Hawassa university
Faculty of Medicine

Introductory Physiology

Course Title: Human Physiology

Group: Health science

Instructor: Tesfaye Teshome

Session outline

. Body fluid compartments

- Total body water
- Extracellular and intracellular fluid compartments
- Composition of body fluid compartments
- Measurement of body fluid compartments
- Fluid and electrolyte homeostasis

Session outline…ctd

- Clinical correlates: Disturbances of body fluid and electrolytes
- Dehydration: types, causes
- Overhydration: types, causes
- Edema: ECF and ICF edema, Pitting and non-pitting edema

Medical PHYSIOLOGY

- Life is not always about homeostasis and balance. The body must also adapt to changing requirements, such as during exercise.

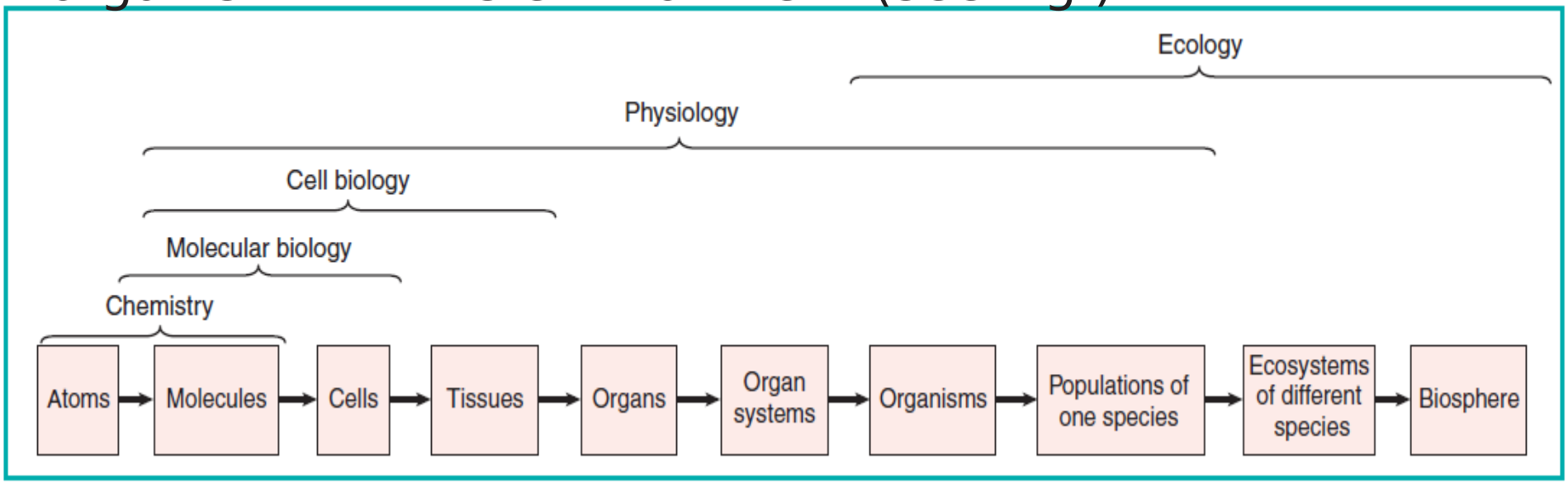
- Physiology studies the adaptive adjustments to new challenges.

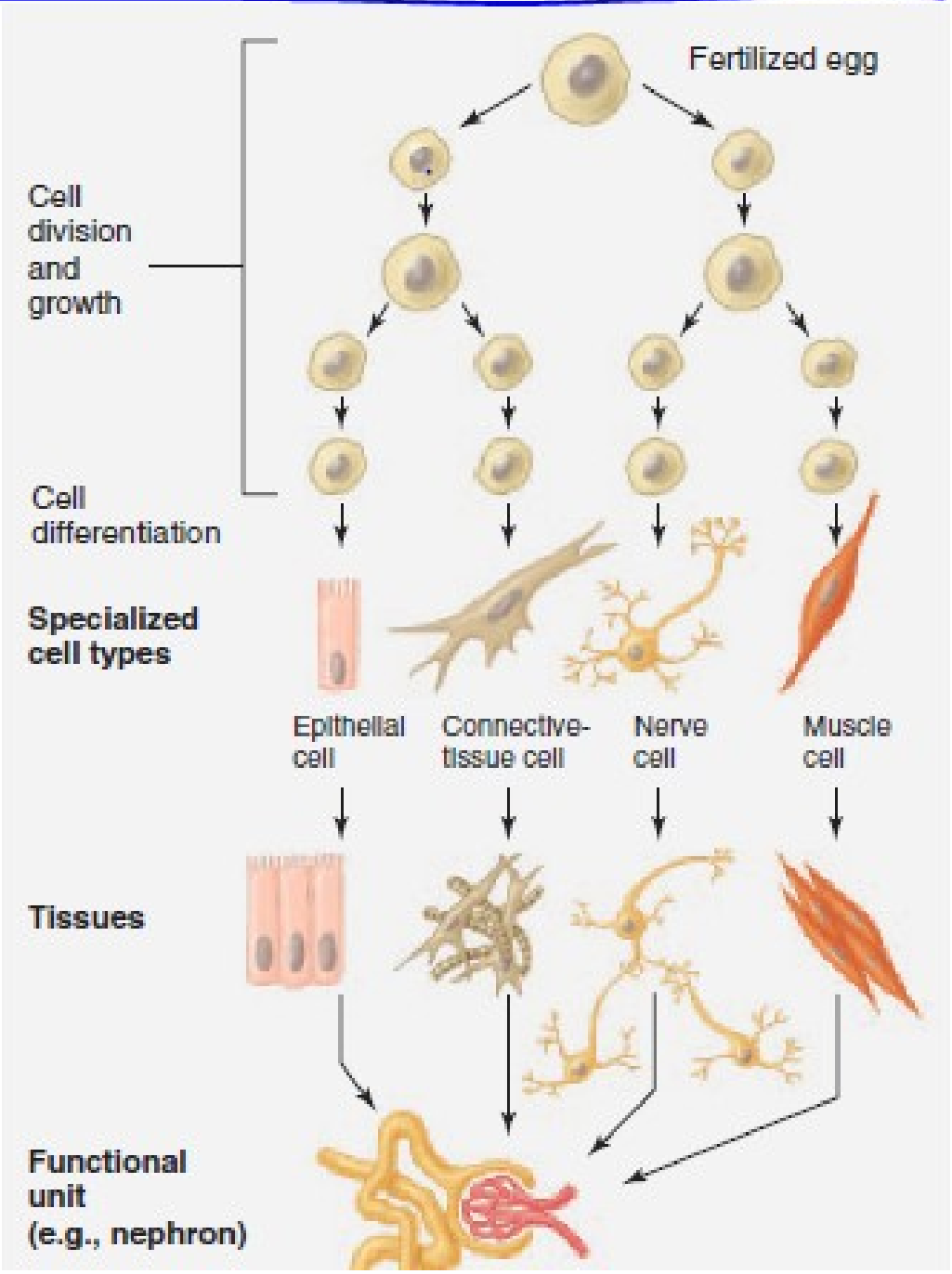
- Life is a state of constant change. The physiology of the body alters as we age

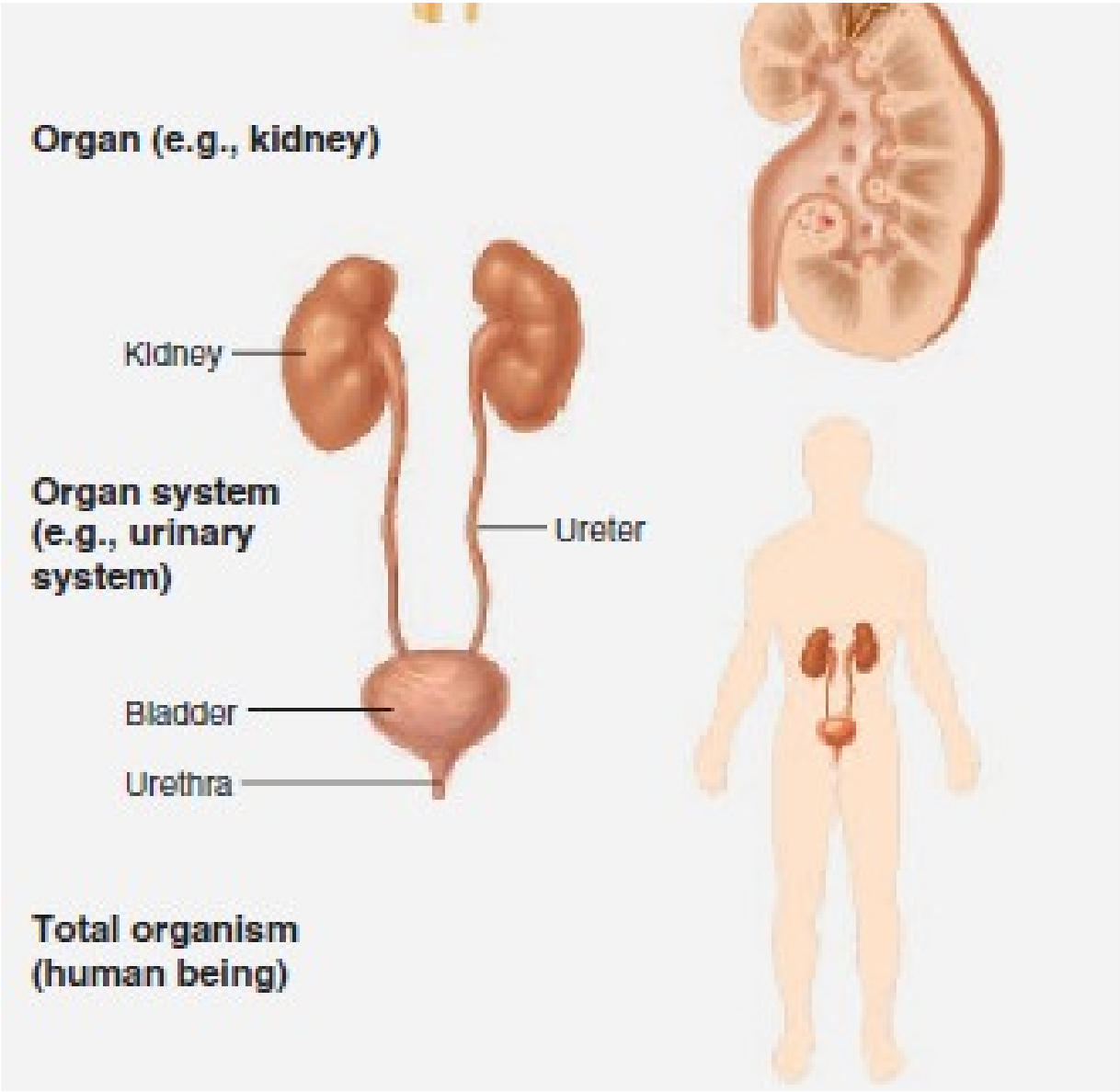
Medical PHYSIOLOGY

- Physiology is the study of normal body function.
- Physiology extends to the molecular level, the study of the regulation of the synthesis of biomolecules, and to the subcellular level, details of the provision of nutrients to support mitochondrial metabolism.
- Physiology includes cellular function, the study of the role of membrane transport, and describes organ function, including the mechanics of pressure generation by the heart.
- Body function requires a stable internal environment, described by Claude Bernard as the “milieu intérieur,” in spite of a changing outside world.

Medical physiology applies basic principles from chemistry, physics, and biology to the study of human life. Atoms are safely in the realm of chemistry. Physiologic study begins with molecules and continues through the interaction of the organism with its environment (see Fig.).



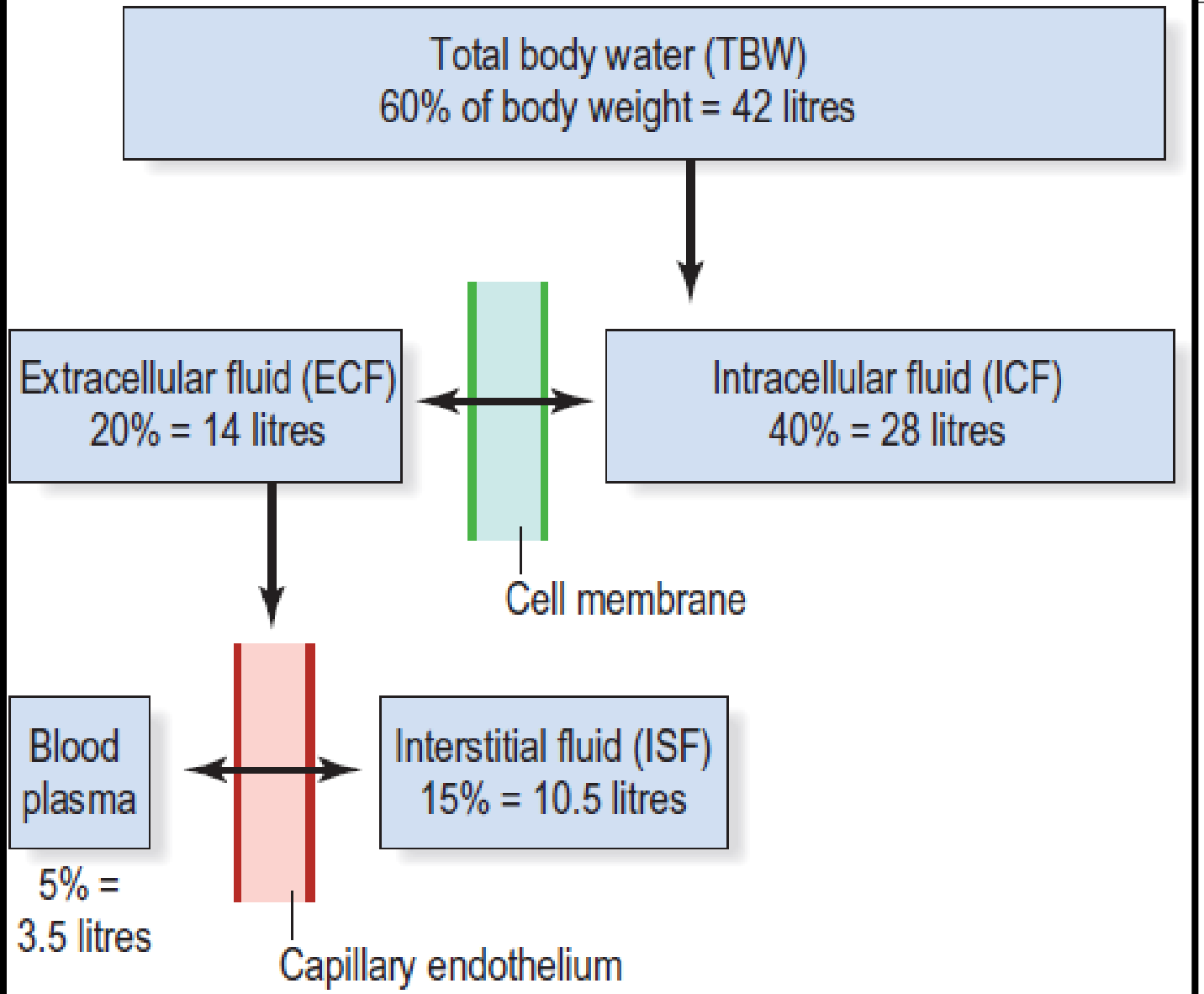

Fertilized egg
Cell division and growth
Cell differentiation
Specialized cell types
Epithelial cell
Connective-tissue cell
Nerve cell
Muscle cell
Tissues
Functional unit (e.g., nephron)


Organ (e.g., kidney)
Kidney
Organ system (e.g., urinary system)
Ureter
Bladder
Urethra
Total organism (human being)

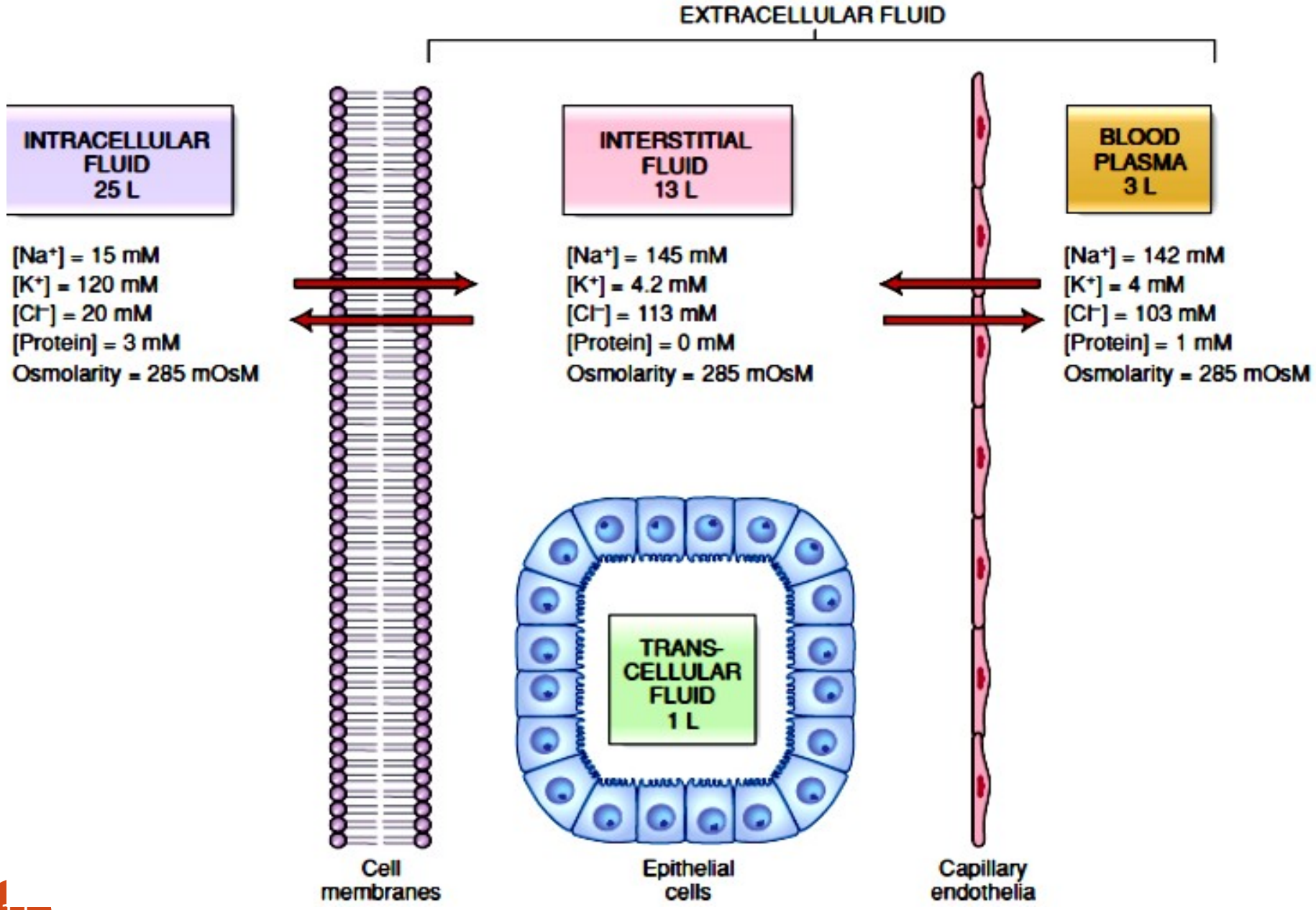
Body fluids

Water contents and distribution

- Percent of body water varies between 45-75% in adults (average is 60% of body weight in males and 50% in females)
  - The fraction is **higher** in **lean body mass** because fat has low water content
  - The fraction is **lower** in **females** due to higher adiposity in females
  - In either sex **lean body mass** contains **73% water**
  - In infants it is between 65-75%
  - **Lean body mass** refers to 75% tissue, 15% bone and 10% fat
  - Adpose tissue has 10% water content



Fluid compartments of the body. These are approximate values for a 70 kg person (per cent of total body water (TBW)).


EXTRACELLULAR FLUID
INTRACELLULAR FLUID 25 L
[Na+] = 15 mM
[K+] = 120 mM
[Cl−] = 20 mM
[Protein] = 3 mM
Osmolarity = 285 mOsM
INTERSTITIAL FLUID 13 L
[Na+] = 145 mM
[K+] = 4.2 mM
[Cl−] = 113 mM
[Protein] = 0 mM
Osmolarity = 285 mOsM
BLOOD PLASMA 3 L
[Na+] = 142 mM
[K+] = 4 mM
[Cl−] = 103 mM
[Protein] = 1 mM
Osmolarity = 285 mOsM
TRANS-CELLULAR FLUID 1 L
Cell membranes
Epithelial cells
Capillary endothelia

Tonicity

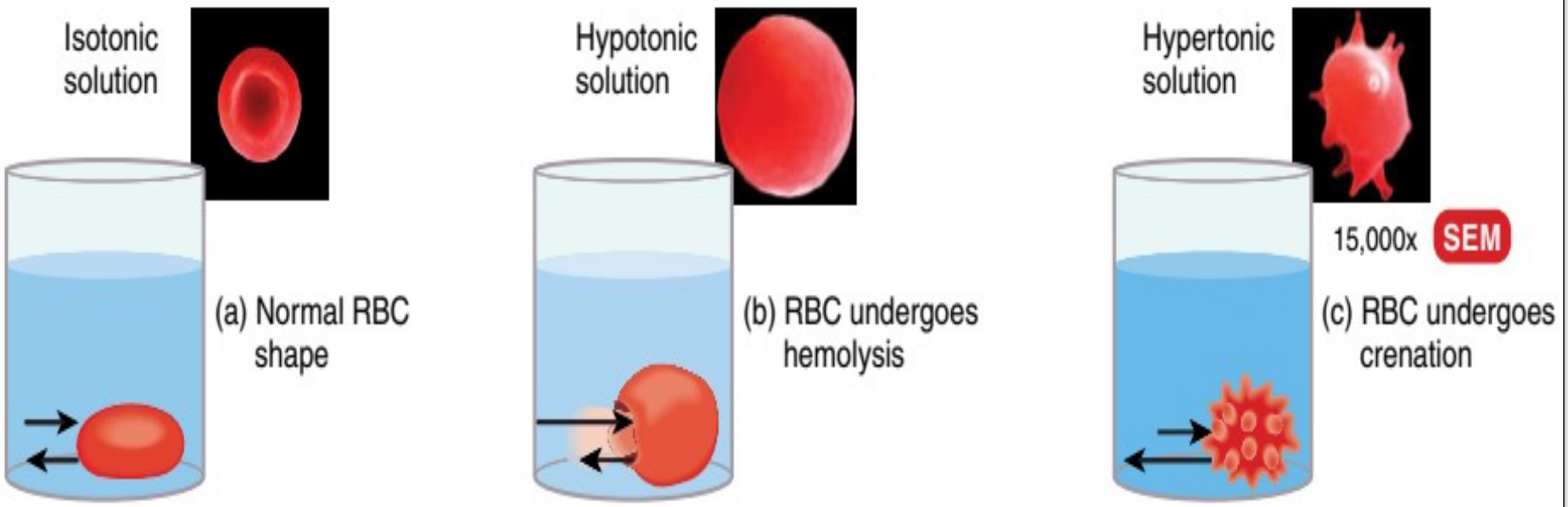
- When body cells are placed in a solution having a different osmotic pressure than cytosol, the **shape** and **volume** of the **cells change**.
- A solution's **tonicity**; *tonic* tension is a measure of the solution's ability to change the volume of cells by altering their water content. Eg. RBC maintains its normal shape and volume is an **isotonic solution**
- The concentrations of solutes that cannot cross the plasma membrane are the same on both sides of the membrane in this solution. For instance, a 0.9% NaCl solution (0.9 gram of sodium chloride in 100 mL of solution), called a *normal (physiological) saline solution,* is isotonic for RBCs.

- **Hypotonic solution-** a solution that has a *lower* concentration of solutes than the cytosol inside the RBCs.
- So water molecules enter the cells and causing the RBCs to swell and eventually to burst. The rupture of RBCs in this manner is called **hemolysis**

- A **hypertonic solution:** a solution that has *higher* concentration of solutes than does the cytosol inside RBCs
- Example- 2% NaCl solution. In such solution water molecules move out of the cells and causing the cells to **shrink**. Such shrinkage of cells is called **crenation**

Medical Uses of Isotonic, Hypertonic, and Hypotonic Solutions

- RBCs and other body cells may be damaged or destroyed if exposed to hypertonic or hypotonic solutions. For this reason, most **intravenous (IV) solutions**, liquids infused into the blood of a vein, are isotonic.
- Eg isotonic saline (0.9% NaCl) and D5W, which stands for dextrose 5% in water.
- Sometimes infusion of a hypertonic solution such as mannitol (sugar alcohol) is useful to treat patients who have ***cerebral edema***, excess interstitial fluid in the brain. Infusion of such a solution relieves fluid overload by causing osmosis of water from interstitial fluid into the blood


Isotonic solution
(a) Normal RBC shape
Hypotonic solution
(b) RBC undergoes hemolysis
Hypertonic solution
15,000x
SEM
(c) RBC undergoes crenation

Dehydration

- ***Dehydration*** is defined as an excessive loss of body fluid.
- Dehydration occurs when more fluids are lost than taken in and the body doesn’t have enough water and other fluids to carry out its normal functions.

Dehydration…ctd

- **Three main types of dehydration based on type of fluid loss:**
  - **Hypotonic or hyponatremic** – primarily a loss of electrolytes, particularly sodium
  - **Hypertonic or hypernatremic** – primarily a loss of water
  - **Isotonic or isonatremic** – equal loss of water and electrolytes

Skin with decreased turgor remains elevated after being pulled up and released

Water intoxication (Overhydration)

- When too much water is drunk too fast or there is a complete blockage of urine production, there is a dilution of body fluids.
- The sodium concentration of the ECF is reduced causing an osmotic shift of water into cells and cell swelling.

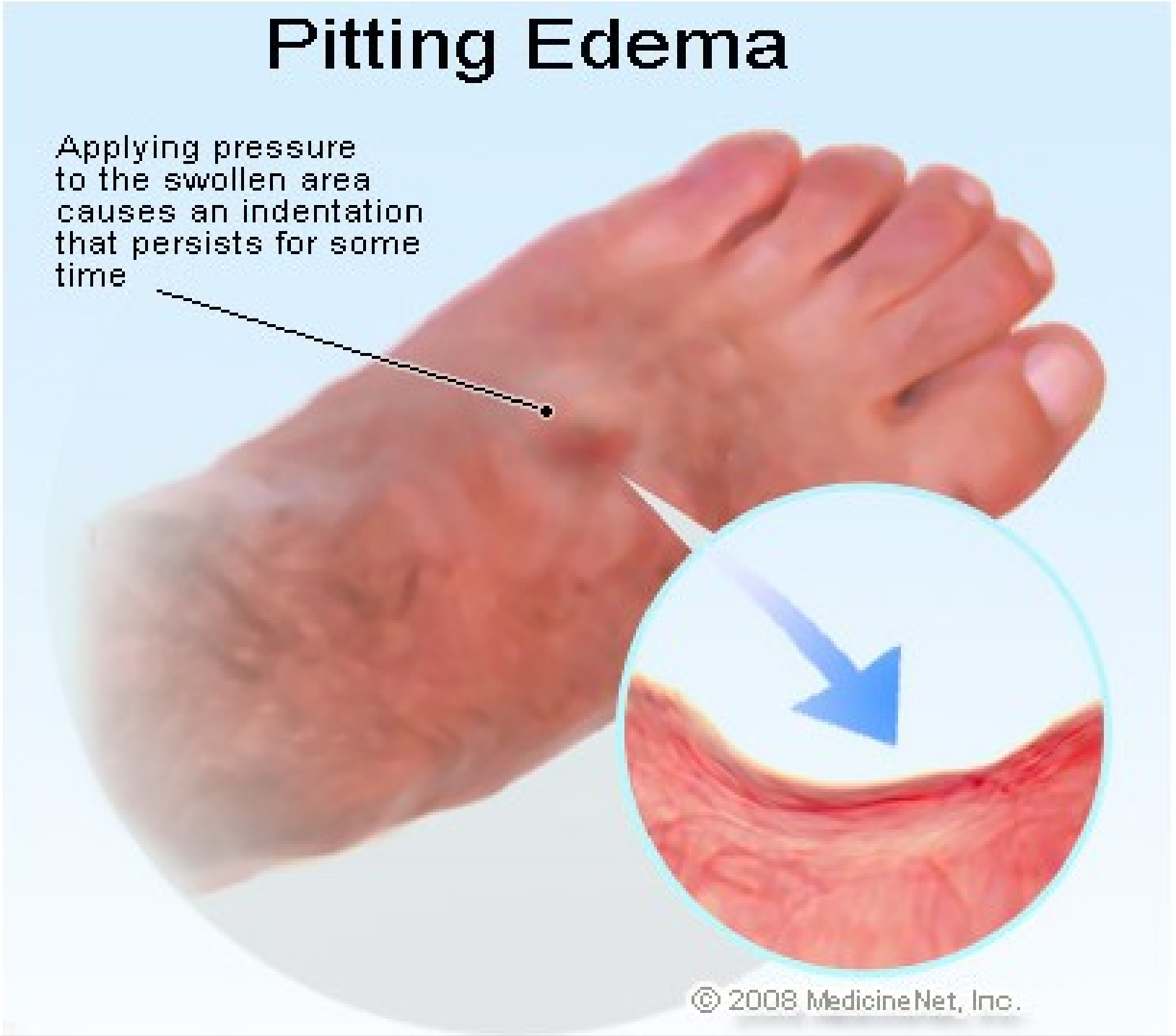
Oedema

- Swelling of the tissues due to the accumulation of fluid is called **oedema.**

- It has many different causes, several of which have little to do with overall fluid balance.

- Pitting & Non-pitting (ECF & ICF)
- This is particularly dangerous in the brain, where swelling can cause convulsions, coma and death.

Pitting Edema

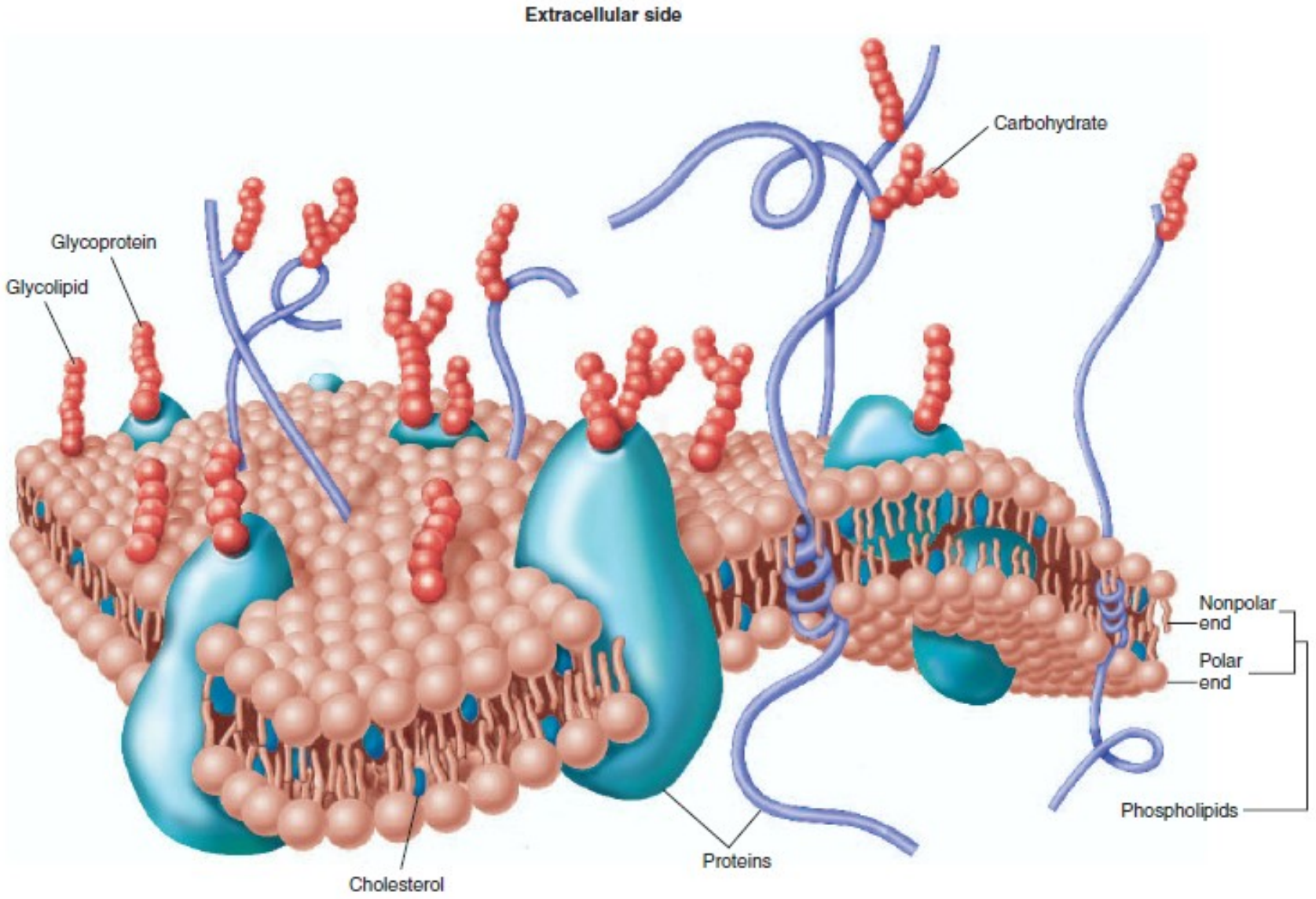


The cell

- **Number**
- ~ 100 trillions in adult human body
- **Size:**
- Human egg cell ~ 140 µm
- RBC ~ 7.5 µm
- White blood cells 10-12 µm
- Smooth muscle (20-500 µm)
- **The cell theory**
- All free-living organisms are composed of cells and their products
- All cells are basically similar in their chemical construction
- New cells are formed from preexisting cells by cell division

Cell membrane structure

- The lipid bilayer 50%
- Cholesterol
- Integral proteins 45%
- Peripheral proteins
- Carbohydrates 5%
- Glycolipids


Extracellular side
Carbohydrate
Glycoprotein
Glycolipid
Nonpolar end
Polar end
Phospholipids
Proteins
Cholesterol
Intracellular side

Cell Membrane Carbohydrates

- Is known as **Cell coat or "Glycocalyx"**
- Carbohydrates occur almost invariably in combination with proteins or lipids in the form of *glycoproteins* or *glycolipids*.
- In addition to lipids and proteins, the plasma membrane also contains carbohydrates, which are primarily attached to the outer surface of the membrane as glycoproteins and glycolipids.
- These surface carbohydrates have numerous negative charges and, as a

- The carbohydrate moieties attached to the outer surface of the cell have several important functions:

- Short-chain carbohydrate on the outer membrane surface serves as **self-identity marker** enabling cells to identify and interact with each other in the following ways:

- Recognition of "**self**" and **cell-to-cell** interactions.

- Carbohydrate-containing surface markers are important in growth. Cells do not overgrow their own

Electrolyte balance and Imbalance

Sodium

- Attracts water into the ECF
- Nerve impulse
- Muscle contractions

Hypernatremia

- Excess sodium in the blood
- Hypertension
- Muscle twitching

Hyponatremia

- Deficiency of sodium in the blood
- Hypotension
- Tachycardia
- Hypotonicity is always associated with hyponatremia

Potassium

- Attracts water into the ICF

- Nerve impulse

Hyperkalemia

- Excess potassium in the blood

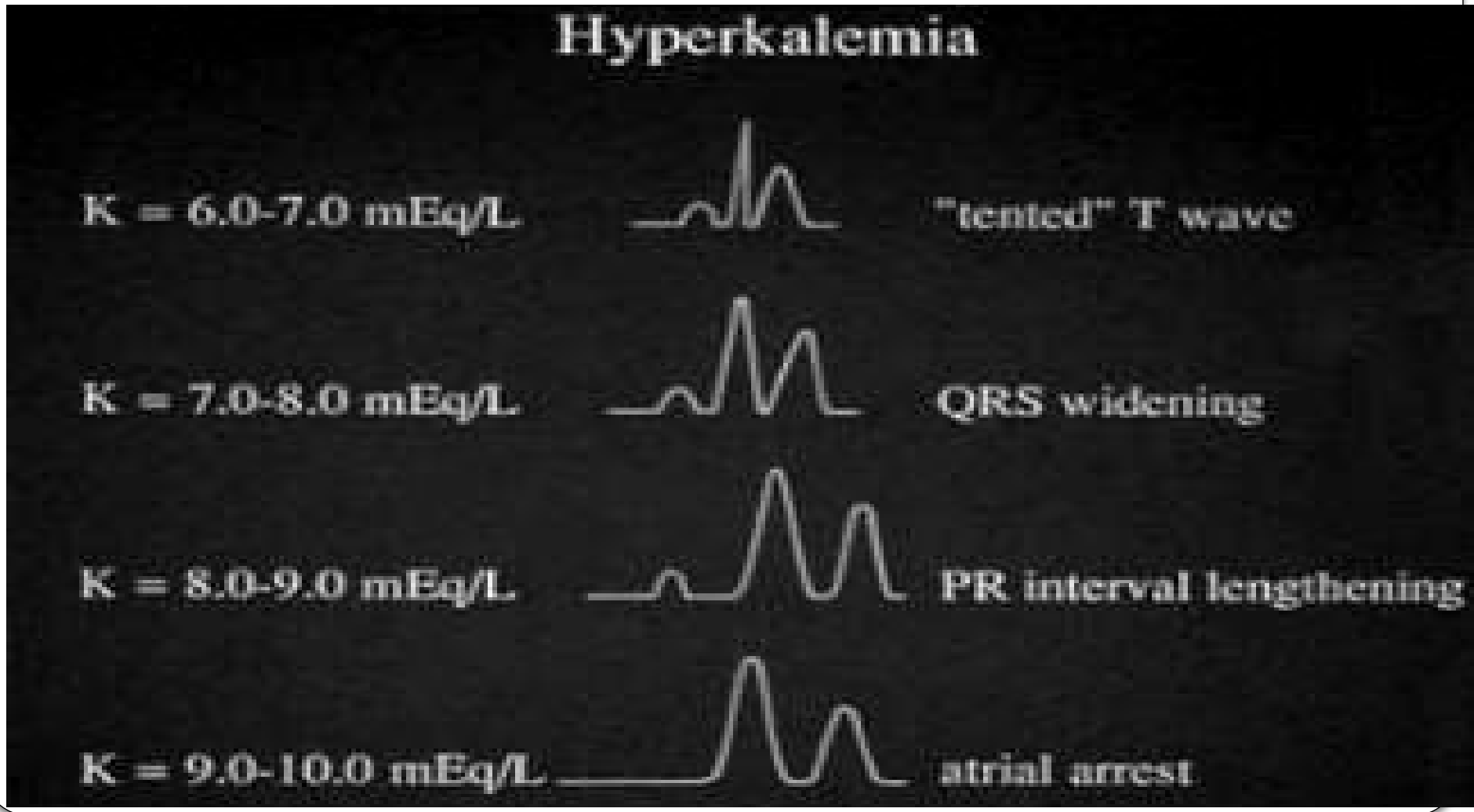
- Cardiac arrhythmias and cardiac arrest

- Elevated T wave

Causes

- decreased renal excretion of K^+

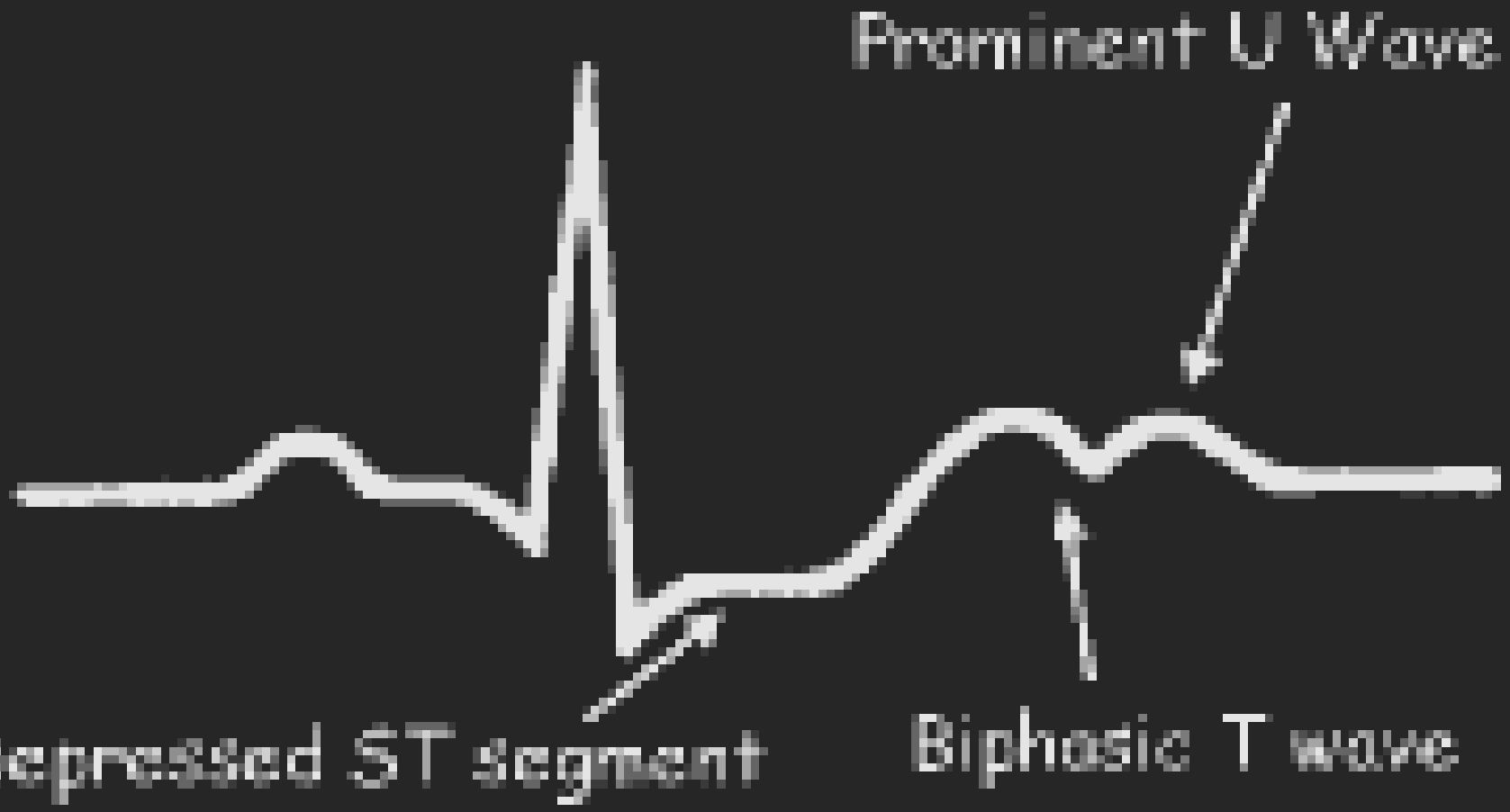
- Serum K^+/level
- ECG



Hypokalemia

- Deficiency of potassium in the blood (< 3.5 meq/l
- Cardiac arrhythmias and cardiac arrest
- Flatened T wave
- Muscle weakness

ECG Pattern of Hypokalemia



Calcium

- Most in bones and teeth
- Blood clotting
- Nerve impulse
- Muscle contraction

Range = 2.5mM or 10mg/dl

Hypercalcemia

- Excess calcium in the blood
- Kidney stones
- Bone pain
- Cardiac arrhythmias

Hypocalcemia

- Deficiency of calcium in the blood
- Tetany/ Spasms - muscle of the extremities and face
- Weak heart muscle
- Increased clotting time

Causes

- Bed rest in elderly person with osteoporosis is hazardous because impaired Ca metabolism with increased bone resorption is associated with immobilization
- Inadequate Vitamin D

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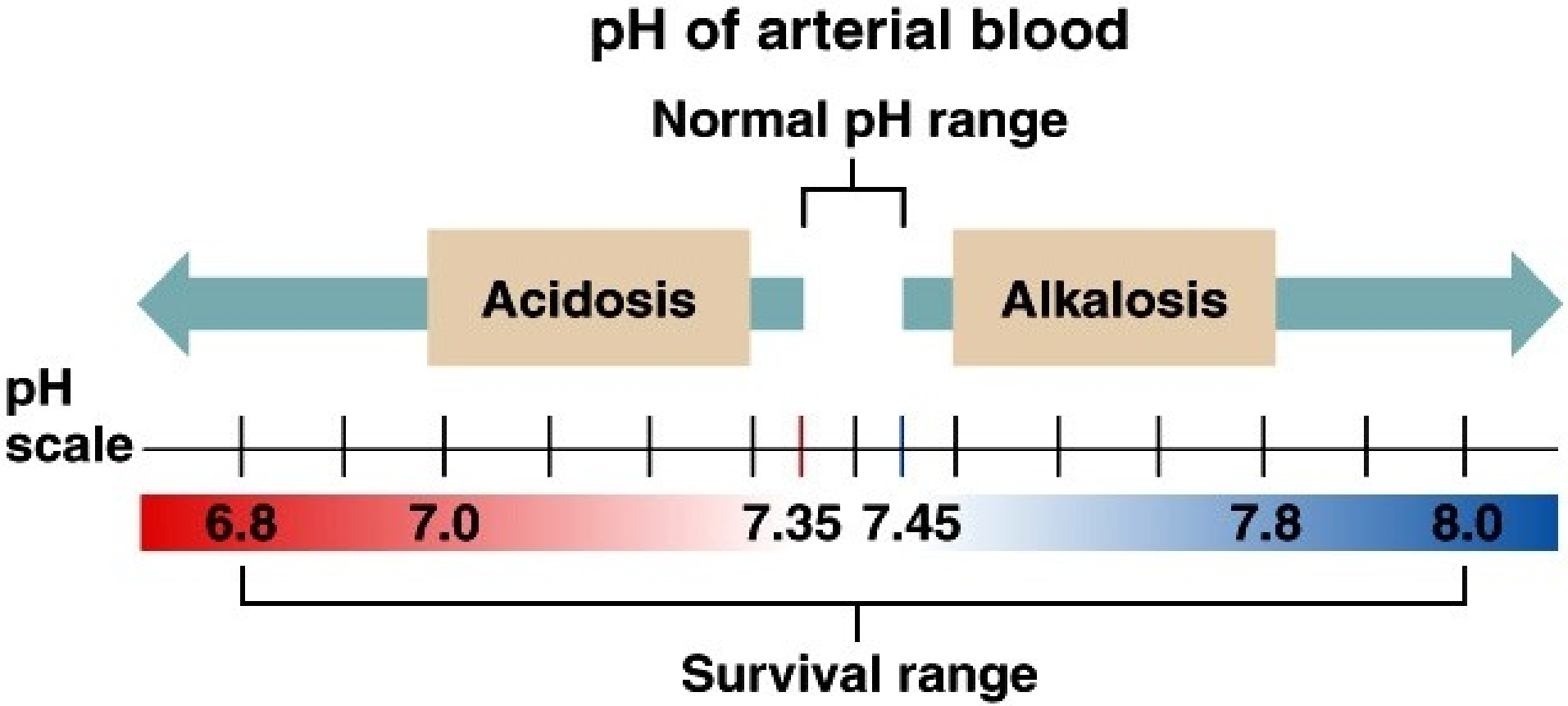
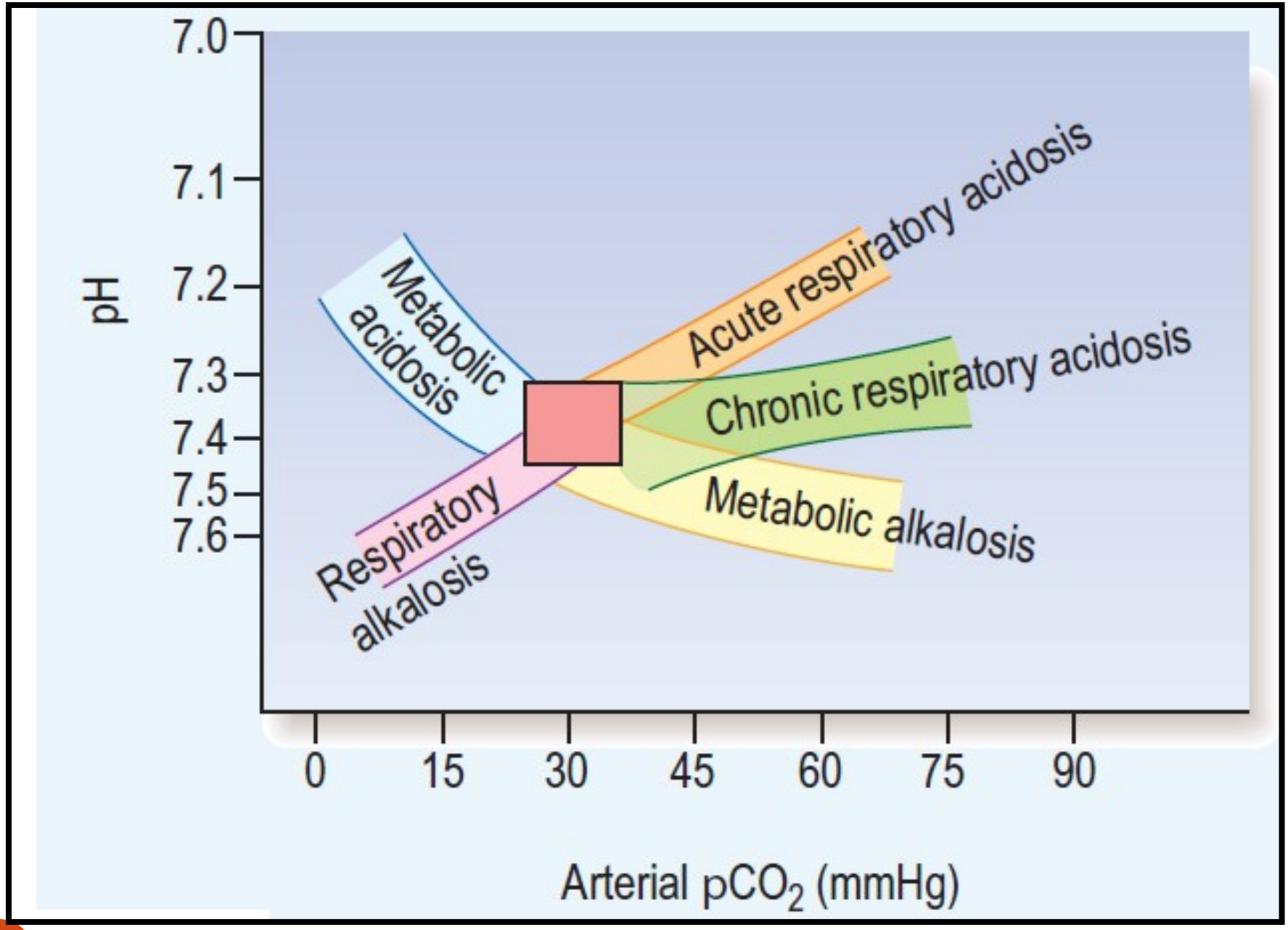



7.0
7.1
7.2
7.3
7.4
7.5
7.6
pH
Metabolic acidosis
Acute respiratory acidosis
Chronic respiratory acidosis
Metabolic alkalosis
Respiratory alkalosis
0
15
30
45
60
75
90
Arterial pCO_2 (mmHg)

Membrane Transport

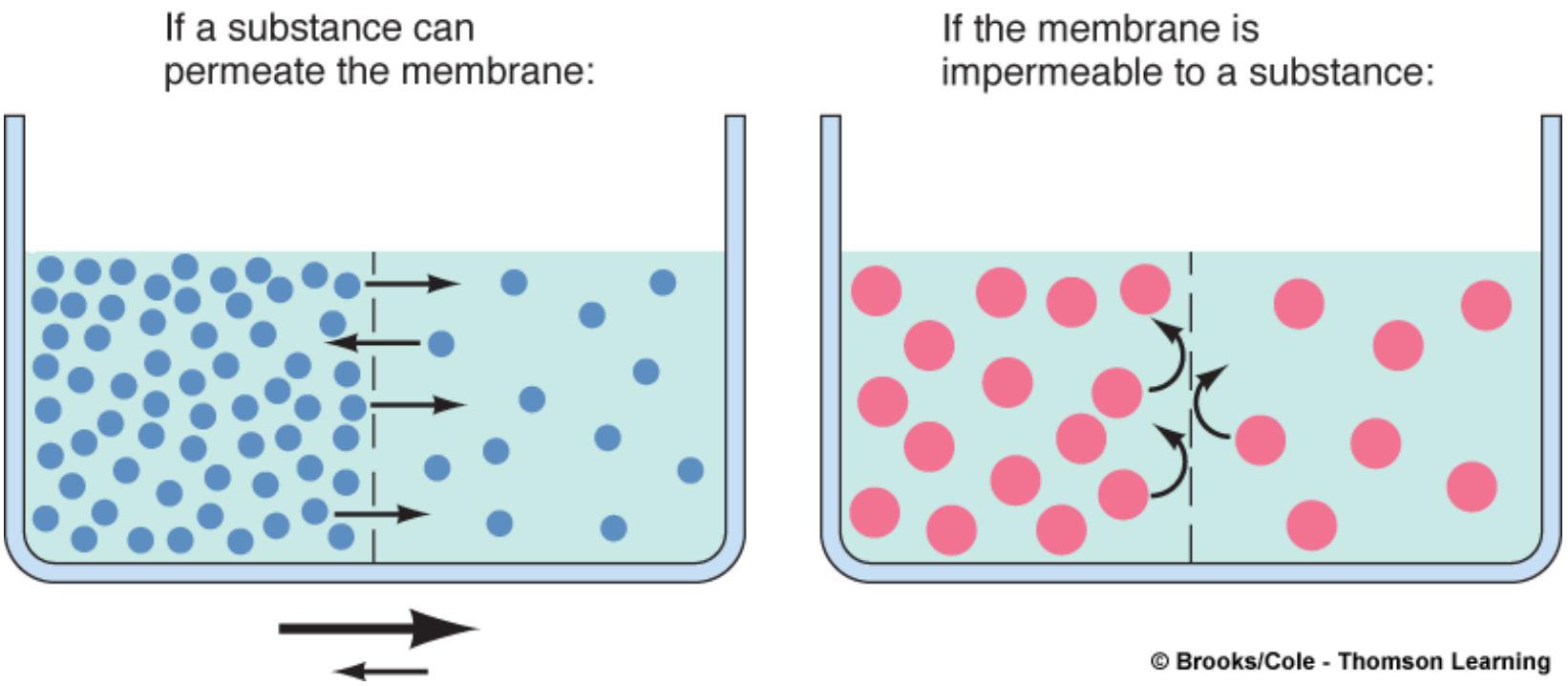
- Lipid-soluble substances and small ions can passively diffuse through the plasma membrane down their electro-chemical gradients.
- The plasma membrane is selectively permeable.
- Highly lipid-soluble particles are able to dissolve in the lipid bilayer and pass through the membrane.
- **Uncharged/non-polar** molecules O2, CO2 and FAs are highly lipid-soluble and readily permeate the membrane.
- The lipid layer in the middle of the membrane is impermeable to the usual water-soluble substances, such as **ions**, **glucose**, and **urea**.

Membrane Transport

- Unassisted membrane transport
  - Diffusion
  - Osmosis
- Assisted membrane transport
  - Carrier-mediated transport
  - Facilitated transport
  - Active transport

Membrane Transport

Diffusion

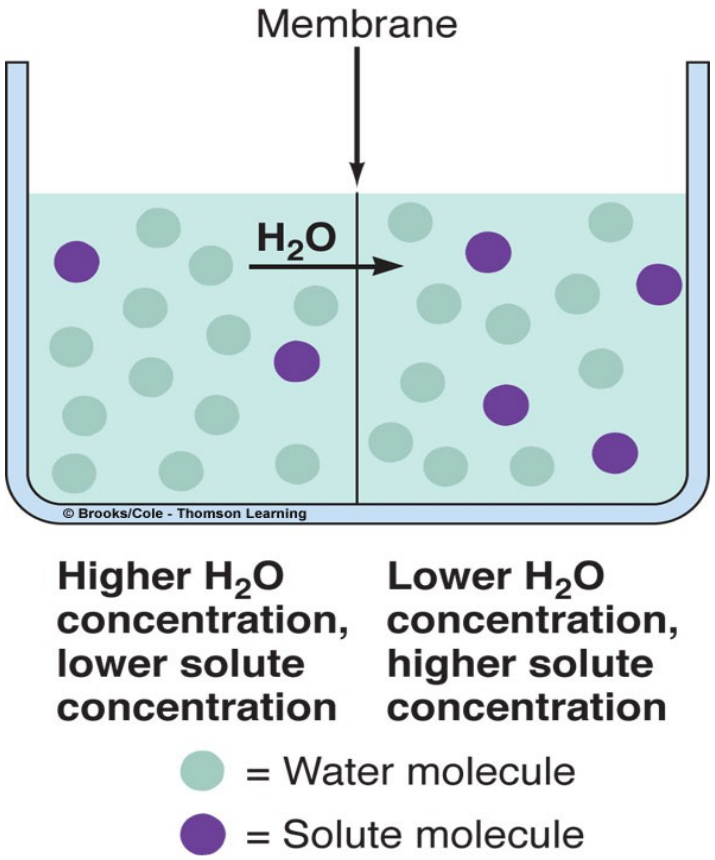


Membrane Transport

- Factors affecting rate of diffusion collectively make up Fick's law of diffusion:
- ✓ Magnitude (steepness) of the concentration gradient
- ✓ Permeability of the membrane to the substance
  - Charge?
- ✓ Surface area of the membrane across which diffusion is taking place
- ✓ Molecular weight of the substance

Membrane Transport

- Osmosis
  - Net diffusion of water down its own concentration gradient



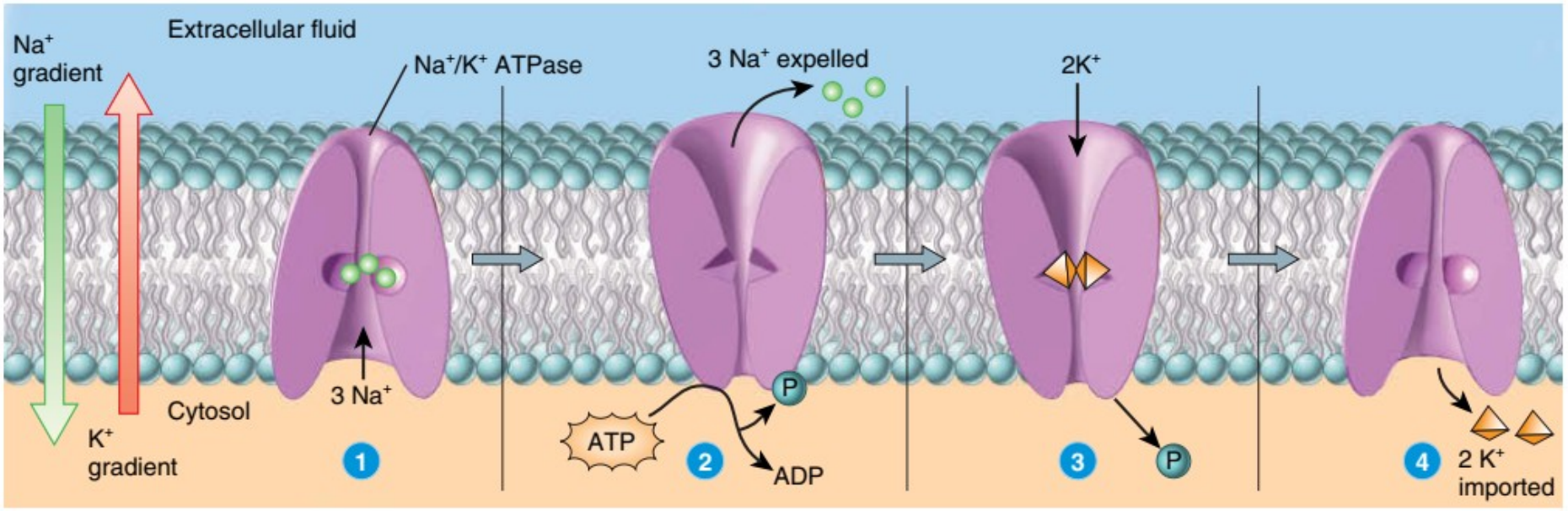
Transport

Active Processes

- Some polar or charged solutes that must enter or leave body cells cannot cross the plasma membrane through any form of passive transport because they would need to move "**uphill**," ***against*** their concentration gradients.
- Such solutes may be able to cross the membrane by a process called **active transport**
- In active transport energy is required for carrier proteins to move solutes across the membrane against a concentration

Primary Active Transport

- In **primary active transport**, energy derived from hydrolysis of ATP changes the shape of a carrier protein, which "pumps" a substance across a plasma membrane **against** its concentration gradient **sodium–potassium pump**.
- Sodium-potassium pump acts as an *ATPase,* an enzyme that hydrolyzes ATP, another name for this pump is **Na–K ATPase**



3 sodium ions (Na^+) from the cytosol bind to the inside surface of the sodium–potassium pump.

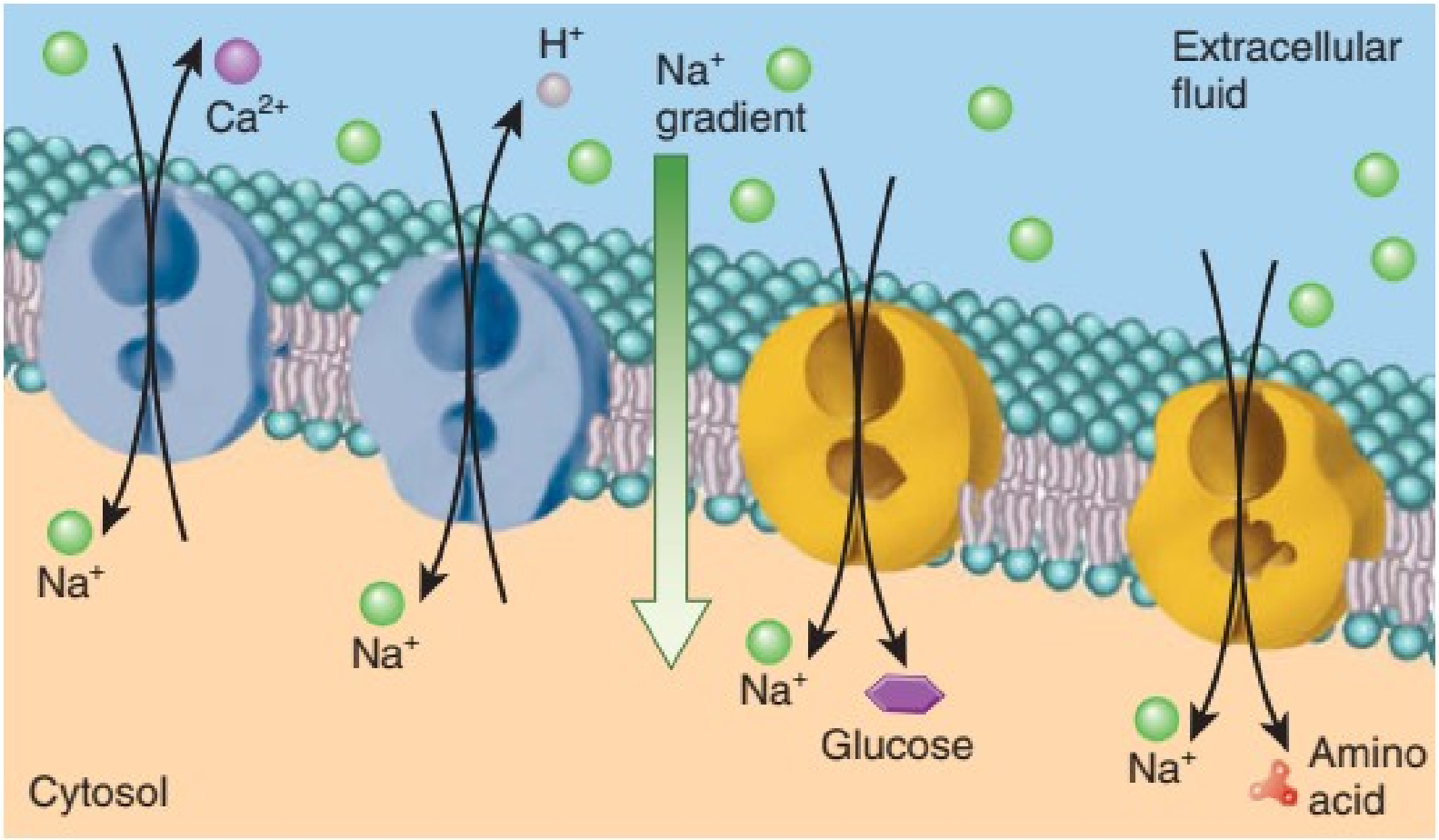
Na^+ binding triggers ATP to bind to the pump and be split into ADP and P (phosphate). The energy from ATP splitting causes the protein to change shape, which moves the Na^+ to the outside.

2 potassium ions (K^+) land to the outside surface of the pump and cause the P to be released.

The release of the P causes the pump to return to its original shape, which moves the K^+ into the cell.

Secondary Active Transport

- In **secondary active transport**, the energy stored in a Na or H concentration gradient is used to drive other substances across the membrane against their own concentration gradients.
- secondary active transport *indirectly* uses energy obtained from the hydrolysis of ATP
- E.g. **symporters-** If the transporters move two substances in the same direction
- **Antiporters -** move two substances in



(a) Antiporters

(b) Symporters

Vesicular Transport

- Vesicles also import materials from and release materials into extracellular fluid.
- **Endocytosis -** materials move into a cell in a vesicle formed from the plasma membrane.
- **Exocytosis -** materials move out of a cell by the fusion with the plasma membrane of vesicles formed inside the cell.
- Both endocytosis and exocytosis require energy supplied by ATP
- **Three types** of **endocytosis**: receptor-mediated endocytosis, phagocytosis, and bulk-phase endocytosis.
- Receptor-mediated endocytosis is a highly selective type of endocytosis by which **cells take up specific ligands**.

- **Phagocytosis**; (*phago*- to eat) is a form of endocytosis in which the cell engulfs large solid particles, such as worn-out cells, whole bacteria, or viruses.
- Only a few body cells, termed **phagocytes**, are able to carry out phagocytosis.
  Two main types of phagocytes are
- *macrophages,* located in many body tissues
- *neutrophils,* a type of white blood cell.
- Phagocytosis begins when the particle binds to a plasma membrane receptor on the phagocyte, causing it to extend **pseudopods**