LECTURE 1

PART 1: INTRODUCTION AND BACKGROUND

Read Chapter 1 in your text before proceeding. Pay particular attention to the membrane transport mechanisms described in the text.

PATHOPHYSIOLOGY (definition)- the disruption of normal physiological mechanisms to the extent that a disease state results. Usually, disruptions resulting from trauma are excluded from the definition.

Because of the prevalence of head trauma in modern clinical situations, we will violate the rule and consider head and spinal injuries in this course.

ORGANIZATIONAL LEVELS OF THE HUMAN BODY:

Chemically speaking, the human consists of the same basic elements of the periodic chart that occur throughout the universe with carbon, hydrogen, oxygen, and nitrogen being the most common. In this regard, the human is not unique from any other entity on earth. So, what makes the human uniquely different from anything else? Simply speaking it is just the organization of these elements. For example, instead of the carbon occurring in pure state like you might see in soot or lamp black, carbon in the human forms the chemical skeleton of the numerous complex organic compounds that comprise the protein, lipid, carbohydrate and nucleic acid molecules of the human body. In fact, these organizational levels can be arranged to form a hierarchy from simple to more complex (see below):

Sub-Atomic particles – protons, neutrons and electrons

Atoms – an arrangement of protons and neutrons in the nucleus surrounded by a “cloud” of electrons

Molecules – an interaction of atoms with others through chemical bonding

Macromolecules (polymers) - large molecules (carbohydrates, lipids, proteins, nucleic acids) made up of small **monomer** subunit molecules.

Macromolecular Complexes – an aggregate of macromolecules (examples - cell membrane comprised of phospholipids, proteins and carbohydrates and a chromosome comprised of DNA, RNA and histone proteins)

Organelles – the **"**small organs" that comprise individual cells (mitochondria, Golgi, lysosome, endoplasmic reticulum, flagella, etc).

Cells - collections of organelles interacting with each other within a cytoplasmic "matrix" and surrounded by a cell membrane**.**

Tissues – similarly specialized cells grouped together to perform a specific function.

Organs – collections of different tissues, each contributing a specific function to the organ as a whole. **What specific tissues comprise the heart?**

Organ System - a group of related organs interacting to perform specific functions for the entire organism (ex. Circulatory System – the heart along with arteries and veins are specialized for material transport and interstitial fluid formation and reclamation). Each organ system is specialized for maintaining some parameter/s of homeostasis. For example, the respiratory system not only controls blood gas levels but also regulates pH. **What is the relationship between blood carbon dioxide levels and blood pH?**

Organism - a collection of organ systems, each interacting with all others and each specialized to maintain some parameter (aspect) of homeostasis.
For general review, look into each human organ system and identify the parameters of homeostasis that each controls.

IMPORTANT NOTE:

In order for a human organism to function normally, all of these levels not only have to be intact and functional, but must interact correctly with each other. Thus, pathophysiological disease states can be explained as a disruption of one or more of these organizational levels or their interactions with each other.

RELATED PROBLEM:

Since these interactions are so complex, it is often difficult to assess a client's problem by noting just signs and symptoms. A disruption at one point can produce signs and symptoms in different but interrelated organ systems. Sickle cell anemia serves as an excellent example of this assessment difficulty. In this condition, red blood cells distort and assume a "sickle" shape when exposed to low oxygen. These distorted cells can rupture to cause anemia or they can lodge in small diameter vessels causing an infarction and resultant pain wherever the obstruction occurs. Signs and symptoms might suggest muscle or vascular problems when, in reality, the problem is genetic. A single point mutation substituting valine for a glutamic acid molecule in the 6^{th} position of the beta hemoglobin chain changes normal hemoglobin into sickle hemoglobin, which crystallizes and distorts RBC's when exposed to low oxygen tension. Thus, being unaware of all the facts could lead you to an incorrect assessment.

GOAL OF COURSE: TO AVOID ASSESSMENT ERRORS!

Consequently, patient histories, interviews, physical examinations and lab values all must be considered in the assessment process to avoid being misled and making serious errors. As the course progresses, you will be given exercises that will help you to develop sound assessment skills in your further education. You will learn to collect the necessary information in order to make an accurate assessment without being misled by distracting peripheral information.

PART 2: HOMEOSTASIS AND CAPILLARY HEMODYNAMICS

HOMEOSTASIS – (homeo= uniform; stasis= static, unchanging) The concept of homeostasis refers to the maintenance of a "constant" internal environment for body cells. It is within this environment where cellular activities involving nutrient uptake and waste elimination continually threaten the stability of chemical and physical parameters. In reality, the normal cellular environment is not static, but fluctuates within a normal range of values. For example, pH can normally vary between 7.35 and 7.45.

This environment of individual cells is the **interstitial fluid**, which is formed by filtration from blood plasma across capillary walls, flows through interstitial spaces among cells, and is returned to circulation by osmosis at the venous ends of capillary beds.

For background review, identify the organ systems that are responsible for the following homeostatic parameters: (1) pH; (2) temperature; (3) calcium and phosphorous levels; (4) blood gases; (5) blood sugar and other nutrients; (6) urea levels; (7) blood pressure.

Since interstitial fluid, one of the fluid compartments of the body, represents the environment for body cells, its stable composition is vital to survival. Nutrients can not become depleted nor can wastes be allowed to accumulate in this fluid environment. Two other fluid compartments interact with the interstitial fluid, intravascular (plasma) and intracellular fluids that comprise cellular cytoplasm. Consequently, changes in one fluid compartment can result in changes in one or both of the others. Such changes can be detrimental to cells and can constitute a disruption leading to a pathophysiological disease state. In all, three fluid compartments contain all the fluids of the human body, and these fluids combined represent 60% to 80% of body weight depending upon age of the individual. The proportion of fluid body weight diminishes with age and other factors.

Read about fluid compartments in your text (Chapter 10) and study the graphic on page 194 for differences in composition. Pay particular attention to the "partitions" that separate the three fluid compartments from each other and their unique permeability properties.

REVIEW QUESTIONS:

1. Which fluid compartment is most easily collected for laboratory analysis and why would this fluid's composition reflect changes in the other two?

2. In which fluid compartment is most protein found? Why?

3. What is albumin and what function does it perform?

4. In which fluid compartment is albumin found?

5. How does the albumin location relate to its function?

DISCUSSION QUESTIONS: (Post to the "Patho Discussion Group")

1. **What forces are primarily responsible for interstitial fluid formation and reclamation?**

2. **Compare and contrast "intracellular" and "extracellular" fluid compositions and identify the pedominant intracellular and extracellular electrolytes?**

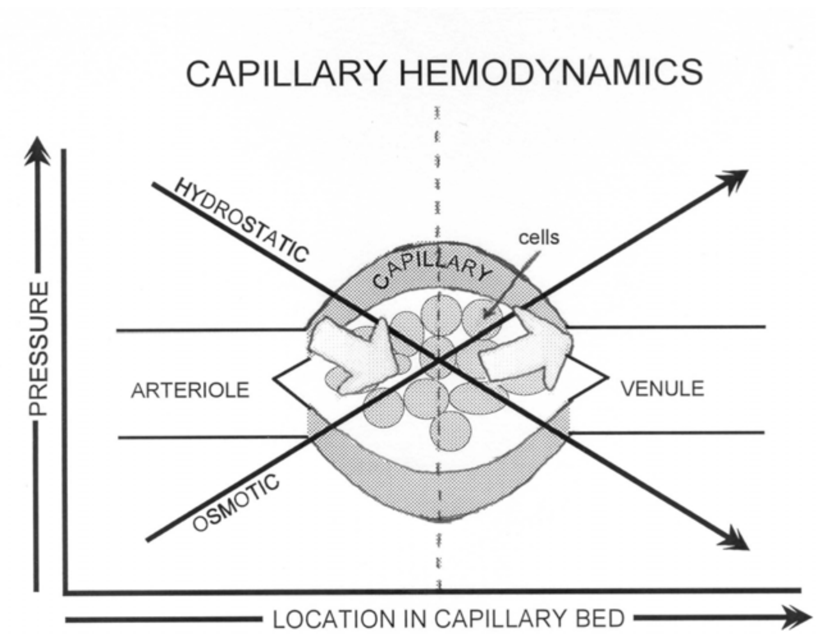
CAPILLARY HEMODYNAMICS: FLUID SHIFTS AMONG BODY FLUID COMPARTMENTS

As suggested in the previous section, fluids from blood plasma and interstitial compartments are exchanged very readily. Recall that their compositions were very similar. Recall also that typical capillaries are **fenestrated** (have holes). As blood flows through an arteriole and into capillaries under pressure (hydrostatic blood pressure), plasma fluid, along with all small molecules dissolved in it, leak out into the interstitial spaces to form interstitial fluid. However, albumin protein (high mol. wt) does not pass through capillary pores and becomes more concentrated in the capillaries as fluid is lost around it. Since albumin is osmotically active, its high concentration serves do draw interstitial fluid back into capillaries on the venous end of capillaries. This returning fluid has lost nutrients and gained wastes as it flowed through the interstitial spaces across cells. If filtration does not match reabsorption, interstitial spaces either swell (edema) or dry out (dehydration). It is by this continuing process that cells are nourished and wastes are removed. Blood that has passed through tissue capillary beds must be purified to keep its composition constant and stable. This is homeostasis, and requires normal functioning organ systems for the process to continue!

Notice that the capillary wall separates plasma and interstitial fluid, whereas the interstitial and intracellular fluids are separated by cell membranes. Cell membranes are much more selective as to what crosses them accounting for the major difference in intracellular fluid composition. However, water crosses cell membranes readily and can cause cellular shrinking (crenation) or swelling (-lysis) if osmotic differences should occur.

The figure below illustrates the three fluid compartments and their interactions. Notice particularly how hydrostatic blood pressure and blood osmotic pressure changes across a capillary bed. The figure allows you to understand how changes in the two pressures affect interstitial space status (edema or dehydration). The capillary bed is divided approximately in the middle where the two pressure lines cross in a normal person so that filtration and reabsorption are closely matched. The arteriolar ends of capillaries primarily filter fluids out since hydrostatic pressures exceed osmotic on that end. Conversely, the venous halves of capilllaries have greater osmotic pressure and tend to favor reabsorption of fluids back into circulation.

PRACTICE EXERCISE: Redraw either the hydrostatic or osmotic pressure line higher or lower to simulate an increase or decrease in that pressure and note how the point where they cross shifts. Be sure to keep the redrawn lines parallel to the original ones. A shift to the right of center means more of the capillaries are engaged in filtration than in reabsorption leading to edema.



Experiment with other situations by redrawing different pressure lines and predict the signs each might produce and speculate about ways you might correct each situation.

What happens with shifts to the left?

How might osmotic pressure be used to correct for cerebral edema.

DISCUSSION QUESTION: (Post answer to the "Patho Discussion Group")

1. **Explain why alcoholics who have damaged their livers often have ascites and puffy, edematous features.**