Cardiovascular System
The Heart

What is the Cardiovascular System?

Blood circulated in Arteries, veins, and capillaries by the Pumping action of the heart

Functions of the Heart

• Generating blood pressure sufficient to efficiently cause blood to flow from heart to veins
• Keeping oxygenated and low-oxygen blood separate
• Adjusting blood pressure as conditions change (maintain homeostasis)
  – Changes in contraction rate and force match blood delivery to changing metabolic needs

Heart Anatomy

The Pulmonary and Systemic Circuits

• Heart is a transport system consisting of two side-by-side pumps
  – Right side receives low-oxygen blood from tissues
    • Moves blood to lungs to get rid of CO₂, pick up O₂, and return via pulmonary circuit
  – Left side receives oxygenated blood from lungs
    • Moves blood to body tissues via systemic circuit
Location of the heart in the mediastinum.

- **Midsternal line**
- **2nd rib**
- **Diaphragm**

**Sternum**

**Diaphragm**

- **(a)** - Base (posterior surface) leans toward right shoulder
- Apex points toward left hip
- More of mass on left – lack of bilateral symmetry
- Fist-sized, 250-350 g
- Mediastinum = medial cavity of thorax

### Chambers and Associated Great Vessels

- **Internal features**
  - Four chambers
    - Two superior **atria** (singular atrium)
    - Two inferior **ventricles**
  - **Interalatrial septum**: separates atria
    - **Fossa ovalis**: remnant of foramen ovale of fetal heart
  - **Interventricular septum**: separates ventricles
- ‘Walls’ consist of cardiac muscle, fibrous connective tissue, others in lesser amounts
Chambers and Associated Great Vessels (cont.)

**Atria**
- Small, thin-walled
  - Receive blood from veins
  - Convey blood to ventricles below
  - Auricle vs atrium
- **Right atrium**: receives deoxygenated (aka low-oxygen) blood from body
  - Superior & inferior vena cava, coronary sinus
- **Left atrium**: receives oxygenated blood from lungs
  - Four pulmonary veins

**Ventricles**
- Contain most of the volume of heart
- Primary pump
  - Thickness of ventricular myocardium reflects workload
- Right ventricle
  - Pumps blood into pulmonary trunk and pulmonary circulation
- Left ventricle
  - Pumps blood into aorta (largest artery in body) and begins systemic circulation
- Trabeculae carneae
  - Prevent suction, aid papillary muscles
- Papillary muscles
  - Anchor chordae tendineae that are attached to heart valves

The layers of the pericardium and of the heart wall.

1. **Superficial fibrous pericardium**: functions to protect, anchor heart to surrounding structures, and prevent overfilling
2. **Deep two layered serous pericardium**
   - **Parietal layer** lines internal surface of fibrous pericardium
   - **Visceral layer (epicardium)** on external surface of heart
   - Two layers separated by fluid-filled pericardial cavity (decreases friction)
Three Layers Of Heart Wall

1. **Epicardium**: visceral layer of serous pericardium

2. **Myocardium**: circular or spiral bundles of contractile cardiac muscle cells
   - **Cardiac skeleton**: crisscrossing, interlacing layer of connective tissue
     - Anchors cardiac muscle fibers
     - Supports great vessels and valves
     - Limits spread of action potentials to specific paths

3. **Endocardium**: innermost layer; is continuous with endothelial lining of blood vessels
   - Lines heart chambers and covers cardiac skeleton of valves

Heart valves

![Heart Valves Diagram](image)

The function of the atrioventricular (AV) valves

1. Blood returning to the heart fills atria, pressing against the AV valves. The increased pressure forces AV valves open.
2. As ventricles fill, AV valve flaps hang limply into ventricles.
3. Atria contract, forcing additional blood into ventricles.

(a) AV valves open; atrial pressure greater than ventricular pressure
The function of the semilunar (SL) valves

As ventricles contract and intraventricular pressure rises, blood is pushed up against semilunar valves, forcing them open.

(a) Semilunar valves open

As ventricles relax and intraventricular pressure falls, blood flows back from arteries, filling the cusps of semilunar valves and forcing them to close.

(b) Semilunar valves closed

Pathway of Blood Through Heart and Connected Vessels

- Equal volumes of blood are pumped to pulmonary and systemic circuits
- Pulmonary circuit is short, low-pressure circulation – ‘reoxygenation’ of blood returned to heart from body
- Systemic circuit is long, high-friction circulation – ‘distribution’ of oxygen-saturated pulmonary blood
- Anatomy of ventricles reflects differences – Left ventricle walls are much thicker than right
  - Pumps with greater pressure
Coronary Circulation

• Coronary arteries and veins
  – Functional blood supply to heart muscle itself
    • Living muscle tissue with limited anaerobic capabilities
    – Delivered when heart is relaxed, too much pressure in cardiac arteries for blood to flow while myocardium contracted
    – Shortest circulation in body
    – Left ventricle receives most of coronary blood supply; Heart receives 1/20th of body’s blood supply

• Arteries contain many anastomoses (junctions)
  – Provide additional routes for blood delivery
  – Cannot compensate for coronary artery occlusion
  – Narrowing, closing, plugging leads to ischemia and/or infarction

• Branching of coronary arteries varies among individuals
Microscopic anatomy of cardiac muscle fibers

- Muscle contraction is preceded by depolarizing action potential
- Depolarization wave travels down T tubules; causes sarcoplasmic reticulum (SR) to release Ca^{2+}
- Excitation-contraction coupling occurs – Ca binds to troponin causing filaments to slide

Microscopic anatomy of cardiac muscle.
Differences in the Physiology of Skeletal and Cardiac Muscle

- **Heart contracts as a unit**
  - All cardiomyocytes contract as a unit (functional syncytium) for effective pumping action, or none contract
  - Skeletal muscle fibers contract independently
- **Influx of Ca\(^{2+}\) from extracellular fluid triggers Ca\(^{2+}\) release from SR**
  - Depolarization opens slow Ca\(^{2+}\) channels in sarcolemma, allowing Ca\(^{2+}\) to enter cell
  - Extracellular Ca\(^{2+}\) then causes SR to release its intracellular Ca\(^{2+}\)
  - Skeletal muscles do not use extracellular Ca\(^{2+}\)

Differences in the Physiology of Skeletal and Cardiac Muscle

The heart relies almost exclusively on aerobic respiration

- Cardiac muscle has more mitochondria than skeletal muscle so has greater dependence on oxygen
- Skeletal muscle (depending on type) can go through fermentation when oxygen not present
- Both types of tissues can use other fuel sources
  - Cardiac is more adaptable to other fuels, including lactic acid, but must have oxygen
Setting the Basic Rhythm: The Intrinsic Conduction System

Coordinated heartbeat is a function of:

1. Presence of gap junctions
2. **Intrinsic cardiac conduction system**
   - Network of noncontractile (autorrhythmic) cells
   - **Cardiac pacemaker cells** have unstable resting membrane potentials called **pacemaker potentials** or **prepotentials**
   - Initiate and distribute impulses to coordinate depolarization and contraction of heart

What is extrinsic control?

The Intrinsic Conduction System

**Action potential initiation by pacemaker cells**

1. Pacemaker potential: K⁺ channels are closed, but slow Na⁺ channels are open, causing interior to become more positive
2. Depolarization: Ca²⁺ channels open (around −40 mV), allowing huge influx of Ca³⁺, leading to rising phase of action potential
3. Repolarization: K⁺ channels open, allowing efflux of K⁺, and cell becomes more negative

Pacemaker and action potentials of typical cardiac pacemaker cells

- **Pacemaker potential** This slow depolarization is due to both opening of Na⁺ channels and closing of K⁺ channels. Notice that the membrane potential is never a flat line.
- **Depolarization** The action potential begins when the pacemaker potential reaches threshold. Depolarization is due to Ca²⁺ influx through Ca⁺⁺ channels.
- **Repolarization** is due to Ca⁺⁺ channels deactivating and K⁺ channels opening. This allows K⁺ efflux, which brings the membrane potential back to its most negative voltage.
The Intrinsic Conduction System

1. Sinoatrial (SA) node
   - Primary pacemaker of heart in right atrial wall
     • Spontaneously depolarizes faster than rest of myocardium
     • Generates impulses about 75×/minute
       • sinus rhythm
         • Inherent rate of 100×/minute tempered by extrinsic factors including parasympathetic inhibition
     • Impulse spreads across atria cell to cell, reaching AV node

2. Atrioventricular (AV) node
   - In inferior interatrial septum
   - Delays impulses approximately 0.1 second
     • Cause: fibers are smaller in diameter, have fewer gap junctions
     • Allows atrial contraction prior to initiation of ventricular contraction
     • Inherent rate of 50×/minute in absence of SA node input
     • “ectopic focus” if it becomes primary pacemaker
The Intrinsic Conduction System

3. **Atrioventricular (AV) bundle** (bundle of His)
   - In superior interventricular septum
   - Only electrical connection between atria and ventricles
     - Atria and ventricles not connected via gap junctions
   - Carries AP through electrically-neutral cardiac skeleton

4. **Right and left bundle branches**
   - Two pathways in interventricular septum
   - Carry impulses toward apex of heart

The Intrinsic Conduction System

5. **Subendocardial conducting network**
   - Also referred to as **Purkinje fibers**
   - Complete pathway through interventricular septum into apex and ventricular walls, then cell to cell
   - AV bundle and subendocardial conducting network depolarize 30/min in absence of AV node input
     - “ectopic focus”
   - Ventricular contraction initiates at apex toward atria
   - Process from initiation at SA node to complete contraction takes ~0.22 seconds

Heartbeat modified by ANS via cardiac centers in medulla oblongata
- Cardioacceleratory center: sends signals through sympathetic trunk to increase both rate and force
- Stimulates SA and AV nodes, heart muscle, and coronary arteries
- Cardioinhibitory center: parasympathetic signals via vagus nerve to decrease rate
- Inhibits SA and AV nodes via vagus nerve
- Remember: nervous stimulation is dependent on AP frequency, type of neurotransmitter, type of receptor

Autonomic (extrinsic) innervation of the heart
Action Potentials of Contractile Cardiac Muscle Cells

- Contractile muscle fibers make up bulk of heart and are responsible for pumping action
  - Different from skeletal muscle contraction; cardiac muscle action potentials have plateau
- Steps involved in AP:
  1. Depolarization opens fast voltage-gated Na\(^+\) channels; Na\(^+\) enters cell

Action Potentials of Contractile Cardiac Muscle Cells (cont.)

2. Depolarization by Na\(^+\) also opens slow Ca\(^{2+}\) channels
   - At +30 mV, Na\(^+\) channels close, but slow Ca\(^{2+}\) channels remain open, prolonging depolarization
     - Seen as a plateau
3. After about 200 ms, slow Ca\(^{2+}\) channels close, and voltage-gated K\(^+\) channels open
   - Rapid efflux of K\(^+\) repolarizes cell to RMP
   - Ca\(^{2+}\) is pumped both back into SR and out of cell into extracellular space

Action Potentials of Contractile Cardiac Muscle Cells (cont.)

- More differences between contractile muscle fiber and skeletal muscle fiber contractions
  - AP in skeletal muscle lasts 1–2 ms; in cardiac muscle it lasts 200 ms
  - Contraction in skeletal muscle lasts 15–100 ms; in cardiac contraction lasts over 200 ms
- Benefit of longer AP and contraction:
  - Sustained contraction ensures efficient ejection of blood
  - Longer refractory period prevents tetanic contractions
The action potential of contractile cardiac muscle cells.

Mechanical Events

- **Systole**: period of heart contraction
- **Diastole**: period of heart relaxation
- **Cardiac cycle**:
  - Atrial systole and diastole and ventricular systole and diastole
  - Cycle represents series of pressure and blood volume changes leading to movement of blood in vessels
  - Mechanical events follow electrical events seen on ECG
- Blood flows from area of high pressure to area of low pressure unless impeded (by things like valves)

Mechanical Events of Heart and Phases of the Cardiac Cycle

**Ventricular filling**
1. Passive filling phase = atrial and ventricular diastole, all chambers filling
2. Active filling phase = atrial systole but ventricles relaxed – ‘forced’ filling of ventricles
   - End diastolic volume (EDV): volume of blood in each ventricle at end of ventricular diastole

**Ventricular systole**
3. Isovolumetric contraction phase: all valves are closed
4. Ejection phase: ventricular pressure exceeds pressure in large arteries, forcing SL valves open
   - Pressure in aorta around 120 mm Hg
   - End systolic volume (ESV): volume of blood remaining in each ventricle after systole
5. Isovolumetric relaxation phase: early ventricular diastole, atria already in diastole and accepting venous blood
Heart Sounds
• Two sounds (lub-dup)
• Associated with closing of heart valves
  – First sound is closing of AV valves at beginning of ventricular systole
  – Second sound is closing of SL valves at beginning of ventricular diastole
• Pause between lub-dups indicates heart relaxation

Electrocardiography
• Electrocardiograph can detect electrical currents generated by heart
• Electrocardiogram (ECG or EKG) is a graphic recording of electrical activity
  – Composite of all action potentials at given time; not a tracing of a single AP
  – Electrodes are placed at various points on body to measure voltage differences
• A diagnostic tool

An electrocardiogram (ECG) tracing.
Atrial depolarization, initiated by the SA node, causes the P wave.

With atrial depolarization complete, the impulse is delayed at the AV node.

Ventricular depolarization begins at apex, causing the QRS complex. Atrial repolarization occurs.

Ventricular depolarization is complete.

Ventricular repolarization begins at apex, causing the T wave. Ventricular repolarization is complete.

**Cardiac Output (CO)**

- Volume of blood pumped by each ventricle in 1 minute
- Highly variable
  - CO changes (increases/decreases) if either or both SV or HR is changed

**CO = heart rate (HR) x stroke volume (SV)**
- HR = number of beats per minute
- SV = volume of blood pumped out by one ventricle (left) with each beat

- At rest:
  \[
  CO (\text{ml/min}) = \text{HR (75 beats/min)} \times \text{SV (70 ml/beat)}
  \]
  \[
  = 5.25 \text{ L/min}
  \]

**Putting it all together!**
Cardiac Reserve

Difference between resting and maximal CO

• Maximal CO is 4–5 times resting CO in nonathletic people (20–25 L/min)
• Maximal CO may reach 35 L/min in trained athletes

Regulation of Cardiac Output

Stroke Volume
• Mathematically: \( SV = EDV - ESV \)
  – EDV is affected by length of ventricular diastole and venous pressure (~120 ml/beat)
  – ESV is affected by arterial BP and force of ventricular contraction (~50 ml/beat)
  – Normal \( SV = 120 \text{ ml} - 50 \text{ ml} = 70 \text{ ml/beat} \)
• Three main factors that affect SV:
  – Preload
  – Contractility
  – Afterload

Regulation of Stroke Volume

Preload: degree of stretch of heart muscle
• Just before systole
• Cardiac muscle exhibits a length-tension relationship
  – At rest, cardiac muscle cells are shorter than optimal length
  – When stretched by increases in EDV a big increase in contractile force results
• Most important factor in preload stretching of cardiac muscle is venous return—amount of blood returning to heart
Regulation of Stroke Volume (cont.)

Preload (cont.)
- Slowed heart rate or exercise increase venous return
- Increased venous return distends (stretches) ventricles and increases contraction force
- **Frank-Starling law of the heart**
  - "ability of the heart to change its force of contraction and therefore stroke volume in response to changes in venous return"

\[
\text{Venous Return} \rightarrow \text{EDV} \rightarrow \text{SV} \rightarrow \text{CO}
\]
Frank-Starling Law

Regulation of Stroke Volume (cont.)

**Contractility**
- Contractile strength at given muscle length
  - Independent of muscle stretch and EDV
- Increased contractility lowers ESV; caused by:
  - Sympathetic epinephrine release stimulates increased Ca^{2+} influx, leading to more cross bridge formations
  - Positive inotropic agents increase contractility
    - Thyroxine, glucagon, epinephrine, digitalis, high extracellular Ca^{2+}
- Decreased by negative inotropic agents
  - Acidosis (excess H^+), increased extracellular K^+, calcium channel blockers
Regulation of Stroke Volume (cont.)

**Afterload**: back pressure exerted by arterial blood on semilunar valves
- Ventricles must overcome afterload to eject blood
  - Back pressure from arterial blood pushing on SL valves is major pressure
    - Aortic pressure is around 80 mm Hg
    - Pulmonary trunk pressure is around 10 mm Hg
- Hypertension increases afterload, resulting in increased ESV and reduced SV

Factors involved in determining cardiac output.

<table>
<thead>
<tr>
<th>Exercise (by sympathetic activity, skeletal muscle and respiratory pumps; see Chapter 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular filling time (due to heart rate)</td>
</tr>
<tr>
<td>Bloodborne epinephrine, thyroxine, excess Ca$^{2+}$</td>
</tr>
<tr>
<td>CNS output in response to exercise, fright, anxiety, or blood pressure</td>
</tr>
<tr>
<td>Venous return</td>
</tr>
<tr>
<td>Contractility</td>
</tr>
<tr>
<td>Sympathetic activity</td>
</tr>
<tr>
<td>Parasympathetic activity</td>
</tr>
</tbody>
</table>

Initial stimulus | Physiological response | Result |
--- | --- | --- |
Cardiac output ($CO = SV \times HR$)