Cardiovascular Physiology

Part 3
Cardiac Control, Capillary Exchange & Disorders

Cardiac Physiology

Neural Regulation of Blood Pressure

• CNS contains the Medullary Cardiovascular Control Center
  – Receives inputs from carotid and aortic baroreceptors
  – Creates outflow to sympathetic and parasympathetic pathways
    • Sympathetic to SA & AV nodes and myocardium as well as to arterioles and veins
    • Parasympathetic to the SA Node
  – Baroreceptors initiate the baroreceptor reflex

Lecture Outline

• Medullary Center for Cardiovascular Control & the Baroreceptor Reflex
• Capillary Exchange
• The Lymphatic System
• Blood

The Baroreceptor Reflex Pathways
Lecture Outline

• Medullary Center for Cardiovascular Control & the Baroreceptor Reflex
• Capillary Exchange
• Blood

Capillary Exchange

• The physics involved:
  – velocity of blood flow
    • Influenced by?

Capillary Exchange

• Cardiovascular process involving
  – all three functional systems
    • heart, blood & blood vessels
  – and physics
    • velocity of blood flow
    • cross-sectional area of capillaries
    • Exchange processes
      – diffusion & transcytosis
    • Pressures
      – Filtration
        » Influenced by capillary hydrostatic pressure
      – colloid osmotic pressures (oncotic pressure)
        » Influence bulk flow

• Capillary Exchange

• The physics involved: Exchange Processes
  – Diffusion factors
    • Surface area for diffusion
      – 6300 m² (two football field surfaces)
      – Direct result of the large cross-sectional area and length of capillaries (~50,000 miles)
    • membrane permeability
      – Differing capillaries have differing permeability’s
        » Continuous vs. Fenestrated vs. Sinusoid
      – Also influenced by surrounding cells
        » Pericytes are weakly contractile cells that form a network around capillaries...
        » The more pericytes the less permeable the capillaries are
        » Can be associated with other cells to form barriers
Capillary Exchange

• The physics involved:
  – Exchange processes
    • Diffusion of smaller molecules between the cells
      – paracellular pathway
    • Diffusion of larger molecules through the cells via
      – endothelial transport (transcytosis)

Capillary Exchange

• The physics involved:
  – Pressures
    • Capillary hydrostatic pressure ($P_{out}$)
      – The filtration force in the capillaries
      – Created by the fluid pressure of blood entering the capillaries
      – Variable throughout the length of the capillary
        - highest on arteriole end ($32 \text{ mm Hg}$)
        - lowest on venule end ($15 \text{ mm Hg}$)
    • Direct relationship between capillary hydrostatic pressure (CHP) and movement of fluids across the capillary membrane
    • There should be no filtration pressure moving fluid back into the capillary (interstitial fluid hydrostatic pressure)
      \[ P_{IF} = 0 \text{ mm Hg} \]
      ...So the outward filtration pressure ($P_{out}$) is attributable to the capillary hydrostatic pressure ($P_{cap}$)

Capillary Exchange

• All the major factors
  – Filtration Pressure ($P_{out}$) is equal to the change in capillary hydrostatic pressure
    \[ \Delta P_{CHP} = (P_{cap} - P_{IF}) \]
  – Absorption Pressure ($\pi_{in}$) is equal to the change in colloid osmotic pressure
    \[ \Delta P_{\pi} = (\pi_{IF} - \pi_{cap}) \]
  • Coming together to create
    – Net Pressure = $P_{out} - \pi_{in}$
Capillary Exchange

- The Net Pressure will change in a gradient along the length of the capillary.
  - Net Pressure \(_{\text{arterial end}} = (P_{\text{cap}} - P_{\text{IF}}) + (\pi_{\text{cap}} - \pi_{\text{IF}})\)
    - (32 mm Hg – 0 mm Hg) + (0 mm Hg – 25 mm Hg) = (32 mm Hg + -25 mm Hg) = 7 mm Hg
  - This is a filtration pressure
  - Net Pressure \(_{\text{venous end}} = (P_{\text{cap}} - P_{\text{IF}}) + (\pi_{\text{cap}} - \pi_{\text{IF}})\)
    - (15 mm Hg – 0 mm Hg) + (0 mm Hg – 25 mm Hg) = (15 mm Hg + -25 mm Hg) = -10 mm Hg
  - This is a reabsorption pressure
  - filtration pressure is greater than the reabsorption pressure \((P_{\text{out}} > \pi_{\text{in}})\)
  - This means there is a net loss of capillary fluid to the interstitial fluid on a constant basis

Capillary Exchange

- The return of the fluid gained in the interstitial space due to a greater filtration force than reabsorption force is done by
  - the lymphatic system

The Lymphatic System

- Collects the excess fluid “lymph” and returns it to venous circulation at the junction of the subclavian and internal jugular veins
The Lymphatic System

- What does the lymphatic System do for us?
  - Returns the excess fluid
  - In doing so prevents edema
  - Absorbs and transports fats from the GI tract
    - Through specialized lymphatic capillaries called lacteals
  - Filters the returning fluid for purposes protection
    - Occurs at the lymph nodes
- More on the lymphatic system and its functions later as it relates to digestive system and immunity

A Little Disease & Disorder

- Greater than 50% of the deaths in the U.S. have links to cardiovascular disease!
  - Net cost is around $450 billion

- What are the risk factors for CVD?
  - Controllable
    - Smoking & Obesity
    - Activity level
    - Untreated hypertension
  - Uncontrollable
    - Familial history (genetics)
    - Age & Gender
      - early on males in more danger later in life it equalizes

The Lymphatic System

A Little Disease & Disorder

Diabetes

- What does diabetes have to do with CVD?
  - 2/3 of people with diabetes will die as a result of cardiovascular problems

Why?
  - blood glucose that is normally available for cellular metabolism is not
  - fats and proteins are metabolized instead and fatty acids are released into the blood
  - LDL-cholesterol levels rise
  - leads to atherosclerosis and its progression
A Little Disease & Disorder
Atherosclerosis Progression

- Low Density Lipoprotein-Cholesterol (LDL-C) is required for normal cell function... transporting cholesterol to the cells for use in synthesis of hormones as well as maintenance of cell membranes
- Excess LDL-C is taken in by the endothelial cells (especially areas of low endothelial sheer – where blood doesn’t move fast or turbulenty)
- Endothelial cells move it to the interstitial space between the two layers of the artery
- Macrophages consume it and become lipid filled foam cells
  - In response they release cytokines which causes smooth muscle growth in the area & forms a lesion on the arterial wall
- Additional LDL-C and macrophages will form an increasingly large plaque which shrinks the volume of the lumen
- Advanced plaques may develop collagenous and calcified areas
- Plaques tend to have one of two states seemingly controlled by macrophage inflammation processes
  - Stable plaques just reduce blood flow but don’t activate platelets
  - Vulnerable plaques are so called because they do activate platelets and can therefore cause a thrombus

A Little Disease & Disorder
Atherosclerosis

Notice the narrowing of the lumen within artery within the circle!
A Little Disease & Disorder
Atherosclerosis

• So what is good cholesterol?
  – HDL-C (high density lipoprotein-cholesterol)
  – Should be carry about 30% of your total cholesterol
  – Why is it “healthy”?
    • It is associated with a lower risk of heart attack
      – Hypothesis is that it picks up cholesterol from plaques and transports it away = reverse cholesterol transport hypothesis
      – It also is involved with reducing inflammation and platelet activation/aggregation

• What are the recommended levels?

A Little Disease & Disorder
Cholesterol Levels

Normal ranges
In the USA, the American Heart Association, NIH, and NCEP provide a set of guidelines for fasting LDL-Cholesterol levels, estimated or measured, and risk for heart disease. As of 2003, these guidelines were:

<table>
<thead>
<tr>
<th>Level (mg/dl)</th>
<th>Level (mmol/L)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>&lt;2.6</td>
<td>Optimal LDL cholesterol, corresponding to reduced, but not zero, risk for heart disease</td>
</tr>
<tr>
<td>100 to 129</td>
<td>2.6 to 3.3</td>
<td>Near optimal LDL level</td>
</tr>
<tr>
<td>130 to 159</td>
<td>3.3 to 4.1</td>
<td>Borderline high LDL level</td>
</tr>
<tr>
<td>160 to 189</td>
<td>4.1 to 4.9</td>
<td>High LDL level</td>
</tr>
<tr>
<td>&gt;190</td>
<td>&gt;4.9</td>
<td>Very high LDL level, corresponding to highest increased risk of heart disease</td>
</tr>
</tbody>
</table>

A Little Disease & Disorder
Hypertension and CVD

• Uncontrolled for 90%
  – There is no underlying cause other than genetics
  – Over a period of time, the receptors in the carotid and aortic bodies “reset” or down-regulate their activity and the elevated bp becomes the norm!
  – What is the relationship between elevated bp and CVD?
A Little Disorder & Disease
Hypertension and CVD

- Prolonged high pressure will cause the heart to fatigue leading to heart failure
  - Usually starts with the left side weakening leading to pulmonary edema and lack of O2
  - Further weakening occurs and congestive heart failure occurs

A Little Disease & Disorder
CVD and fixing it

- How do we fix it?
  - Healthy lifestyle is number one
  - If it is uncontrollable (genetic, age…) then
    - Pharmacology is the ticket!