Cells to Systems: Lecture 7

TRANSPORT OF MOLECULES AROUND THE BODY

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Learning Objectives:

- Describe the major body fluid compartments and the composition of intracellular and extracellular body fluid
- Explain how water and solutes traverse the capillary wall, using Fick's equation and Starling's hypothesis
- Describe the organization of the cardiovascular and lymphatic systems and their role in fluid homeostasis
- Explain the mechanisms underlying disruptions to fluid homeostasis including oedema and lymphoedema

Volume and composition of the fluid compartments of the body

- Body fluids are 60-70% of body weight
- Body fluids are in two main compartments.
  - The intracellular compartment contains 2/3 of total body water
  - The extracellular compartment contains 1/3 of total body water
    - Lies outside cell membranes and consists of plasma, lymph, interstitial fluid and fluid in transcellular compartment (eg. CSF)
    - ¼ of extracellular fluid is intravascular
    - ¾ of extravascular fluid is interstitial
- The composition of extracellular and intracellular compartments is very different.
  - Extracellular fluid contains high concentrations of Na^+, Cl^-, Ca^{2+}, HCO_3^-
    - Extracellular fluid solute concentration can fluctuate
  - Intracellular fluid contains high concentrations of K^+, Mg^{2+}, phosphates, phospholipids and proteins.
    - Intracellular fluid solute content is normally fixed and maintained by active transport mechanisms (covered in Lecture 9)
  - For an animal to survive and function correctly the volume and composition of the intracellular and extracellular compartments must be rigorously maintained.
  - Tonicity (measure of osmotic pressure) can be isotonic, hypertonic or hypotonic.

Transport of fluid and solutes

- Two body systems transport fluid and solutes around the body; the cardiovascular and the lymphatic systems.
- Both have thin walled vessels that allow molecules to diffuse over short distances between the vessel and the interstitial fluid

Cardiovascular system

- Transports blood and is composed of:
  - Heart
  - Arterial system
  - Capillaries/exchange network
  - Venous system
- Blood transports:
  - Nutrients and waste products
  - Gases
  - Water, electrolytes and hormones
  - Cells of the immune system
- Capillaries allow the exchange of nutrients and metabolic products by diffusion across the endothelial wall of the capillary
- Capillaries consist of a single layer of endothelial cells surrounded by a basement membrane made up of a fine network of reticular collagen fibres.
- Venules have a discontinuous layer of vascular smooth muscle cells. They carry blood back into low-pressure veins that return blood to the heart

There are several types of capillaries:

- Continuous capillaries
  - Found in muscle, skin, lung, fat and connective tissues.
  - Contain 10-15nm wide junctions or clefts between endothelial cells
  - Hydrophilic molecules must pass through the clefts or small, coated pits in the endothelial cell membrane called caveolae.
- Fenestrated capillaries – more ‘leaky’
  - Found in kidneys, intestines, endocrine glands, and joints.
  - Endothelial cells contain pores called fenestrae that enhance the permeability to small hydrophilic molecules.
- Discontinuous capillaries – very ‘leaky’
  - Found in bone marrow, liver, and spleen.
  - They have wide clefts (100-1000nm) between adjacent endothelial cells that are permeable to large molecules
  - They also have large pores or fenestrations, which increases movement of large molecules.
- Neural capillaries
  - Found in brain
  - Special case of continuous capillaries with tight junctions and no caveolae.
  - Endothelial cells have tight junctions and capillary is surrounded by a basement membrane and enclosed by the endfeet of astrocytes (glial cells)
  - Water diffuses, but solutes require transport mechanisms

Movement across the capillary wall

- Water crosses by osmosis
  - Capillary walls are highly permeable to water
- Lipid soluble molecules like gases are able to cross endothelial cells by diffusion
- Other molecules and ions pass through water filled clefts and pores between adjacent endothelial cells (1% of total area of capillary endothelium)
- Capillary endothelial cells can exchange small amounts of protein by endocytosis and exocytosis, but albumin and other plasma proteins cannot cross continuous

capillary walls

- Some capillaries are leaky (wide clefts and fenestrae, eg. liver) and some are tight (eg. brain)
- Leaky capillaries allow more macromolecules and proteins to escape

Forces that govern fluid exchanges between blood and interstitial fluid across capillaries

- Passive diffusion (Fick's law)

Fick's equation describes factors that influence the rate of net diffusion across a membrane:

1. **Magnitude of concentration gradient**
    - ➢ Greater the difference in concentration, faster the rate of net diffusion
2. **Permeability of the membrane to the substance**
    - ➢ Greater the permeability, faster the rate of net diffusion
3. **Surface area of membrane available for diffusion**
    - ➢ Larger the surface area, faster the rate of net diffusion
4. **Molecular weight of substance**
    - ➢ Heavier the molecule, the slower the rate of net diffusion
5. **Distance of diffusion**
    - ➢ Greater the distance, the slower the rate of net diffusion

- Bulk flow across capillaries: Starling's forces
- **The four Starling's forces that regulate fluid movement filtration across the wall of a capillary are:**
    - Hydrostatic pressure in the capillary (Pc).
        - Capillary hydrostatic pressure is the pressure exerted on the inside of the capillary walls by the blood (35 mm Hg at the arterial end of the capillary and 15 mm Hg at the venous end)
    - Hydrostatic pressure in the interstitial fluid (Pif), which works in the reverse direction
    - Oncotic pressure in the capillary (□c)
        - Osmotic force exerted by plasma proteins which is equal to about 25 mmHg and drives fluid back into the capillary
    - Oncotic pressure in the interstitial fluid (□if)
        - This is very low and has minimal effect

The net fluid flux:

- Depends upon the surface area and permeability of the capillaries
- The balance of these forces allows the calculation of the net driving pressure and dictates the direction and magnitude of flow
- At the arterial end of the capillary there is a net movement of fluid out of the capillary and at the venous end fluid is reabsorbed
- Overall there is a small net filtration of fluid out of the capillary (and some protein loss)
    - Only about 90% of fluid is returned at the venous end and the remaining 10% of fluid and any proteins are returned to the blood by the lymphatic system

Lymphatic system

Lymphatic pathways form a distinct circulation of fluid and cells, which is separate from, but closely integrated with, the cardiovascular system, although the two circulations differ considerably in the composition of their fluids, their cellular content and their hydrodynamics.

The lymphatic system:

- Returns fluid, protein and cells from interstitial spaces to the cardiovascular system
- Network of vessels lined by endothelial cells
    - Initial lymphatics start in the interstitial spaces
        - The spaces where fluids, nutrients and metabolites are exchanged between parenchymal cells and blood
    - Collecting lymphatic ducts take fluid to regional lymph nodes (afferent lymphatics)
    - Efferent lymphatics take lymph from one or more lymph nodes to the thoracic duct or the right lymphatic duct, which then join the great veins in the neck

Functions:

1. **Return of excess filtered fluid to the bloodstream**
2. **Defence against disease:** lymph passes through lymph nodes located within the lymphatic system
3. **Transport of absorbed fat:** fat absorbed in the GI system is unable to access capillaries but can enter initial lymphatics
4. **Return of filtered proteins:** when plasma proteins do leak from capillaries, they travel within the lymphatics back to the intravascular space

Oedema

- Oedema is defined as the accumulation of excess body fluid, which can be intracellular or extracellular
- Intracellular oedema: due to physical damage to cell membrane or failure of cell metabolism leading to excessive Na^+ and water entry
- Extracellular oedema: accumulation in interstitial tissues or in body cavities
- Five major mechanisms of extracellular odema:
    1. Increased plasma hydrostatic pressure
    2. Decreased plasma colloid oncotic pressure
    3. Lymphatic obstruction (= lymphoedema)
    4. Increased vascular permeability
    5. Sodium retention
- Lymphoedema is the build-up of excess fluid due to the obstruction of lymph drainage
    - Can be due to blocked or damaged lymphatics

FURTHER READING

Hall JE: *Guyton and Hall Textbook of Medical Physiology*, Elsevier, 2021.Ebook. Chapters 1&2.
Klein BG: *Cunningham's textbook of veterinary physiology*. Elsevier, 2020. Available in BioMed and Werribee libraries.