Ch 14: Cardiovascular Physiology, Part 1

concepts:

- Fluid flow
- APs in contractile & autorhythmic cells
- Cardiac cycle (elec. & mech. events)
- HR regulation
- Stroke volume & cardiac output

Running Problem: Heart Attack

Developed by John Gallagher, MS, DVM
Overview of Cardiovascular System

The heart is a dual pump!
Circulation Review

Fig 14-1

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Blood Flow

- Why does blood flow through cardiovascular system? (teleological vs. mechanistic answers)
  - *Teleological*: Because diffusion is too slow to support a large and complex organism
  - *Mechanistic*: Because the contractions of the heart produce a hydrostatic pressure gradient and the blood wants to flow to the region of lesser pressure. Therefore, the Pressure gradient ($\Delta P$) is main driving force for flow through the vessels

**Blood Flow Rate** $\propto \Delta P / R$
Pressure

- Hydrostatic pressure is in all directions
  - Measured in mmHg: The pressure to raise a 1 cm column of Hg 1 mm
  - Sphygmomanometer

- Flow is produce by Driving Pressure

- Pressure of fluid in motion decreases over distance because of energy loss due to friction

Blood Flow Rate $\propto \Delta P/R$
Plumbing 101: Resistance Opposes Flow

3 parameters determine resistance ($R$):

1. Tube length (L)
   
   1. Constant in body

2. Tube radius (r)
   
   1. Can radius change?

3. Fluid viscosity ($\eta$ (eta))
   
   1. Can blood viscosity change??

Poiseuille’s law:

$$R = \frac{8L \eta}{\pi r^4}$$

$$\Rightarrow R \propto \frac{1}{r^4}$$

Blood Flow Rate $\propto \Delta P / R$

Fig 14-5
Velocity (v) of Flow

Depends on Flow Rate and Cross-Sectional Area:

- **Flow rate (Q) = volume of blood passing one point in the system per unit of time (e.g., ml/min)**
  - If flow rate ↑ ⇒ velocity ↑

- **Cross-Sectional area (A) (or tube diameter)**
  - If cross sectional area ↑ ⇒ velocity ↓

\[ v = \frac{Q}{A} \]
The pathway of a blood cell should be well known to you!
Unique Microanatomy of Cardiac Muscle Cells

- 1% of cardiac cells are autorhythmic
  - Signal to contract is myogenic
- Intercalated discs with gap junctions and desmosomes
  - Electrical link and strength
- SR smaller than in skeletal muscle
  - Extracellular Ca$^{2+}$ initiates contraction (like smooth muscle)
- Abundant mitochondria extract about 80% of O$_2$
Excitation-Contraction (EC) Coupling in Cardiac Muscle

- Contraction occurs by the same sliding filament activity as in skeletal muscle.
- Relaxation similar to skeletal muscle:
  - Ca\(^{2+}\) removal requires Ca\(^{2+}\)-ATPase (into SR) & Na\(^+/Ca^{2+}\) antiport (into ECF).

\([Na^+]\) restored via

- AP is from pacemaker cells (SA node), not neurons.
- AP opens voltage-gated Ca\(^{2+}\) channels in cell membrane.
- Ca\(^{2+}\) induces Ca\(^{2+}\) release from SR stores.

Fig 14-11
1. Action potential enters from adjacent cell.
2. Voltage-gated Ca²⁺ channels open. Ca²⁺ enters cell.
3. Ca²⁺ induces Ca²⁺ release through ryanodine receptor-channels (RyR).
4. Local release causes Ca²⁺ spark.
5. Summed Ca²⁺ sparks create a Ca²⁺ signal.
6. Ca²⁺ ions bind to troponin to initiate contraction.
7. Relaxation occurs when Ca²⁺ unbinds from troponin.
8. Ca²⁺ is pumped back into the sarcoplasmic reticulum for storage.
9. Ca²⁺ is exchanged with Na⁺.
10. Na⁺ gradient is maintained by the Na⁺-K⁺-ATPase.
Cardiac Muscle Cell Contraction is Graded

- **Skeletal muscle cell**: all-or-none contraction in any single fiber for a given fiber length.
  
  Graded contraction in skeletal muscle occurs through?

- **Cardiac muscle**:
  - force $\propto$ to sarcomere length (up to a maximum)
  - force $\propto$ to # of Ca$^{2+}$ activated crossbridges
    (Function of intracellular Ca$^{2+}$: if $[Ca^{2+}]_{in}$ low $\rightarrow$
    not all crossbridges activated)

*Fig 12-16*
Foxglove for a Failing Heart

See cardiac glycosides p. 492

- **Cardiac glycosides** from *Digitalis purpurea*
  - **digoxin**

- Highly toxic in large dosage: destroys all Na\(^+\)/K\(^+\) pumps

- In low dosage: partial block of Na\(^+\) removal from myocardial cells

- The Na\(^+\) - Ca\(^{2+}\) pump is less effective and there will be more Ca\(^+\) for coupling

**Explain mechanism of action!**
APs in Contractile Myocardial Cells

- Similar to skeletal muscle
- Phase 4: Stable resting pot. ~ -90 mV
- Phase 0: Depolarization due to voltage-gated Na\(^+\) channels (Na\(^+\) movement?)
- Phase 1: Partial Repolarization as Na\(^+\) channels close and voltage-gated K\(^+\) channels open (K\(^+\) movement?)
- Phase 2: Plateau: ↑ K\(^+\) permeability and ↓ Ca\(^{2+}\) permeability
- Phase 3: Repolarization: Back to resting potential

Fig 14-13
APs in Contractile Myocardial Cells

- **Much longer AP**

- **Refractory period and contraction end simultaneously - Why important?**

AP in skeletal muscle: 1-5 msec
AP in cardiac muscle: 200 msec

Fig 14-14
Myocardial Autorhythmic Cells

- Anatomically distinct from contractile cells – Also called **pacemaker** cells

- Membrane Potential = – 60 mV

- Spontaneous AP generation as gradual depolarization reaches threshold
  - Unstable resting membrane potential (= pacemaker potential)
  - The cell membranes are “leaky”
  - Unique membrane channels that are permeable to both Na\(^+\) and K\(^+\)
Myocardial Autorhythmic Cells, cont’d.

**I_f-channel Causes Mem. Pot. Instability**

- **Autorhythmic cells have different membrane channel:**
  - $I_f$ - channel

- $I_f$ channels let $K^+$ & $Na^+$ through at -60mV
- $Na^+$ influx $> K^+$ efflux
- slow depolarization to threshold

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- allow current ($= I$) to flow
- $f = “funny”$: researchers didn’t understand initially
Myocardial Autorhythmic Cells, cont’d.

“Pacemaker potential” starts at ~ -60mV, slowly drifts to threshold

Heart Rate = Myogenic
Skeletal Muscle contraction = ?

Fig 14-15