Cardiovascular Physiology

Part 3
Cardiac Control, Capillary Exchange & Disorders

Lecture Outline

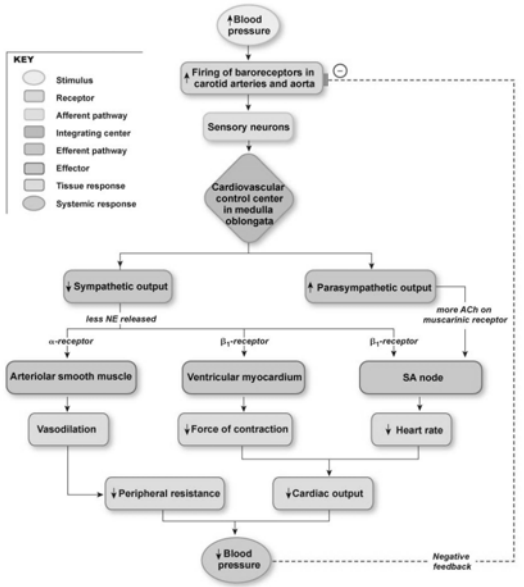
- **Medullary Center for Cardiovascular Control & the Baroreceptor Reflex**
- **Capillary Exchange**
- **The Lymphatic System**
- **Blood**

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**

The Baroreceptor Reflex Pathways



Lecture Outline

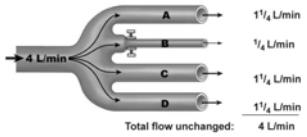
- **Medullary Center for Cardiovascular Control & the Baroreceptor Reflex**
- **Capillary Exchange**
- **Blood**

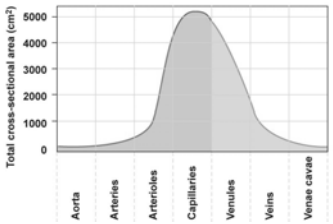
Capillary Exchange

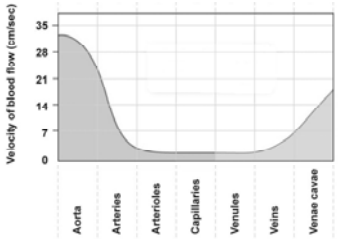
- Cardiovascular process involving
  - all three functional systems
    - heart, blood & blood vessels
  - and physics
    - velocity of blood flow
    - cross-sectional area of capillaries
    - Exchange processes
      - diffusion & transcytosis
    - Pressures
      - Filtration
        - » Influenced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

Capillary Exchange

- The physics involved:
  - velocity of blood flow
    - Influenced by?

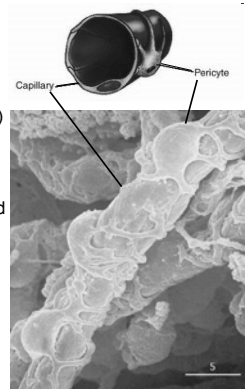






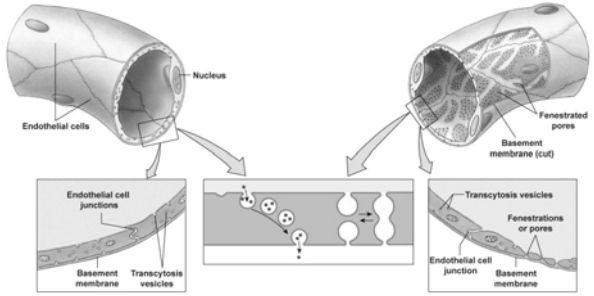
Capillary Exchange

- The physics involved: Exchange Processes
  - Diffusion factors
    - Surface area for diffusion
      - 6300 m^2 (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 mm Hg**)
      - lowest on venule end (**15 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 mm Hg

      …So the outward filtration pressure (P_{out}) is attributable to the capillary hydrostatic pressure (P_{cap})

Capillary Exchange

- The physics involved:
  - colloidal osmotic pressures (π)
    - Created by the "solids" in the blood that are not capable of crossing through the capillary.
    - Inverse relationship between fluid movement and colloid osmotic pressure or *oncotic pressure*
      - π_{cap} remains constant
        - » However the effect of this is variable again from ateriolar end to venule end as the filtration pressure is reduced due to the length of the capillary and the loss of fluid
      - π_{IF}
        - » The interstitial colloid osmotic pressure should be 0 mm Hg
        - » This is what makes colloidal osmotic pressure in the capillary a reabsorption pressure

        $\pi_{in} = (\pi_{IF} - \pi_{cap})$ = (0 mm Hg – 25 mm Hg) = **-25 mm Hg**

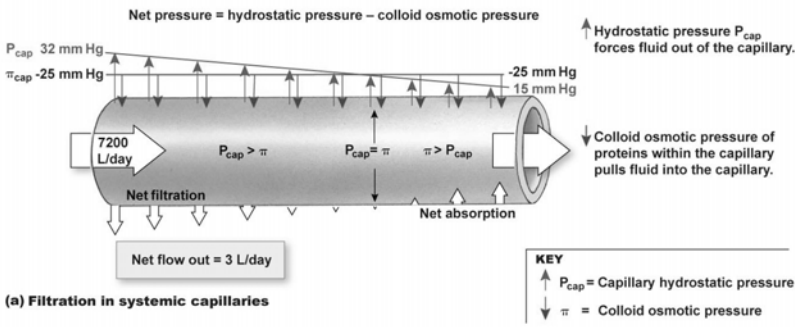
Capillary Exchange

- All the major factors
  - Filtration Pressure (P_{out}) is equal to the change in capillary hydrostatic pressure ΔP_{CHP} ($P_{cap} - P_{IF}$)
  - Absorption Pressure (π_{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 $_{arterial\ end}$ = ($P_{cap} - P_{IF}$) + ($\pi_{cap} - \pi_{IF}$)
    (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 $_{venous\ end}$ = ($P_{cap} - P_{IF}$) + ($\pi_{cap} - \pi_{IF}$)
    (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 ($P_{out} > \pi_{in}$)
- This means there is a net loss of capillary fluid to the interstitial fluid on a constant basis

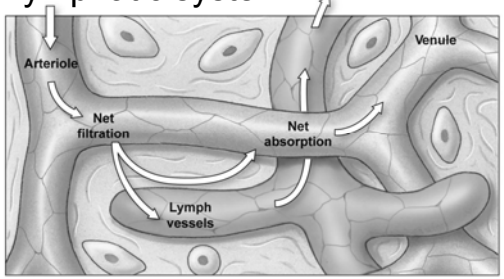
Capillary Exchange



Where does the excess fluid of 3 L/day go?

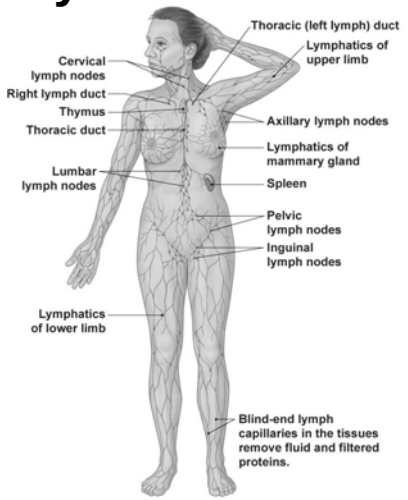
Capillary Exchange

- 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

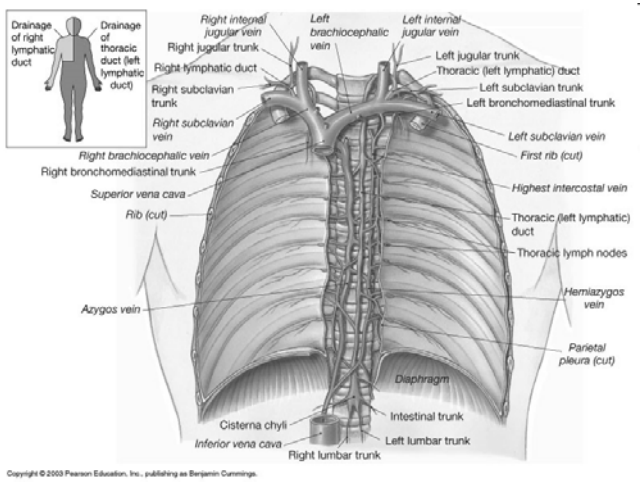


The Lymphatic System

- Collects the excess fluid "lymph" and returns it to venous circulation at the junction of the subclavian and internal jugular veins



The Lymphatic System



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

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

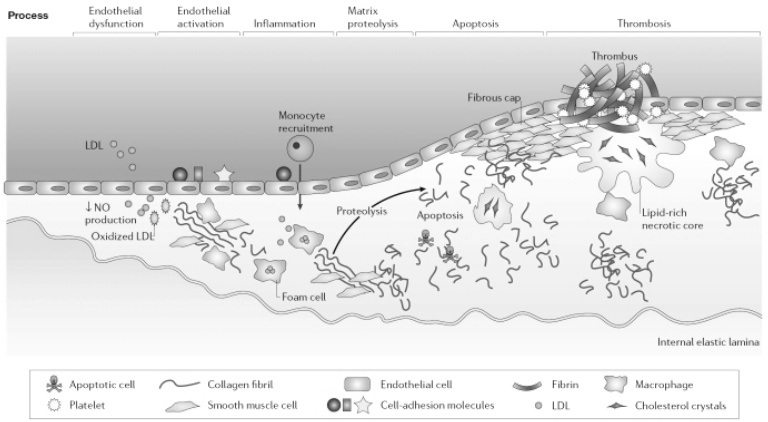
A Little Disease & Disorder

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 turbulently)
- 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 calicified 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

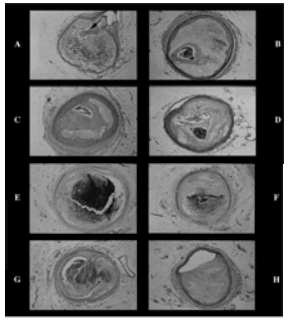
A little Disease & Disorder

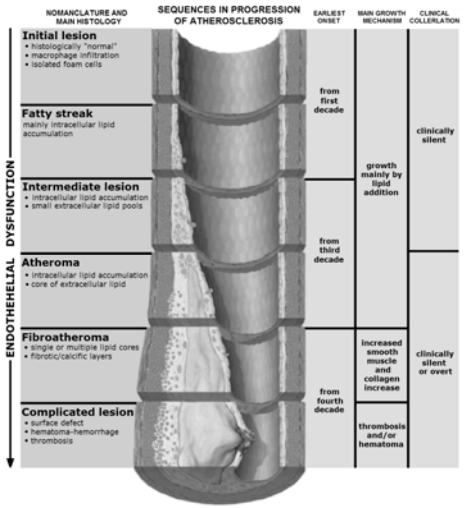
Atherosclerosis Progression



A Little Disease & Disorder

Atherosclerosis

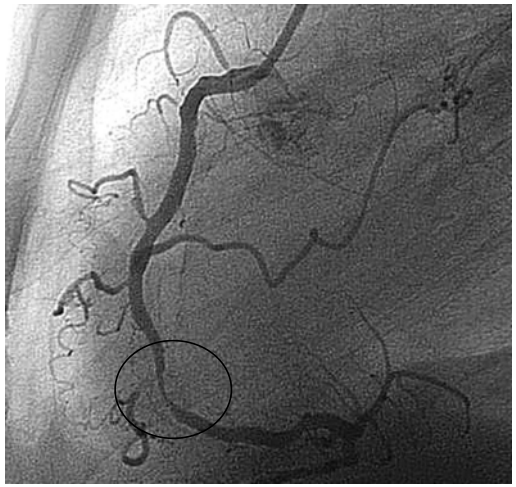




A Little Disease & Disorder

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:

Level mg/dl	**Level** mmol/L	**Interpretation**
<100	<2.6	Optimal LDL cholesterol, corresponding to reduced, but not zero, risk for heart disease
100 to 129	2.6 to 3.3	Near optimal LDL level
130 to 159	3.3 to 4.1	Borderline high LDL level
160 to 189	4.1 to 4.9	High LDL level
>190	>4.9	Very high LDL level, corresponding to highest increased risk of heart disease

A Little Disease & Disorder
Cholesterol Levels

Recommended range
The American Heart Association, NIH and NCEP provides a set of guidelines for fasting HDL levels and risk for heart disease.

Level mg/dL	**Level** mmol/L	**Interpretation**
<40 for men, <50 for women	<1.03	Low HDL cholesterol, heightened risk for heart disease
40–59	1.03–1.55	Medium HDL level
>60	>1.55	High HDL level, optimal condition considered protective against heart disease

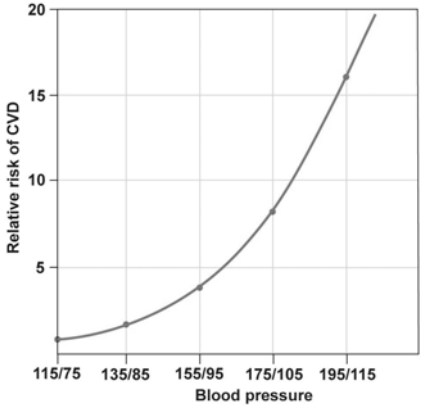
A Little Disease & Disorder
Hypertension and CVD

- 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!