**Myocardial Cell Action Potentials**

- **4 Phases:**

  A. *Phase 0*: Rapid depolarization (+20mV)
  -
  B. *Phase 1*: Initial Repolarization
  -
  -
  C. *Phase 2*: Plateau Phase (+10mV)
  - Slow Ca^{2+} channels open
  - Fast K^{+} channels close
  -
  D. *Phase 3*: Rapid Repolarization (-85mV)
  - Slow Ca^{2+} channels close
  - Slow K^{+} channels open
  -
  E. *Phase 4*: Resting membrane potential (-85mV)
  -
Plateau Phase: Refractory Phase

- Ensure:

Plateau Phase on ECG

- Effect of Myocardial Action Potential on Muscle Contraction:
  - Action Potentials stimulate 2 Ca\(^{2+}\) Sources
    1. Plateau Phase:
    2. Terminal Cisternae:
      - Ryanodine Receptor Channel:
        ✓
        - BOTH sources of Ca\(^{2+}\) increase:
          ✓ Cardiac Contractions are NOT:
          ✓ Cardiac Contraction strengths altered by:

Controlling Cardiac Tissue:

1. Rate Changes = Chronotropic
   - Extrinsic Mediation:
     a. Sympathetic Nervous System
        ✓
        ☆ Tachycardia:
Adrenergic Mechanism: 2 Effects

1. cAMP sensitizes :
   - Increases :
   - Increases :

2. cAMP activates :
   - Phosphorylation increases activity of sacroplasmic :
   - Increases :
   - Increases readiness for :

b. Parasympathetic Nervous System

☆

☆ Bradycardia:

Cholinergic Mechanism:

• Acetylcholine: Binds
  - Opens :
  - Hyperpolarize :
  - Lengthens time / “ramp” to:

2. Contractility Changes = Inotropic Effect

2 Controlling Sources

1. Intrinsic Control: “Built in”

a. Length-Tension Relationship

  ✅ Degree of :
  
  ✅ Increasing cardiac stretch increases:

  - Resting cardiac cell length is :

  ✅ Increasing stretch increases :

  ✡ Increasing :

  ✅ Mechanism: Ventricular filling
\[ \uparrow \text{Ventricular Filling} = \]
\[ \uparrow \text{Stretch} = \]
\[ = \text{Positive} \]

* Frank-Starling Law*

b. Excitation Contraction Coupling

\[ \Rightarrow \text{Effect of frequency of Myocardial Potentials on :} \]

✓ Greater frequency of Action Potentials
  
  • Increase \textit{influxing}:
  
  • Increase \textit{ryanodine}:

\[ \Rightarrow \text{Positive} : \]

2. \textbf{Extrinsic Control}:

a. Sympathetic Nervous System:

• Positive

• Mechanism:

\[ \Rightarrow \text{Norepinephrine: Binds :} \]

\[ \Rightarrow \text{cAMP activates :} \]

1. Phosphorylate: \textbf{L-Type Voltage gated Calcium Channel} :

  ✓ Influx :

  ✓ More calcium produces :

2. Phosphorylate: \textbf{Ryanodine channels}

  ✓ Release :

  ✓ More calcium produces :

3. Phosphorylate: \textbf{Phospholamban}

  ✓ Reuptake :

  ✓ Faster

  ✓ Faster
b. Parasympathetic Nervous System:

- **Mechanism: *Indirect affect***

  ➔ Acetylcholine: Binds:

  * Slows SA Node: *Fewer*
  * Less influxing:

Additional Cardiac Function Modifier

Adenosine: Produced in response to:

- *Large amounts of:*

  Adenosine receptors: G-protein moderated Second Messenger Operated Response

Myocardial effect:

- Slows pacing and Conduction velocity of Nodal Cells: Important mechanism to slow pacing when:

  - **Mechanisms of action:**

    1. Inhibit Adenylate Cyclase: Decrease
1. Decrease :

2. Increase :

3. Slow :

4. Negative Chronotropic effect (pacing)

2. Inhibit Adenylate Cyclase: Decrease

- Decrease L-Type Voltage gated Ca\(^{2+}\) channel
- Slow conduction velocity (esp AV node)

*Negative Dromotrophic Effect*

- Clinical Use: Antiarrhythmic drug

- Rapid treatment of Supraventricular Tachycardia
- Especially in AV node re-entry

**Study Questions :**

1. What are the main differences between the pacemaker potentials and cardiac myocardial cell potentials? Which cells within the myocardium produce the myocardial potentials and which ones produce pacemaker potentials?

2. What are the four phases in myocardial action potentials? Which channels produce the rapid depolarization? Which channels are responsible for the initial repolarization? Which channels are responsible for the plateau phase? Which channels are responsible for the fast repolarization?

3. What is the functional significance of the plateau phase? (what does it prevent from happening in myocardial cells)?

4. Diagram the neuronal action potential, the pacemaker potential and the myocardial action potential.

5. How is the plateau phase presented on the ECG?

6. What is the difference between chronotropic and inotropic effects on the heart?

7. What is the sympathetic nervous system chronotropic effect on the heart: positive or negative? How is this effect produced by the sympathetic nervous system?

8. What is the parasympathetic nervous system chronotropic effect on the heart: positive or negative? How is this effect produced by the parasympathetic nervous system?

9. What is the difference between bradycardia and tachycardia? Which branch of the autonomic nervous system causes each?

10. What is the sympathetic nervous system inotropic effect on the heart: positive or negative? How is this effect produced by the sympathetic nervous system? What is the parasympathetic nervous system indirect affect on cardiac contractility? How are these affects mediated?

11. What effect does cardiac muscle stretch have on the heart? What is this effect called? How does muscle stretch affect contractility? Under normal circumstances what stretches the heart?

12. Skeletal muscle uses recruitment to achieve stronger muscle contractions. Explain why cardiac muscle cannot use recruitment. Why does it make sense then that contractility if altered by muscle stretch and calcium concentration?

13. What effect does the myocardial action potential have on the strength of myocardial contraction? When calcium influxes during the plateau phase what additional affects can this calcium cause? (hint think sarcoplasmic reticulum)
14. What is the ryanodine channel? Where is it located and what is its function? What causes it to open? How does cAMP presence affect the ryanodine channels and how does this affect contractility?

15. When is adenosine in high concentrations in the heart? What mechanism do adenosine receptors use to mediate their affects?

16. What is the effect of adenosine on vascular smooth muscle? How does this effect aide in supporting appropriate cardiac function?

17. What mechanisms are initiated by adenosine resulting in slower pacing by nodal cells?

18. Clinically how is adenosine used?