Chapter 14
Cardiac Output, Blood Flow and Blood Pressure

Adjusting the pumping mechanism on demand.

Calculating Cardiac Output

- **Stroke volume**
  - volume of blood ejected by each ventricle during each contraction.
- **Cardiac rate**
  - Beats per minute
- **Cardiac output**
  \[ \text{Cardiac output} = \text{Stroke volume} \times \text{Cardiac Rate} \]

Regulation of Cardiac Rate

- Regulation of HR (chronotropic effect):
  - Positive or negative chronotropic effect.
- Autonomic control:
  - Major means by which cardiac rate is regulated.
- Cardiac Control Center (medulla):
  - Coordinates activity of autonomic innervation.

Effects on stroke volume

- Norepinephrine
  - From sympathetic nerve endings
  - Opens Na⁺ and Ca²⁺ channels
- Epinephrine
  - From adrenal medulla
  - Opens Na⁺ and Ca²⁺ channels
- Acetylcholine
  - Parasympathetic endings
  - Opens K⁺ channels.

Chronotropic Effect

Question of the day: Fill in third bullet and explain why occurs mechanistically.
### Effects of Autonomic Nerve Activity on Heart

<table>
<thead>
<tr>
<th>Region affected</th>
<th>Sympathetic Nerve Endings</th>
<th>Parasympathetic Nerve Endings</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA node</td>
<td>Increased rate diastolic depolarization; increased cardiac rate</td>
<td>Decreased rate diastolic depolarization; decreased cardiac rate.</td>
</tr>
<tr>
<td>AV Node</td>
<td>Increased conduction rate</td>
<td>Decreased conduction rate</td>
</tr>
<tr>
<td>Atrial muscle</td>
<td>Increased strength of contraction</td>
<td>Decreased strength of contraction</td>
</tr>
<tr>
<td>Ventricular muscle</td>
<td>Increased contraction strength</td>
<td>No significant effect</td>
</tr>
</tbody>
</table>

### Factors determining Stroke Volume

- **End diastolic volume (EDV).**
  - Volume of blood in ventricles immediately before contraction (preload).
- **Strength of ventricular contraction.**
- **Total peripheral resistance**
  (resistance to blood flow in the arteries).

### Frank-Starling Mechanism (Law of the Heart)

#### Frank-Starling Law and Sympathetic Nerve Effects

- **Frank-Starling law**
  - Increased contractility caused by sympathetic nerve stimulation

- **Stroke volume (ml)**
  - Ventricular end-diastolic volume (ml)

### Factoring in the Sympathoadrenal System: norepinephrine and epinephrine.

- **Produce increase in contraction strength.**
- **Positive inotropic effect**
  - Results from increased amount of Ca²⁺ to sarcomeres.
- **Increased Cardiac Output from**
  - Positive inotropic effect
  - Positive chronotropic effect

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Frank-Starling and adjustment to rise in total peripheral resistance.
Contribution of venous return to cardiac output.

- Venous pressure
  - Return of blood to the heart via veins.
  - Driving force for return of blood to the heart.
- Depends on
  - Total blood volume
  - Venous pressure
- Veins have thinner walls = higher compliance.
- Capacitance vessels.
  - 2/3 blood volume in veins.
  - Therefore can "store" blood.

Variables that Affect Venous Return and End-diastolic Volume

- End-diastolic volume
- Venous return
- Blood volume
- Negative intrathoracic pressure
- Breathing
- Venous pressure
- Urine volume
- Tissue-fluid volume
- Venoconstriction
- Skeletal muscle pump
- Sympathetic nerve stimulation

Total Body Water

- Distribution of H₂O within the body:
- Intracellular compartment:
  - 2/3 of total body H₂O within the cells.
- Extracellular compartment:
  - 80% interstitial fluid.
  - 20% blood plasma.
- Maintained by constant balance between H₂O loss and gain.
Fluid Equilibrium

- Distribution of ECF between plasma and interstitial compartments is in state of dynamic equilibrium.
  - Balance between tissue fluid and blood plasma.
- Hydrostatic pressure:
  - Exerted against the inner capillary wall.
  - Promotes formation of tissue fluid.
- Colloid osmotic pressure:
  - Exerted by plasma proteins.
  - Promotes fluid reabsorption into circulatory system.

Filtration Pressure

- Net filtration pressure:
  - Hydrostatic pressure of blood minus the hydrostatic pressure in the interstitial fluid.
  - Blood hydrostatic pressure (arteriolar pressure) = 37 mm Hg.
  - Blood hydrostatic pressure (venular end) = 17 mm Hg.
  - Interstitial hydrostatic pressure = 1 mm Hg.

Colloid Osmotic Pressure

- Pressure exerted by plasma proteins or interstitial proteins.
- Oncotic pressure
  - Difference between plasma osmotic pressure and interstitial osmotic pressure
  - Colloid osmotic pressure of the plasma = 25 mm Hg.
  - Colloid osmotic pressure of the interstitium = 0 mm Hg.

Determining fluid movement into or out of the capillaries:

- \((P_c + \pi_t) - (P_i + \pi_p)\)
  - \(P_c\) = hydrostatic pressure in the capillary
  - \(\pi_t\) = colloid osmotic pressure in the interstitium
  - \(P_i\) = hydrostatic pressure of interstitium
  - \(\pi_p\) = colloid osmotic pressure of blood plasma
Edema

• Excessive accumulation of tissue fluid.
• Edema may result from:
  – High arterial blood pressure.
  – Venous obstruction.
  – Leakage of plasma proteins into interstitial fluid.
  – Myxedema.
  – Decreased plasma protein.
  – Obstruction of lymphatic drainage.
• Look at Table 14.2

Severe edema of elephantiasis

Pictures and more information can be found at http://circuit.neb.com/fgn/pnb/wuchban.html#lifecycle

Kidney Regulation of Blood Volume

• Formation of urine begins by filtration of plasma through glomerular capillary pores.
• Volume of urine excreted can be varied by changes in reabsorption of filtrate.
• Adjusted according to needs of body by action of hormones.
Aldosterone

- Mechanism to maintain blood volume and pressure through absorption and retention of Na⁺ and Cl⁻.
  - Stimulates reabsorption of NaCl.
  - Increases H₂O reabsorption.
  - Does not dilute osmolality.

Renin-angiotensin-aldosterone System

Angiotensin II
- Powerful vasoconstrictor.
- Stimulates production of aldosterone.
- Stimulates thirst.

ANF

- Atrial natriuretic factor.
- Stretch of atria stimulates production of ANF.
  - Antagonistic to aldosterone and angiotensin II.
  - Promotes Na⁺ and H₂O excretion by the kidney.

Arterial pressure/blood volume

Steady-state blood volume changes are the single most important long-term determinant of blood pressure!!!
Blood Flow = F

- Hydrostatic pressure
- Always from region of higher pressure to lower pressure.
- Generated by contraction of heart.
- Magnitude varies throughout system.
- \( F = \frac{\Delta P}{R} \)
  - \( F \) = flow
  - \( \Delta P \) = pressure difference (mmHg)
  - \( R \) = resistance to flow.

Flow between two points

\[
\begin{align*}
P_1 &= 100 \text{ mmHg} \\
P_2 &= 10 \text{ mmHg} \\
\Delta P &= 90 \text{ mmHg}
\end{align*}
\]

Flow rate = 10 ml/min

\[
\begin{align*}
P_1 &= 500 \text{ mmHg} \\
P_2 &= 410 \text{ mmHg} \\
\Delta P &= 90 \text{ mmHg}
\end{align*}
\]

Flow rate = 10 ml/min

Resistance

- Opposition to blood flow.
- Resistance directly proportional to length of vessel and to the viscosity of the blood.
- Inversely proportional to the 4th power of the radius of the vessel.
- \( R = \frac{L \cdot \eta}{r^4} \)
  - \( L \) = length of the vessel
  - \( \eta \) = viscosity of blood
  - \( r \) = radius of the vessel

Components contributing to resistance

- \( R = (\frac{\eta L}{r^4}) \frac{8}{\pi} \)
  - \( \eta \) = fluid viscosity
  - \( L \) = Length
  - \( r \) = inside radius of tube.
  - \( \frac{8}{\pi} \) = constant
- Usually viscosity and length does not change in blood system.
- Major regulators of blood flow through an organ are:
  - Mean arterial pressure.
  - Vascular resistance to flow.

Changing the radius = changing the flow.

- Extrinsic Regulators - autonomic nervous and endocrine system.
  - Sympathoadrenal system
  - Parasympathetic system
  - Paracrine regulation
- Intrinsic Regulators - “built-in” mechanisms
  - Myogenic
  - Metabolic
Important hormones of the sympathetic nervous system.

- Epinephrine
- Norepinephrine
- Angiotensin II
- Vasopressin
- Atrial natriuretic factor.

Note: go through and fill in what each of these hormones do to the arteries. See table 14.4

Paracrine release by ENDOTHELIAL cells.

- Nitric oxide.
- Bradykinin
- Prostacyclin (PGL$_2$, an eicosanoid).
- Endothelin-1 (ET-1).

Note: again, look these up to find out what they do!

Intrinsic Regulation of Blood Flow

**Myogenic:**
- Occurs because of the stretch of the vascular smooth muscle.
  - A decrease in systemic arterial pressure causes cerebral vessels to dilate.
  - Maintains adequate flow.

**Metabolic:**
- Intrinsic receptors sense chemical changes in environment

**Vasodilation:**
- Decreased O$_2$:
  - Increased metabolic rate.
- Increased CO$_2$:
  - Decreased ventilation.
- Decreased pH:
  - Lactic acid.
- Increased adenosine or increased K$^+$:
  - From tissue cells.
Keeping the flow to the heart

- Alpha-adrenergic sympathetic stimulation
  - Results in vasoconstriction
- Beta-adrenergic and sympathetic cholinergic stimulation
  - Results in vasodilation
- Intrinsic metabolic control

Controlling blood flow and cardiac output during exercise

- Cardiac output increases.
- Blood flow to brain stays same.
- HR increases to maximum of 190 beats/min.
- Stroke Volume increases.
- Ejection fraction increases due to increased contractility.
- Vascular resistance:
  - Decreases to skeletal muscle.
  - Increases to GI tract and skin.

Cerebral Circulation

- Cerebral blood flow not normally influenced by sympathetic nerve activity.
- Normal range of arterial pressures:
  - Cerebral blood flow regulated by intrinsic mechanisms.
    - Myogenic:
      - Maintain constant flow rate.
    - Metabolic:
      - Sensitive to changes in metabolic activity.

Cutaneous Blood Flow

- Blood flow through the skin is adjusted to maintain deep-body temperatures about 37°C.
- Occur due to:
  - Vasoconstriction/vasodilation arteries.
  - Arteriovenous anastomoses:
    - Divert blood to deep venules.
- Bradykinin:
  - Sweat glands secrete bradykinin which increases blood flow to skin and sweat glands.
Blood Pressure

- Pressure of arterial blood is regulated by blood volume, TPR, and cardiac rate.
  - Arteriole resistance is greatest because they have the smallest diameter.
  - Capillaries BP is reduced because of the total cross-sectional area.
- 3 most important variables are HR, SV, and TPR.
Atrial Stretch Reflexes

- Located in the atria of the heart.
- Receptors activated by increased venous return.
  - Stimulate reflex tachycardia.
  - Inhibit ADH release.
  - Promote secretion of ANF.

Measurement of Blood Pressure

- Auscultation:
  - Art of listening.
- Laminar flow:
  - Normal blood flow. Blood in the central axial stream moves faster than blood flowing closer to the artery wall.
  - Turbulent flow and vibrations produced in the artery when cuff pressure is greater than diastolic pressure and lower than systolic pressure.
## Recall: Pulse Pressure
- The expansion of the artery in response to the volume of blood ejected.
- **Pulse pressure = systolic pressure – diastolic pressure**
- Mean arterial pressure:
  - Average arterial pressure during the cardiac cycle.
  - Is closer to diastolic pressure, as the period of diastole is longer than the period of systole.
- **Mean arterial pressure = diastolic pressure + 1/3 pulse pressure**

## Hypertension
- Blood pressure in excess of normal range for age and gender.
- > 140/90 mm Hg.
- Primary or essential hypertension:
  - Result of a complex or poorly understood process.
- Secondary hypertension:
  - As a result of a known disease.

## Essential Hypertension
- 95% of population with hypertension.
  - Increase in TPR is a universal characteristic.
  - Secretion of renin, angiotensin II, and aldosterone is variable.
  - Sustained high stress (via SNS) and high Na\(^+\) intake act synergistically in development of hypertension.
  - Adaptive response is thickening of arterial wall, resulting in atherosclerosis.
  - Kidneys may not be able to properly excrete Na\(^+\) and H\(_2\)O.

## Dangers of Hypertension
- Silent killer:
  - Patients are asymptomatic until substantial vascular damage occurs.
  - Atherosclerosis.
- Increases afterload:
  - Increases workload of the heart.
  - Congestive heart failure.
- Damage cerebral blood vessels.
  - Stroke.

## Treatment of Hypertension
- **Modification of lifestyle:**
  - Cessation of smoking.
  - Moderation in alcohol intake.
  - Weight reduction.
  - Reduction in Na\(^+\) intake.
- Medications (exercise: work out how these counteract hypertension)
  - Diuretics.
  - Beta-blockers.
  - Calcium antagonists.
  - ACE inhibitors.

## Circulatory Shock
- **Hypovolemic shock:**
  - Circulatory shock that is due to low blood volume.
  - Decreased Cardiac Output and blood pressure.
- **Compensations:**
  - Baroreceptor reflex:
    - Tachycardia.
  - Vasconstriction to GI, skin, kidneys and muscles.
  - Kidneys stimulate production of renin-angiotensin-aldosterone system.
  - Increase in ADH.
### Circulatory Shock

- **Septic shock:**
  - Dangerously low blood pressure as a result of sepsis.
  - Occur through the action of endotoxin.
    - Endotoxin activates nitric oxide synthetase, producing NO.
    - NO causes vasodilation.
- Treat with drugs that inhibit the production of NO.

### Congestive Heart Failure

- Cardiac output is insufficient to maintain the blood flow required by the body.
- Caused by:
  - MI (most common cause).
  - Congenital defects.
  - Hypertension.
  - Disturbances in electrolyte concentrations.
    - $K^+$ and $Ca^{++}$.
- Compensations similar to those of hypovolemic shock.
- Treated with medications:
  - Digitalis and vasodilators, and diuretics.