HISTOLOGY
Cardiac Muscle

FIGURE 20.12

1. Comparison to skeletal muscle.
   A. Cardiac muscle has actin and myosin myofibrils arranged to form sarcomeres and the mechanism of contraction is like that in skeletal muscle.

   B. Cardiac muscle has a T tubule system and sarcoplasmic reticulum similar to skeletal muscle. A T tubule next to the sarcoplasmic reticulum is called a diad (recall the triad of skeletal muscle). The excitation-contraction mechanism in cardiac muscle is similar to that in skeletal muscle, but it is slower.

   C. Cardiac muscle cells typically have a single nucleus, whereas skeletal muscle cells are multinucleated.

   D. Cardiac muscle cells are smaller in diameter, shorter, and branched compared to skeletal muscle. Cardiac muscle cells are also connected to each other by intercalated disks (a type of gap junction).
      1) The intercalated disks have very low electrical resistance and action potentials readily pass from one cardiac muscle cell to the next.
      2) When one cardiac muscle cell contracts they all contract (this is not the case for skeletal muscle, in which motor units can contract independently of each other). Thus cardiac muscle functions as a single unit.

2. Energy metabolism.
   A. Cardiac muscle is well supplied with blood vessels (coronary circuit) to support aerobic respiration.

   B. Cardiac muscle aerobically uses glucose, fatty acids, and lactic acid to produce ATP molecules for energy.

   Explain where the lactic acid comes from and why it is advantageous for cardiac muscle to use it as a source of energy (hint: think of an exercising person).
C. Cardiac muscle does not develop a significant oxygen debt.
   1) Recall that an oxygen debt is the oxygen needed for the chemical reactions of aerobic respiration that produce the ATP molecules used to convert the lactic acid produced by anaerobic respiration to glucose.

   2) Cardiac muscle has little ability to perform anaerobic respiration and produce lactic acid, i.e., develop an oxygen debt. Instead, cardiac muscle uses lactic acid as an energy source.

**ELECTRICAL PROPERTIES**

1. Cardiac muscle has a resting membrane potential like that in skeletal muscle and neurons.

2. Stimulation of the cardiac cell membrane results in an action potential. Action potentials are the signal that results in contraction of cardiac muscle.

**Action Potentials**

1. Reminder: The depolarization phase of the action potential results from the movement of $\text{Na}^+$ into a cell, whereas the repolarization phase results from the movement of $\text{K}^+$ out of the cells.

2. General principle: The movement of a positive ion into a cell causes depolarization, whereas the movement of a positive ion out of a cell causes repolarization.

![FIGURE 20.14](image)

<table>
<thead>
<tr>
<th>Channel Activity</th>
<th>Ion Movement</th>
<th>Membrane Potential Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{Na}^+$ channels open</td>
<td>$\text{Na}^+$ move into the cell</td>
<td>Depolarization</td>
</tr>
<tr>
<td>$\text{Na}^+$ channels close $\text{K}^+$ channels open</td>
<td>$\text{K}^+$ move out of the cell</td>
<td>Repolarization</td>
</tr>
<tr>
<td>$\text{K}^+$ channels close</td>
<td></td>
<td>Return to resting membrane potential</td>
</tr>
</tbody>
</table>
3. Action potentials in cardiac muscle also result from the movement of ions through ion channels.
   A. As in skeletal muscle there are voltage-gated Na⁺ channels and voltage-gated K⁺ channels.

   B. In addition, there are voltage-gated Ca²⁺ channels.

   C. The voltage-gated Na⁺ channels are sometimes called fast channels and the voltage-gated Ca²⁺ channels are sometimes called slow channels because of the speeds at which they open.

4. Cardiac muscle cells have action potentials with depolarization and repolarization phases. However, there is a prolonged period of repolarization, called the plateau phase.

   ![FIGURE 20.14b](image)

<table>
<thead>
<tr>
<th>Channel Activity</th>
<th>Ion Movement</th>
<th>Membrane Potential Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺ channels open K⁺ channels close (end of previous cycle)</td>
<td>Na⁺ move into the cell</td>
<td>Depolarization</td>
</tr>
<tr>
<td>Na⁺ channels close Some K⁺ channels open</td>
<td>K⁺ move out of the cell</td>
<td>Early repolarization</td>
</tr>
<tr>
<td>Ca²⁺ channels are open</td>
<td>Potential change caused by K⁺ movement out of the cell is counteracted by Ca²⁺ movement into the cell</td>
<td>Plateau phase</td>
</tr>
<tr>
<td>Many K⁺ channels open Ca²⁺ channels close</td>
<td>K⁺ move out of the cell</td>
<td>Final repolarization</td>
</tr>
</tbody>
</table>
Autorhythmicity of Cardiac Muscle

1. Cardiac muscle is autorhythmic. This means that it can contract without any external stimulation at a regular rate.
   A. If the heart is removed from the body and maintained at the proper temperature with the appropriate nutrients it will continue to beat.

   B. In a heart transplant, the nerve supply to the donor heart is severed. When the heart is placed in the recipient, there is no longer a nerve supply.

2. Normally only certain cardiac muscle cells, called pacemakers, are autorhythmic. In the embryo, all cardiac muscle cells are autorhythmic. Most cardiac muscle cells lose this ability.
   A. The pacemaker cells have Na\(^+\) channels that allow leakage of Na\(^+\) into the cell. This produces a slow depolarization, which causes voltage-gated Ca\(^{2+}\) channels to begin opening. The movement of Na\(^+\) and Ca\(^{2+}\) into the cell produces a local potential called the prepotential.

   B. When the prepotential reaches threshold, an action potential results. Unlike skeletal and most cardiac muscle, depolarization results from the movement of Ca\(^{2+}\) into the cell.

   C. The action potential can spread to other cardiac muscles cells across intercalated disks. An action potential reaching a nonpacemaker cardiac muscle cell is a stimulus that causes voltage-gated Na\(^+\) channels to open, producing an action potential.

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**FIGURE 20.15**

<table>
<thead>
<tr>
<th>Channel Activity</th>
<th>Ion Movement</th>
<th>Membrane Potential Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some Na(^+) channels are open</td>
<td>Some Na(^+) move into the cell</td>
<td>Prepotential</td>
</tr>
<tr>
<td>Some Ca(^{2+}) channels begin</td>
<td>Some Ca(^{2+}) move into the cell</td>
<td></td>
</tr>
<tr>
<td>to open</td>
<td>Have opened</td>
<td></td>
</tr>
</tbody>
</table>

| Ca\(^{2+}\) channels open         | Ca\(^{2+}\) move into the cell         | Depolarization            |
| K\(^+\) channels close            |                                       |                           |

| Ca\(^{2+}\) channels close         | K\(^+\) move out of the cell           | Repolarization            |
| K\(^+\) channels open              |                                       |                           |

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20-4
3. Drugs are available that can block the fast and slow channels.
   A. Tetrodotoxin blocks fast channels.
   B. Manganese and verapamil [ver-ap′a-mil] block the slow channels. Because slow channel blockers prevent the entry of $\text{Ca}^{2+}$ into the cardiac muscle, they are called calcium blockers.

Would you use a calcium blocker to treat tachycardia (more rapid than normal heart rate) or bradycardia (slower than normal heart rate)? Explain (Hint: prepotential).

4. Although cardiac muscle is autorhythmic, the inherent rate can be modified by the autonomic nervous system and by chemicals.

   Predict the effect on heart rate of stimulating the branches of the vagus nerve supplying the heart.

   Predict the effect on heart rate of stimulating the sympathetic nerves going to the heart.

   Predict the effect on heart rate of injecting epinephrine into the blood supplying the heart.
Refractory Period of Cardiac Muscle
1. As in a skeletal muscle cell, the action potential of a cardiac muscle cell has an absolute and relative refractory period.
   A. During the absolute refractory period a stimulus, no matter how strong, will not produce an action potential.
   B. During the relative refractory period an above threshold stimulus ("a stronger than normal stimulus") will produce an action potential.

2. Because the plateau phase is prolonged, the refractory periods are prolonged. This allows the cardiac muscle to relax before the next action potential can cause a contraction.
   Because the heart relaxes between contractions, the heart cannot maintain a sustained contracted state (i.e., tetanus). Explain why this is advantageous.

Contraction Characteristics of Cardiac Muscle
1. The all-or-none law of cardiac muscle. Cardiac muscle cells, like skeletal muscle cells, contract as hard as possible, for the existing conditions. With different conditions, the force of contraction can vary.

2. The heart, like an entire skeletal muscle, can produce graded contractions, which are contractions of small, intermediate, or large force. However, the mechanisms are different.
   A. Graded contractions in skeletal muscle can result from recruitment, i.e., the nervous system can selectively stimulate a small, intermediate, or large number of motor units.

   Why doesn't recruitment occur in cardiac muscle?

B. Graded contractions in skeletal muscle can result from summation, i.e., increasing the frequency of stimulation of motor units so that contractions occur "on top of each other."

   Why doesn't summation occur in cardiac muscle?
C. Cardiac muscle, like skeletal muscle (see Figure 9.21), has a **length-tension curve**. The length of the cardiac muscle when it starts to contract affects the force of contraction. A short cardiac muscle produce a weak contraction. If the cardiac muscle is stretched, the force of contraction increases, up to a point.

![Length-Tension Curve](image)

**CONDUCTING SYSTEM OF THE HEART**

**The Problem**
1. In order to pump blood effectively, the heart must function as follows:
   A. Both atria must contract and inject blood into the relaxed ventricles.

   B. The ventricles must both contract after they have been filled with blood by atrial contraction. While the ventricles are contracting, the atria must be relaxed so they can fill with blood.

2. Because cardiac muscle cells are connected by intercalated disks, a mass of cardiac muscle cells would all contract at about the same time. This would not allow the alternating contraction of the atria and ventricles.

**The Solution**
1. The atria and ventricles are electrically isolated from each other by the **skeleton of the heart**, which is a plate of fibrous connective tissue between the atria and ventricles. This prevents the atria and ventricles from contracting at the same time.

2. The **conducting system** of the heart allows the activities of the atria and the ventricles to be coordinated.

**Components of the Conducting System**

1. The **sinoatrial (SA) node**.
   A. The SA node is a small mass of specialized cardiac muscle located near the point of entry of the superior vena cava into the right atrium.

   B. The SA node has the ability to contract spontaneously. Because its rate of spontaneous contraction is faster than the spontaneous rate of contraction of other cardiac tissue, the SA node can control the rate of contraction of the entire heart. For this reason, the SA node is called the **pacemaker**.
C. Once the SA node depolarizes, action potentials spread to all the cardiac cells of both atria (through intercalated disks), causing them all to contract at about the same time.

D. The atrial action potentials do not go to the ventricles because of the skeleton of the heart, so the ventricles do not contract at this time.

2. The **atrioventricular (AV) node**.
   A. The AV node is specialized cardiac muscle located in the interatrial septum just superior to the ventricles.
   
   B. Action potentials generated by the SA node reach the AV node.
   
   C. The AV node functions to transmit the action potentials from the atria to the ventricles. However, the action potentials are delayed for about 0.1 of a second before they are transmitted to the ventricles.
   
   ❍ Why is it advantageous for there to be a delay?

3. The **atrioventricular bundle** is specialized cardiac muscle that transmits action potentials from the AV node to the interventricular septum.

4. The **bundle branches** are specialized cardiac muscle formed by a division of the atrioventricular bundle into two parts. Each bundle branch carries action potentials down the interventricular septum.

5. **Purkinje fibers** are specialized cardiac muscle cells that carry action potentials from the bundle branches to the walls of the ventricles and to the papillary muscles.
   A. The **moderator band** (septomarginal trabecula) conducts action potentials from the interventricular septum to the right ventricular wall.
   
   B. At one time, it was believed that the moderator band prevented overextension of the right ventricle. This is doubtful.

6. The rate of transmission of action potentials through the atrioventricular bundle, the bundle branches, and the Purkinje fibers is very rapid. Therefore the ventricles depolarized almost immediately after the AV node.

   ❍ The inferior part of the ventricles contract before the superior part contracts. Explain.
The Electrocardiogram (ECG)
1. As the action potentials generated by the SA node travel through the heart, electrical currents are generated that pass through the fluids of the body.

2. By placing electrodes on various parts of the body, it is possible to measure and record the electric currents. This is called an electrocardiogram (ECG; EKG in England).

3. Note that an ECG measures electrical events and NOT the actual contraction of the heart. However, since the electrical events and the contraction of the heart are intimately related, much can be learned about heart function from the ECG.

4. The normal ECG produces a series of deflections on a graph that are designated as P, Q, R, S, and T waves. The letters have no significance except to indicate the order of appearance of the deflections.

   FIGURE 20.16

A. Each deflection or wave corresponds to an electrical event in the heart and therefore to a mechanical event (contraction or relaxation).

<table>
<thead>
<tr>
<th>Wave</th>
<th>Electrical Event</th>
<th>Mechanical Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>Atria depolarize</td>
<td>Atria contract</td>
</tr>
<tr>
<td>QRS</td>
<td>Ventricles depolarize</td>
<td>Ventricles contract</td>
</tr>
<tr>
<td>T</td>
<td>Ventricles repolarize</td>
<td>Ventricles relax</td>
</tr>
</tbody>
</table>

B. Atrial repolarization (corresponding to atrial relaxation) is not normally seen because it is masked by the QRS complex.
Route of Blood Flow Through the Heart

1. Blood enters the right atrium from the superior and inferior vena cava (systemic circuit) and the coronary sinus (coronary circuit).

2. Blood passes from the right atrium to the right ventricle. An atrioventricular (AV) valve, the tricuspid valve, prevents backflow of blood into the right atrium when the right ventricle contracts.

3. Blood flows from the right ventricle through the pulmonary trunk toward the lungs. The pulmonary semilunar valves prevent backflow of blood into the relaxed right ventricle.

4. Blood from the lungs enters the left ventricle through the pulmonary veins.

5. Blood passes from the left atrium to the left ventricle. An atrioventricular (AV) valve, the bicuspid valve, prevents backflow of blood into the left atrium when the left ventricle contracts.

6. Blood flows from the left ventricle through the aorta. The aortic semilunar valves prevent backflow of blood into the relaxed left ventricle.

CARDIAC CYCLE
1. The conducting system of the heart generates and conducts action potentials that stimulate the contraction of the heart chambers.
   A. Systole (G., a contracting) occurs when a heart chamber contracts. During systole the heart chamber is emptying.
   
   B. Diastole (G., a dilation) occurs when a heart chamber relaxes. During diastole the heart chamber fills with blood.
   
   C. Although both atria and ventricles undergo repeated systole and diastole, the terms, unless otherwise indicated, refer just to the ventricles.

2. The cardiac cycle consists of systole followed by diastole, repeated over and over. At rest (heart rate = 72 beats/min) the cardiac cycle takes approximately 0.8 seconds.
3. The cardiac cycle can be divided into five parts.

<table>
<thead>
<tr>
<th>FIGURE 20.18</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AV Valves</strong></td>
</tr>
<tr>
<td>1. <strong>Systole: Period of Isovolumic Contraction</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>2. <strong>Systole: Period of Ejection</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>3. <strong>Diastole: Period of Isovolumic Relaxation</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>5. <strong>Diastole: Active Ventricular Filling</strong></td>
</tr>
</tbody>
</table>
4. Details of the cardiac cycle.

**Electrocardiogram (ECG).** The electrical events in the heart cause contraction and relaxation of the atria and ventricles.

**Pressure graphs.** The contraction and relaxation of the atria and ventricles produces pressure changes that cause blood to flow through the heart and the aorta.

**Volume graph.** Changes in ventricular volume as blood flows into and out of the left ventricle.

**Sound graph.** Blood flow cause the AV and semilunar valves to close, producing the first and second heart sounds. Turbulent blood flow into the ventricles sometimes produces a third heart sound.

**Systole: Period of Isovolumic Contraction.**
1. **ECG.** The QRS complex is completed and the ventricles depolarize and contract.
2. **Pressure graph.** Ventricular contraction causes ventricular pressure to increase.
3. **Valves.** Blood flowing toward the atria causes the AV valves to close.
4. **Volume graph.** The volume of blood left in a ventricle from the previous cardiac cycle is called the **end-diastolic volume.** No change in volume occurs at this time because all the valves are closed.
5. **Sound graph.** Closure of the AV valves produces the **first heart sound,** which marks the beginning of systole.

**Systole: Period of Ejection.**
1. **ECG.** T wave begins.
2. **Pressure graph.** Ventricular pressure increases as the ventricles continue to contract. Then, ventricular pressure begins to drop as the ventricles empty.
3. **Valves.** The semilunar valves open as blood is ejected from the heart.
4. **Volume graph.** Ventricular volume decreases as the contracting ventricles push blood out of the heart. The volume of blood left in a ventricle after it has contracted is called the **end-systolic volume.**
5. **Sound graph.** No sound.
Diastole: Period of Isovolumic Relaxation.
1. *ECG*. T wave is completed, indicating ventricular relaxation.
2. *Pressure graph*. Pressure within the relaxed ventricle decreases rapidly.
3. *Valves*. Blood flowing back toward the relaxed ventricles causes the semilunar valves to close.
4. *Volume graph*. No change in volume occurs at this time because all the valves are closed.
5. *Sound graph*. Closure of the semilunar valves produces the **second heart sound**, which marks the beginning of diastole.

1. *ECG*. P wave begins at the end of this period.
2. *Pressure graph*. Ventricular pressure drops to near zero.
3. *Valves*. The AV valves open as ventricular pressures drops below atrial pressures.
4. *Volume graph*. Ventricular volume increases as blood flows into the ventricle. Approximately 70% of ventricular filling takes place during the first two-thirds of diastole as a result of passive blood flow.
5. *Sound graph*. Sometimes a **third heart sound** is produced by turbulent blood flow into the ventricles.

Diastole: Active Ventricular Filling.
1. *ECG*. The P wave is completed and the atria depolarize and contract.
2. *Pressure graph*. Ventricular pressures increase slightly as blood is pushed into the ventricles by the atria.
4. *Volume graph*. The last part of ventricular filling occurs during the last third of diastole. End-diastolic volume is established.
5. *Sound graph*. No sound.

* Explain why malfunction of the atria is a much less serious problem than malfunction of the ventricles.
Heart Sounds
1. Definitions.
   A. The **first heart sound** (the lubb of lubb-dupp) is produced by vibrations of the AV valves when they close.

   B. The **second heart sound** (the dupp of lubb-dupp) is produced by vibrations of the semilunar valves when they close.

   C. Sometimes a **third heart sound** is heard near the end of the first third of ventricular diastole. It results from turbulent blood flow into the ventricles.

2. **Heart murmurs** are abnormal sounds resulting from improperly functioning valves.
   A. Types of valve dysfunction.
      1) **Incompetent valve.** The valves don't close properly and blood moves backward into the atria or ventricles. This means that the same blood must be pumped again.
      2) **Valvular stenosis.** The valve opening is too narrow and it is harder than normal to push blood through the valve opening.

   B. Valvular dysfunction places an additional load on the heart. The disorder may produce no noticeable effects (other than the sounds produced) or may be life threatening.

   C. Valvular defects can be congenital (present at birth), can be due to disease (atherosclerosis, rheumatic fever), or can be due to simply wearing out.

   D. Valvular defects can be surgically corrected.

3. Detecting heart murmurs.
   
   ![FIGURE 20.20](image)

   A. By knowing the location of the heart in the thoracic cavity a stethoscope can be placed where the heart sounds are best heard.

   B. Types of abnormal heart sounds.
      1) An incompetent valve produces a swish sound immediately after the valve closes. The sound is caused by blood being pushed backwards through the valve.

      2) A stenosed valve produces a rushing sound immediately before the valve closes. The sound is caused by the rapid movement of blood through the narrow valve opening.

   Given the following heart sounds, at the indicated point would you expect a swish or rushing sound? Is the heart murmur caused by a faulty atrioventricular valve or semilunar valve?

   lubb - dupp - lubb - dupp - lubb - dupp
Aortic Pressure Curve

1. **Systolic pressure** is the highest pressure in the aorta. It occurs during the period of ejection because of the pressure generated by the contracting ventricle. In the average young adult at rest it is 120 mm Hg.

2. After the peak of systolic pressure, aortic pressure decreases as blood moves from the aorta into other arteries.

3. The movement of blood from the aorta is assisted by the elastic recoil of the aorta.
   A. Ejection of blood into the aorta causes its elastic walls to expand.
   B. Elastic recoil of the aorta pushes blood toward the body and back toward the heart.
   C. Blood moving back toward the heart causes the semilunar valves to close. As aortic recoil continues, pressure within the aorta increases slightly, producing a **dicrotic notch**, or **incisura**, in the aortic pressure curve. Dicrotic means double-beating; when increased pressure caused by recoil is large, a double pulse can be felt. Incisura means a cutting into and refers to the appearance of the curve.

4. Pressure within the aorta continues to decrease. **Diastolic pressure** is the lowest pressure in the aorta. It occurs just before the semilunar valves open and blood is pushed into the aorta by the contracting left ventricle. In the average young adult at rest it is 80 mm Hg.

**MEAN ARTERIAL BLOOD PRESSURE**
1. **Blood pressure (BP)** is responsible for the movement of blood.
   A. Blood flows from areas of higher blood pressure (the ventricles during systole) to areas of lower blood pressure (the ventricles during diastole).
   B. Maintenance of blood pressure is essential to life because the movement of blood is necessary to supply tissues with nutrients and to remove waste products.

2. **Mean arterial blood pressure (MAP)** is the average blood pressure between systolic and diastolic pressure in the aorta. MAP is determined by **cardiac output (CO)** and **peripheral resistance (PR)**.

   \[ \text{MAP} = \text{CO} \times \text{PR} \]

3. Changes in MAP result in changes in blood delivery. MAP can be changed by altering PR and CO.
A. **Peripheral resistance (PR)** is the total resistance within the blood vessels against which blood must be pumped. As blood vessels *vasoconstrict* (decrease in diameter), PR increases. As blood vessels *vasodilate* (increase in diameter), PR decreases.

\[
\text{Vasoconstrict, PR } \uparrow \\
\text{Vasodilate, PR } \downarrow 
\]

If blood vessels vasoconstrict, does MAP increase or decrease?

B. **Cardiac output** is the amount of blood moved per minute by the heart.

If cardiac output increases, does MAP increase or decrease?

---

**Changing Cardiac Output**

1. Cardiac output (CO) is equal to heart rate (HR) times stroke volume (SV). Thus, cardiac output can be changed by changing heart rate or stroke volume.

\[
\text{CO} = \text{HR} \times \text{SV} \\
\text{(mL/min)} \times \text{(beats/min)} = \text{(mL/beat)}
\]

2. **Stroke volume (SV)** is the difference between the end-diastolic volume and the end-systolic volume.
   
   A. The *end-diastolic volume (EDV)* is the amount of blood that fills the ventricles at the end of diastole. A typical resting EDV is 125 mL.

   B. The *end-systolic volume (ESV)* is the amount of the blood left in the ventricles at the end of systole. The ventricles are unable to completely empty. A typical resting ESV is 55 mL.

\[
70 \text{ mL} = 125 \text{ mL} - 55 \text{ mL} \\
\text{SV} = \text{EDV} - \text{ESV}
\]

Stroke volume \hspace{1cm} End-diastolic volume \hspace{1cm} End-systolic volume
   A. **Sponge analogy.** Imagine that you are rinsing out a sponge under a running water faucet.  
      1) As you relax your hand, the sponge fills with water; as your fingers contract, water is 
         squeeze out of the sponge; and after you have squeezed, some water is left within the 
         sponge.  
      2) EDV is analogous to the amount of water in the filled sponge, ESV is analogous to 
         the amount of water left in the squeezed sponge, and SV is analogous to the amount 
         of water squeezed out of the sponge. 
      3) The more the heart fills up (EDV) and the less it has in it after contracting (ESV), the 
         greater is the stroke volume.  
   B. Stoke volume can be increased by increasing EDV.  
      1) Increased venous return increases EDV. **Venous return** is the amount of blood 
         returning to the heart.  
      2) During exercise, blood flow increases and venous return increases, resulting in 
         greater ventricular filling and an increase in EDV. For example, EDV can increase 
         from a resting value of 125 mL to 145 mL. 
   C. Stroke volume can be increased by decreasing ESV.  
      1) Increased force of contraction of the ventricles results in decreased ESV as more 
         blood is ejected from the heart.  
      2) During exercise, force of contraction increases and ESV decreases from a resting 
         value of 55 mL to 30 mL. 

   At rest, SV is 70 mL. If EDV increases to 145 mL and ESV decreases to 30 mL, how 
   much does SV increases?

   A. In the average resting adult:  
      \[
      \begin{align*}
      \text{HR} &= 72 \text{ beats/min} \\
      \text{SV} &= 70 \text{ mL/beat} \\
      \text{CO} &= 72 \times 70 = 5040 \text{ mL/min} = \text{approximately 5 L/min}
      \end{align*}
      \]
   B. Because the average adult has approximately 5 liters of blood, this means that the entire 
      blood volume is circulated every minute in a person at rest.
C. During exercise, heart rate can increase to 190 beats/min and stroke volume can increase to 115 mL/beat. Therefore cardiac output can increase to 22 L/min.

\[
\begin{align*}
HR &= 190 \text{ beats/min} \\
SV &= 115 \text{ mL/beat} \\
CO &= 190 \times 115 = 21,850 \text{ mL/min} = \text{approximately } 22 \text{ L/min}
\end{align*}
\]

5. The difference between CO at rest and during exercise is called cardiac reserve. Cardiac reserve is a measure of the ability of the heart to do work.

The size of the heart can increase with exercise training. What effect would this have on resting heart rate? Explain.

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REGULATION OF THE HEART

Introduction

1. The amount of blood pumped by the heart varies depending upon the circumstances. For example, less blood is pumped at rest than during exercise.

2. Two basic types of regulatory mechanisms control the heart.
   A. Intrinsic mechanisms involve functional characteristics of the heart independent of any neural or hormonal control.
   B. Extrinsic mechanisms are neural or hormonal.

Intrinsic Regulation

1. Recall that cardiac muscle can produce graded contractions, i.e., the force of contraction can range from weak to strong.

2. Graded contractions depend upon the length of the cardiac muscle prior to contraction.
   A. A cardiac muscle in a shorten state produces a small contraction.
   B. As the cardiac muscle is stretched (within limits), the force of contraction increases.

3. Venous return determines the amount of stretch of cardiac muscle, which is called the preload.
   A. A small venous return produces a small amount of stretch and a small force of contraction. A large venous return produces a large amount of stretch and a large force of contraction.
   B. Venous return (preload) determines the strength of contraction, which determines the amount of blood ejected per beat (stroke volume). Thus, venous return equals stroke volume.
   C. If venous return increases, stroke volume and cardiac output increase.
4. The relationship between venous return and cardiac output is described by Starling's law of the heart: venous return is equal to cardiac output.

5. Afterload is the pressure the contracting ventricles must overcome to push blood out of the heart. Stroke volume is relatively unaffected by afterload until aortic pressure increases to 170 mm Hg or above. However, stroke volume is very sensitive to small changes in preload.
Extrinsic Regulation

FIGURE 20.22

1. The heart is innervated by the parasympathetic and sympathetic divisions, which can affect both heart rate and stroke volume.

2. Hormones from the adrenal gland can affect both heart rate and stroke volume.

Parasympathetic Control
1. The parasympathetic division innervates the heart (e.g., the SA node) through the vagus nerves (cranial nerves X).

2. Parasympathetic stimulation decreases heart rate.
   A. Without extrinsic nervous system or hormonal control, the intrinsic resting heart rate is about 100 beats/minute. For example, the resting heart rate in a heart transplant recipient is 100 beats/minute.
   B. Normally the parasympathetic division continually stimulates the heart, which results in a continual "brake" on heart rate. Thus normal, resting heart rate is 72 beats/minute.
   C. Strong parasympathetic stimulation can greatly decrease heart rate but has little effect on stroke volume.
   D. Withdrawal of parasympathetic stimulation results in an increase in heart rate.

3. Acetylcholine, released by the ends of the vagus nerves, binds to ligand-gated $K^+$ channels and increases membrane permeability to $K^+$. This hyperpolarizes the cell membrane (farther from threshold), which decreases the excitability of cardiac muscle cells.

Sympathetic Control
1. The sympathetic division innervates the heart (e.g., the SA node) through cardiac nerves from the cervical sympathetic chain ganglia.

2. Sympathetic stimulation increases heart rate.

   A. Stroke volume increases because the increased force of contraction of cardiac muscle moves more blood out of the heart, thereby decreasing end-systolic volume.
   B. During heavy exercise with a very rapidly beating heart, SV may decrease compared to SV during moderate exercise. This occurs because there is less time for the ventricles to fill during diastole, which decreases end-diastolic volume.

4. Norepinephrine, released by the ends of the cardiac nerves, increases membrane permeability to $Ca^{2+}$ by causing $Ca^{2+}$ channels to open. This causes depolarization (closer to threshold) that increases the excitability of cardiac muscle cells. The increased movement of $Ca^{2+}$ into cardiac muscle also increases the force of contraction.
Contrasting Parasympathetic and Sympathetic Control
1. Recall that the parasympathetic division is involved with “day-to-day” functions, whereas the sympathetic division is involved with “fight-or-flight” events, such as exercise.

2. Heart rate increases up to approximately 100 beats/min as a result of parasympathetic withdrawal. Heart rate above 100 beats/min results from increased sympathetic stimulation.

3. Although stroke volume increases during exercise, most of the increase in cardiac output results from an increase in heart rate.

Hormonal Regulation
1. Epinephrine and norepinephrine released from the adrenal medulla travels by blood to the heart.

2. Epinephrine and norepinephrine increase heart rate and the force of contraction of the heart.

THE HEART AND HOMEOSTASIS
1. The cardioregulatory center in the medulla regulates the heart through the parasympathetic (vagus nerves) and sympathetic (cardiac nerves) divisions.

2. Input to the cardioregulatory center.

A. Higher centers in the brain. For example, emotions can affect heart rate.

B. Receptors in the peripheral nervous system send nerve impulses through the glossopharyngeal nerves (cranial nerves IX).
   1) Baroreceptors respond to changes in blood pressure. Some baroreceptors are located in the wall of the carotid sinus, which is an expansion of the internal carotid artery just after it branches from the common carotid artery. The carotid sinus baroreceptors monitor the blood going to the brain. Other baroreceptors in the wall of the aorta monitor blood going to the body.
      a) The baroreceptors continually send action potentials to the cardioregulatory center.
      b) An increase in blood pressure results in an increased number of action potentials, and a decrease in blood pressure results in a decreased number of action potentials.
   2) Peripheral chemoreceptors respond primarily to changes in oxygen. Normally few action potentials are produced, unless oxygen levels dramatically decrease. The carotid bodies, are chemoreceptors located near the bifurcation of the common carotid artery, and the aortic bodies are located along the aorta.

C. Central chemoreceptors in the medulla oblongata respond primarily to changes in pH (often caused by changes in carbon dioxide).
Effect of Blood Pressure

FIGURE 20.23

1. Blood delivery depends on adequate blood pressure. The baroreceptor reflex monitors and maintains blood pressure.

2. If blood pressure is too low there is inadequate delivery of blood to tissues.
   A. The decrease in blood pressure is detected by the baroreceptors.
   B. The cardioregulatory center decreases parasympathetic stimulation, which increases heart rate, and increases sympathetic stimulation, which increases heart rate and force of contraction.

3. If blood pressure is too high, the heart is working too hard. The baroreceptor reflex causes the heart rate and force of contraction to decrease.

Effect of pH, Carbon Dioxide, and Oxygen

FIGURE 20.24

1. Central chemoreceptors in the medulla oblongata respond to changes in pH. Because carbon dioxide levels affect blood pH, it indirectly affects the central chemoreceptors.

\[
\text{CO}_2 \uparrow + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \\
\text{(higher than normal)}
\]

- Lowers pH as H\(^+\) accumulate

A. A decrease in blood pH can be caused by an increase in carbon dioxide, an increase in lactic acid, ketosis (excess ketones as in diabetes), etc. The decrease in blood pH stimulates an increase in heart rate and stroke volume. The resulting increase in cardiac output causes increased blood movement.

B. As blood delivery to the lungs increases, blood carbon dioxide levels decrease, pH increases, and homeostasis is maintained.

\[
\text{CO}_2 \downarrow + \text{H}_2\text{O} \leftarrow \text{H}_2\text{CO}_3 \leftarrow \text{H}^+ + \text{HCO}_3^- \\
\text{(eliminated in lungs)}
\]

- Increases pH as H\(^+\) decrease

C. The chemoreceptors in the medulla are activated in emergency situations (e.g., blood loss). The most important effect of activating these receptors is the resulting vasoconstriction of blood vessels (more later).
2. Peripheral chemoreceptors in the carotid and aortic bodies are most sensitive to changes in oxygen levels.
   A. The peripheral chemoreceptors are not very important in the regulation of the heart. They are important for regulating respiration. When blood oxygen levels decrease, respiration increases.

   B. A decrease in blood oxygen is detected by the receptors. Through the peripheral chemoreceptor reflex, heart rate decreases.
      1) Possible explanation: under conditions of low oxygen, slowing the heart enables the heart to keep pumping for a longer time.

      2) Many animals exhibit a diving response, in which heart rate decreases when the animal is submerged. Just placing a human's face in cold water can evoke a diving response. The arterial chemoreceptor reflex may be part of such a response.

   C. Two mechanisms counteract the peripheral chemoreceptor reflex effect on the heart, typically resulting in an increase in heart rate.
      1) Increased respiration results in reflexes that also increase heart rate.

      2) Normally, when blood oxygen levels are low, blood carbon dioxide levels are high. The central chemoreceptor reflex increases heart rate and stroke volume.

   D. The bottom line is that when oxygen levels decrease, heart rate increases as a result of the combined effect of all the reflexes. The peripheral chemoreceptors are not normally important in regulating the heart. However, they are important in regulating respiration.

3. Important contrast: the baroreceptor reflex is most important for maintaining "tonic" cardiovascular function; the central chemoreceptors reflexes are most important under emergency conditions.

**Effect of Extracellular Ion Concentration**

1. Sodium ions. Usually not clinically significant because normal heart function is affected only by very large changes in Na⁺ levels.

2. Potassium ions. Increased K⁺ decreases heart rate and stroke volume. The rate of conduction of action potentials through cardiac muscle decreases, and heart block can develop in the AV node. If ectopic foci develop, arrhythmias or fibrillation can result.

   A. Increased Ca²⁺ increases the force of contraction of cardiac muscle and decreases heart rate.

   B. Clinically, decreased Ca²⁺ levels lead to death by tetany of skeletal (respiratory) muscles before the heart is significantly affected.
Effect of Body Temperature
1. An increase in temperature (fever, exercise) increases heart rate and stroke volume.

2. A decrease in temperature (hypothermia, e.g., for heart surgery) lowers heart rate and stroke volume.

Practice Problems
1. Predict the effect on heart rate if the vagus nerves to the heart were cut.

2. Predict the effect on Starling's law of the heart if the vagus nerves to the heart were cut.

3. Predict the effect on heart rate if the glossopharyngeal nerves from the baroreceptors to the heart were cut.

4. During defecation it is not uncommon to "strain" by holding the breath and compressing the thoracic and abdominal muscles. Assume that the increased pressure in the thoracic and abdominopelvic cavities compresses the superior and inferior vena cava. What would happen to arterial blood pressure as result of compression of the vena cava? Describe the compensatory mechanisms that would be activated to correct this change in blood pressure.