinin
  - Substances released during injury
  - Nitric oxide

**Arteriolar smooth muscle**
- Altered arteriolar radius
Capillaries

- Movement between plasma and IF
  - Diffusion
  - Vesicle transport
  - Bulk flow
  - Mediated transport (brain)

- Movement between IF and cytoplasm
  - Diffusion
  - Mediated transport

- 5% of blood in capillaries

Low resistance to flow due to large cross-sectional area
Diffusion Gradients
Movement of Nutrients and Metabolic End Products

- Easily diffuse
  - Lipid soluble substances
    - \( \text{O}_2, \text{CO}_2 \)
- Small, water-filled channels in the endothelium
  - Water soluble substances
    - Ions
    - Polar molecules
  - Makes permeability of these substances high

*Cellular metabolism creates pressure and concentration gradients*
Leakiness
Movement of Nutrients and Metabolic End Products

- Due to variations in the size of the water-filled channels
- Tight capillaries of the brain
  - No clefts
  - Only tight junctions
  - Water-soluble substances only move by carrier-mediated transport
- Liver capillaries
  - Large clefts
  - Large holes in the membranes of the endothelial cells
  - Large enough for proteins to pass through
Bulk Flow
Movement of Protein-Free Fluid

- Distribution of ECF
- Bulk flow of protein-free plasma
  - Remember...the capillary wall acts as a filter and proteins typically do not diffuse across
- Driven by hydrostatic pressure gradients
Osmotic Force ($\pi$)
Protein Concentrations Drive Movement

- **Crystalloids**
  - Large amounts of crystalloids in plasma and ICF
  - low-molecular-weight penetrating solutes
  - $\text{Na}^+$, $\text{Cl}^-$, $\text{K}^+$
  - Move with water

- **Colloids**
  - Non-penetrating
  - Plasma proteins
  - $[\text{colloid}]_{\text{plasma}} > [\text{colloid}]_{\text{IF}}$

- Concentrations of crystalloids *do not* change
- Volume of water and amount of crystalloids *do* change
- Increased filtration from plasma to IF
  - Increases volume of IF
  - Decreases volume of plasma
Net Filtration Pressure (NFP)

\[ \text{NFP} = P_c + \pi_{IF} - P_{IF} - \pi_C \]

- Opposing forces move **protein-free fluid** across the capillary wall
  - Filtration (capillary \(\rightarrow\) IF)
  - Absorption (IF \(\rightarrow\) capillary)
Net Filtration Pressure (NFP)

\[
NFP = P_C + \pi_{IF} - P_{IF} - \pi_C
\]

• **Starling Forces**
  – The 4 factors that determine NFP
  – Only difference is capillary pressure
  – Positive NFP favors filtration
    • Arteriole end
  – Negative NFP favors absorption
    • Venule end
Veins

- Factors determining pressure in any elastic tube
  - Volume
  - Compliance
    - $\Delta \text{volume}/\Delta \text{pressure}$
    - Higher the compliance, the easier it stretches
    - Veins can hold large amounts of blood with a small increase in pressure
  - Veins have high compliance. Why?
  - Venous pressure average $<10 \text{ mmHg}$
Venous Pressure

• Pressure differences between peripheral veins (all veins not within the thoracic cavity) and the right atrium
  – Peripheral veins 10-15 mmHg
  – Right atrium 0 mmHg
• Low pressure difference is sufficient because veins offer low resistance to flow
• Diameters of veins are altered in response to blood volume
Venous Pressure and SV

1. Sympathetic PostG neurons release NE
   – Causes contraction of venous smooth muscle
   – Decreases diameter
   – Decreases compliance
   – Raising venous pressure

2. Also respond to hormones and paracrine agents

3. Skeletal muscle pump

4. Respiratory pump
   – Inspiration enhances venous return
Lymphatic System

- Large water-filled channels permeable to all IF constituents
- IF enters lymphatic capillaries by bulk flow
- Capillary filtration exceeds capillary absorption by 4 L/day
  - 4 L/day returned to blood via lymphatic system
Regulation of Systemic Arterial Pressure

• Major cardiovascular variable regulated is MAP in systemic circulation

• MAP in systemic circulation
  – CO $\times$ total peripheral resistance (TPR)

• All changes in MAP must be the result of changes in CO and/or TPR

• Changes in TPR is normally due to changes in resistance of arterioles
Regulation of Systemic Arterial Pressure

- **Activity of sympathetic nerves to veins**
- **Venous pressure**
- **Blood volume**
- **Skeletal muscle pump**
- **Inspiration movements**
- **Venous return**
- **Atrial pressure**
- **End-diastolic ventricular volume**
- **Plasma epinephrine**
- **Activity of sympathetic nerves to heart**
- **Activity of parasympathetic nerves to heart**
- **Cardiac muscle Stroke volume**
- **SA node Heart rate**

**Local controls**
- Vasopressors
- Vasoconstrictors
- Neurons that release nitric oxide
- Bradykinin
- Substances released during injury
- Nitric oxide

**Neural controls**
- Sympathetic nerves
- Vasodilators

**Hormonal controls**
- Angiotensin II
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**Arteriolar smooth muscle**
- Arteriolar radius
- **Blood viscosity**
- **Hematocrit**

**Total peripheral resistance**

**Mean arterial pressure** = **Cardiac output** × **Total peripheral resistance**
Regulation of Systemic Arterial Pressure

- A change in a single variable will produce a change in CO or TPR
- Any deviation in blood pressure will elicit homeostatic reflexes so that CO and/or TPR will adjust to accommodate the change in arteriole pressure
Arterial Baroreceptors

- **Baroreceptors**
  - Sensitive to stretch or distortion
  - Degree of wall stretching is directly related to pressure within the artery
    - *Carotid sinus*
    - *Aortic arch baroreceptor*

- Afferent neurons travel from baroreceptors to the cardiovascular control center in the medulla
The Baroreceptor Reflex

- Response to a decrease in arterial blood pressure
- Net result:
  - Increased CO
    - Increased HR
    - Increased SV
  - Increased TPR
    - Vasoconstriction
  - Return of blood pressure to normal
- Baroreceptor reflex is a short-term regulator of arterial blood pressure
  - < a few days
Cardiovascular Center
Medulla Oblongata

• Primary integrating center for the baroreceptor reflexes

• Input from baroreceptors regulate activity of:
  – Vagus nerve
  – Sympathetic nerves
    • Heart
    • Arterioles
    • Veins
Long-Term Regulation of Arterial Pressure

- Baroreceptors adapt to prolonged changes in pressure.
- Primary mechanism for long-term regulation is blood volume.
- Blood volume determines arterial pressure by influencing:
  - Venous pressure
  - EDV
  - SV
  - CO
Other Cardiovascular Reflexes and Responses

**Increase in blood pressure**
- Decrease arterial \([O_2]\)
- Increase arterial \([CO_2]\)
- Decreased blood flow to the brain
- Pain in skin
- Stress
- Anxiety
- Anger
- Walking

**Decrease in blood pressure**
- Pain in viscera or joints
- Sleeping
- Good mood