Faculty of Veterinary and Agricultural Sciences

Cells to Systems Lecture 8: Transport of molecules around the body Video 1

VETS30015 / VETS90121

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Lecture 8: ILOs

- 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

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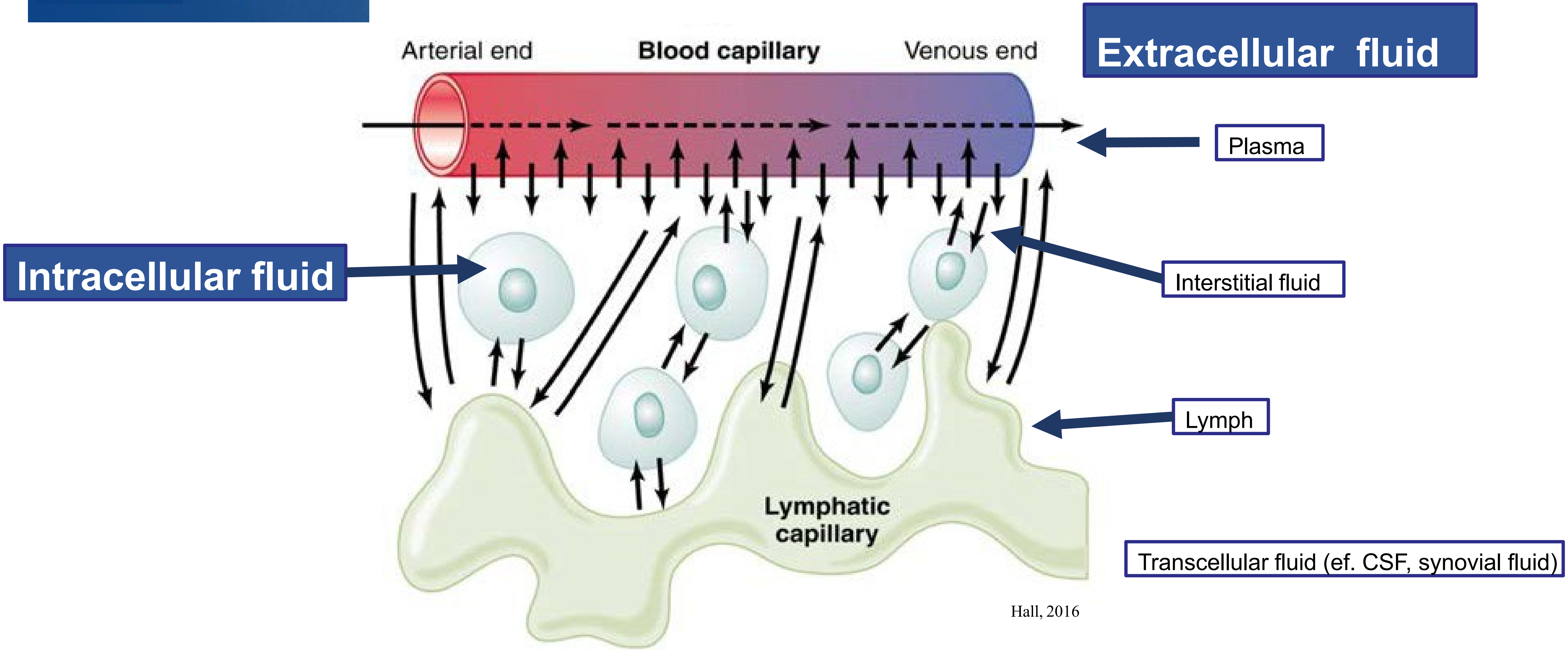
Why do vets need to understand fluid balance?

Water homeostasis is critical for life!

Water comprises approx. 60% of BW

istockphotos.com

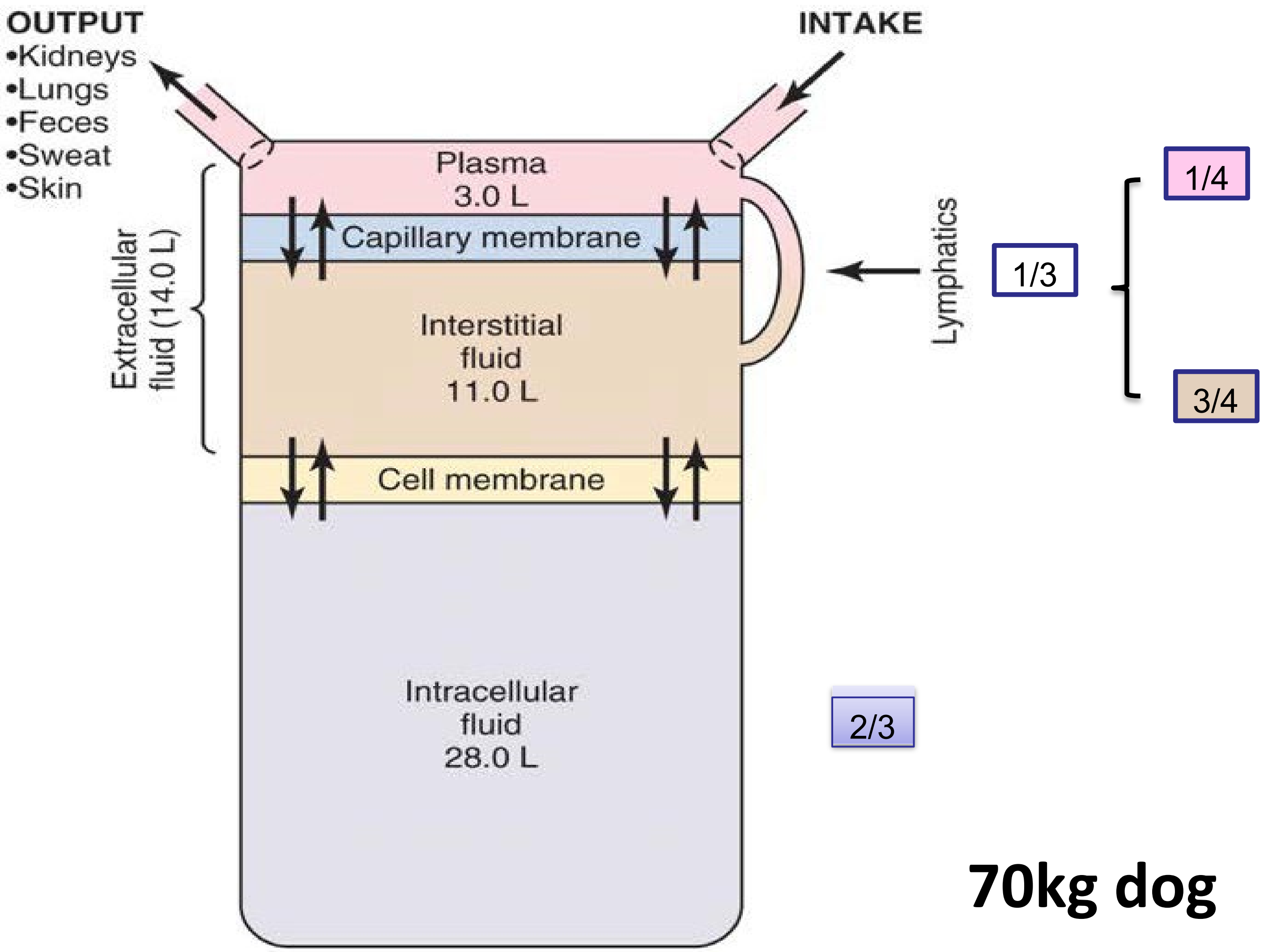
Body fluid compartments: overview



Hall, 2016

Body fluid compartments: ECF and ICF

- Total body water (TBW)
  - 60% of lean body weight
- 1/3 of TBW is extracellular
  - ¼ extracellular water = plasma
  - ¾ extracellular water = interstitial
  - Exchange of water, solutes, nutrients and gases occurs via diffusion and osmosis driven by hydrostatic and oncotic pressures
- 2/3 of TBW is intracellular
  - Water, solutes, nutrients and gases must cross the cell membrane
  - Simple diffusion and osmosis occurs for some molecules
  - Additional transport mechanisms are required for others – next lecture



70kg dog

Guyton & Hall, 2007

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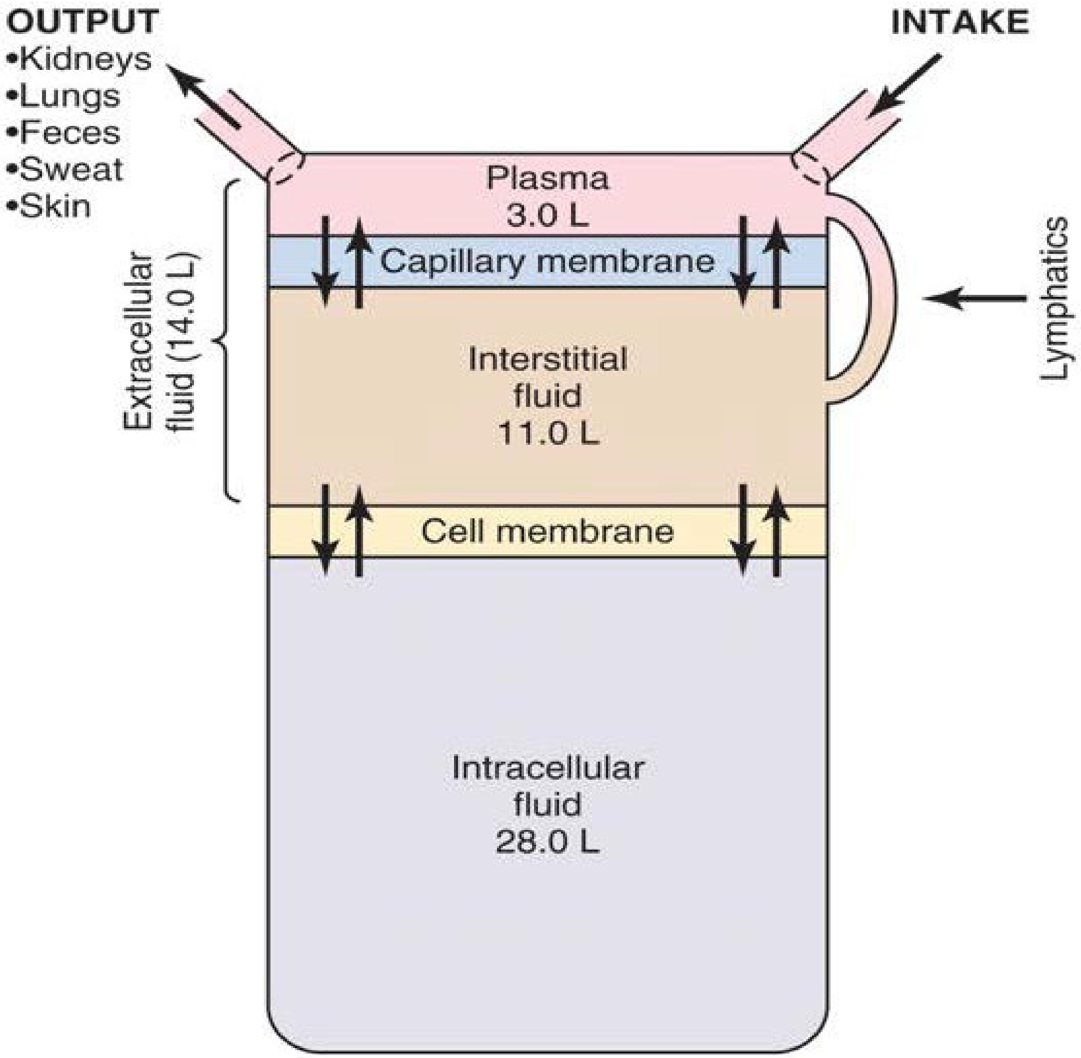

Capillary membrane:

- H20 and most plasma constituents (except plasma proteins) freely exchanged
- ➢ Composition of plasma and interstitial fluid is similar

- Plasma is the only fluid compartment that can be actively modified

Cell membrane:

- Highly selective, permits movement of some molecules but not others
- Passive and active mechanisms – next lecture

Composition of Body Fluid Compartments

	Extracellular fluid		Intracellular fluid
	Blood plasma	Interstitial fluid	Intracellular fluid
	1.0 litre*	3 litre*	8 litres*
	[Na+]= 153 mM	[Na+]= 145 mM	[Na+]= 10-15 mM
	[K+]= 4.7 mM	[K+]= 4.5 mM	[K+]= 120-140 mM
	[Cl-]= 110 mM	[Cl-]= 116 mM	[Cl-]= 20 mM Range 3-30mM
	[Ca2+]= 1.3 mM (ionized)	[Ca2+]= 1.2 mM	[Ca2+]=0.001 uM
	[Protein]= 1 mM Range 1-10 mM	[Protein]= 0 mM	[Protein]= 4 mM Range 4-50mM
	Osmolality=290mOsm/kg	Osmolality=290mOsm/kg	Osmolality=290mOsm/kg
	HCO_3= 24 (mM)	Also high in HCO_3	Also high in phosphates & Mg^{2+}

* Some fluid in transcellular compartments

* For 20kg dog – this will vary with size of animal

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Clinical Assessment of Dehydration

Clinical Sign	Dehydration estimate (% BW)
Normal	<5%
Dry mucous membranes	5%
Reduced Skin turgor	6-8%
Increased HR	8-10%
Weak pulses	10-12%
Collapse, shock	12-15%

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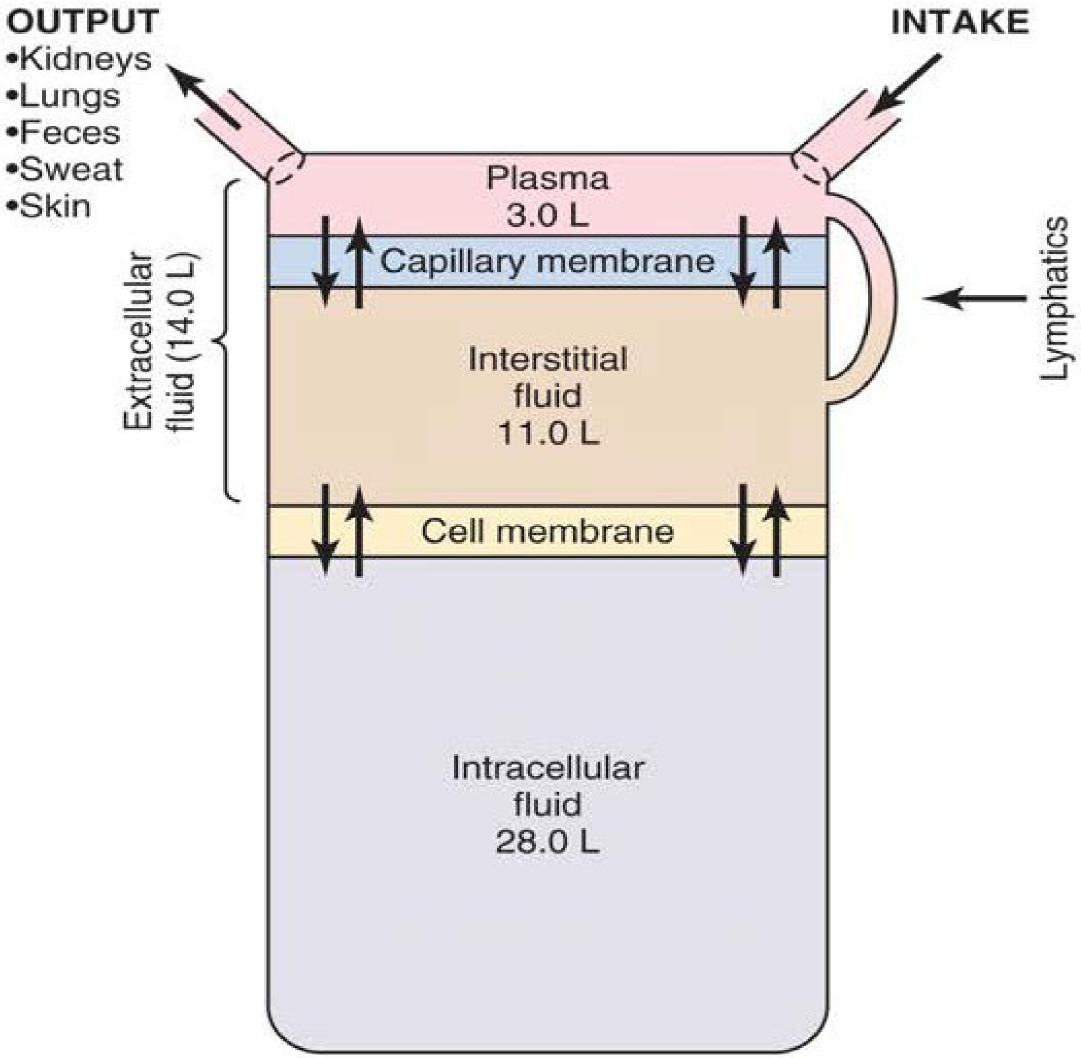
Clinical signs of dehydration

Mucous membranes

Skin tenting

Pulse strength, HR



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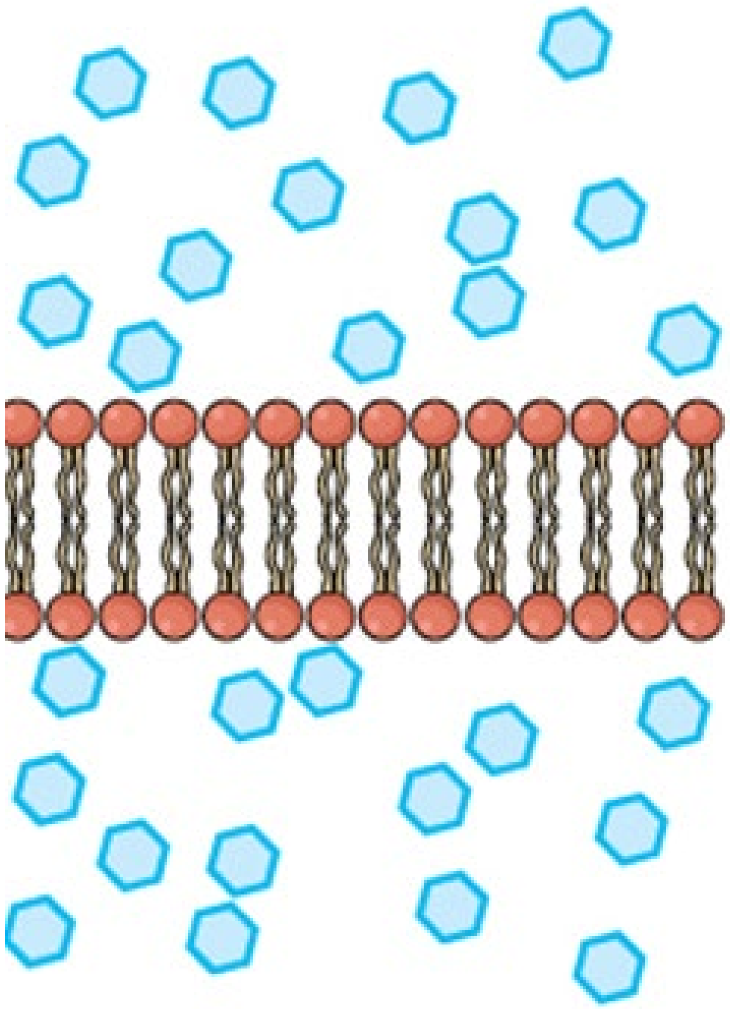
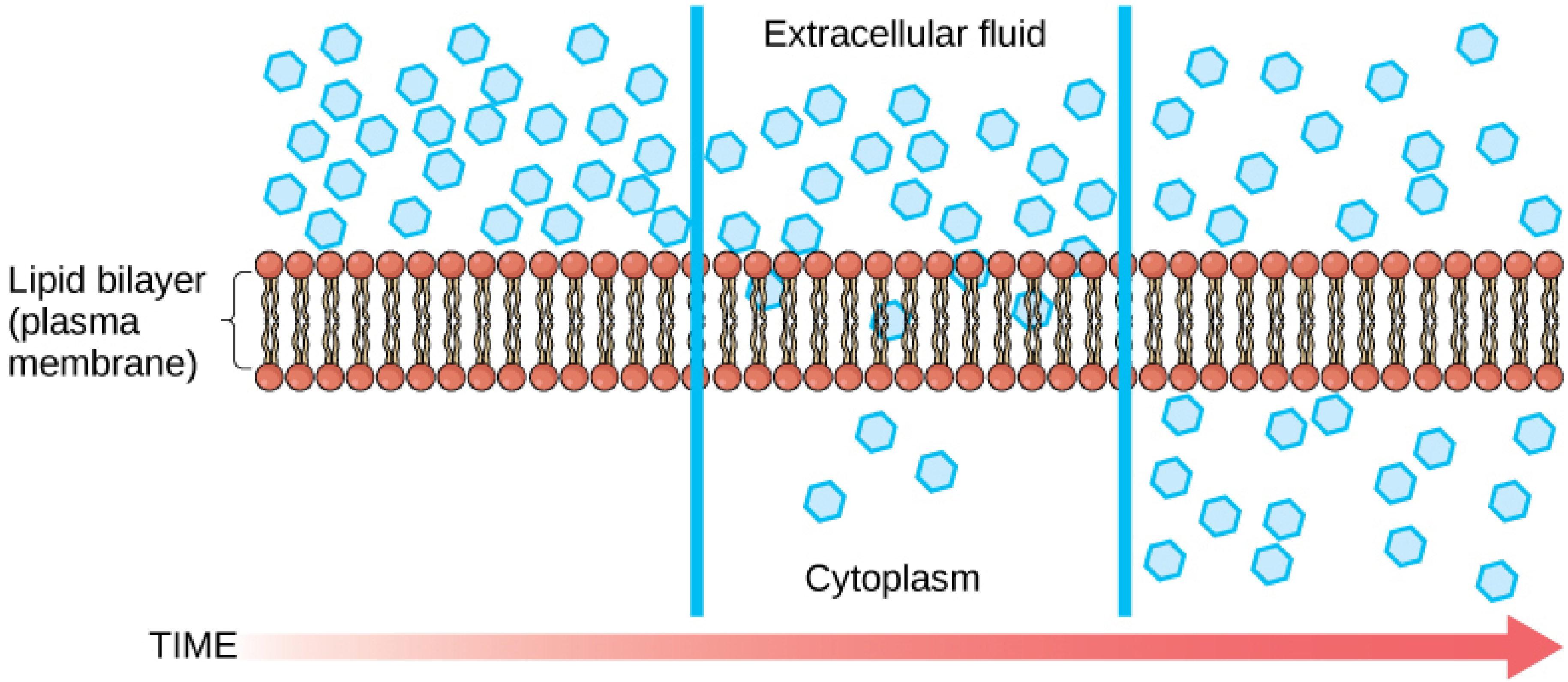
Transport across membranes

- Molecules or ions that are able permeate the plasma membrane unassisted will move passively across the membrane

- Two forces involved in passive movement:
  1. Diffusion down a ***concentration gradient***
  2. Movement along an ***electrical gradient***



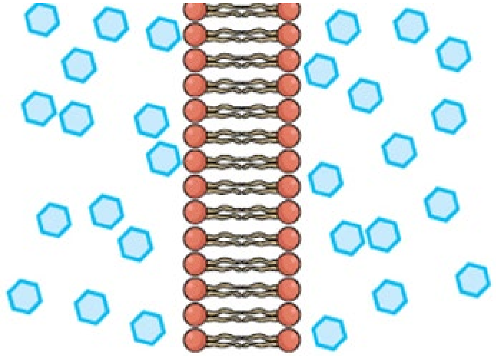
Diffusion



- Movement of a molecule down a concentration gradient – due to random molecular collisions
- Where there is a membrane barrier and the substance can permeate the membrane, it will move from an area of high concentration to low concentration

  e.g. diffusion of oxygen from the lungs into the blood

Fick's equation



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

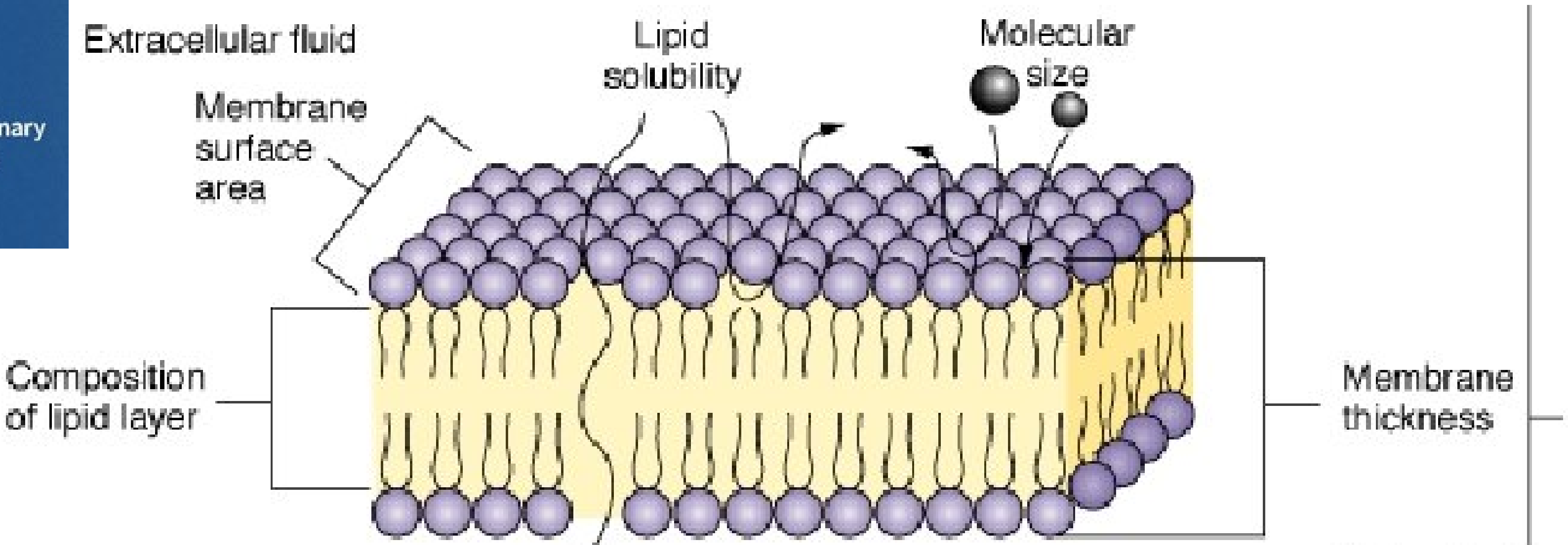


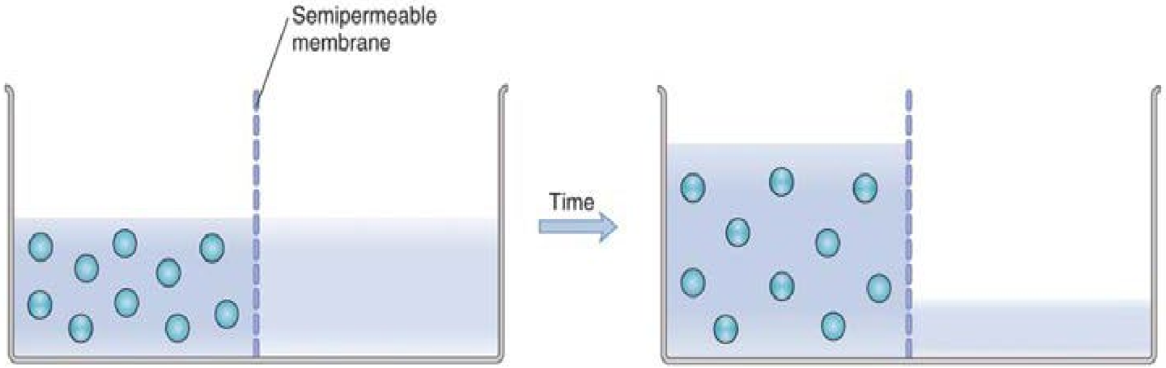
Fig 5-6

Fick's law of Diffusion

$$\text{Diffusion rate} \propto \frac{\text{surface area} \times \text{conc. gradient} \times \text{membrane permeability}}{\text{membrane thickness}}$$

Osmosis: *net diffusion of water down it's own concentration gradient*

- Specific type of diffusion
- Flow of water across a membrane that is permeable to water but not to solutes



- Water is a small polar molecule
  - ➢ Passes through lipid bilayer of cell membrane
  - ➢ Also passes through channels (aquaporins) in cell membrane

Water passes by osmosis from a region of higher water concentration to a region of lower water concentration (i.e. higher solute concentration)

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Osmosis: *net diffusion of water down it's own concentration gradient*

1. Pure water

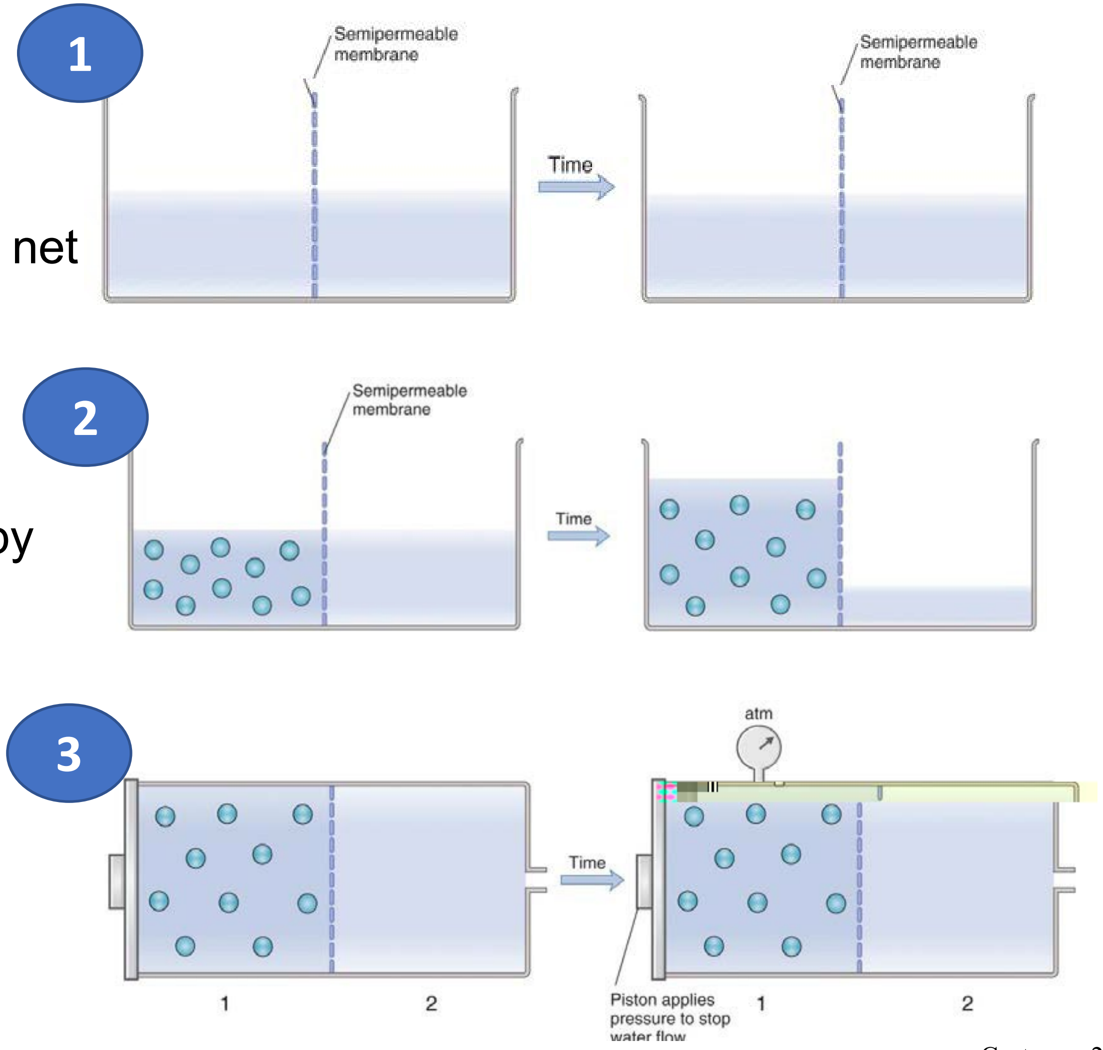
- Semipermeable membrane
- Constant movement of water molecules, but no net diffusion or flux of water

2. Presence of solute produces directional water movement

- Reduces water concentration → water moves by osmosis to area of lower water concentration (higher solute concentration)
  - 'Water follows salt'

3 Osmotic pressure

- Amount of pressure required to stop osmotic water movement



Costanzo, 2013

Maintaining fluid balance

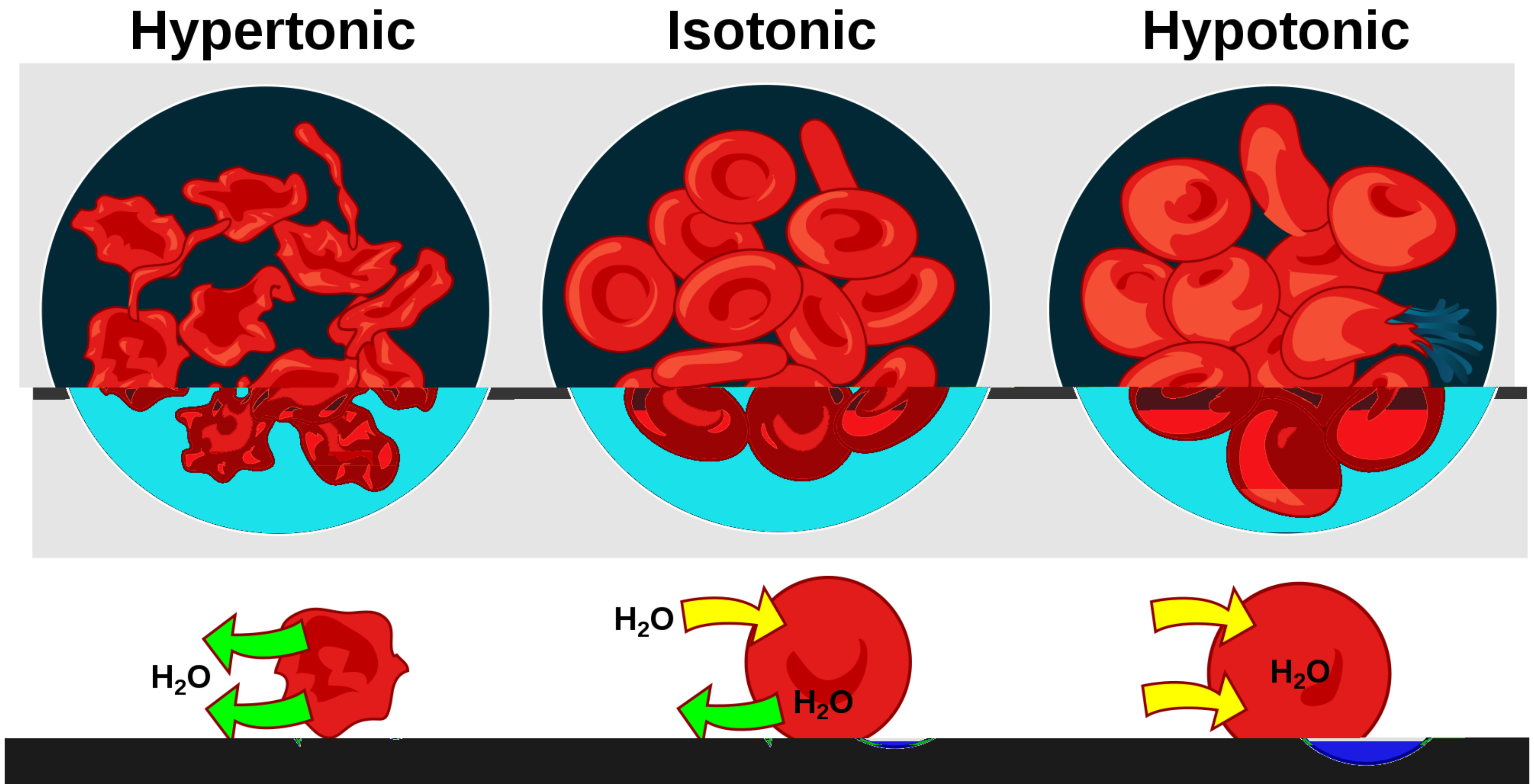
- *ECF volume* and *ECF osmolarity* are tightly regulated

- Maintenance of *ECF volume* critical for blood pressure – this will be discussed in cardiovascular unit

- *Maintenance of ECF osmolarity* critical to prevent swelling/shrinking of cells (due to osmosis)

Tonicity

- *Tonicity* is the effect the solution has on cell volume
- Determined by the concentration of non-penetrating solutes



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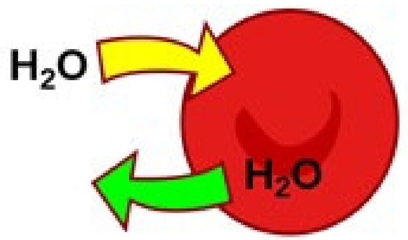
Tonicity

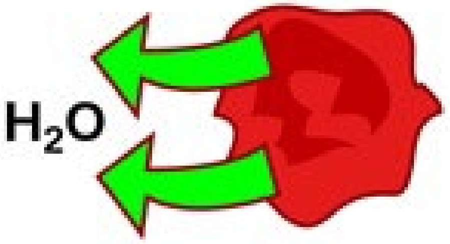
Isotonic

- Concentration of solutes on both sides of the membrane is equal
- **No net movement of water occurs**



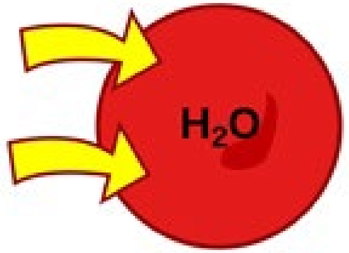
Hypertonic compartment or solution

- Osmotic pressure of the solution outside the cells is higher than the osmotic pressure inside the cells
- **Net movement of water out of cell → cell shrinks & crenates**



Hypotonic compartment or solution

- Osmotic pressure of solution outside of the cells is lower than the cytoplasm of the cells
- **Net movement of water into cell → cell expands, can cause lysis**



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Why understand tonicity?

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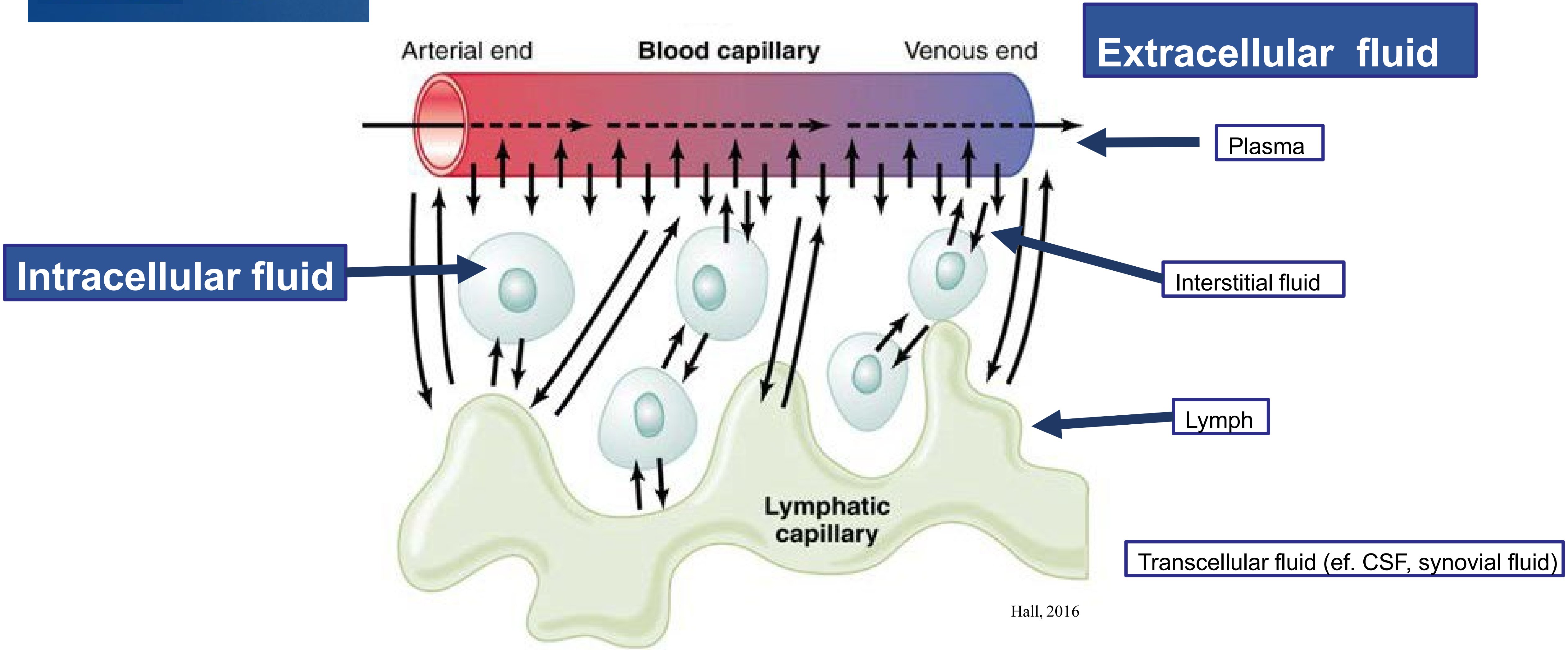
Body fluid compartments: overview



Hall, 2016

Cardiovascular System

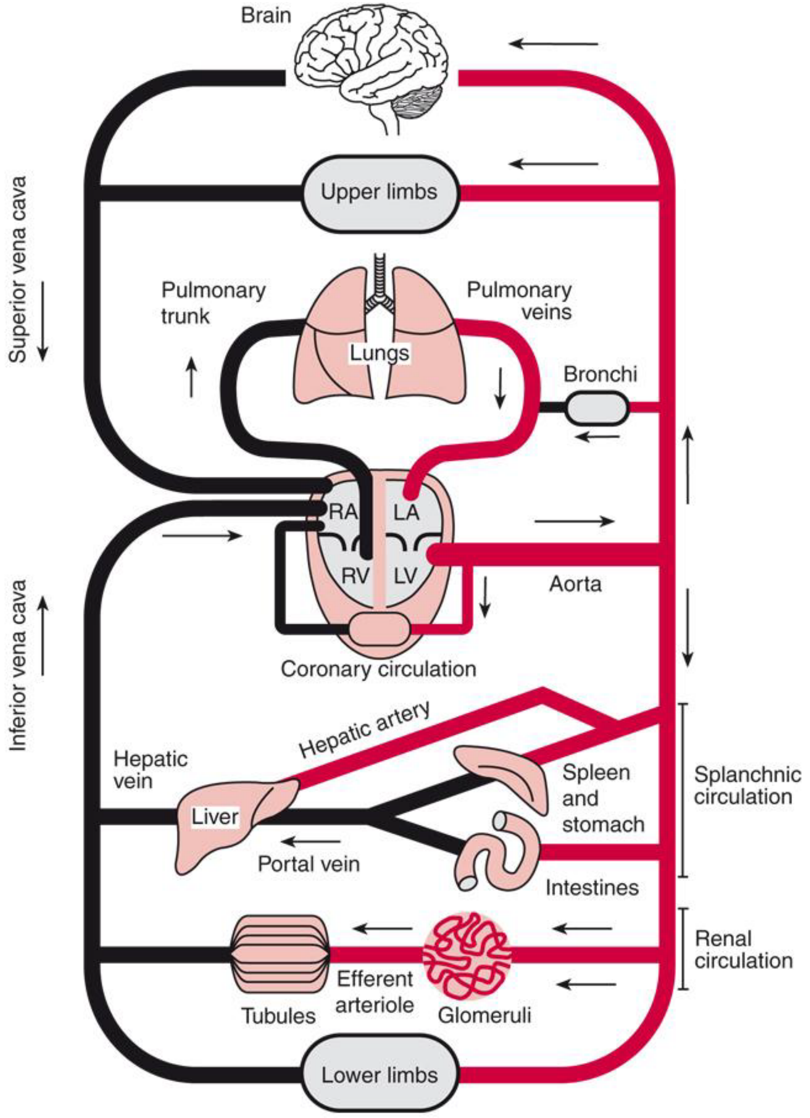
- The heart - the driving force

  propels blood around the body
- Arterial system

  the distribution channels
- The microcirculation

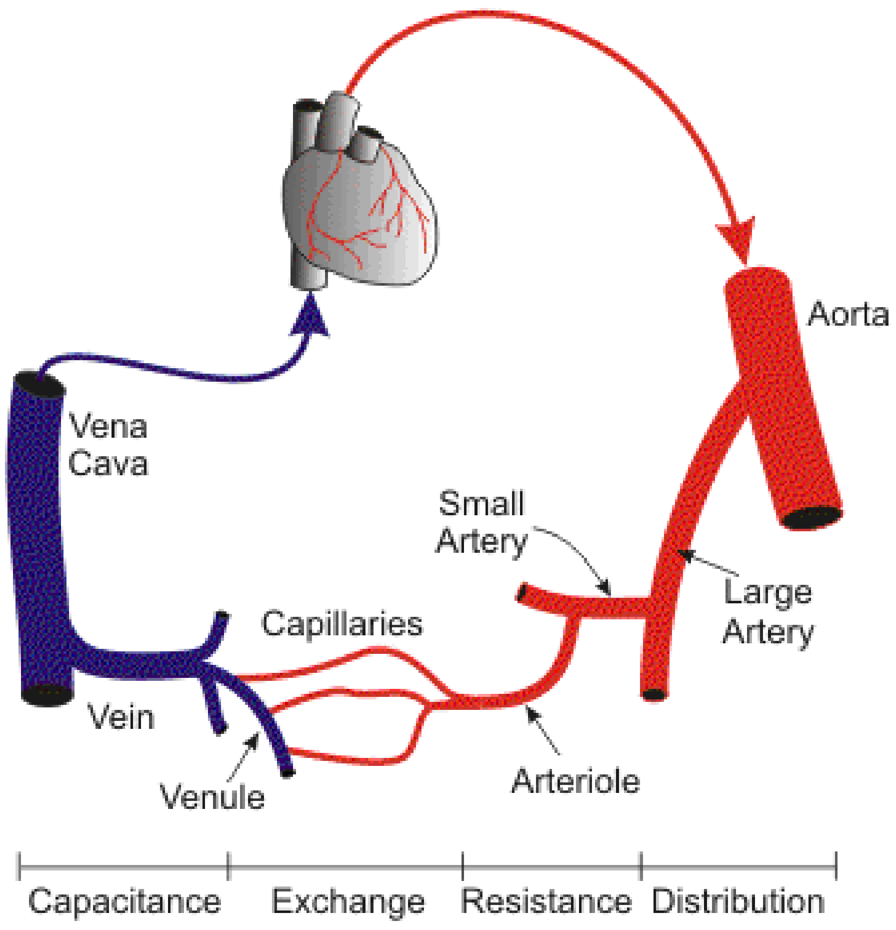
  the exchange vessels
- The venous system

  the blood reservoirs, return blood to the heart



An Introduction to Cardiovascular Physiology/Hodder Arnold © 2010 JR Levick

Overview: functions of blood vessels



http://www.cvphysiology.com/Blood%20Pressure/BP019.htm

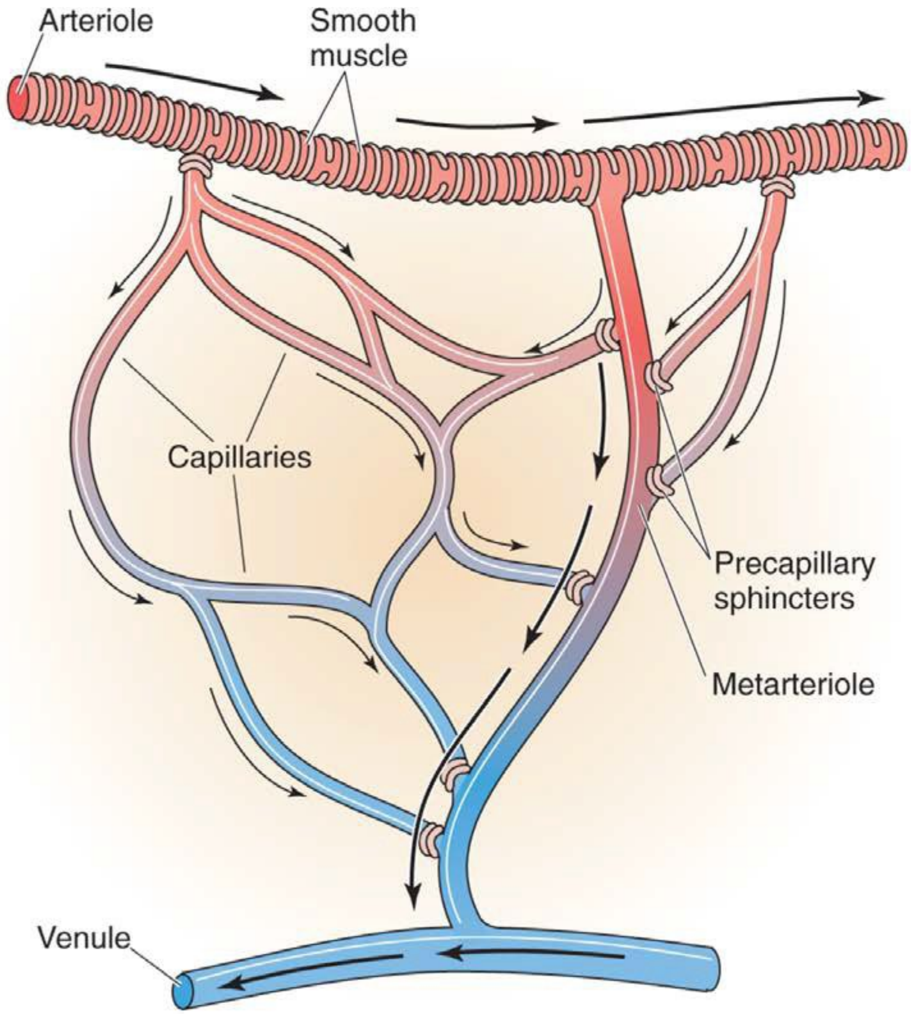
FUNCTIONAL GROUP	FUNCTION
Conducting arteries	Elastic arteries that act as a pressure reservoir – elastic recoil continues driving blood forward during diastole
Distributing arteries	Primary role to conduct flow to smaller arteries, can change diameter actively
Resistance vessels	Control local blood flow to tissues. Main source of peripheral resistance, control arterial pressure
Exchange vessels	Site of metabolic exchange. Low resistance, high cross-sectional area to facilitate exchange
Capacitance vessels	Act as a reservoir of blood, stabilise and regulate venous return to the heart

Capillaries: sites of exchange

- Exchange of fluid (nutrients & metabolic products) between blood and interstitial fluid

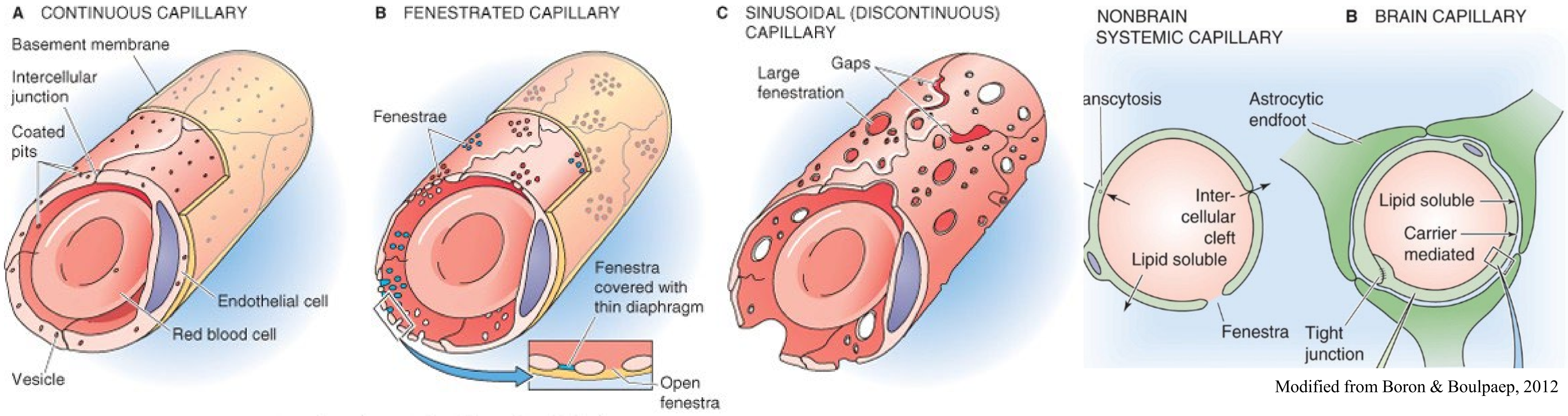
- Capillary walls are made up of a single layer of endothelial cells (~2μm thick)

- Capillaries are located close to every cell in body (30-100μm distance)



Boron & Boulpaep, 2012

Types of capillaries



Modified from Boron & Boulpaep, 2012

Continuous:
- Muscle
- Skin
- Lung
- Fat
- Connective tissue

Contain narrow junctions (clefts) & small, coated pits (caveolae)

Fenestrated:
- Kidneys
- Intestines
- Endocrine glands
- Joints

Contain pores or fenestrae – permeable to small molecules

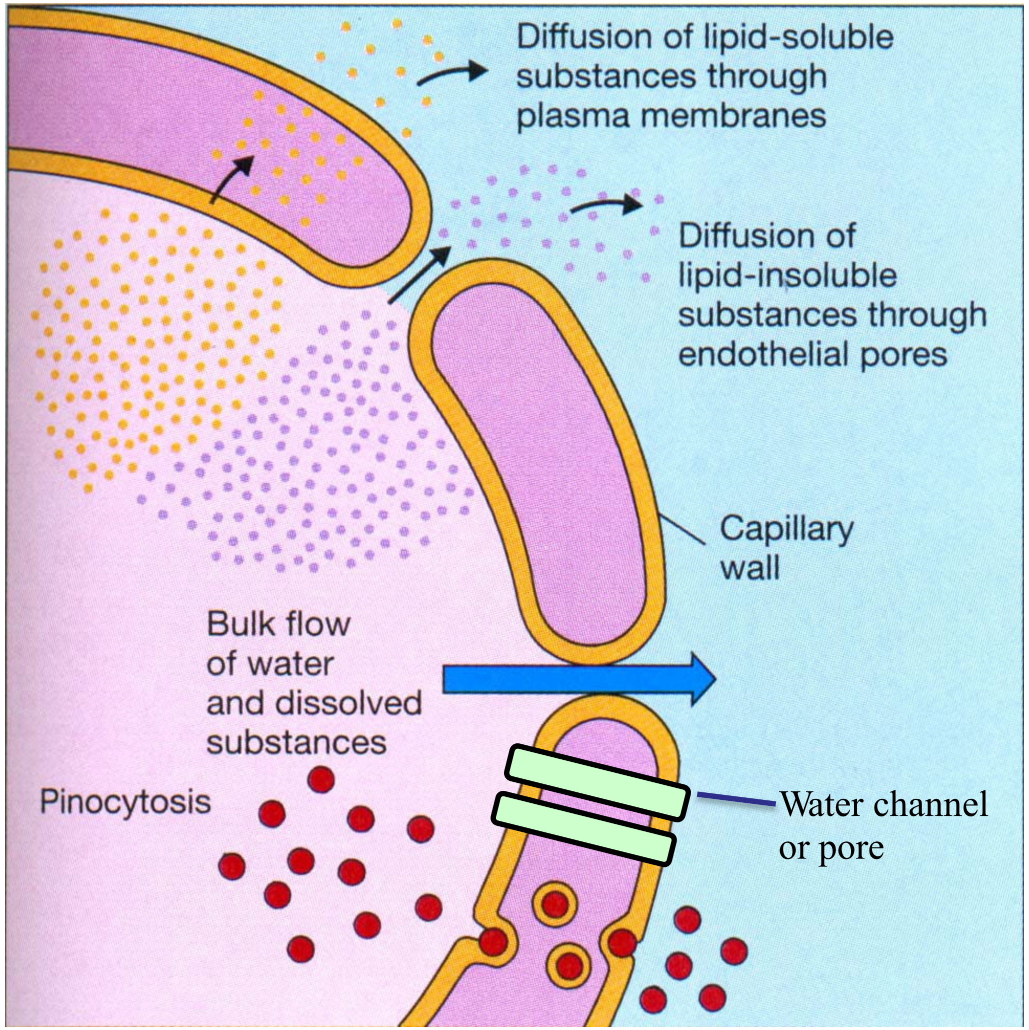
Discontinuous:
- Bone marrow
- Liver
- Spleen

Wide gaps between endothelial cells – permeable to large molecules

Neural:
- Brain

Endothelial cells fused together by tight junctions and covered by thick basement membrane and astrocyte processes. Water diffuses, solutes require specific transport

Movement of substances across capillary walls



Modified from Rhoades & Pflanzer 2003

1. Diffusion

- Lipid-soluble molecules cross EC membranes
- Lipid-insoluble molecules pass between ECs and through pores
- Rate of diffusion described by Fick's Law

2. Transcytosis or pinocytosis

- Movement of macromolecules across ECs in vesicles

3. Bulk flow via Starling's Forces – driving force

- Bulk flow of fluid through channels in capillary wall – molecules moving together in bulk
- Transfer of water and dissolved substances across capillaries depends on net hydrostatic and osmotic forces

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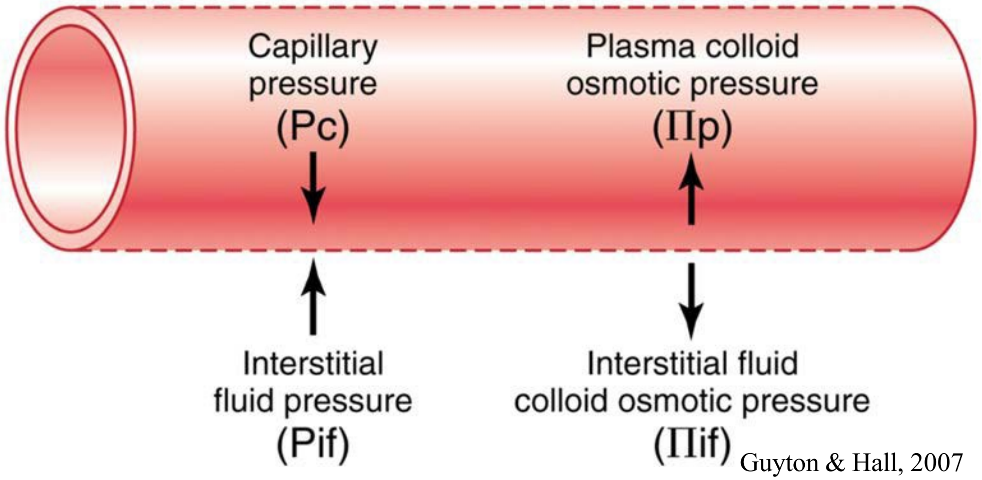
Forces influencing bulk flow: Starling's forces

Four forces influencing bulk flow:

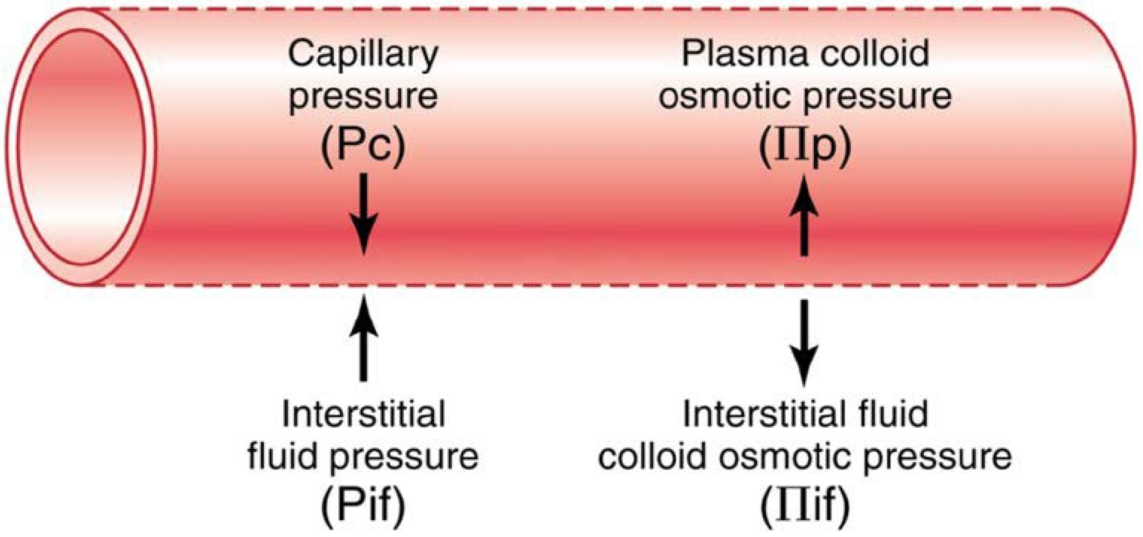
1. Capillary blood pressure: hydrostatic pressure exerted on the capillary wall by the blood. Forces fluid out of capillary
2. Plasma colloid osmotic pressure (also known as oncotic pressure): force caused by plasma proteins which remain in plasma, which exerts an osmotic effect on water. Forces fluid into the plasma compartment
3. Interstitial fluid pressure: hydrostatic pressure exerted by the interstitial fluid on the outside of the capillary wall. Forces fluid into capillaries.
4. Interstitial fluid colloid osmotic pressure: the protein concentration in the interstitium is normally very low, and so this force is close to zero.



Guyton & Hall, 2007

$$NFP = \underbrace{(Pc + \prod if)}_{\text{Filtration forces}} - \underbrace{(Pif + \prod p)}_{\text{Absorption forces}}$$

Forces influencing bulk flow: Starling’s forces



Guyton & Hall, 2007

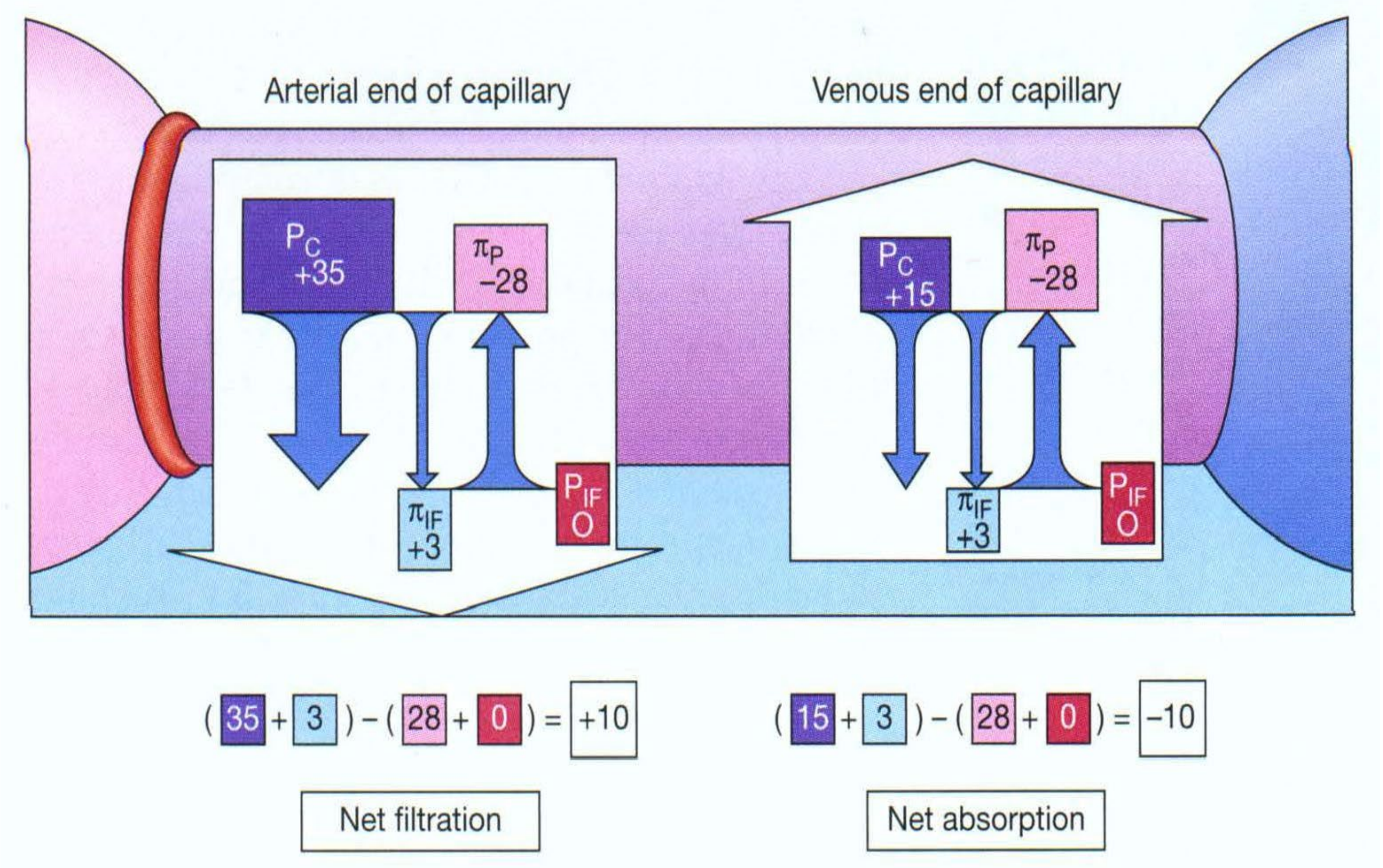
$$NFP = \underbrace{(Pc + \prod if)}_{\text{Filtration forces}} - \underbrace{(Pif + \prod p)}_{\text{Absorption forces}}$$

Net filtration pressure (NFP) is the difference between forces driving fluid from the capillary to interstitial fluid and forces driving fluid from interstitial fluid into the capillary

Filtration is greatest at the arterial end of the capillary

- Hydrostatic forces favouring filtration are greatest at the arterial ends of capillaries

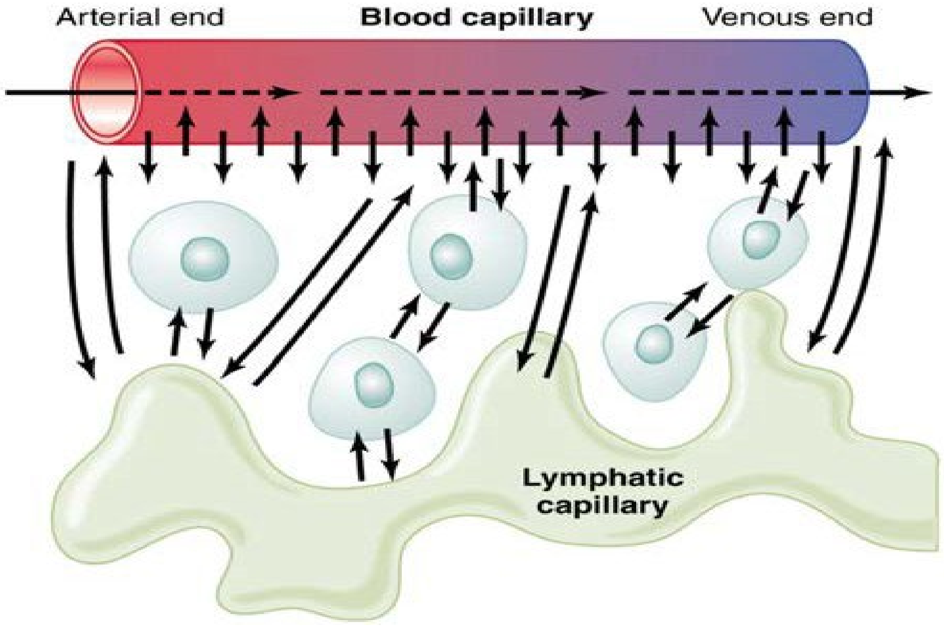
- Oncotic osmotic pressure predominates at the venous ends of the capillaries ensuring 90% of the fluid is reabsorbed → this creates a filtration-absorption imbalance



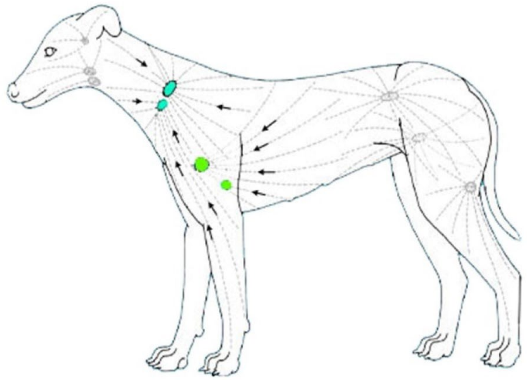
Rhoades & Pflanzer, 2003

Lymphatic system: role in fluid balance

- In normal circumstances, slightly more fluid is filtered out of capillaries than is reabsorbed back into plasma
- This 'extra' fluid is picked up by the lymphatic system, and is called 'lymph'
- Lymphatic system returns this extra interstitial fluid to the blood



Lymphatic system



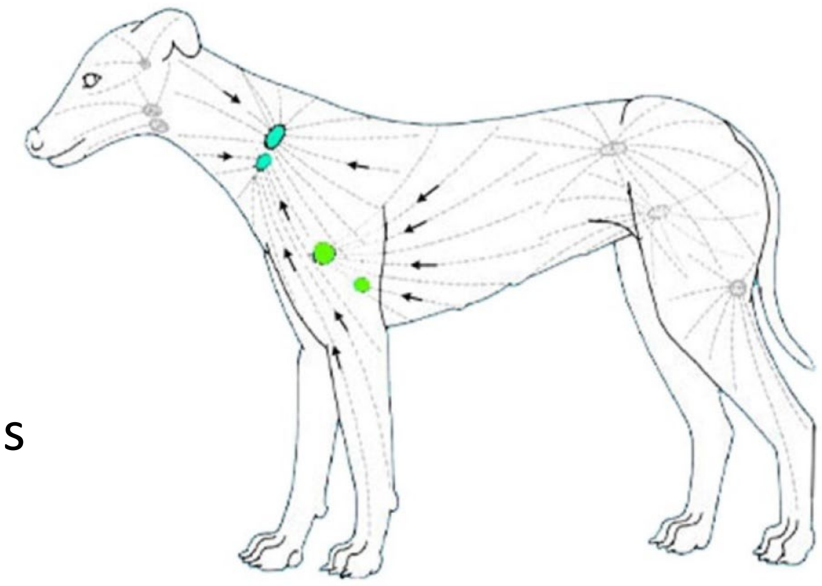
- *Extensive network of one-way vessels*
- *Functions as a tissue drainage system and is responsible for returning excess interstitial fluid back to the venous circulation*

<u>FUNCTIONS:</u>

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

Lymphatic system: structure

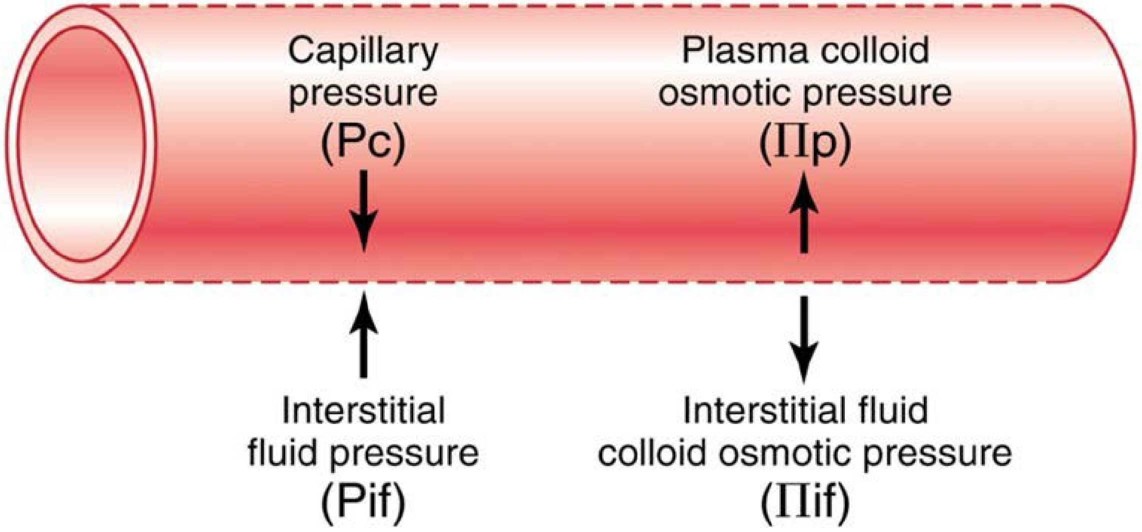
- Lymphatic capillaries form plexuses that give rise to larger lymphatic vessels
- These converge into large trunks which open into the major veins in the thorax
- Lymph nodes are placed along lymph pathways – lymph passes through a node before entering the blood stream
- In lymph nodes, it is exposed to lymphocytes and phagocytes → provides for immune surveillance



Oedema

- Oedema: the accumulation of excess body fluid → can be ECF or ICF
- 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

Extracellular oedema is caused by a disturbance in Starling's forces



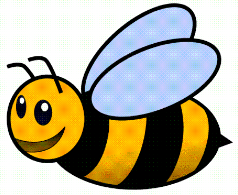
Guyton & Hall, 2007

Causes of extracellular oedema

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

Example: Bee sting



Lymphoedema

- Impairment of lymphatic drainage causes lymphoedema upstream
- Generally localised to the drainage field of the damaged/obstructed area
- Can be caused by damage to, or obstruction of, lymphatic vessels or nodes (trauma, inflammation, infection)

Kang, 2007

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