Physiology Lecture 4 & 5

# Transport of substances through cell membranes

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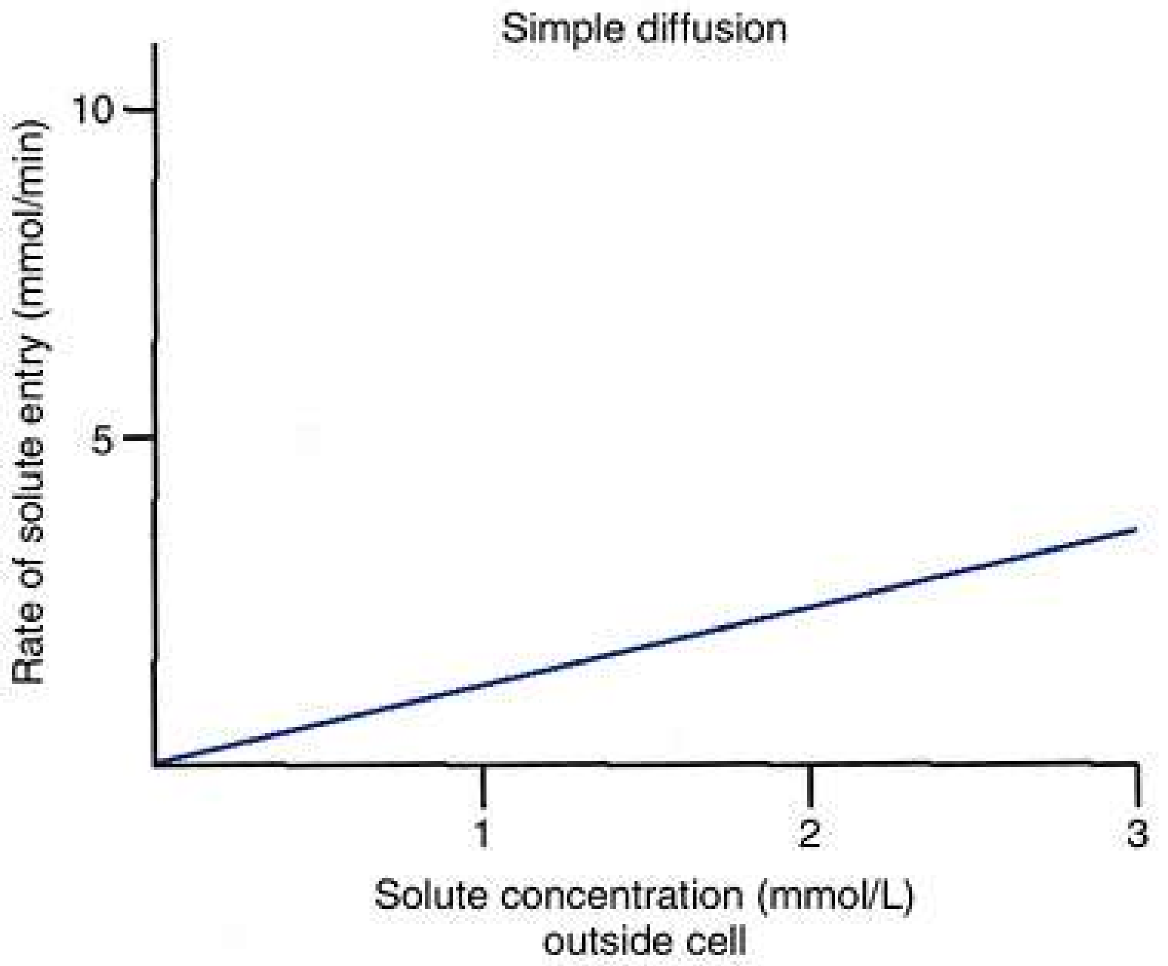
# Lecture Objectives:

- Define diffusion and describe the factors that affect the rate of diffusion of substances across cell membranes.
- Describe facilitated diffusion.
- Compare and contrast facilitated diffusion and simple diffusion.
- Explain characteristics of carrier mediate transport, (specificity, saturation, and competition).
- Define and explain primary active transport, using the $Na^{+}$-$K^{+}$ pump, and proton pump as examples of primary active transport.
- Discuss the characteristics of primary active transport.
- Define and explain the mechanism of secondary active transport.
- Explain how glucose is transported across epithelial cells in the kidney and the gut by secondary active transport.
- Define vesicular transport, transcellular transport, and their functions.
- Define osmosis and explain how osmosis takes place.
- Define osmotic pressure and explain the determinants of osmotic pressure.
- Understand how to calculate osmotic pressure.
- Describe water movement across the plasma membrane and explain the role of water channels.

# Diffusion

- It is the random movement of substances molecules, ions, or suspended colloid particles either through membrane openings or through intermolecular spaces in the membrane, or in combination with a carrier protein.
- Diffusion through cell membrane is either *simple* or *facilitated*.
- **Simple diffusion** is passive process (no energy is required) by which particles in solution flow down a concentration gradient. Diffusion rate is determined by the (1) concentration gradient, (2) electrical gradient, and by (3) membrane permeability. It is the only form of transport that is **not carrier-mediated**.
- Lipid-soluble particles can diffuse easily, their permeability is proportional to (1) their lipid solubility and (2) the size of the particle.
- The **selective** rapid passage of water through the membrane is achieved through *aquaporins,* which are channels used for the passage of water.




**A graph of solute transport across a plasma membrane by simple diffusion**

# Diffusion (cont.)

- ***Permeability*** describes the ease with which a solute diffuses through a membrane. It depends on the characteristics of the solute and the membrane.
- The permeability increases if:
  1. Solute is lipid soluble
  2. The radius of the solute is small
  3. The membrane thickness is small
- Uncharged or nonpolar molecules such as $O_2$, $N_2$, $CO_2$, fatty acids, and alcohols can diffuse through lipid membrane because of their high lipid solubility.
- Water-soluble ions less than 0.8 nm in diameter diffuse through protein pore channels. Their permeability is proportional to their size, shape, and charge; as well as the number of channels through which they can diffuse.

# Diffusion (cont.)

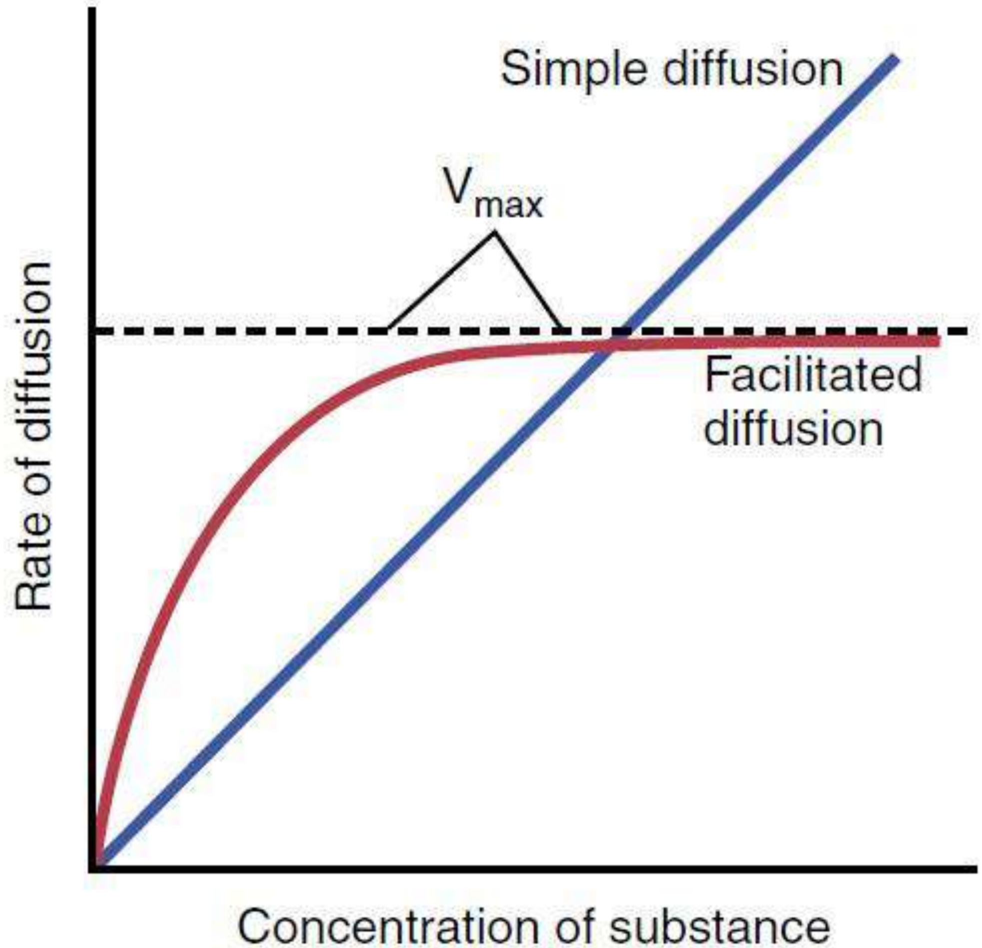
- Some lipid-insoluble molecules (such as urea) can use less selective water channels to pass.
- In **facilitated diffusion** carrier protein aids passage of too large molecules or ions by binding chemically with the molecule or ion and shuttling them through the membrane in this form down an electrochemical gradient (e.g. *glucose* and *amino acids*). It does not require metabolic energy (i.e. *passive*) and is more rapid than simple diffusion.
- As facilitated diffusion is carrier-mediated, therefore, it displays three important characteristics that determine the kind and amount of material that can be transferred across the membrane: ***stereospecificity***, ***saturation***, and ***competition***.
- **Stereospecificity:** Each carrier protein is specialized to transport a specific substance or, at most, a few closely related chemical compounds. Example, amino acids cannot bind to glucose carriers.

# Diffusion (cont.)

- **Saturation:** A limited number of carrier binding sites are available within a particular plasma membrane for a specific substance. Therefore, there is a limit to the amount of a substance a carrier can transport across the membrane in a given time. This limit is known as the **transport maximum** (***Tm*** or ***Vmax***).

  This means that initially facilitated diffusion depends on the concentration gradient until all binding sites are filled (saturated); at this point, the rate of diffusion can no longer rise with increasing the concentration gradient.

- **Competition:** Closely related compounds may compete for a ride across the membrane on the same carrier. Example the amino acid ***glycine*** can compete with ***alanine*** for the same carrier. The rate of transport of each amino acid is less when both amino acid molecules are present than when either is present by itself.




Effect of concentration of a substance on the rate of diffusion through a membrane by simple diffusion and facilitated diffusion. This graph shows that facilitated diffusion approaches a maximum rate, called the $V_{max}$.

# Active transport

It is the movement of molecules or ions by a cell membrane (or intracellular membranes) uphill against a concentration or electrical gradient.

Ions actively transported are $Na^+$, $K^+$, $Ca^{2+}$, iron, $H^+$, $I^-$, and urate ions.

Molecules that are actively transported are different ***sugars*** and most of the ***amino acids***.

Transport depends on carrier proteins in cell membrane.

# Types of active transport

- Secondary active transport
- Primary active transport

# Primary active transport

Uses the hydrolysis of ATP as source of energy. Ions transported by this mechanism are $Na^+$, $K^+$, $Ca^{2+}$,$H^+$, $Cl^-$, and few other ions. Examples are;

A. **$Na^+$- $K^+$ pump** ($Na^+$- $K^+$ ATPase) is a clear example of this mechanism. Both $Na^+$ and $K^+$ are transported against their electrochemical gradients. Each cycle of the pump uses 1 molecule of ATP to remove 3 $Na^+$ ions from the ICF and transport 2 $K^+$ ions into the ICF. The $Na^+$-$K^+$ pump controls ***cell volume*** and creates ***electrical potential*** across the cell membrane as it pumps.

   This pump is inhibited by **digitalis**, a drug used in the treatment of heart failure. Also this pump stops functioning if no $Na^+$, $K^+$, or ATP is available.

B. **$Ca^{2+}$ pump** on the sarcoplasmic reticulum (SR) of muscle cells, which maintains the intracellular ionic $Ca^{2+}$ concentration below 0.1 μmol/L.

C. **$H^+$-$K^+$ ATPase or proton pump**. This pump is found in (1) the gastric glands of the stomach and in (2) the late distal tubules and cortical collecting ducts of the kidneys.

# Secondary active transport

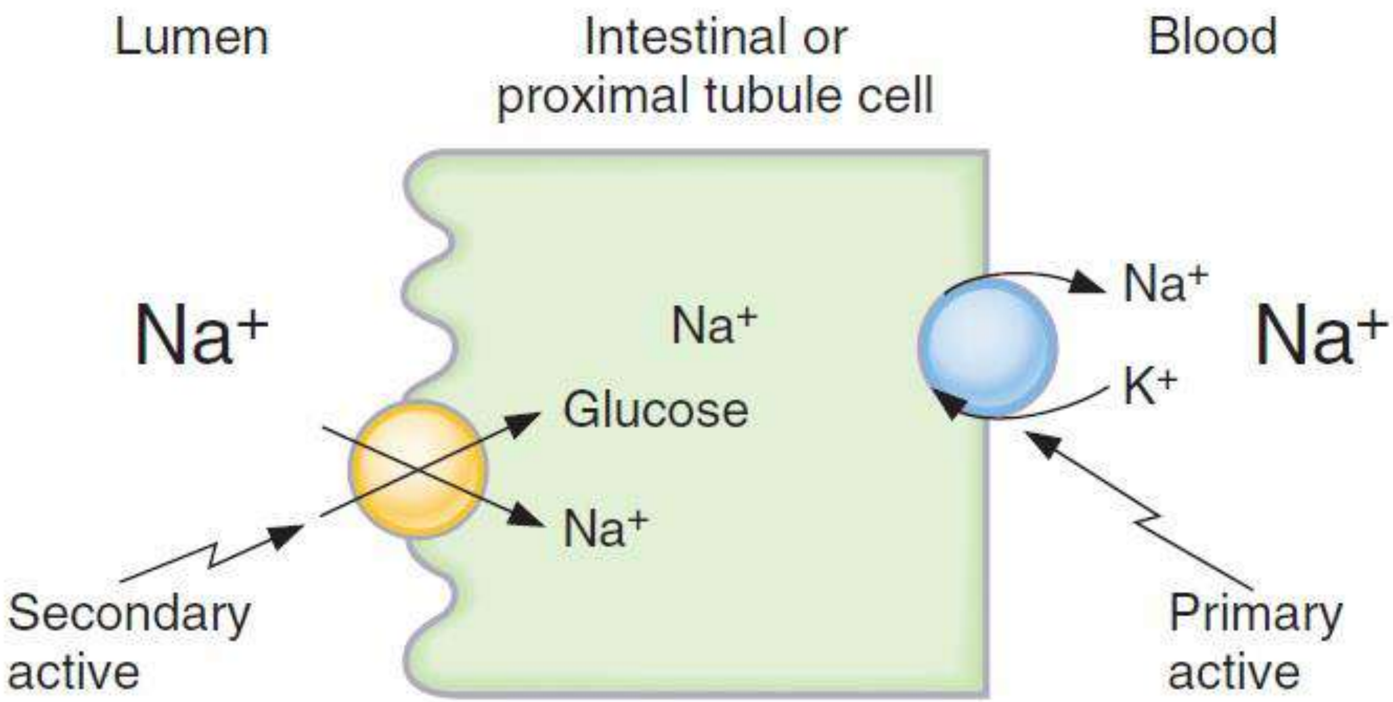
- Metabolic energy is not provided directly, but indirectly from the ***$Na^+$ gradient*** that is maintained across cell membranes (potential energy).
- Two or more solutes are coupled to the carrier protein; one of the solutes ($Na^+$) is transported ***downhill*** and provides the energy for the uphill transport of the other solute(s). Thus, inhibition of $Na^+$-$K^+$ pump eventually inhibits secondary active transport.
- If $Na^+$ ions pull other substances along with them while diffusing to the interior (solutes move in the same direction), the phenomenon is called ***co-transport***. **Glucose** and many **amino acids** are transported by this mechanism (such as in intestinal epithelial cells and in the renal proximal tubules of the kidney).

# Secondary active transport (cont.)

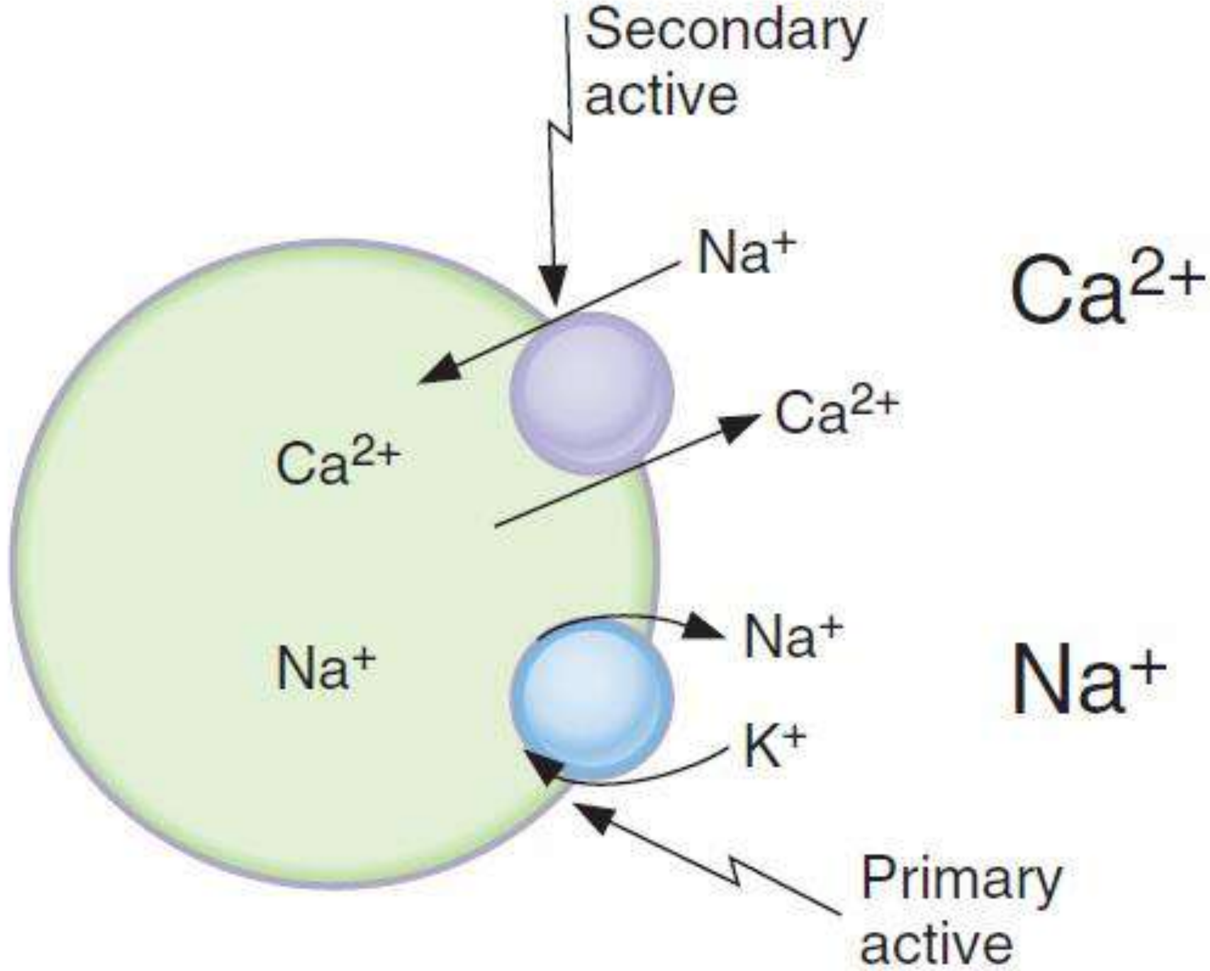
- Other form of secondary active transport is the ***counter-transport*** or **exchange** phenomenon. Here $Na^+$ ions diffuse in replacement for intracellular substances that must be transported to the outside.

- Two counter-transport mechanisms are especially important; they are:

  * The **$Na^+$-$Ca^{2+}$ exchanger** (responsible for the removal of calcium from the cytoplasm of myocardial cells)
  * The **$Na^+$-$H^+$ counter-transport**. This latter mechanism is responsible for the removal of $H^+$ ions produced by cellular metabolism to the ECF. The same mechanism is also responsible for the reabsorption of bicarbonate ions in the proximal tubule of the kidney.




$Na^+$–glucose cotransport (symport) in intestinal or proximal tubule epithelial cell




$Na^{+}$–$Ca^{2+}$ countertransport (antiport)

# Vesicular transport

This mechanism is applied for the transport of large polar molecules or even multimolecular materials that must ***leave*** or ***enter*** the cell- such as during secretion of protein hormones by endocrine cells, or during ingestion of invading bacteria by white blood cells.

Vesicular transport <u>requires energy</u> expenditure by the cell, so it is an active method of membrane transport. Energy is needed to accomplish ***vesicle formation*** and ***vesicle movement*** within the cell.

Vesicular transport includes **endocytosis** and **exocytosis**.

A. In **endocytosis** the material to be transported first binds to a receptor, and then the receptor-substance complex is surrounded by the plasma membrane substance forming endocytic vesicle to be ingested by endocytosis. Endocytosis is of three types;
    1. Phagocytosis (cell eating), for bacteria, dead tissue, and bits of material. Few specialized cells (such as WBC) are capable of phagocytosis. A lysosome fused with the membrane of the internalized vesicle releases its hydrolytic enzymes into the vesicle, breaking down the engulfed material into reusable raw ingredients.

# Vesicular transport (cont.)

2. Receptor-mediated endocytosis. is a highly selective process that enables cells to import specific large molecules that it needs from its environment. **Iron**, **cholesterol**, **vitamin B12**, and the **hormone insulin** are important examples.
3. Pinocytosis (cell drinking), the ingested substances are in solution and cannot be seen under the microscope. Pinocytosis provides a way to retrieve extra plasma membrane that has been added to the cell surface during exocytosis.

B. In **exocytosis**, intracellular material is trapped within vesicles, the vesicles fuse with the cell membrane and release the content to the ECF. ***Hormones***, ***digestive enzymes***, and ***synaptic transmitters*** are examples of materials transported by such mechanism.

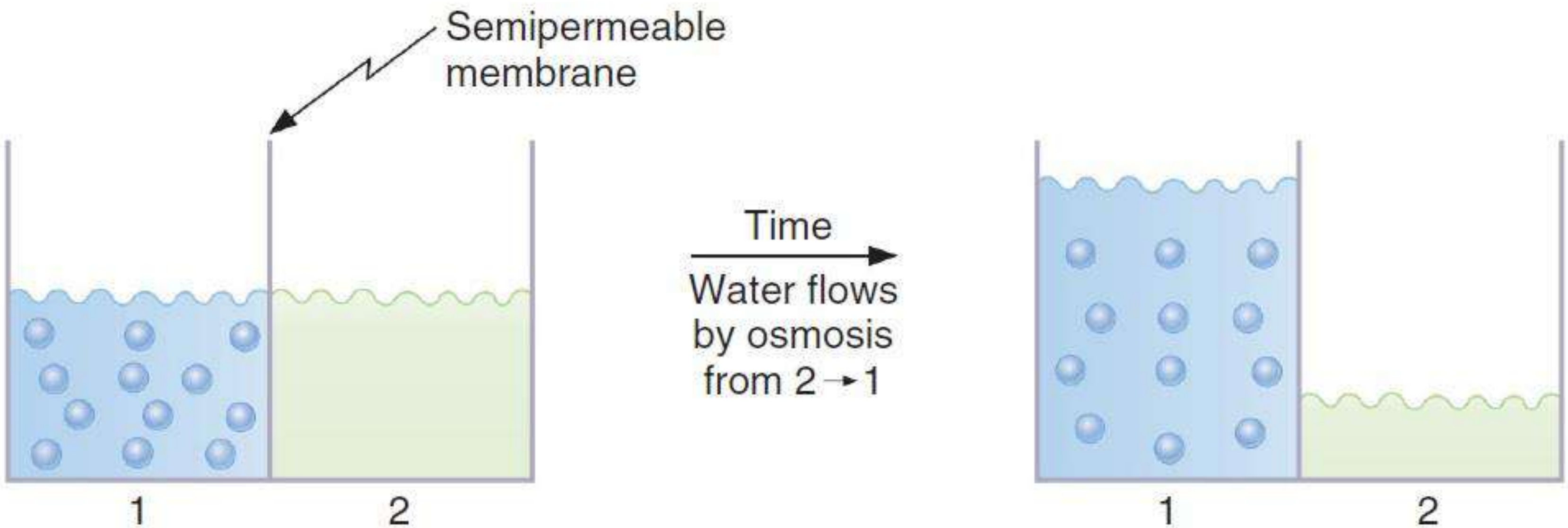
Exocytosis enables the cell to add specific components to the membrane, such as selected carriers, channels, or receptors, depending on the cell's needs. Exocytosis is a process that requires $Ca^{2+}$ and energy.

**Notes**: Exocytosis-endocytosis coupling maintains the surface area of the cell at its normal size.

Flu viruses and HIV, the virus that causes AIDS, gain entry to cells via receptor-mediated endocytosis.

# Osmosis

- It is the net *passive* flow of water across a selectively permeable membrane down an osmotic pressure gradient.
- The driving force for movement of water is the same as for any other diffusing molecule, i.e. from a region of high water concentration to one that has a lower water concentration.
- It is important to recognize, however, that adding a solute to pure water in effect decreases the water concentration.
- In general, adding one molecule of a solute displaces one molecule of water.
- Therefore, water flows from pure water to salty solution (i.e. ***water moves by osmosis to the area of higher solute concentration***).




Osmosis of $H_2O$ across a semipermeable membrane

# Osmosis (cont.)

- **Osmotic pressure (π)** of a solution is a measure of the tendency for water to move ***into that solution***. It is equal to the hydrostatic pressure needed to stop osmosis.

  It is determined by the number of particles in a solution per unit volume of fluid (i.e. molar concentration). The osmotic pressure increases when the solute concentration increases.

- The higher the osmotic pressure of a solution, the greater the water flow ***into it***.

- The **Osmole** of a substance = 1 gram molecular weight of undissociated solute of that substance.

  **Osmolarity = concentration X number of dissociable particles**

  **mOsm/L = mmol/L X number of particles/mole**

- The **Osmolality** = the number of osmoles per kilogram of water. The normal osmolality of the extracellular and intracellular fluids is about 300 milliosmoles per a kilogram of water.

  The average osmotic pressure of the body fluids is about 5500 mmHg, since one milliosmole per liter is equivalent to 19.3 mmHg osmotic pressure.

- The **Osmolarity** = the number of osmoles per liter of solution ≈ osmolality for dilute solution, such as those in the body.

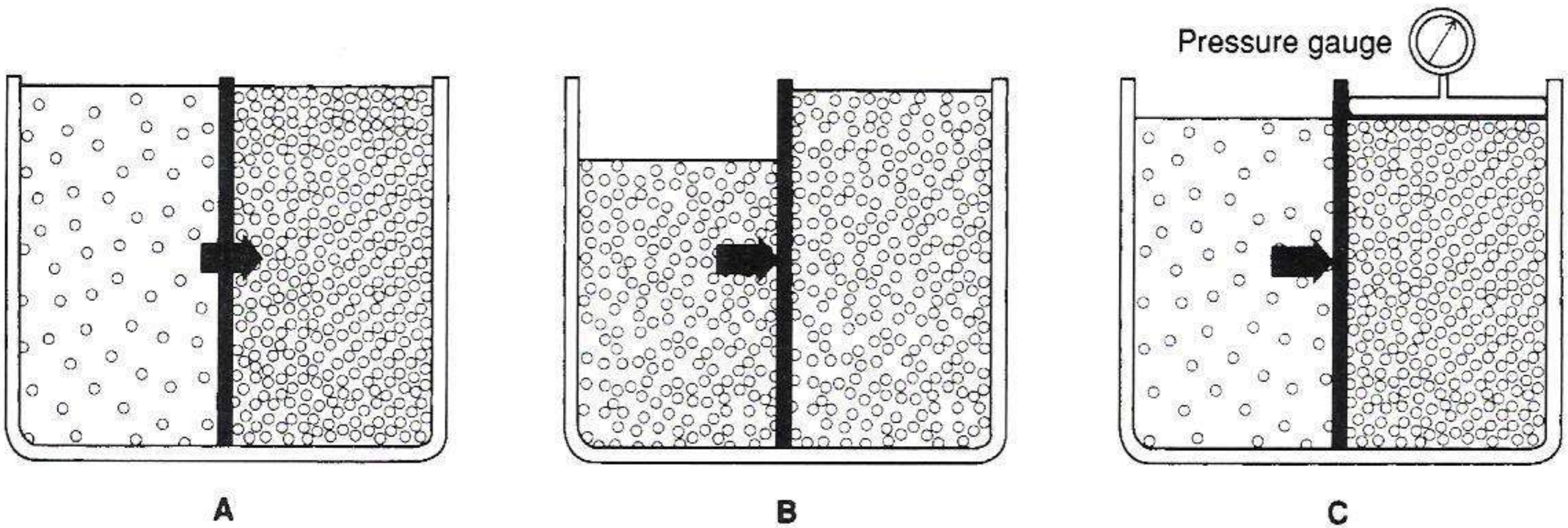



**FIGURE .** When a selectively permeable membrane separates two solutions of different osmolalities (*A*), water flows from the solution with the lower osmotic pressure (concentration) to the solution with the higher osmotic pressure (concentration). (*B*) Water flows into the chamber until the pressure (i.e., hydrostatic and osmotic) difference between the two chambers is zero. (*C*) The application of pressure to the chamber that contains the higher solute concentration prevents the flow of water. The amount of pressure that must be applied to prevent the flow of water is a measure of the osmotic pressure between the two chambers.

# Osmosis (cont.)

- **Colloid osmotic pressure**, or **oncotic pressure**, is the osmotic pressure created by proteins (e.g. plasma proteins). As proteins do not cross the capillary wall, they cause colloid osmotic (oncotic) pressure gradient between the capillary and the interstitial fluid.
- Cell volume can change if the cell is placed in a solution with different osmolality. The new cell volume can be calculated by the formula:

$$\Pi 1 \cdot V1 = \Pi 2 \cdot V2$$

- If the concentration of a substance increases in the ECF compartment the ECF becomes **hyperosmotic**. If the cell membrane is impermeable to this substance the ECF becomes **hypertonic** too. Hypertonic ECF causes water to flow out of the cell (vice versa for hypotonic ECF).
- A solution that causes no change in intracellular volume is called **isotonic**.
- In ***renal failure*** the ECF is hyperosmotic but not hypertonic (as cell membrane is permeable to urea), whereas the rise in glucose produced by ***diabetes*** causes water to flow out of cells as ECF is both hyperosmotic and hypertonic.

# Test Question

**Q1. Which is incorrect?**

A. Diffusion of a solute through a membrane is considerably quicker than diffusion of the same solute through a water layer of equal thickness.

B. A single ion, such as $K^+$, can diffuse through more than one type of channel.

C. Lipid-soluble solutes diffuse more readily through the phospholipid bilayer of a plasma membrane than do water-soluble ones.

D. The rate of facilitated diffusion of a solute is limited by the number of transporters in the membrane at any given time.

E. A common example of cotransport is that of an ion and an organic molecule.

# Test Question

**Q2. If a small amount of urea were added to an iso-osmotic saline solution containing cells, what would be the result?**

A. The cells would shrink and remain that way.
B. The cells would first shrink but then be restored to normal volume after a brief period of time.
C. The cells would swell and remain that way.
D. The cells would first swell but then be restored to normal volume after a brief period of time.
E. The urea would have no effect, even transiently.