Ch 1: Membrane Dynamics

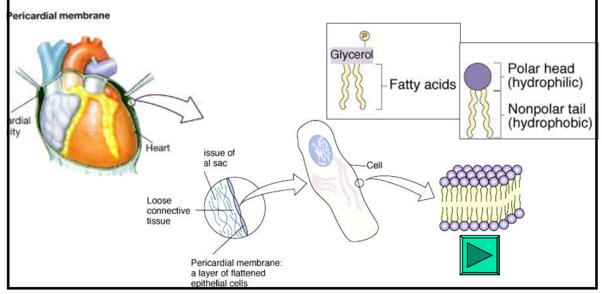
Cell membrane structures and functions
- Membranes form fluid body compartments
- Membranes as barriers and gatekeepers
- How products move across membranes
  - i.e., methods of transport
- Distribution of water and solutes in cells & the body
- Chemical and electrical imbalances
- Membrane permeability and changes

Membrane – 2 Meanings!

- **Epithelial membranes**

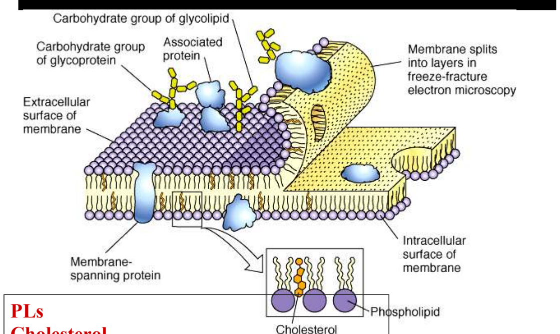
vs.

- **Cell membranes and Membranes around organelles**



Cell Membrane Structure: Fluid Mosaic Model

Thickness ~ 8nm



PLs
Cholesterol
Proteins: peripheral (associated) or integral

Membrane Structure: Protein to Lipid Ratio varies from cell type to cell type

Table 5-1: Composition of Selected Membranes

MEMBRANE	PROTEIN	LIPID	CARBOHYDRATE
Red blood cell membrane	49%	43%	8%
Myelin membrane around nerve cells	18%	79%	3%
Inner mitochondrial membrane	76%	24%	0%

Ratio for cells with high metabolic activity?

Membrane Proteins

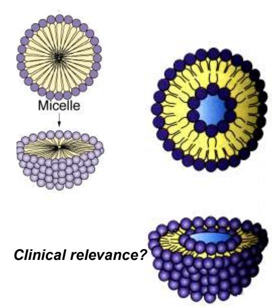
Integral
(Membrane-spanning or intrinsic)
- Can span membrane several times
- Either move around or are kept in place by cytoskeleton proteins

Allows for cell polarity

Associated
(peripheral or extrinsic)
- Loosely bound to membrane
- Enzymes and structural proteins

Other Phospholipid Behaviors in H_2O:

- ***Phospholipid bilayer***
- **Micelle**
  - **Role in digestion and absorption of fats in GI tract**
- **Liposome**
  - **Larger, bilayer, hollow center with aqueous core**



Clinical relevance?

Movement across Membrane

Membrane permeability varies for different molecules & cell types

Two movement categories: *depends on??*

- **Passive** **and**
- **Active**

Passive Transport

= **Diffusion** (*Def?*) – 3 types:

1. **simple diffusion**
2. **osmosis**
3. **facilitated diffusion** (= mediated transport)

Active Transport

Always protein-mediated – 3 types:

1. **co-transport**
2. **vesicular transport**
3. **receptor mediated transport**

Membrane Spanning Protein

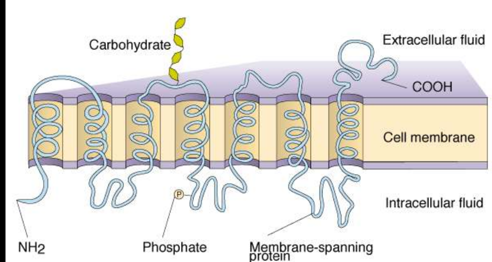
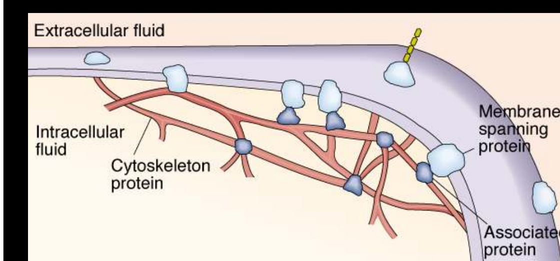


Fig 5-5

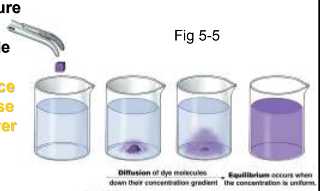
Cytoskeleton Proteins



Diffusion Process (Passive)

- **Uses energy of concentration gradient**
- **Net movement until state of equilibrium reached (no more conc. gradient)**
- **Direct correlation to temperature** (why?)
- **Indirect correlation to molecule size**
- **Slower with increasing distance**
- **Lipophilic molecules can difuse through the phospholipid bilayer**

Fig 5-5



Distance – Time Relationship

Time for diffusion to progress to given distance ~ to distance squared

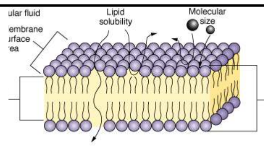
diffusion over 100 µm takes 5 sec.

diffusion over 200 µm takes ??

diffusion over 400 µm takes ??

diffusion over 800 µm takes ??

Diffusion effective only over short distances!



Fick's law of Diffusion (p 135)

$$\text{rate of diffusion} = \frac{\text{surface area} \times \text{conc. gradient}}{\text{membrane resistance} \times \text{membrane thickness}}$$

depends on
size and lipid-solubility of molecule and composition of lipid bilayer

Membrane Proteins

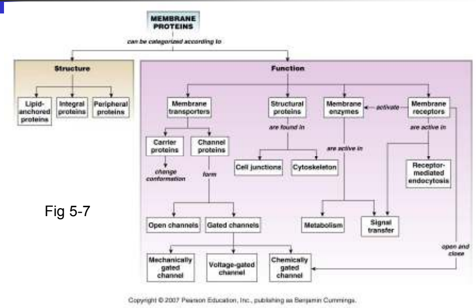


Fig 5-7

Protein-Mediated Transport

- More selective
  - Active or Passive
- Membrane Proteins
  - Structural
  - Enzymes
  - Receptors
  - Transporters (allows Specificity, Competition, Saturation p 145)
    - Channel
    - Gated

Transporters

Cell Membrane Regulates Exchange with Environment

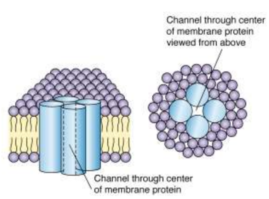
Many molecules use transporters to cross cell membrane. ***Why? Examples ?***

Two categories of transporter proteins

1. **Channel proteins (rapid but not as selective – for small molecules only, e.g., water and ions)**
2. **Carrier proteins (slower but very selective – also works for large molecules)**

1. Channel Proteins

- **For small molecules such as ??**
- **Aquaporin; plus > 100 ion channels**
- **Selectivity based on size & charge of molecule**
- **All have gate region**
  - **Open**
  - **Gated**



Open Channels vs. Gated Channels

= pores

Have gates, but gates are open most of the time.

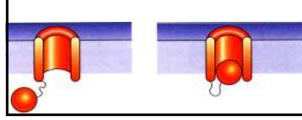
Also referred to as "leak channels".

Gates closed most of the time

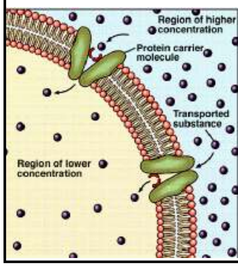
Chemically gated channels (controlled by messenger molecule or ligand)

Voltage gated channels (controlled by electrical state of cell)

Mechanically gated channels (controlled by physical state of cell: temp.; stretching of cell membrane etc.)



2. Carrier Proteins

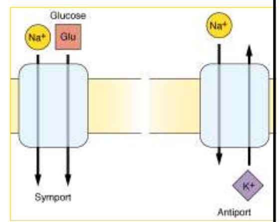


- Never form direct connection between ECF and ICF – 2 gates!
- Bind molecules and change conformation
- Used for small organic molecules *(such as?)*
- Ions may use channels or carriers
- Rel. slow (1,000 to 1 Mio / sec)

Cotransport

Symport
- Molecules are carried in same direction
- Examples: Glucose and Na^+

Antiport
- Molecules are carried in opposite direction
- Examples: Na^+/K^+ pump

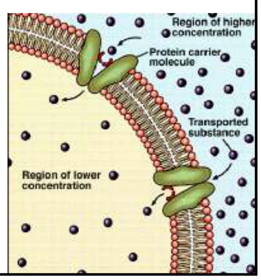


Facilitated Diffusion (as a form of carrier mediated transport)

Some characteristics same as simple diffusion

but also:
- specificity
- competition
- saturation

Figs 5-18/20



Active Transport

- Movement from low conc. to high conc.
- ATP needed
- Creates state of disequilibrium
- 1° (direct) active transport
  - ATPases or "pumps" (uniport and antiport)– examples?
- 2° (indirect) active transport
  - Symport and antiport

TABLE 5-2 Primary Active Transporters

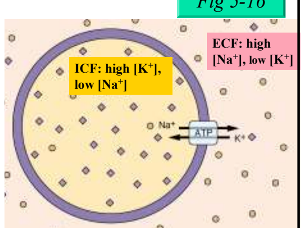
NAMES	TYPE OF TRANSPORT
Na^+-K^+-ATPase or sodium-potassium pump	Antiport
Ca^{2+}-ATPase	Uniport
H^+-ATPase or proton pump	Uniport
H^+-K^+-ATPase	Antiport

1° (Direct) Active Transport

- ATP energy directly fuels transport
- Most important example: Na^+/K^+ pump = sodium-potassium ATPase (uses up to 30% of cell's ATP)

Fig 5-16

- Establishes Na+ conc. gradient ⇒ $E_{pot.}$ can be harnessed for other cell functions



Mechanism of the Na^+/K^+-ATPase

start

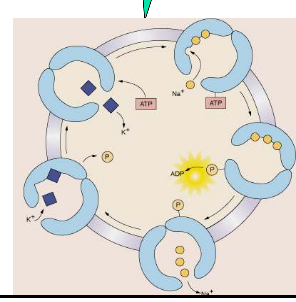
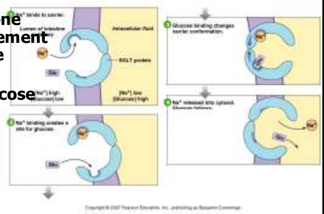


Fig 5-17

2º (Indirect) Active Transport

- Indirect ATP use: uses $E_{pot.}$ stored in concentration gradient (of Na^+ and K^+)
- Coupling of E_{kin} of one molecule with movement of another molecule
- Example: Na^+ / Glucose symporter
  - other examples
- 2 mechanisms for Glucose transport



Body Fluid Compartments

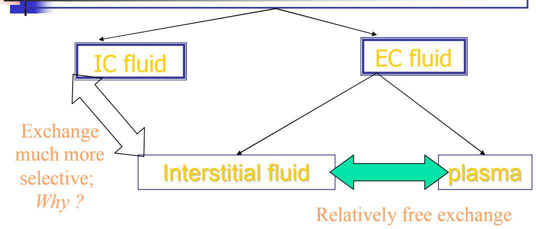
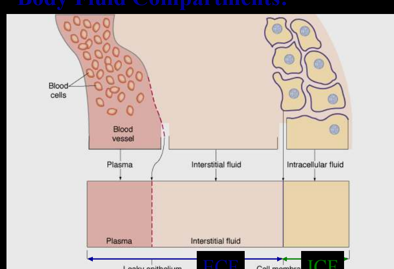


Fig 5-13

Body Fluid Compartments:



Competition and Saturation

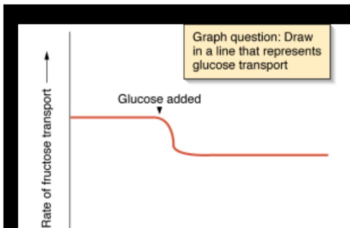


Fig 5-18

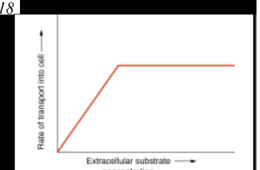


Table 5-4

Secondary Active Transporters

Sodium-dependent transporters	
Symport Carriers	*Antiport Carriers*
Na^+/glucose	Na^+/H^+
Na^+/amino acids (several types)	Na^+/Ca^{2+}
Na^+/K^+/2 Cl^-	
Na^+/bile salts (small intestine)	
Na^+/choline uptake (nerve cells)	
Na^+/neurotransmitter uptake (nerve cells)	
Nonsodium-dependent transporters	
	HCO_3^-/Cl^-
	H^+/K^+

Vesicular Transport

Movement of macromolecules across cell membrane:

1. Phagocytosis (specialized cells only)
2. Endocytosis
   - Pinocytosis
   - Receptor mediated endocytosis
   - (Caveolae) Potocytosis
3. Exocytosis

1. Phagocytosis

Requires energy

- Cell engulfs particle into vesicle via pseudopodia formation
- *E.g.:* some WBCs engulf bacteria
- Vesicles formed are much larger than those formed by endocytosis
- Phagosome fuses with lysosomes ⇒ ? *(see Fig. 5-23)*

2. Endocytosis

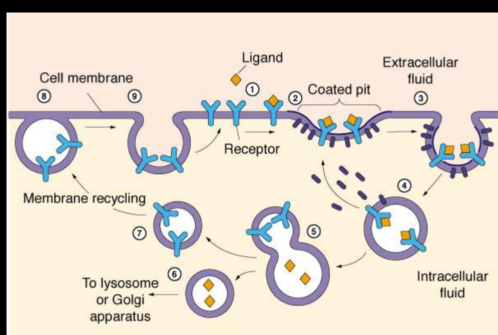
Requires energy

No pseudopodia - Membrane surface indents

- Smaller vesicles
- Nonselective: Pinocytosis for fluids & dissolved substances
- Selective:
  - Receptor Mediated Endocytosis via clathrin-coated pits - Example: LDL cholesterol and Familial Hypercholesterolemia
  - Podocytosis via caveolae

Fig 5-24

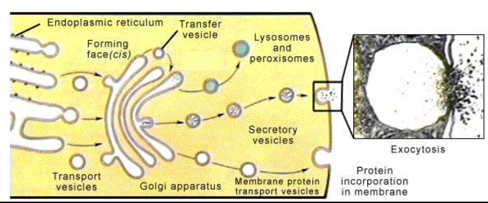
Receptor Mediated Endocytosis and Membrane Recycling



3. Exocytosis

Intracellular vesicle fuses with membrane → Requires energy (ATP) and Ca^{2+}

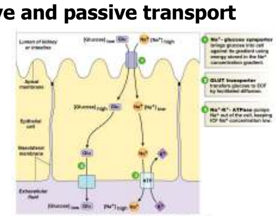
Examples: large lipophobic molecule secretion; receptor insertion; waste removal



Movement through Epithelia: Transepithelial transport

Uses combination of active and passive transport

Molecule must cross two phospholipid bilayers



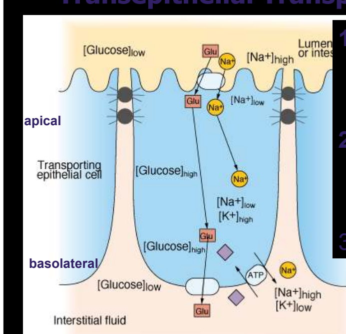
Apical and basolateral cell membranes have different proteins*:*

Na^+- glucose transporter on apical membrane

Na^+/K^+-ATPase only on basolateral membrane

Fig 5-26

Transepithelial Transport of Glucose

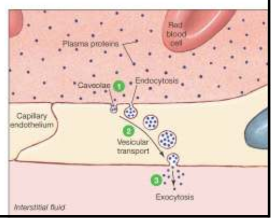


1. **Na⁺/Glucose** symporter only found on apical side
2. **Na⁺/K⁺-ATPase** only found on basolateral side
3. Facilitated diffusion

Concept check: Apply Ouabain to either side of cell, what happens?

Transcytosis

- Endocytosis → vesicular transport → exocytosis
- **Moves large proteins intact**
- **Examples:**
  - Absorption of maternal antibodies from breast milk
  - Movement of proteins across capillary endothelium



Distribution of Solutes in Body

Depends on

- **selective permeability of cell membrane**
- **transport mechanisms available**

Water is in osmotic equilibrium (free movement across membranes)

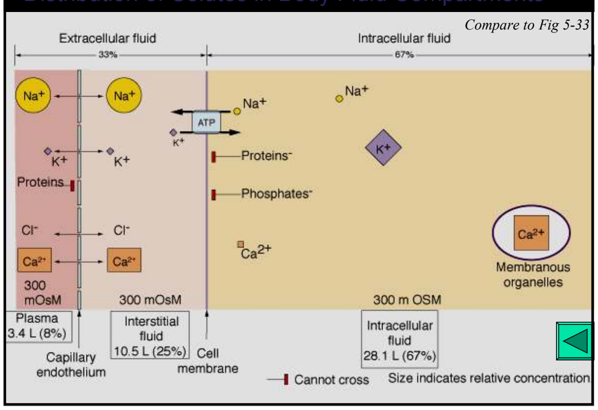
Ions and most solutes are in chemical disequilibrium (e.g., Na-K ATPase Pump)

Electrical disequilibrium between ECF and ICF

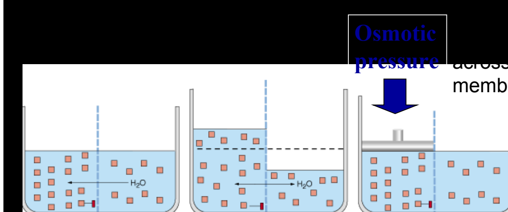
Fig 5-33

Distribution of Solutes in Body Fluid Compartments

Compare to Fig 5-33



Osmosis



Molarity vs. Osmolarity

In chemistry:

- Mole / L
- Avogadro's # / L

In Physiology

Important is not # of molecules / L but

# of particles / L: osmol/L or OsM

Why?

Osmolarity takes into account dissociation (solubility) of molecules in solution

Osmolality = OsM/Kg of sol'n

Convert Molarity to Osmolarity

Osmolarity = # of particles / L of solution

- **1 M glucose = 1 OsM glucose**
- **1 M NaCl = 2 OsM NaCl**
- **1 M $MgCl_2$ = 3 OsM $MgCl_2$**
- **Osmolarity of human body ~ 300 mOsM**
- **Compare isosmotic, hyperosmotic, hyposmotic (p 156)**

Tonicity

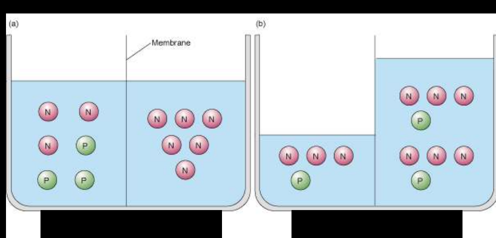
- **Physiological term describing how cell volume changes if cell placed in the solution**
- **Always comparative. Has no units.**
  - **Isotonic sol'n = No change in cell**
  - **Hypertonic sol'n = cell shrinks**
  - **Hypotonic = cell expands**
- **Depends not just on osmolarity but on nature of solutes and permeability of membrane**

Penetrating vs. Nonpenetrating Solutes

- **Penetrating solute: can enter cell (glucose, urea)**
- **Nonpenetrating solutes: cannot enter cell (sucrose, NaCl*)**
- **Determine relative conc. of nonpenetrating solutes in solution and in cell to determine tonicity.**
  - **Water will move to dilute nonpenetrating solutes**
  - **Penetrating solutes will distribute to equilibrium**

Fig 5-30

Osmolarity and Tonicity Comparison



Compare to Fig 5-35

IV Fluid Therapy

2 different purposes:

- **Get fluid into dehydrated cells or**
- **Keep fluid in extra-cellular compartment**

Table 5-9: Intravenous Solutions

SOLUTION	ALSO KNOWN AS	OSMOLARITY	TONICITY
0.9% saline*	Normal saline	Isosmotic	Isotonic
D_5—0.9% saline	5% dextrose** in normal saline	Hyperosmotic	Isotonic
D_5W	5% dextrose in water	Isosmotic	Hypotonic
0.45% saline	Half-normal saline	Hyposmotic	Hypotonic
D_5—0.45% saline	5% dextrose in half-normal saline	Hyperosmotic	Hypotonic

*Saline = NaCl.   **Dextrose = glucose.

Electrical Disequilibrium and Resting Membrane Potential (pp.156-163) will be covered at the beginning of Ch 8

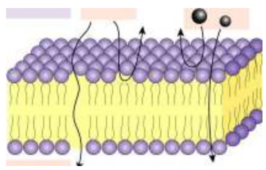
the end

Ch 5: Membrane Dynamics, Part 2

Cell membrane structures and functions
- Membranes form fluid body compartments
- Membranes as barriers and gatekeepers
- How products move across membranes
  - i.e., methods of transport
    - Vesicular
    - Transepithelial
    - Osmosis
- Distribution of water and solutes in cells & the body
- Chemical and electrical imbalances
  - Resting Membrane Potential
- Membrane permeability and changes

Membrane Dynamics, Part 1 Review

- Law of Mass Balance
  - Ins = outs
- Diffusion
  - Too slow for many processes
- Facilitated Diffusion
  - Carrier proteins
- Protein-mediated Transport
  - Very selective
- Active Transport uses ATP
  - Na^+ - K^+ ATPase pump



Vesicular Transport

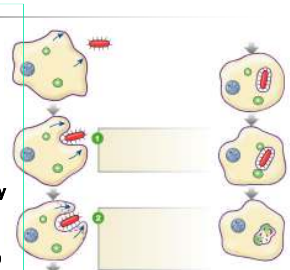
Movement of macromolecules across cell membrane:

1. **Phagocytosis (specialized cells only)**
2. **Endocytosis**
   - **Pinocytosis**
   - **Receptor mediated endocytosis**
   - **(Caveolae) Potocytosis**
3. **Exocytosis**

1. Phagocytosis

Requires energy

- **Cell engulfs particle into vesicle via pseudopod formation**
- ***E.g.:* some WBCs engulf bacteria**
- **Vesicles formed are much larger than those formed by endocytosis**
- **Phagosome fuses with lysosomes ⇒ ?** ***(see Fig. 5-23)***



2. Endocytosis

- **Requires energy**
- **No pseudopodia - Membrane surface indents**
- **Smaller vesicles**
- **Nonselective: Pinocytosis for fluids & dissolved substances**
- **Selective:**
  - **Receptor Mediated Endocytosis via clathrin-coated pits - Example: LDL cholesterol and** Familial Hypercholesterolemia
  - **Potocytosis via caveolae**

Fig 5-24

Receptor Mediated Endocytosis and Membrane Recycling

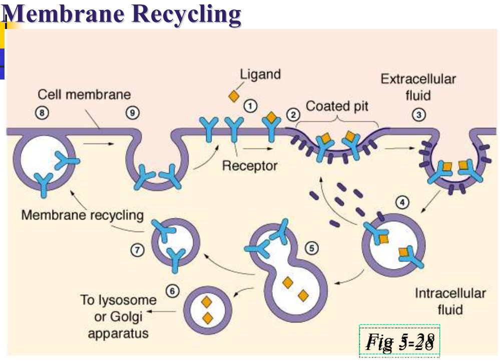
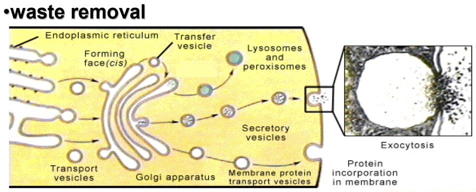


Fig 5-28

3. Exocytosis

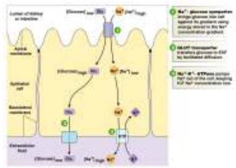
- **Intracellular vesicle fuses with membrane →**
- **Requires energy (ATP) and Ca^{2+}**
- *Uses:*
  - **large lipophobic molecule secretion;**
  - **receptor insertion;**
  - **waste removal**



Movement through Epithelia: Transepithelial Transport

Uses combination of active and passive transport

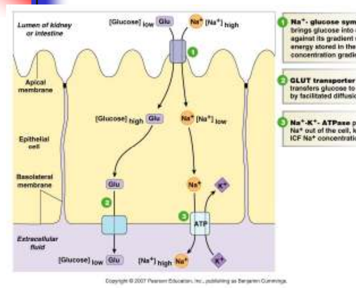
Molecule must cross two phospholipid bilayers



Apical and basolateral cell membranes have different proteins:
- Na^+- glucose transporter on apical membrane
- Na^+/K^+-ATPase only on basolateral membrane

Fig 5-26

Transepithelial Transport of Glucose



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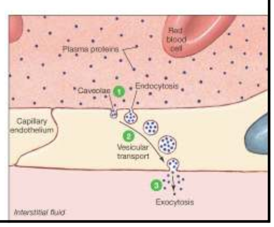

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Depends on
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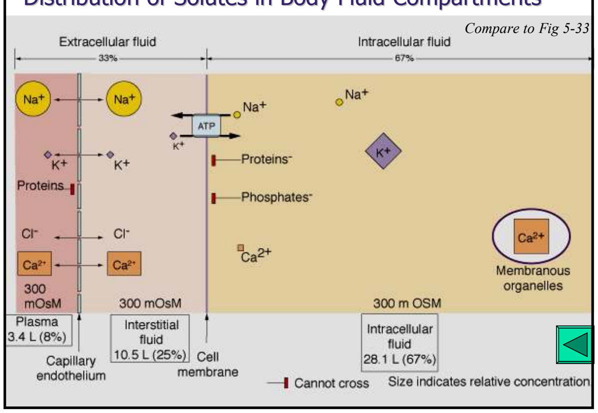
Ions and most solutes are in chemical disequilibrium (e.g., Na-K ATPase Pump)

Electrical disequilibrium between ECF and ICF

Fig 5-33

Distribution of Solutes in Body Fluid Compartments

Compare to Fig 5-33

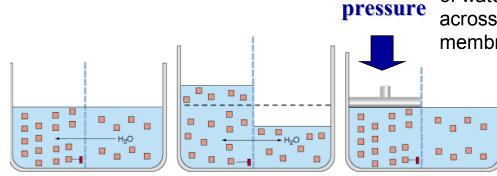


Osmosis

Compare to Fig. 5-29

Movement of ***water*** down its concentration gradient.

Osmotic pressure Opposes movement of water across membrane



Water moves freely in body until osmotic equilibrium is reached

Molarity vs. Osmolarity

In chemistry:
- Mole / L
- Avogadro's # / L

In Physiology

Important is not # of molecules / L but

# of particles / L: osmol/L or OsM

Why?

Osmolarity takes into account dissociation (solubility) of molecules in solution

Osmolality = OsM/Kg of sol'n

Convert Molarity to Osmolarity

Osmolarity = # of particles / L of solution

- **1 M glucose = 1 OsM glucose**
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- **1 M $MgCl_2$ = 3 OsM $MgCl_2$**
- **Osmolarity of human body ~ 300 mOsM**

- **Compare isosmotic, hyperosmotic, hyposmotic (p 156)**

Tonicity

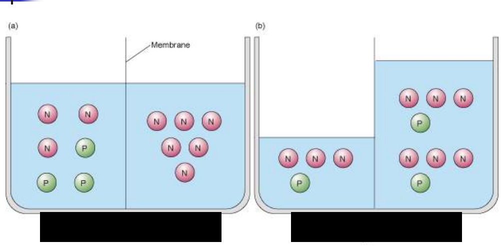
- **Physiological term describing how cell volume changes if cell placed in the solution**
- **Always comparative. Has no units.**
  - **Isotonic sol'n = No change in cell**
  - **Hypertonic sol'n = cell shrinks**
  - **Hypotonic = cell expands**
- **Depends not just on osmolarity but on nature of solutes and**

Penetrating vs. Nonpenetrating Solutes

- **Penetrating solute: can enter cell (glucose, urea)**
- **Nonpenetrating solutes: cannot enter cell (sucrose, NaCl*)**
- **Determine relative conc. of nonpenetrating solutes in solution and in cell to determine tonicity.**
  - **Water will move to dilute nonpenetrating solutes**
  - **Penetrating solutes will distribute to equilibrium**

Fig 5-30

Osmolarity and Tonicity Comparison



Compare to Fig 5-35

IV Fluid Therapy

2 different purposes:
- **Get fluid into dehydrated cells or**
- **Keep fluid in extra-cellular**

Table 5-9: Intravenous Solutions

SOLUTION	ALSO KNOWN AS	OSMOLARITY	TONICITY
0.9% saline*	Normal saline	Isosmotic	Isotonic
D_5—0.9% saline	5% dextrose** in normal saline	Hyperosmotic	Isotonic
D_5W	5% dextrose in water	Isosmotic	Hypotonic
0.45% saline	Half-normal saline	Hyposmotic	Hypotonic
D_5—0.45% saline	5% dextrose in half-normal saline	Hyperosmotic	Hypotonic

* Saline = NaCl. ** Dextrose = glucose.

Electrical Disequilibrium and Resting Membrane Potential (pp.156-163) will be covered at the beginning of Ch 8

the end

Which of the following is a way for solutes in a aqueous solution to move from an area of high solute concentration to an area of low solute concentration?

Facilitated diffusion
Osmosis
Active transport
A and B
None of these

Which of the following defines the term specificity?

movement of molecules by the use of vesicles
the energy required to move molecules
a group of carrier proteins operating at their maximum rate
carrier transport of a group of closely related molecules
none of these

Water will always move from ____________ situations to ________ situations.

Hyperosmotic, hyposmotic
Hyposmotic, hyperosmotic
Hyposmotic, isosmotic
Hyperosmotic, isosmotic

Which of the following pairs of molecular characteristics favors diffusion through the cell membrane?

Large, polar
Large, non-polar
Small, polar
Small, non-polar

Which of the following is a way for solutes in a aqueous solution to move from an area of high solute concentration to an area of low solute concentration?

- Facilitated diffusion
- Osmosis
- Active transport
- A and B
- None of these