Cardiovascular Physiology

Lecture Outline

• Cardiovascular System Function
• Functional Anatomy of the Heart
• Myocardial Physiology
• Cardiac Cycle
• Cardiac Output Controls & Blood Pressure

Cardiovascular System Function

• Functional components of the cardiovascular system:
  – Heart
  – Blood Vessels
  – Blood
• General functions these provide
  – Transportation
    • Everything transported by the blood
  – Regulation
    • Of the cardiovascular system
      – Intrinsic v extrinsic
  – Protection
    • Against blood loss
  – Production/Synthesis

Functional Anatomy of the Heart

• To create the “pump” we have to examine
  – Cardiac muscle
  – Chambers
  – Valves
  – Intrinsic Conduction System
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**Functional Anatomy of the Heart**

**Cardiac Muscle**

• Characteristics
  – Striated
  – Short branched cells
  – Uninucleate
  – Intercalated discs
  – T-tubules larger and over z-discs

**Chambers**

• 4 chambers
  – 2 Atria
  – 2 Ventricles

• 2 systems
  – Pulmonary
  – Systemic

**Valves**

• Function is to prevent backflow
  – Atrioventricular Valves
    • Prevent backflow to the atria
    • Prolapse is prevented by the chordae
      – Tensioned by the papillary muscles
  – Semilunar Valves
    • Prevent backflow into ventricles
Functional Anatomy of the Heart
Intrinsic Conduction System

• Consists of “pacemaker” cells and conduction pathways
  – Coordinate the contraction of the atria and ventricles

Myocardial Physiology
Autorhythmic Cells (Pacemaker Cells)

• Characteristics of Pacemaker Cells
  – Smaller than contractile cells
  – Don't contain many myofibrils
  – No organized sarcomere structure
  • do not contribute to the contractile force of the heart

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Myocardial Physiology
Autorhythmic Cells (Pacemaker Cells)

• Characteristics of Pacemaker Cells
  – Unstable membrane potential
    • “bottoms out” at -60mV
    • “drifts upward” to -40mV, forming a pacemaker potential
  – Myogenic
    • The upward “drift” allows the membrane to reach threshold potential (-40mV) by itself
    • This is due to
      1. Slow leakage of K⁺ out & faster leakage Na⁺ in
         » Causes slow depolarization
         » Occurs through Iₚ channels (funny) that open at negative membrane potentials and start closing as membrane approaches threshold potential
      2. Ca²⁺ channels opening as membrane approaches threshold
         » At threshold additional Ca²⁺ ion channels open causing more rapid depolarization
         » These deactivate shortly after and
      3. Slow K⁺ channels open as membrane depolarizes causing an efflux of K⁺ and a repolarization of membrane
Myocardial Physiology
Autorhythmic Cells (Pacemaker Cells)

- Characteristics of Pacemaker Cells
  - Altering Activity of Pacemaker Cells
    - Sympathetic activity
      - NE and E increase \( I_f \) channel activity
        - Binds to \( \beta \_1 \) adrenergic receptors which activate cAMP and increase \( I_f \) channel open time
        - Causes more rapid pacemaker potential and faster rate of action potentials
      - Sympathetic Activity Summary:
        - Increased chronotropic effects
          \[ \uparrow \] heart rate
        - Increased dromotropic effects
          \[ \uparrow \] conduction of APs
        - Increased inotropic effects
          \[ \uparrow \] contractility
    - Parasympathetic activity
      - ACh binds to muscarinic receptors
        - Increases \( K^+ \) permeability and decreases \( Ca^{2+} \) permeability = hyperpolarizing the membrane
        - Longer time to threshold = slower rate of action potentials
      - Parasympathetic Activity Summary:
        - Decreased chronotropic effects
          \[ \downarrow \] heart rate
        - Decreased dromotropic effects
          \[ \downarrow \] conduction of APs
        - Decreased inotropic effects
          \[ \downarrow \] contractility

Myocardial Physiology
Autorhythmic Cells (Pacemaker Cells)

- Altering Activity of Pacemaker Cells
  - Special aspects
    - Intercalated discs
      - Highly convoluted and interdigitated junctions
        - Joint adjacent cells with Desmosomes & fascia adherens
        - Allow for synticial activity
        - With gap junctions
      - More mitochondria than skeletal muscle
      - Less sarcoplasmic reticulum
        - \( Ca^{2+} \) also influxes from ECF reducing storage need
      - Larger t-tubules
        - Internally branching
      - Myocardial contractions are graded!
Myocardial Physiology
Contractile Cells

• Special aspects
  – The action potential of a contractile cell
    • Ca²⁺ plays a major role again
    • Action potential is longer in duration than a “normal” action potential due to Ca²⁺ entry
  – Phases
    4 – resting membrane potential @ -90mV
    0 – depolarization
      » Due to gap junctions or conduction fiber action
      » Voltage gated Na⁺ channels open… close at 20mV
    1 – temporary repolarization
      » Open K⁺ channels allow some K⁺ to leave the cell
    2 – plateau phase
      » Voltage gated Ca²⁺ channels are fully open (started during initial depolarization)
    3 – repolarization
      » Ca²⁺ channels close and K⁺ permeability increases as slower activated K⁺ channels open, causing a quick repolarization
  – What is the significance of the plateau phase?

Myocardial Physiology
Contractile Cells

• Plateau phase prevents summation due to the elongated refractory period
• No summation capacity = no tetanus
  – Which would be fatal

Myocardial Physiology
Contractile Cells

• Skeletal Action Potential vs Contractile Myocardial Action Potential

Summary of Action Potentials
Skeletal Muscle vs Cardiac Muscle

<table>
<thead>
<tr>
<th>TABLE 14-3</th>
<th>Comparison of Action Potentials in Cardiac and Skeletal Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SKELETAL MUSCLE</td>
</tr>
<tr>
<td>Membrane potential</td>
<td>Stable at ~70 mV</td>
</tr>
<tr>
<td>Events leading to threshold potential</td>
<td>Net K⁺ entry through ACCH-operated channels</td>
</tr>
<tr>
<td>Refractory phase</td>
<td>Na⁺ entry</td>
</tr>
<tr>
<td>Repolarization phase:</td>
<td>Rapid, caused by K⁺ influx</td>
</tr>
<tr>
<td>Hyperpolarization</td>
<td>Due to excessive K⁺ efflux at high K⁺ permeability when K⁺ channels close; leak of K⁺ and Na⁺ restores potential to resting state</td>
</tr>
<tr>
<td>Duration of action potential</td>
<td>Short; 1-2 msec</td>
</tr>
<tr>
<td>Refractory period</td>
<td>Generally brief</td>
</tr>
</tbody>
</table>

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Myocardial Physiology
Contractile Cells

• Initiation
  – Action potential via pacemaker cells to conduction fibers

• Excitation-Contraction Coupling
  1. Starts with CICR (Ca\(^{2+}\) induced Ca\(^{2+}\) release)
     • AP spreads along sarcolemma
     • T-tubules contain voltage gated L-type Ca\(^{2+}\) channels which open upon depolarization
     • Ca\(^{2+}\) entrance into myocardial cell and opens RyR (ryanodine receptors) Ca\(^{2+}\) release channels
     • Release of Ca\(^{2+}\) from SR causes a Ca\(^{2+}\) “spark”
     • Multiple sparks form a Ca\(^{2+}\) signal

  2. Ca\(^{2+}\) signal (Ca\(^{2+}\) from SR and ECF) binds to troponin to initiate myosin head attachment to actin

• Contraction
  – Same as skeletal muscle, but…
  – Strength of contraction varies
    • Sarcomeres are not “all or none” as it is in skeletal muscle
      » The response is graded!
      » Low levels of cytosolic Ca\(^{2+}\) will not activate as many myosin/actin interactions and the opposite is true
    • Length tension relationships exist
      – Strongest contraction generated when stretched between 80 & 100% of maximum (physiological range)
      – What causes stretching?
        » The filling of chambers with blood

• Relaxation
  – Ca\(^{2+}\) is transported back into the SR and
  – Ca\(^{2+}\) is transported out of the cell by a facilitated Na\(^{+}\)/Ca\(^{2+}\) exchanger (NCX)
  – As ICF Ca\(^{2+}\) levels drop, interactions between myosin/actin are stopped
  – Sarcomere lengthens

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Cardiac Cycle
Coordinating the activity

• Cardiac cycle is the sequence of events as blood enters the atria, leaves the ventricles and then starts over
• Synchronizing this is the Intrinsic Electrical Conduction System
• Influencing the rate (chronotropy & dromotropy) is done by the sympathetic and parasympathetic divisions of the ANS

Cardiac Cycle
Coordinating the activity

• Electrical Conduction Pathway
  – Initiated by the Sino-Atrial node (SA node) which is myogenic at 70-80 action potentials/minute
  – Depolarization is spread through the atria via gap junctions and internodal pathways to the Atrio-Ventricular node (AV node)
    • The fibrous connective tissue matrix of the heart prevents further spread of APs to the ventricles
    • A slight delay at the AV node occurs
      – Due to slower formation of action potentials
      – Allows further emptying of the atria
  – Action potentials travel down the Atrioventricular bundle (Bundle of His) which splits into left and right atroventricular bundles (bundle branches) and then into the conduction myofibers (Purkinje cells)
    • Purkinje cells are larger in diameter & conduct impulse very rapidly
      – Causes the cells at the apex to contract nearly simultaneously
        » Good for ventricular ejection

• Electrical Conduction Pathway

  – The electrical system gives rise to electrical changes (depolarization/repolarization) that is transmitted through isotonic body fluids and is recordable
    – The ECG!
      • A recording of electrical activity
      • Can be mapped to the cardiac cycle
Cardiac Cycle

Phases

1. Rest
   • Both atria and ventricles in diastole
   • Blood is filling both atria and ventricles due to low pressure conditions
2. Atrial Systole
   • Completes ventricular filling
3. Isovolumetric Ventricular Contraction
   • Increased pressure in the ventricles causes the AV valves to close… why?
     – Creates the first heart sound (lub)
   • Atria go back to diastole
   • No blood flow as semilunar valves are closed as well

Back to Atrial & Ventricular Diastole

Cardiac Cycle

Phases

4. Ventricular Ejection
   • Intraventricular pressure overcomes aortic pressure
     – Semilunar valves open
     – Blood is ejected
5. Isovolumetric Ventricular Relaxation
   • Intraventricular pressure drops below aortic pressure
     – Semilunar valves close = second heart sound (dup)
   • Pressure still hasn’t dropped enough to open AV valves so volume remains same (isovolumetric)

Back to Atrial & Ventricular Diastole
Cardiac Cycle

Phases

1. Hemodynamic ventricular relaxation—ventricles relax, pressure in ventricles falls, valves open, blood begins to flow into ventricles.

2. Atrial systole—atrial contraction pushes a small amount of blood into ventricles, valves close, blood from atria now enters ventricles.

3. Ventricular ejection—ventricular pressure rises, blood is expelled at rate of 70-80 mL/sec.

4. Hemodynamic ventricular systole—last phase of ventricular contraction occurs. AV valves remain closed, but does not exert enough pressure for open semilunar valves.

Cardiac Cycle

Blood Volumes & Pressure

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- Cardiac Output Controls & Blood Pressure… next time!