Chapter 18  Part A

The Cardiovascular System

Human Anatomy & Physiology

Tenth Edition

1/19/16
Similarities of Cardiac and Skeletal Muscle

- RMP
- Ion concentration
- Depolarization
- Action Potential
- Repolarization
- Restoring resting membrane potential
- Types of Cardiac muscle fibers
18.4 Cardiac Muscle Fibers

Microscopic Anatomy

• Cardiac muscle cells: striated, short, branched, fat, interconnected
  – One central nucleus (at most, 2 nuclei)
  – Contain numerous large mitochondria (25–35% of cell volume) that afford resistance to fatigue

• Intercalated discs are connecting junctions between cardiac cells
  – Gap junctions:
  – Desmosomes:
Figure 18.11a Microscopic anatomy of cardiac muscle.

- Cardiac muscle cell
- Nucleus
- Intercalated discs
- Gap junctions (electrically connect myocytes)
- Desmosomes (keep myocytes from pulling apart)
Figure 18.11b Microscopic anatomy of cardiac muscle.

Cardiac muscle cell

Intercalated disc

Mitochondrion

Nucleus

Sarcolemma

I band

A band

Z disc

T tubule

Sarcoplasmic reticulum

(b)
How Does the Physiology of Skeletal and Cardiac Muscle Differ? (cont.)

• Differences between cardiac and skeletal muscle
  – Some cardiac muscle cells are self-excitabile
    – *Pacemaker cells*: noncontractile cells that spontaneously depolarize
      » Initiate depolarization of entire heart
      » Do not need nervous system stimulation, in contrast to skeletal muscle fibers
  – Heart contracts as a unit
    • All cardiomyocytes contract as unit (functional syncytium), or none contract
How Does the Physiology of Skeletal and Cardiac Muscle Differ? (cont.)

- **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\(^{2+}\)

- **Tetanic contractions cannot occur in cardiac muscles**
  - Cardiac muscle fibers have longer absolute refractory period than skeletal muscle fibers
    - Absolute refractory period is almost as long as contraction itself
How Does the Physiology of Skeletal and Cardiac Muscle Differ? (cont.)

– The heart relies almost exclusively on aerobic respiration

  • Cardiac muscle has more mitochondria than skeletal muscle so has greater dependence on oxygen
    – Cannot function without oxygen
  • Skeletal muscle 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
<table>
<thead>
<tr>
<th></th>
<th>Skeletal Muscle</th>
<th>Cardiac Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Structure</strong></td>
<td>Striated, long, cylindrical, multinucleate</td>
<td>Striated, short, branched, one or two nuclei per cell</td>
</tr>
<tr>
<td><strong>Gap junctions</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Contracts as a unit</strong></td>
<td>No, motor units must be stimulated individually</td>
<td>Yes, gap junctions create a functional syncytium</td>
</tr>
<tr>
<td><strong>T tubules</strong></td>
<td>Abundant</td>
<td>Fewer, wider</td>
</tr>
<tr>
<td><strong>Sarcoplasmic reticulum</strong></td>
<td>Elaborate; has terminal cisterns</td>
<td>Less elaborate; no terminal cisterns</td>
</tr>
<tr>
<td><strong>Source of Ca⁺⁺ for contraction</strong></td>
<td>Sarcoplasmic reticulum only</td>
<td>Sarcoplasmic reticulum and extracellular fluid</td>
</tr>
<tr>
<td><strong>Ca⁺⁺ binds to troponin</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Pacemaker cells present</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Tetanus possible</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Supply of ATP</strong></td>
<td>Aerobic and anaerobic (fewer mitochondria)</td>
<td>Aerobic only (more mitochondria)</td>
</tr>
</tbody>
</table>
Figure 18.15 The action potential of contractile cardiac muscle cells.

1. **Depolarization** is due to Na\(^+\) influx through fast voltage-gated Na\(^+\) channels. A positive feedback cycle rapidly opens many Na\(^+\) channels, reversing the membrane potential. Channel inactivation ends this phase.

2. **Plateau phase** is due to Ca\(^{2+}\) influx through slow Ca\(^{2+}\) channels. This keeps the cell depolarized because most K\(^+\) channels are closed.

3. **Repolarization** is due to Ca\(^{2+}\) channels inactivating and K\(^+\) channels opening. This allows K\(^+\) efflux, which brings the membrane potential back to its resting voltage.
Figure 18.12 Pacemaker and action potentials of typical cardiac pacemaker cells.

1. **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.

2. **Depolarization** The action potential begins when the pacemaker potential reaches threshold. Depolarization is due to Ca^{2+} influx through Ca^{2+} channels.

3. **Repolarization** is due to Ca^{2+} channels inactivating and K^+ channels opening. This allows K^+ efflux, which brings the membrane potential back to its most negative voltage.

Review laboratory information on Intrinsic Conduction System
Figure 18.13 Intrinsic cardiac conduction system and action potential succession during one heartbeat.

1. The sinoatrial (SA) node (pacemaker) generates impulses.
2. The impulses pause (0.1 s) at the atrioventricular (AV) node.
3. The atrioventricular (AV) bundle connects the atria to the ventricles.
4. The bundle branches conduct the impulses through the interventricular septum.
5. The subendocardial conducting network depolarizes the contractile cells of both ventricles.

(a) Anatomy of the intrinsic conduction system showing the sequence of electrical excitation

(b) Comparison of action potential shape at various locations
Clinical Applications

• Calcium channel blockers – What effect?
  – Verapamil -
  – Procardia -

• Non-calcium channel blockers
  – Epinephrine and Norepinephrine
  – Lidocaine -

• Digoxin (Digitalis) – increases Ca++ entry
18.6 Mechanical Events of Heart

• **Systole**: period of heart contraction
• **Diastole**: period of heart relaxation
• **Cardiac cycle**: blood flow through heart during one complete heartbeat
  – Atrial systole and diastole are followed by ventricular systole and diastole
  – Cycle represents series of pressure and blood volume changes
  – Mechanical events follow electrical events seen on ECG
• Three phases of the cardiac cycle (following left side, starting with total relaxation)
Figure 18.19 Summary of events during the cardiac cycle.
Cardiac Output (CO)

- Volume of blood pumped by each ventricle in 1 minute
- \( CO = \text{heart rate (HR)} \times \text{stroke volume (SV)} \)
  - HR = number of beats per minute
  - SV = volume of blood pumped out by one ventricle with each beat
- Normal: 5.25 L/min
18.7 Regulation of Pumping

- **Cardiac output**: amount of blood pumped out by each ventricle in 1 minute
  - Equals heart rate (HR) times stroke volume (SV)

- **Stroke volume**: volume of blood pumped out by one ventricle with each beat
  - Correlates with force of contraction

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

• 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
• **Cardiac reserve**: difference between resting and maximal CO
• CO changes (increases/decreases) if either or both SV or HR is changed
• CO is affected by factors leading to:
  — Regulation of stroke volume
Regulation of 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 ml − 50 ml = 70 ml/beat

- Three main factors that affect SV:
  - Preload
  - Contractility
  - Afterload
Preload: degree of stretch of heart muscle

- **Preload**: degree to which cardiac muscle cells are stretched just before they contract
  - Changes in preload cause changes in SV
    - Affects EDV
    - Relationship between preload and SV called **Frank-Starling law of the heart**

- Cardiac muscle exhibits a length-tension relationship
  - At rest, cardiac muscle cells are shorter than optimal length; leads to dramatic increase in contractile force
Regulation of Stroke Volume (cont.)

• **Preload (cont.)**
  – Most important factor in preload stretching of cardiac muscle is **venous return**—amount of blood returning to heart

  • Slow heartbeat and exercise increase venous return

  • Increased venous return distends (stretches) ventricles and increases contraction force

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Venous Return ➔ EDV ➔ SV ➔ CO
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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
Figure 18.22 Norepinephrine increases heart contractility via a cyclic AMP second messenger system.

**Diagram Description**

- **Norepinephrine** interacts with the **Receptor (β₁-adrenergic)**, which activates the **Adenylate cyclase**.
- ATP is converted to **cAMP**.
- **G protein (Gₛ)** binds and activates **GTP**.
- **GTP** activates **inactive protein kinase**.
- **Active protein kinase** phosphorylates the **Sarcoplasmic reticulum (SR)**.
- **Ca²⁺** channels in the SR release **Ca²⁺** into the cytoplasm.
- **Ca²⁺** enters from extracellular fluid and binds to troponin, leading to cross bridge binding and increased force of contraction.

**Key Components**

- **Extracellular fluid**
- **Cardiac muscle cytoplasm**
- **Ca²⁺** channels in the plasma membrane
- **↑ Force of contraction**
• **Afterload**: back pressure exerted by arterial blood
  
  – **Afterload** is pressure that ventricles must overcome 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
Regulation of Heart Rate

• If SV decreases as a result of decreased blood volume or weakened heart, CO can be maintained by increasing HR and contractility
  – *Positive chronotropic* factors increase heart rate
  – *Negative chronotropic* factors decrease heart rate

• Heart rate can be regulated by:
  – Autonomic nervous system
  – Chemicals
  – Other factors
• Autonomic nervous system regulation of heart rate
  – Sympathetic nervous system can be activated by emotional or physical stressors
  – Norepinephrine is released and binds to $\beta_1$-adrenergic receptors on heart, causing:
    • Pacemaker to fire more rapidly, increasing HR
      – EDV decreased because of decreased fill time
    • Increased contractility
      – ESV decreased because of increased volume of ejected blood
• Autonomic nervous system regulation of heart rate (cont.)
  – Because both EDV and ESV decrease, SV can remain unchanged
  – Parasympathetic nervous system opposes sympathetic effects
    • Acetylcholine hyperpolarizes pacemaker cells by opening K^+ channels, which slows HR
    • Has little to no effect on contractility
• Autonomic nervous system regulation of heart rate (cont.)
  – Heart at rest exhibits **vagal tone**
    • Parasympathetic is dominant influence on heart rate
    • Decreases rate about 25 beats/min
    • Cutting vagal nerve leads to HR of ~100
• Autonomic nervous system regulation of heart rate (cont.)
  – When sympathetic is activated, parasympathetic is inhibited, and vice-versa
  – **Atrial (Bainbridge) reflex**: sympathetic reflex initiated by increased venous return, hence increased atrial filling
    • Atrial walls are stretched with increased volume
    • Stimulates SA node, which increases HR
    • Also stimulates atrial stretch receptors that activate sympathetic reflexes
Regulation of Heart Rate (cont.)

- **Chemical regulation of heart rate**
  - **Hormones**
    - Epinephrine from adrenal medulla increases heart rate and contractility
    - Thyroxine increases heart rate; enhances effects of norepinephrine and epinephrine
  - **Ions**
    - Intra- and extracellular ion concentrations (e.g., $\text{Ca}^{2+}$ and $\text{K}^+$) must be maintained for normal heart function
      - Imbalances are very dangerous to heart
Clinical – Homeostatic Imbalance 18.7

• **Hypocalcemia**: depresses heart

• **Hypercalcemia**: increases HR and contractility

• **Hyperkalemia**: alters electrical activity, which can lead to heart block and cardiac arrest

• **Hypokalemia**: results in feeble heartbeat; arrhythmias
Regulation of Heart Rate (cont.)

• Other factors that influence heart rate
  – Age
    • Fetus has fastest HR; declines with age
  – Gender
    • Females have faster HR than males
  – Exercise
    • Increases HR
    • Trained athletes can have slow HR
  – Body temperature
    • HR increases with increased body temperature
Homeostatic Imbalance of Cardiac Output

• Congestive heart failure (CHF)
  – Progressive condition; CO is so low that blood circulation is inadequate to meet tissue needs
  – Reflects weakened myocardium caused by:
    • **Coronary atherosclerosis**: clogged arteries caused by fat buildup; impairs oxygen delivery to cardiac cells
      – Heart becomes hypoxic, contracts inefficiently
• Congestive heart failure (CHF) (cont.)
  • **Persistent high blood pressure:** aortic pressure >90 mmHg causes myocardium to exert more force
    – Chronic increased ESV causes myocardium hypertrophy and weakness
  • **Multiple myocardial infarcts:** heart becomes weak as contractile cells are replaced with scar tissue
  • **Dilated cardiomyopathy (DCM):** ventricles stretch and become flabby, and myocardium deteriorates
    – Drug toxicity or chronic inflammation may play a role
Homeostatic Imbalance of Cardiac Output (cont.)

- Congestive heart failure (CHF) (cont.)
  - Either side of heart can be affected:
    - Left-sided failure results in **pulmonary congestion**
      - Blood backs up in lungs
    - Right-sided failure results in **peripheral congestion**
      - Blood pools in body organs, causing edema
  - Failure of either side ultimately weakens other side
    - Leads to *decompensated*, seriously weakened heart
    - Treatment: removal of fluid, drugs to reduce afterload and increase contractility