Cardiovascular System:

Heart

- Roughly size of human fist (~ 250 – 350 grams)
- Located in the mediastinum (medial cavity of thorax)
- "Double pump" composed of cardiac muscle

Heart layers:

- Epicardium: Anchors cardiac fibers
- Myocardium: Reinforces heart structures, directs electrical signals
- Endocardium: Stays smooth

Heart - Chambers, Vessels & Valves

- Atria: Receiving chambers, small, thin-walled
- Vessels: Return blood above diaphragm
- Valves: Assist in valve closure

Pericardial sac:

- Double-walled sac enclosing the heart

Fibrous pericardium:

- Protects heart
- Anchors heart
- Prevents overfilling

Pericardial cavity:

- Contains serous fluid (friction-free environment)

Pericardial cavity:

- Base: Point of maximum intensity
- Apex
- Coronary sulcus

Pulmonary trunk:

- Returns blood from lungs
- Carries blood to body (largest artery in body)

Superior vena cava:

- Returns blood above diaphragm

Pulmonary veins:

- (4) Returns blood from lungs to body

Inferior vena cava:

- Returns blood below diaphragm

Ligamentum arteriosum:

- Remnant of fetal duct between aorta and pulmonary trunk (ductus arteriosus)

Fossa ovalis:

- Shallow depression; remnants of hole between atria in fetal heart

Trabeculae carnaeae:

- Muscle ridges; assist in maintaining momentum

Papillary muscle:

- Cone-like muscle; assists in valve closure

Pectinate muscles:

- Muscle bundles; assist in atrial contraction

Fossa media:

- Shallow depression; remnants of hole between atria in fetal heart

Auricles:

- (little ears); increase atrial volume

Left atrium:

- Receives systemic blood

Right atrium:

- Receives pulmonary blood

Left ventricle:

- Pumping chamber

Right ventricle:

- Pumping chamber

Rear atrium:

- Receives systemic blood

Front atrium:

- Receives pulmonary blood
Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) - Figure 18.7: Blood in the atria / ventricles provides little nourishment to heart tissue

Heart – Chambers, Vessels & Valves

Blood flows through the heart in a single direction due to the presence of valves

Cusp:
- Flap of endocardium reinforced by connective tissue core

Valves:
- Pulmonary semilunar valve
- Right aortic semilunar valve (tricuspid valve)
- Left aortic semilunar valve (bicuspid valve / mitral valve)

Papillary muscle:
- Coronary circulation delivery limited to when heart is relaxed...

Coronary sinus:
- Great cardiac vein
- Small cardiac vein
- Middle cardiac vein

Valves open / close based on pressure differences

Pulmonary circuit:
- Oxygenated (long, high pressure loop)
- Systemic circuit:
- Deoxygenated (short, low pressure loop)

In steady state, cardiac output from each ventricle must be equal as well as the venous return to each atrium

Valves:
- Semilunar valves
- Aortic semilunar valves
- Pulmonary semilunar valve
- Right aortic semilunar valve (tricuspid valve)
- Left aortic semilunar valve (bicuspid valve / mitral valve)

Conduction system:
- Atrioventricular node
- Bundle of His
- Purkinje fibers

Pathophysiology:

Valvular Regurgitation:
- Valve does not close properly; blood regurgitated
- Causes:
  - Congenitally deformed valve
  - Post-inflammatory scarring
  - Infective endocarditis
  - Rupture of cord / muscle

Valvular Stenosis:
- Valve flaps become stiff; opening constricted
- Causes:
  - Congenitally deformed valve
  - Post-inflammatory scarring
  - Calcification of valve

Treatment = Valve replacement
Cardiac Electrophysiology

Muscle Fiber Anatomy
- Situated, branched cells (~ 85 – 100 μm)
- Single nucleus (sometimes two...)
- Large [mitochondria] (~ 15x skeletal muscle)
- High fatigue resistance
- Electrical synapses (intercalated discs)

Cardiovascular System – Heart

Heart Chambers, Vessels & Valves
Heart designed to create complex flow patterns (direct maintain blood momentum)
1) Chambers arranged in loop pattern
2) Delivery vessels curved
3) Grooves / ridges within chambers

Cardiovascular System – Heart

Cardiac Electrophysiology

Intrinsic Conduction System:
- Normal sinus rhythm: 60 – 100 beats / min
- Connects atria to ventricles
- Slowed conduction velocity
- Connects atria to ventricles
- Atrial fibrillation
- Ventricular filling

Cardiovascular System – Heart

Muscle Fiber Anatomy
- Contractile cell
- Striated, branched cells
- High fatigue resistance
- Large [mitochondria]
- Dense T-tubule system

Cardiovascular System – Heart

Functional synapse: The entire myocardium behaves as a single coordinated unit

Cardiovascular System – Heart

Myocardial Contractions
- Area of contraction: ~ 85% of total myocardium
- Site of contraction: Endocardium
- Sarcomere: Length of contractile unit (l)
- Myosin: Crossbridge (b)

Cardiovascular System – Heart

APs of Atria, Ventricles & Purkinje System
- Long duration AP (~ 150 – 200 ms)
- Net current = 0

Cardiovascular System – Heart

APs of Atria, Ventricles & Purkinje System
- Plateau: Sustained period of depolarization
- Long refractory period
- 245 beats / min

Cardiovascular System – Heart

Regional Synaptogenesis
- Innervation of myocardium
- Synaptic coupling
- Site of innervation
- Site of contraction

Cardiovascular System – Heart

Regulation of Cardiac Function
- Membrane potential determined by relative conductances / concentrations of permeable ions
- Ions flow down electrochemical gradient toward equilibrium potential (Nernst equation)
- Membrane potential expressed in mV
- Inside cell expressed relative to outside
- Resting membrane potential determined primarily by K+ ions (low interstitial K+)
- Na+ / K+ pumps maintain gradients across membranes
- Changes in membrane potential caused by flow of ions into / out of cell
- Threshold potential / represents the point at which a depolarization even becomes self-sustaining (voltage-gated channels)
Cardiac Electrophysiology

APs of Atria, Ventricles & Purkinje System:

Phases of the Action Potential:

- **Phase 3 – Repolarization**
  - Period of rapid repolarization
  - $Ca^{2+}$ channels close ($g_{Ca}$)
  - $K^+$ enters via VG channels ($g_{K}$)

- **Phase 4 – Resting membrane potential**
  - Membrane potential stabilizes
  - $K^+$ exits via leaky channels
  - $Na^+ / K^+$ pumps restore gradients

Changes in RMP (due to gradient issues) directly affect responsiveness of heart.

Changes in RMP (due to gradient issues) directly affect responsiveness of heart.

Cardiac dysrhythmias = irregular heartbeat

Cardiac Electrophysiology

Pacemaker of the Heart:

1) Exhibits automaticity (spontaneous AP generation)
2) Unstable resting membrane potential
3) No sustained plateau

Phase 0 – Upstroke
- Slower than other cardiac tissue
- $Ca^{2+}$ enters via VG channels ($g_{Ca}$)

Phase 1 / Phase 2
- Absent

Phase 3 – Repolarization
- Similar to other cardiac cells

Phase 4 – Spontaneous depolarization
- Accounts for automaticity of SA node
- $Na^+$ enters via VG channels ($g_{Na}$)
- Open via repolarization event

Once threshold reached, VG $Ca^{2+}$ channels open (return in Phase 0)

Rate of depolarization sets heart rate

Cardiac Electrophysiology

Other myocardial cells also have the capacity for spontaneous phase 4 depolarization; these are called latent pacemakers.

Location
- Sinoatrial node: 70 – 80
- Atrioventricular node: 40 – 60
- Bundle of HIs: 40
- Purkinje fibers: 15 – 20

Overdrive suppression: Latent pacemakers own capacity to spontaneously depolarize is suppressed by the SA node.

Ectopic pacemaker: Latent pacemaker takes over and becomes the pacemaker

1) SA node firing rate decreases
2) Intrinsic rate of latent pacemakers increases
3) Blockade in normal conduction pathway

Cardiac Electrophysiology

Conduction velocity (speed at which APs propagate in tissues) differs among myocardial tissues.

Cardiovascular System

Effective refractory period (ERP) = time after which SA node can fire

Relative refractory period (RRP) = time after which atrial or ventricular cells can fire

Supranormal period (SNP) = time after which normal conduction return

Depolarization of ventricles = ventricular AP

Conduction velocity: Graphical recording of electrical currents generated and transmitted through heart.

- **P wave** Depolarization of the atria
- **Q wave** Presence of the heart
- **R wave** Repolarization of the atria
- **S wave** Depolarization of the ventricles
- **T wave** Repolarization of the ventricles

Cardiovascular System

Intrinsic firing rate (impulses/min)
- Sinoatrial node: 70 – 80
- Atrioventricular node: 40 – 60
- Bundle of HIs: 40
- Purkinje fibers: 15 – 20

Cardiovascular System

Net current = 0
The autonomic nervous system can directly affect the heart rate; these effects are called chronotropic effects.

**Positive chronotropic effects:** (increase heart rate)
- Under sympathetic control
  - $\beta_1$ receptors
    - Leads to $T_{Ca^2+}$ release from SR more rapidly
    - Pharmacology: $\beta$ blockers (e.g., propranolol)

**Negative chronotropic effects:** (decrease heart rate)
- Under parasympathetic control
  - $\alpha$ receptors
    - Leads to $T_{Ca^2+}$ release from SR less rapidly

The autonomic nervous system can directly affect heart contractility; these effects are called inotropic effects.

**Positive inotropic effects:** (increase contractility)
- Under sympathetic control
  - $\beta_1$ receptors
    - $Ca^{2+}$ enters cell (plasma phase)
      - $Ca^{2+}$ enters cell via $Ca^{2+}$ channels in sarcolemma
      - $Ca^{2+}$ binds to tropomyosin C, cross-bridging occurs

**Mechanisms of action:**
1) $Phosphorylation$ of $Ca^{2+}$ channels in sarcolemma
   - $Ca^{2+}$ enters during plateau / released from SR
2) $Phosphorylation$ of phospholamban (regulates $Ca^{2+}$ ATPase activity)
   - $Ca^{2+}$ uptake / storage in SR

**Mechanisms of action:**
- $Ca^{2+}$ enters during plateau / released from SR
- Faster relaxation time
- Increased peak tension during subsequent ‘teeth’

The basic contractile machinery between cardiac and smooth muscle is similar.
Cardiac Muscle Contraction

The autonomic nervous system can directly affect heart contractility; these effects are called inotropic effects.

**Positive inotropic effects:**
- **Increase contractility**

**Negative inotropic effects:**
- **Decrease contractility**
- **Increase heart rate**
- **Increase end systolic volume**
- **Decrease ejection fraction**

1) Cardiac glycosides inhibit Na+/K+ ATPase
2) Intracellular [Na⁺] increases
3) Change in Na⁺ gradient slows down Ca⁺-Na⁺ exchanger
4) Intracellular [Ca²⁺] increases
5) [Ca²⁺] increases

Used extensively for the treatment of congestive heart failure.

Changes in heart rate also produce changes in cardiac contractility.

- As heart rate increases, the tension developed in each beat increases, depending on a maximal value.

**Cardiovascular System — Heart**

**Systole = Contraction of heart**

**Diastole = Relaxation of heart**

Ventricular function is described by several parameters:

1) **Cardiac Output:** Total volume of blood ejected by each ventricle per unit time (usually one minute)

   \[ \text{Cardiac output} = \text{Heart rate} \times \text{Stroke volume} \]

2) **Stroke Volume:** Volume of blood ejected by each ventricle per heartbeat

   \[ \text{Stroke volume} = \text{End diastolic volume} - \text{End systolic volume} \]

3) **Ejection Fraction:** Fraction of the end diastolic volume ejected in each stroke volume

   \[ \text{Ejection fraction} = \frac{\text{Stroke volume}}{\text{End diastolic volume}} \]

   - Heart rate = 75 beats/min
   - End diastolic volume = 140 ml
   - End systolic volume = 70 ml
   - Stroke volume = 70 ml
   - Calculate: Ejection fraction = 0.50
   - Cardiac output = 5250 ml/min

Cardiovascular System — Heart

**Cardiovascular System — Heart**

**Figure 4.19**

Fraction of the end diastolic volume ejected in each stroke volume (ml)

**Figure 4.20**

Ejection fraction:

- Cardiovascular System

**Frank-Starling Law of the Heart:**

The volume of blood ejected by the ventricle depends on the volume present in the ventricle at the end of diastole.

- The more the cardiac cells are stretched, the more blood they can pump.

**preload:**

- **Preload:** The resting length from which cardiac muscle contracts

- **optimal length:**
  - Saline length = 1.9 μm
  - Sarcomere length = 2.2 μm

**optimal tension:**

- **optimal tension:**
  - Saline length = 1.9 μm
  - Sarcomere length = 2.2 μm

**Stress:**

- **Stress:**
  - Saline length = 1.9 μm
  - Sarcomere length = 2.2 μm
The volume of blood ejected by the ventricle depends on the volume present in the ventricle at the end of diastole. This relationship ensures that the volume the heart ejects in systole equals the volume it receives in venous return.

For example, if the ventricle is filled with 140 ml of blood at the start of the cardiac cycle, it will eject approximately 90 ml of blood during systole, leaving 50 ml in the ventricle at the end of systole.

The work performed by the heart during a single beat is defined as the stroke work. The stroke work is calculated as the product of the force exerted by the ventricle and the distance over which it is exerted, which is essentially the volume ejected during systole.

The Frank-Starling Law of the Heart states that the stroke work of the heart is directly proportional to the end-diastolic volume. This means that as the end-diastolic volume increases, the force of contraction will also increase, resulting in a greater stroke work.

However, there is a limit to this relationship due to the negative inotropic effect. When the ventricle is overfilled, the myocardial fibers stretch beyond their optimal length, which reduces the force of contraction and therefore the stroke work.

The myocardial O₂ consumption rate correlates directly with the cardiac minute work. Thus, an increase in the cardiac minute work leads to an increase in the O₂ consumption.

The largest percentage of O₂ consumption is for systolic work, which is the work performed by the heart during systole when it is actively generating pressure to eject blood. The Law of Laplace, which describes the relationship between wall tension and radius, is also relevant in this context.

In summary, the Frank-Starling Law of the Heart plays a crucial role in regulating cardiac performance and energy expenditure. Understanding this relationship is essential for comprehending the physiological mechanisms that govern cardiac function and the factors that influence myocardial oxygen consumption.
Cardiac Muscle Contraction

The cardiac output can also be measured using the Fick principle (conservation of mass).

In the steady state, the rate of O₂ consumed by the body must equal the amount of O₂ leaving the lungs (pulmonary veins) minus the amount of O₂ returning to the lungs (pulmonary artery).

\[ O_2 \text{ consumption} = CO_{\text{left ventricle}} \times [O_2]_{\text{pulmonary artery}} - CO_{\text{right ventricle}} \times [O_2]_{\text{pulmonary vein}} \]

Solve for cardiac output:

\[ \text{Cardiac Output} = \frac{O_2 \text{ consumption}}{[O_2]_{\text{pulmonary artery}} - [O_2]_{\text{pulmonary vein}}} \]

Mechanical / Electrical Overview:

Cardiac Cycle: Mechanical and electrical events during single heart beat

- Reduced Ventricular Ejection: (D)
  - Ventricles begin to repolarize (end of T wave)
  - Ventricular / atrial pressure falls (blood still moving out)
  - Atria continue to fill (pressure rising)
- Isovolumetric Ventricular Relaxation: (E)
  - Ventricles fully repolarized (T wave complete)
  - Left ventricular pressure drops rapidly (systole)
  - Aortic valve closes (2nd heart sound – ‘Lub’)
  - No VOLUME CHANGE
- Rapid Ventricular Filling: (F)
  - Mitral valve opens (F_pulmonary > F_venous)
  - Ventricular volume increases rapidly
  - Little change in ventricular pressure (compliance)
  - Aortic pressure decreases (blood carried away)

Cardiovascular System – Heart

A man has a resting O₂ consumption of 250 mL O₂/ min, a femoral arterial O₂ content of 0.20 mL O₂/ mL blood, and a pulmonary arterial O₂ content of 0.15 mL O₂/ mL blood.

What is his cardiac output?

Cardiac Output = \( \frac{250 \text{ mL O}_2/ \text{min}}{0.20 \text{ mL O}_2/ \text{mL} - 0.15 \text{ mL O}_2/ \text{mL}} \)

Cardiac Output = 5000 mL/ min

Mechanical / Electrical Overview:

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Cardiovascular System – Heart

Cardiac Output = \( \frac{250 \text{ mL O}_2/ \text{min}}{0.20 \text{ mL O}_2/ \text{mL} - 0.15 \text{ mL O}_2/ \text{mL}} \)

Cardiac Output = 5000 mL/ min