

Human Kidney Physiology

Fluid Compartments

10 mmol of potassium in banana
omfg woah
he gave chips lmao dkm
water bottles

Dr. Jim Scholey

Professor of Medicine and Physiology

Physician-Scientist

University of Toronto

Senior Scientist

Toronto General Research Institute

Staff Physician

Division of Nephrology

University Health Network and Mount Sinai

Hospital

james.scholey@utoronto.ca

Outline:

1. **General comments** in the next few lectures, there is a case presented to show how renal physiology has a real world impact and understanding how the kidney work and its intricacies is very important in medicine.
2. **Fluid Compartments** kidney marries structure and function damn woah beautiful - like filtration and the anatomy responsible for that.
3. **Water permeability and Solutes** sodium, potassium and water maintaining acid base status.
4. **Movement of water between compartments**
5. **Clinical Aspects**

Case of the Day: The Seizing Marathoner

- A 45 year old woman runs her first marathon after 6 months training. Finished in 5 hours. Rehydrated with water**
- Complained of headache** at the end of the 5 hours.
- Felt nauseated, vomited then had a seizure and taken to medical area**

Outline:

1. General comments
2. **Fluid Compartments**
3. Water permeability and Solutes
4. Movement of water between compartments
5. Clinical Aspects

Text Book Link:

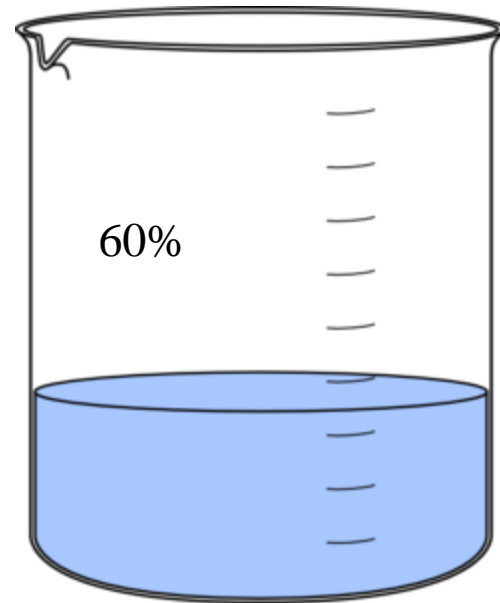
Chapter 5: pages 124-132 (7e)

Chapter 5: pages 132-139 (6e)

Body Fluid Compartments:

On the basis of weight, humans are 50-60% water

body composition is dominated by water
average individual is about 60% water lmao wot -
total body water influenced --> next slide



What Factors Determine Body Water as a Fraction of Weight?

- **Ratio of Fat/Muscle**

most of water exists in muscle --> how much fat and how much muscle you have determines how much body water you have

- **Fat has very little water; muscle has a lot of water; muscle contains most water in the body**

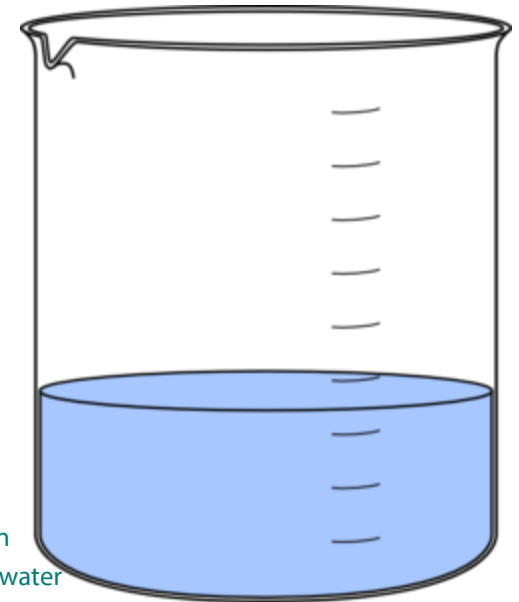
so athletes which are more muscular probably have more water!

On average, there is more fat/muscle in:

- **Women** compared to men (50% vs. 60%)

- **Older** compared to younger aging, it is increasingly difficult to maintain muscle mass, so they have less total body water

- **Chronic illness** compared to healthy declines for chronic illness



average women has less muscle mass compared to an average man, which means that women on average have less water

the average male --> 60% of body weight is water

average female --> 50% of body weight is water --> this is a contributing factor to the marathon women.

TABLE 5-4

Water Content as Percentage of Total Body Weight by Age and Sex

60% is from age 10-40 for males and 17-49 for females

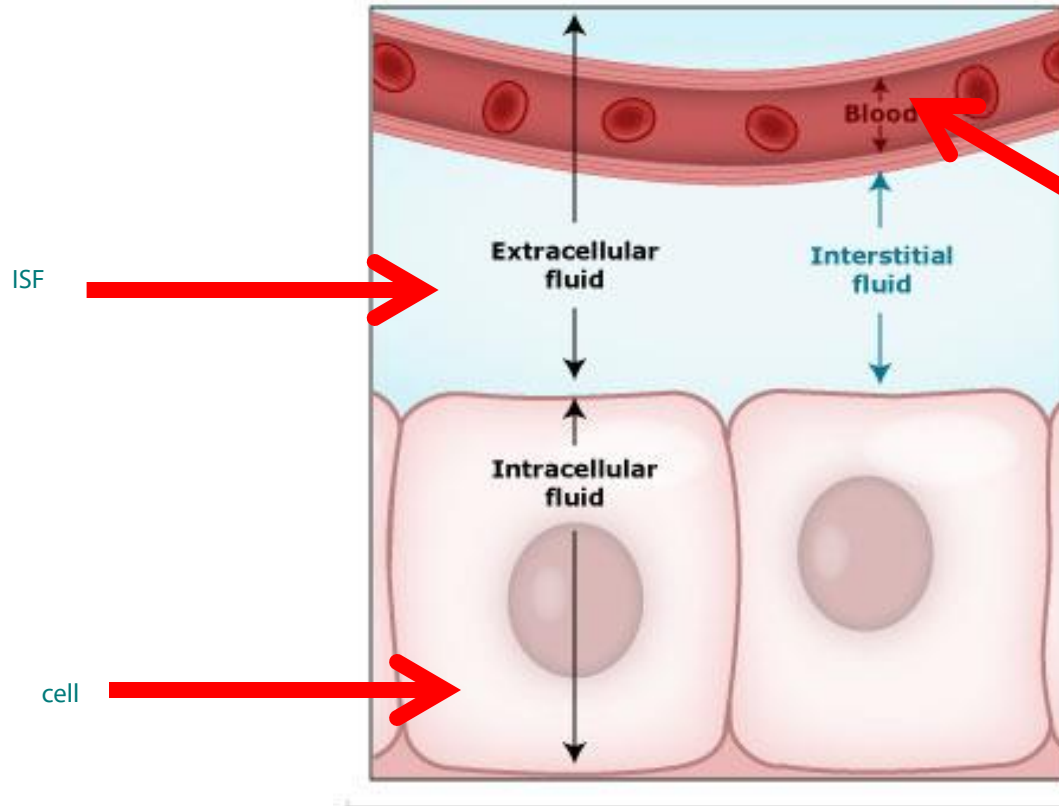
AGE	MALE	FEMALE
Infant	65%	65%
1-9	62%	62%
10-16	59%	57%
17-39	61%	51%
40-59	55%	47%
60+	52%	46%

Adapted from Edelman and Leibman, *American Journal of Medicine* 27; 256-277, 1959.

So where is the water?

Cellular Fluids

water is in each of those compartments

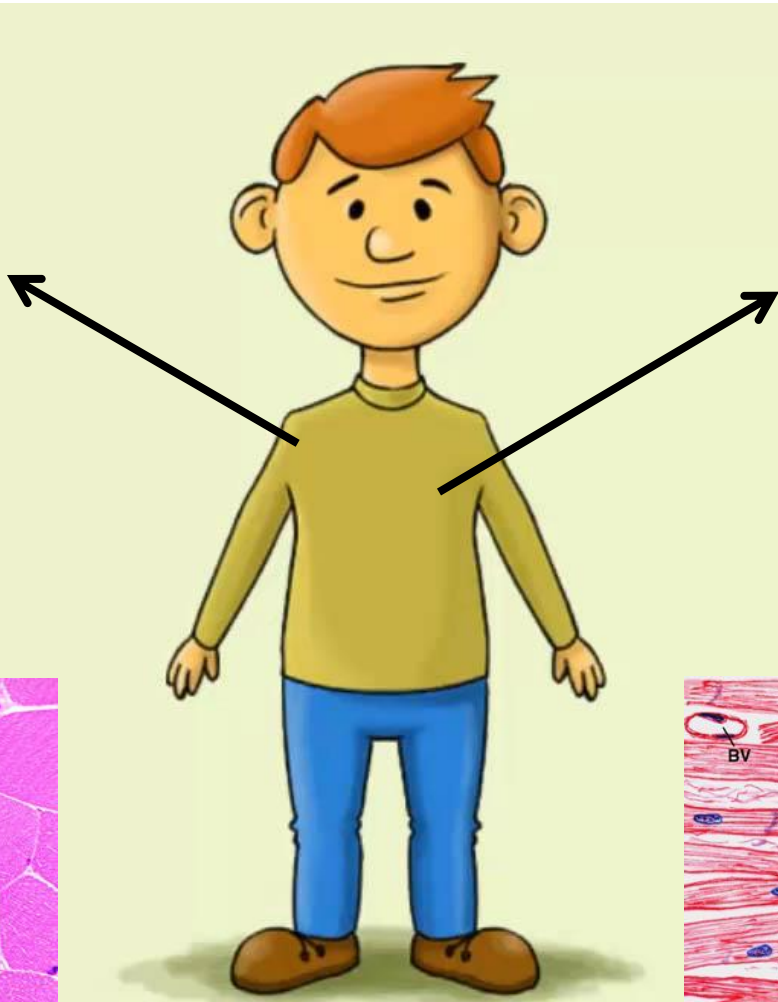
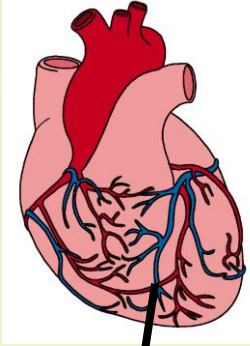
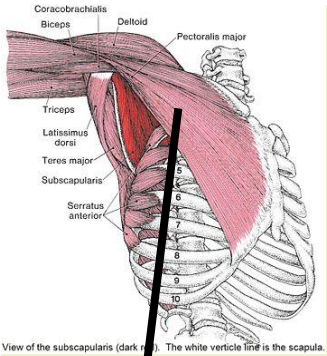


ISF

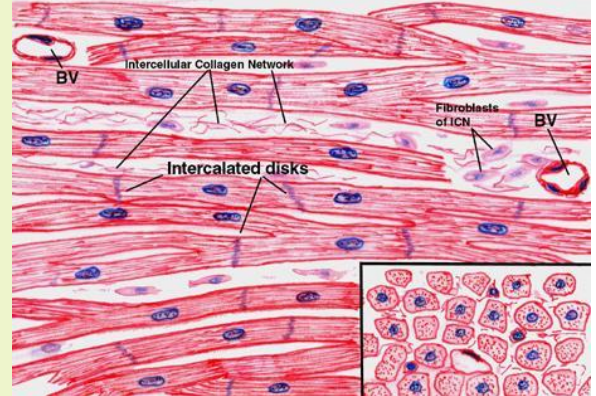
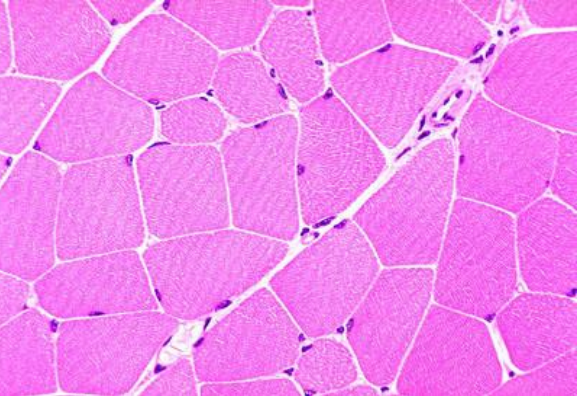
blood compartment

we have 2 large compartments; ICF and ECF. The ECF can be broken up into the ISF and the blood compartment.

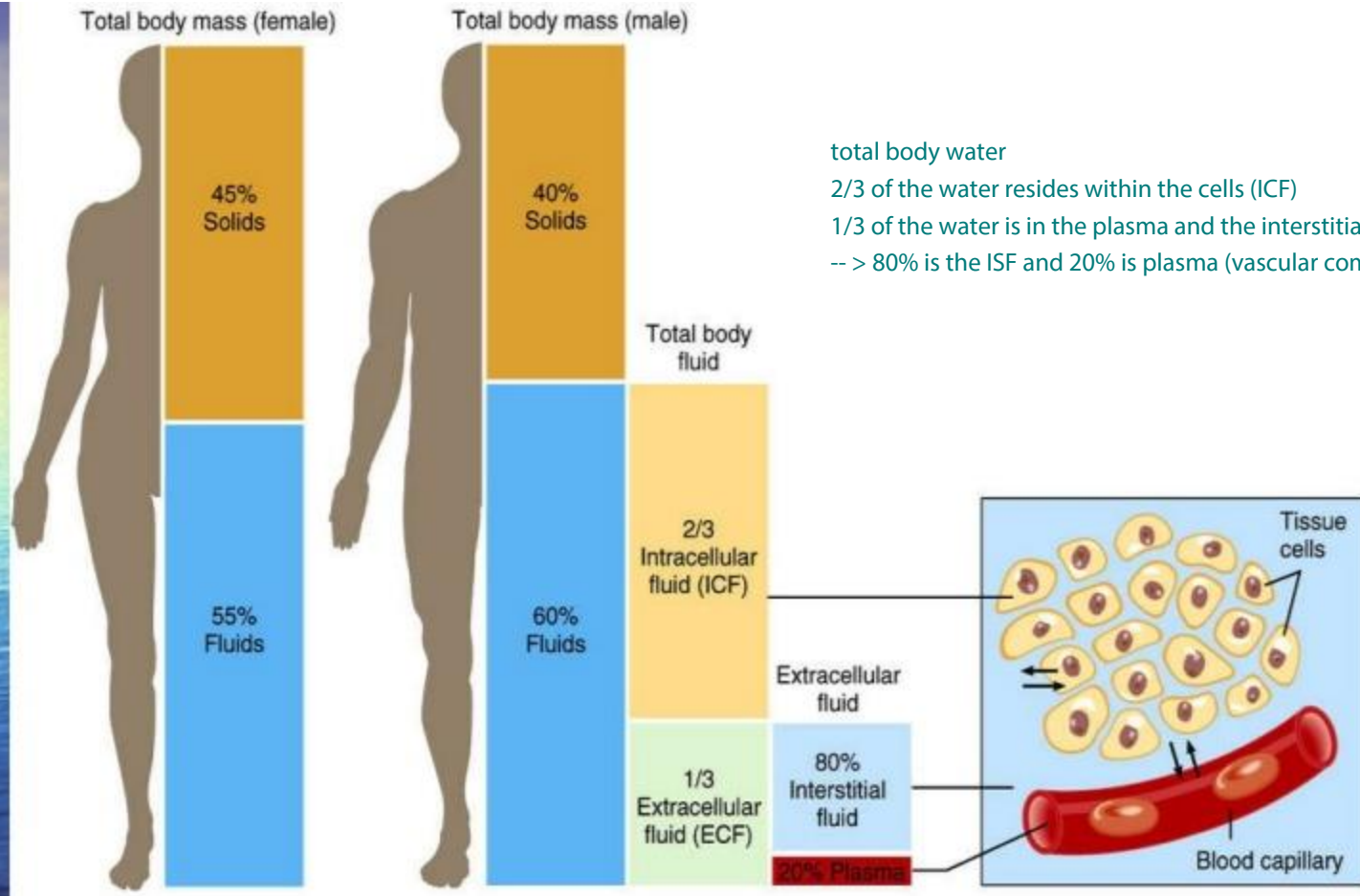
cell



the ISF is tiny!



So let's get quantitative?

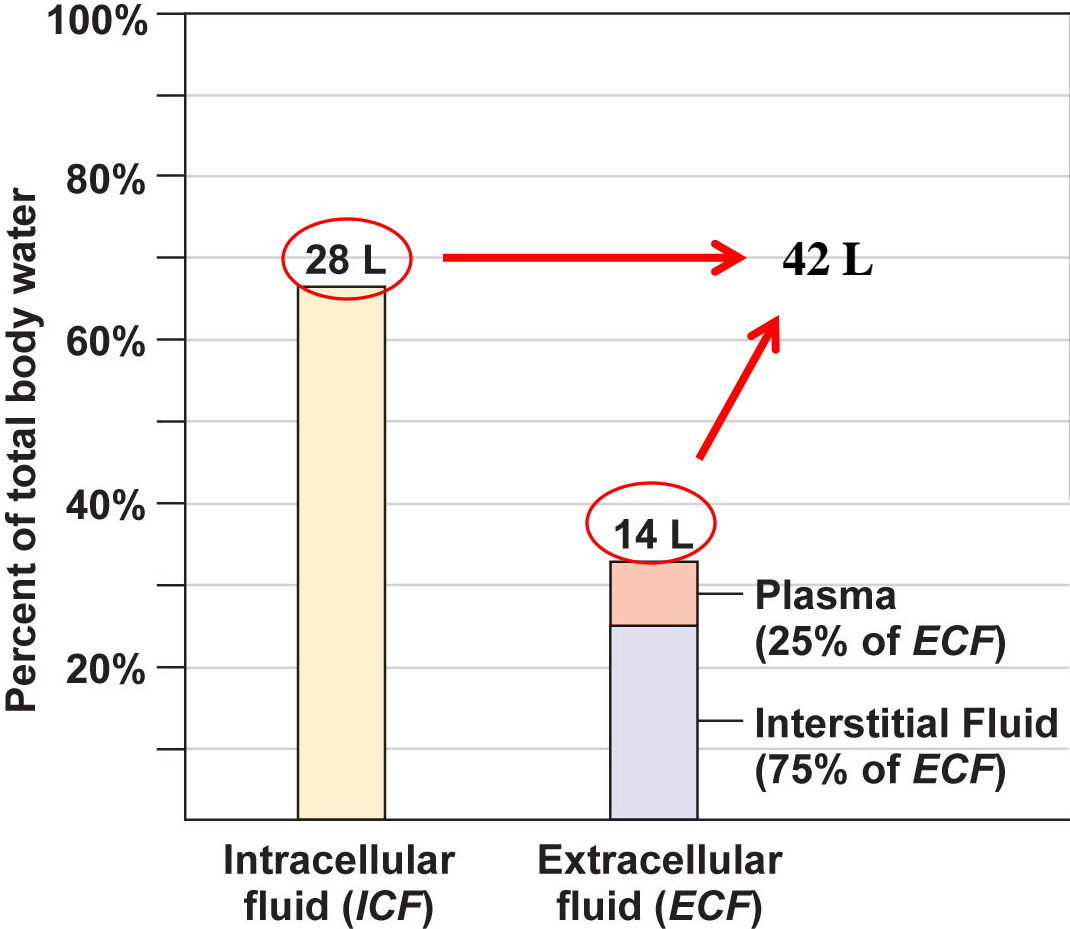


total body water
 2/3 of the water resides within the cells (ICF)
 1/3 of the water is in the plasma and the interstitial fluid, its outside the cell
 --> 80% is the ISF and 20% is plasma (vascular compartment).

(a) Distribution of body solids and fluids in an average lean, adult female and male

(b) Exchange of water among body fluid compartments

Body Fluid Compartments:



70kg person who is male --> 60% of 70 is 42L which is the total body water.
Within that, 2/3 which is 28L is in the cell
1/3 which is 14L resides outside the cell

10-25% of the 1/3 is in plasma
and 75-80% of the 1/3 is in the ISF

1. A person weighs 80 kg. What are the estimated volumes of his body fluid compartments: total body water (TBW), extracellular fluid (ECF) and intracellular Fluid(ICF)?

A. TBW 40 ECF 30 ICF 10

B. TBW 60 ECF 16 ICF 30

C. TBW 48 outside ECF 16 inside ICF 32

D. TBW 48 ECF 32 ICF 16

Outline:

1. General comments
2. Fluid Compartments
3. **Water permeability** and Solutes
4. Movement of water between compartments
5. Clinical Aspects

oil and water don't mix, so how does water get across the cell membrane? This is because all lipid bilayers are permeable to water (but some parts of the kidney are not).

**Cells are surrounded by a
lipid bilayer**

**But they are permeable to
water!**

How?

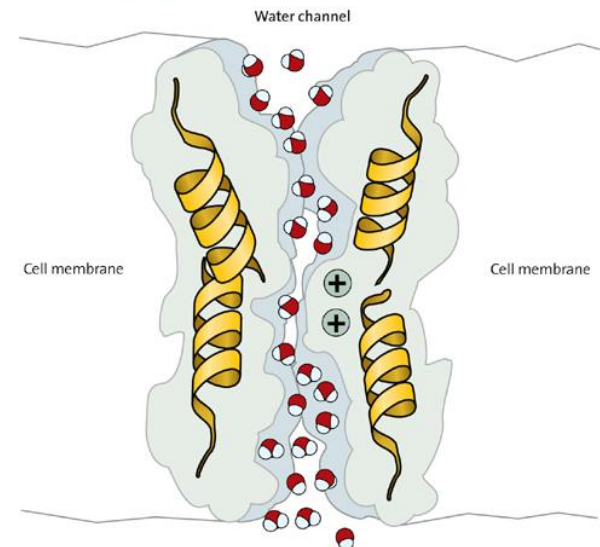
confer water permeability and it is bidirectional

Water channel (Aquaporin)

these are channels which reside in the lipid bilayer making the cell permeable to water.

- Family of Integral membrane proteins.
- Provide channels for rapid movement of water molecules across all plasma membrane.
- Ten aquaporins are known in humans.
- RBC contain 2×10^5 copies of AQP-1 per cell.
- Plasma membrane of PCT cells contain five different aquaporin types.

Structure of Aquaporin





water can move back and forth.

Cell membranes are permeable to water

Outline:

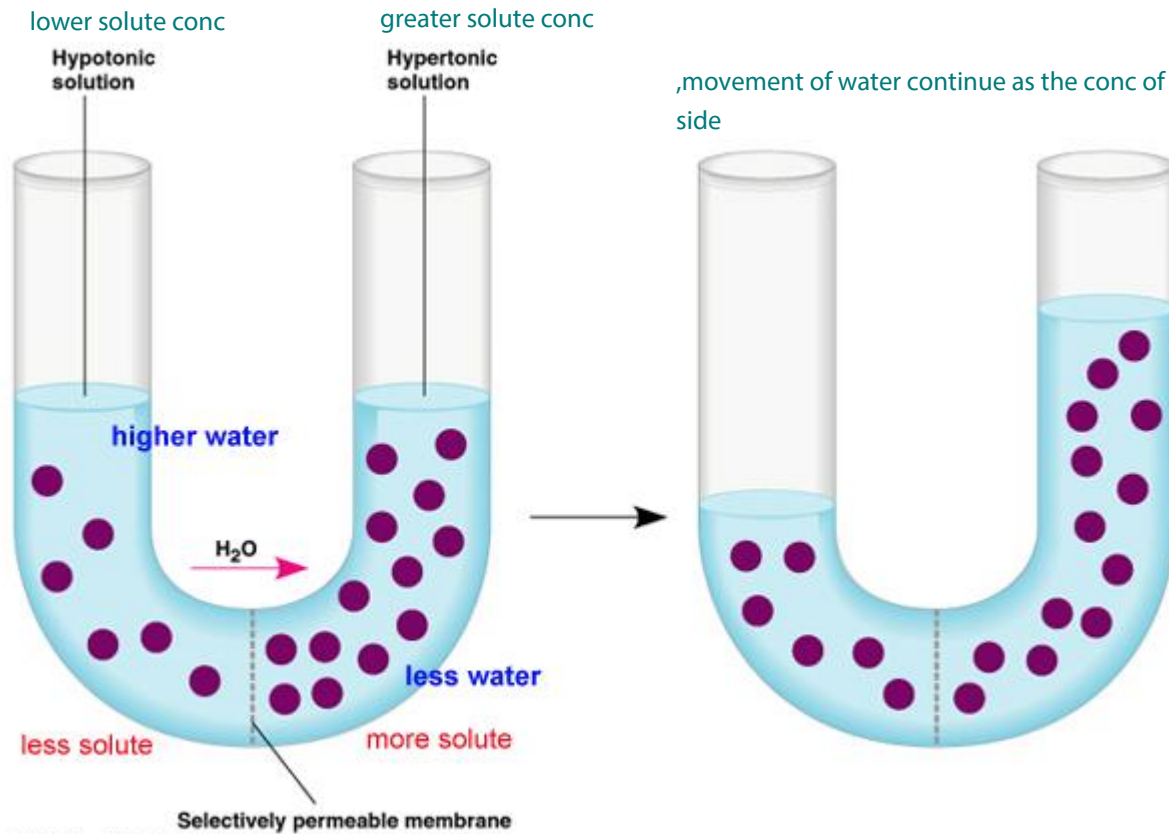
1. General comments
2. Fluid Compartments
3. Water permeability and **Solutes**
4. Movement of water between compartments
5. Clinical Aspects

So now ... some definitions:

- **Solutes** = particles dissolved in a water solution
(Sodium, potassium, glucose) and bicarbonate and hydrogen ions
- **Ions** (electrolytes) = charged solutes (cations are positive + and anions are negative -) e.g. sodium
- **Osmolality** = the concentration of solutes in water which generates an osmotic force

the number of particles or solute within a 1kg of solvent.

Osmolarity - the number of particles or solutes within 1L of solvent



©1999 Addison Wesley Longman, Inc.

semi-permeable membrane
which is like the lipid bilayer
which is perforated with
aquaporins

movement of water continue as the conc of solute are equal on each side

if the number of solutes in any compartment changes, the water will move from a low solute concentration to an area of high solute concentration!

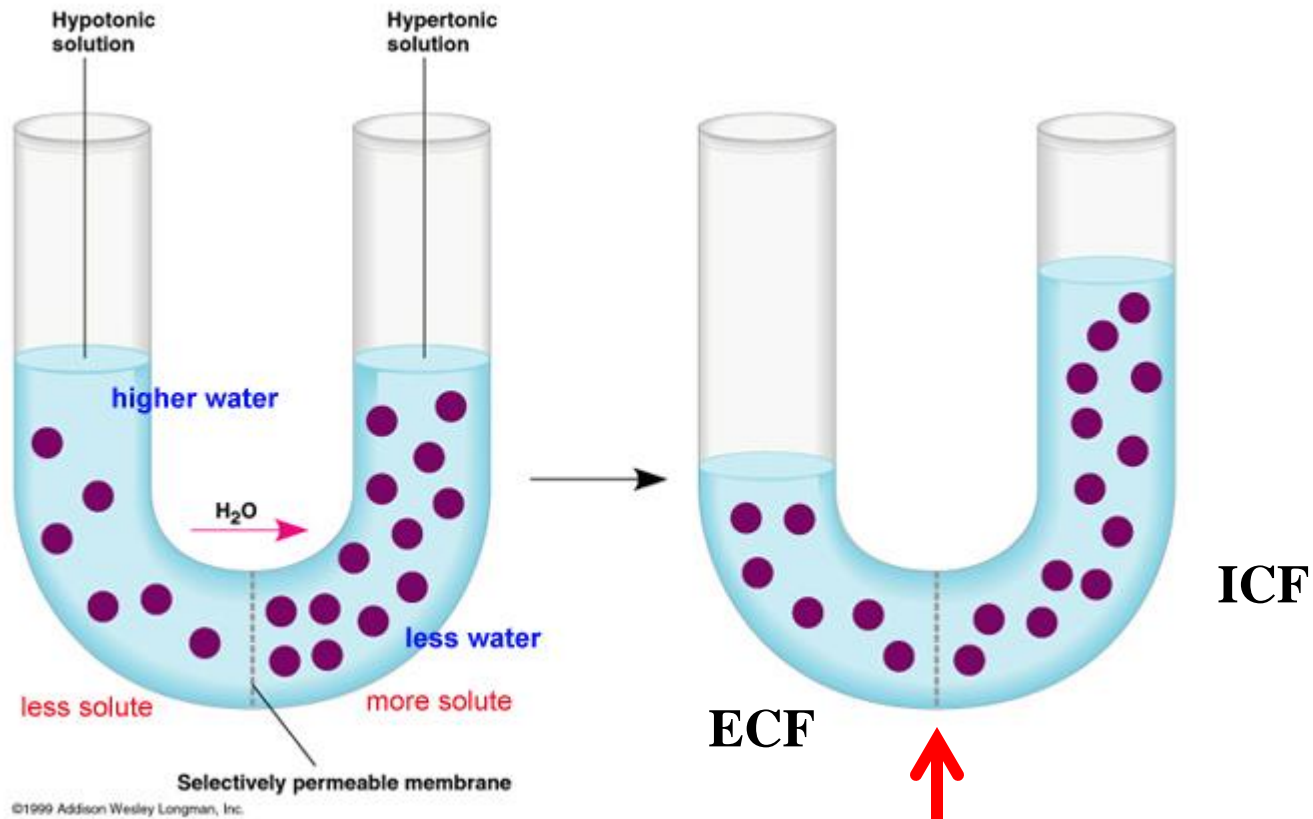
forces water to move AGAINST a solute concentration (low to high) due to solutes generating an osmotic pressure

different in concentration of water separated by a semi-permeable membrane

Osmotic Force:

- The **movement of water across a semi-permeable membrane** in response to an **osmotic gradient**
- The **osmotic gradient = a difference in the osmolality in the compartments** separated by the membrane
- **Water moves** from the compartment with low osmolality to that of high osmolality

no cells can exist in which the solute concentration is different. --> will always want to get to equilibrium! It doesn't want to exist in solute concentrations which are different.



ECF

Cell Membrane

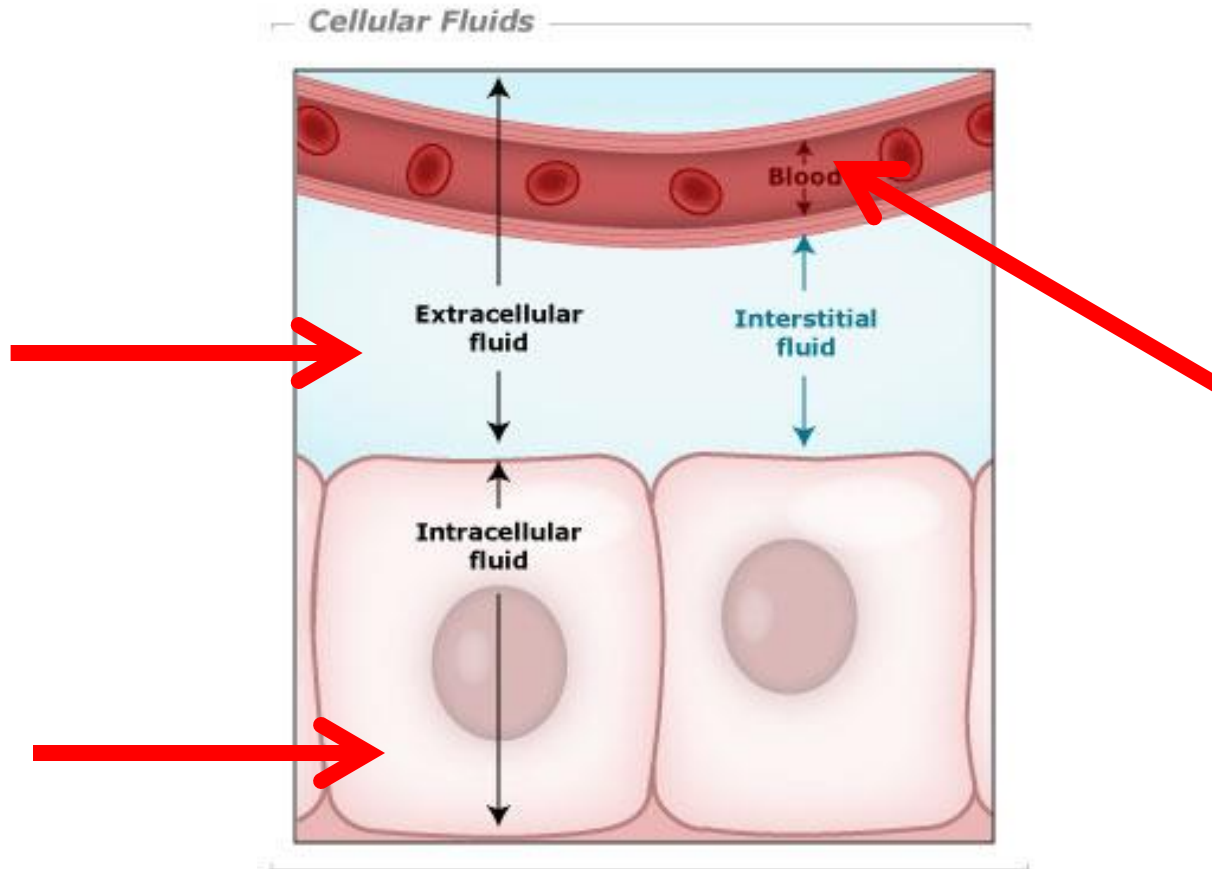
this is semi-permeable

So an important point:

**Is the osmolality the same in all body
fluid compartments?**

YES: osmolality is the same in each fluid compartment

this is because our cell membranes are permeable to water, those water channels allow for the movement of water down its concentration gradient. All cells exist in equilibrium, each fluid compartment is isotonic to one another (since cells want to exist in equilibrium.)

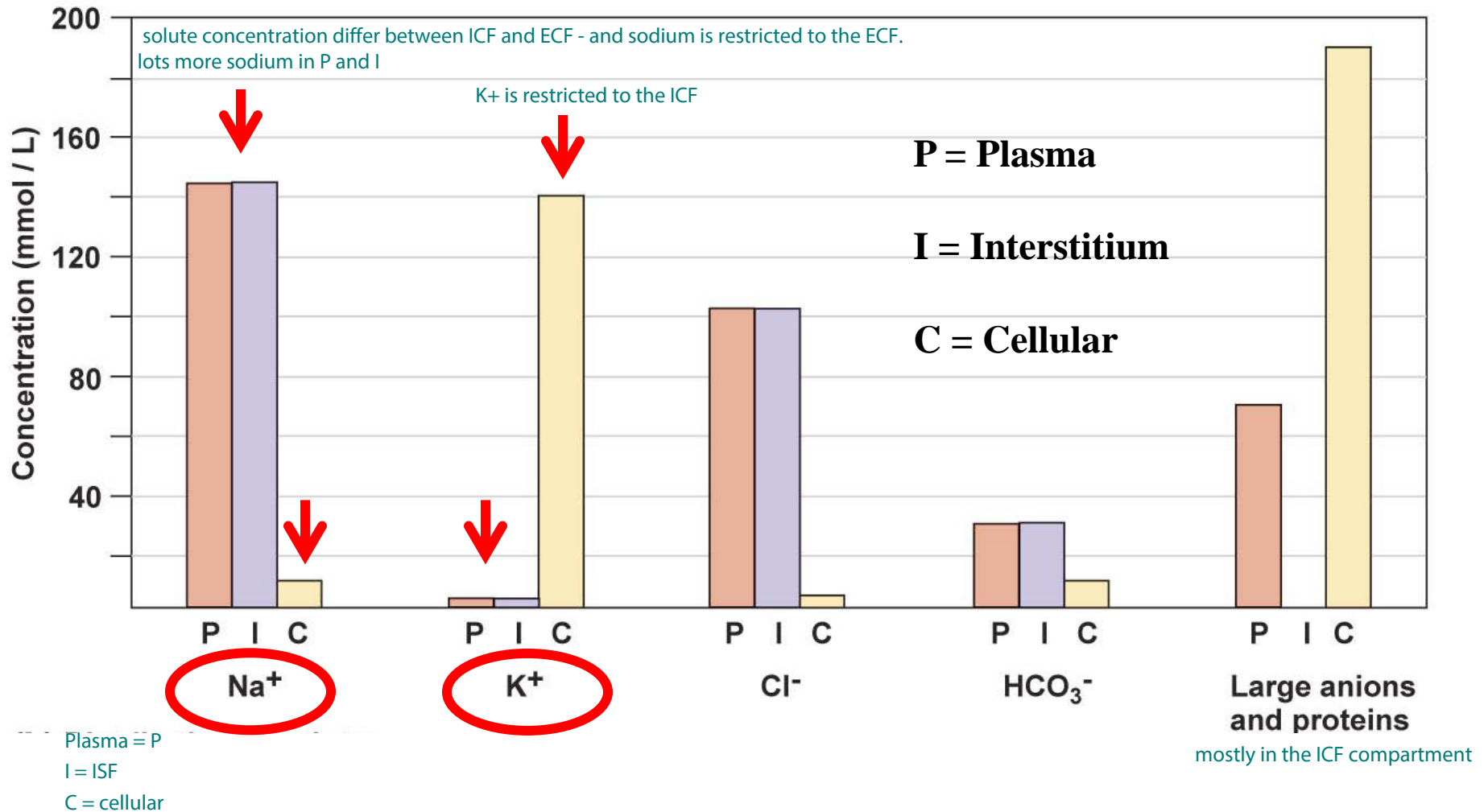


Let's ask another question:

Are the solute concentrations the same in all body fluid compartments?

osmolality is the same in all compartments.

The answer is NO



ICF vs ECF: Osmolality is the same but the dominant positively charged ions differ

how is the ICF is dominated by K^+ and the ECF is dominated by Na^+ ? Due to the membrane protein Na^+/K^+ ATPase, which is an energy consuming pump which moves Na^+ and K^+ in opposite directions.

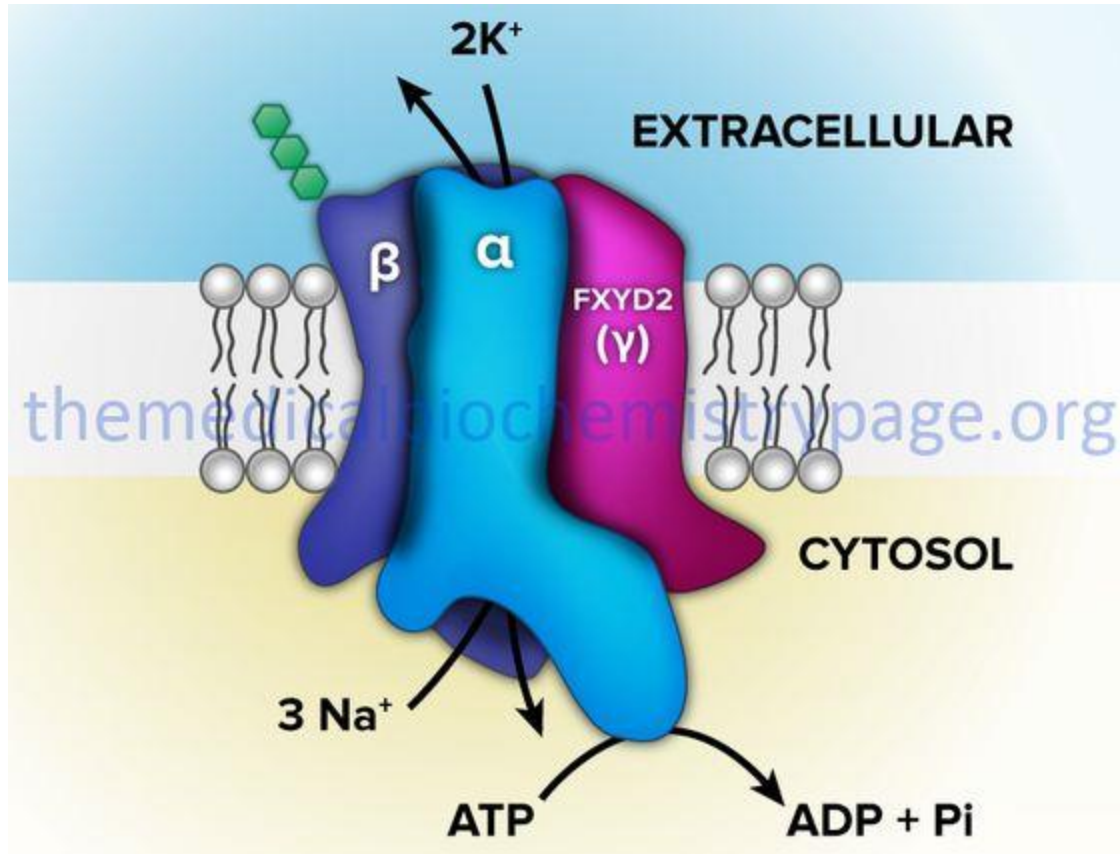
This exists for all the cells in our body and the kidney uses this pump to reabsorb solutes

The Sodium-Potassium Pump (Na^+/K^+ - ATPase)

- A specific case of **active transport**
- This is one of the *best examples* of active transport in animal cells
- This pump transports Na^+ ions *out* of the cell and K^+ ions *into* the cell. Thus keeping the intracellular concentration of Na low compared to outside, and the intracellular concentration of K high
- The pump is driven by hydrolysis of ATP
- It uses about 30% of the energy available to any one animal cell!
- The pump is a **transmembrane carrier protein** made up of 4 subunits (2 large and 2 small)

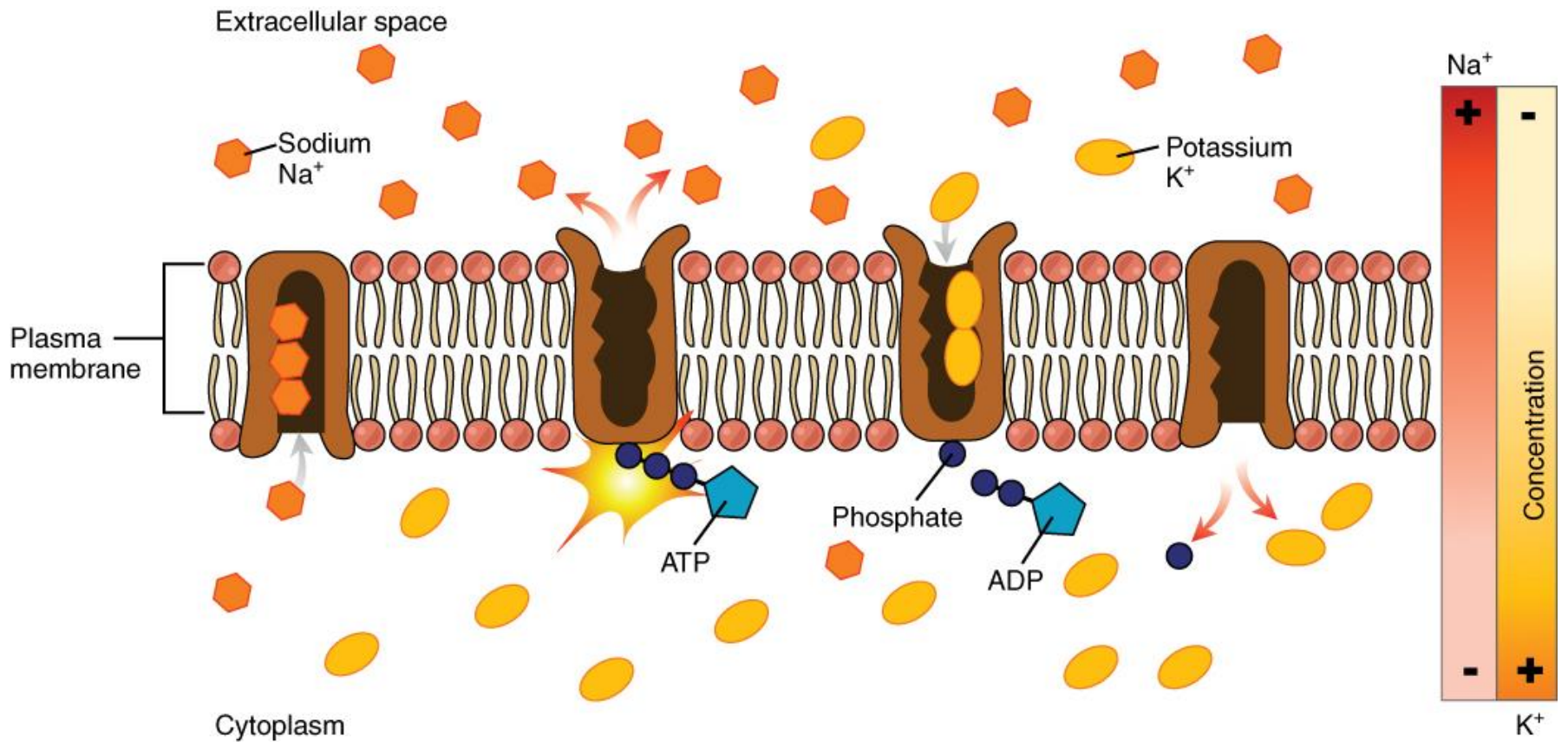
The osmotic pressure doesn't give a shit about the solute is, it just cares about the particles per volume and our cells will always aim for osmotic equilibrium. But we do not have a chemical equilibrium as seen with the previous slide! This different between ion gradients is maintained by the Na^+/K^+ ATPase which is an ATP dependent pump!

in equilibrium - achieved by aquaporins.



3 Na⁺ exits the cell and 2K⁺ enters the cell.

This really requires the hydrolysis of ATP, if you we couldn't make ATP then we would be unable to maintain the gradient and solute concentrations :(and therefore can not maintain the same osmolality.



3 Na⁺ bind --> ATP is bound, hydrolyzed and the configuration of protein changes so Na⁺ is released to the ECF. then K⁺ binds and then configuration changes and potassium released into the cell.

This ATPase allows the solute concentration of the Na⁺ and K⁺ differ across the cell between outside and inside.

THE RULES

- **Sodium (with an anion) is restricted to the ECF and is the main ECF osmole**
- **Water crosses cell membranes to equalize osmolality in the ECF and the ICF**

when eating chips, Na⁺ stays in the ECF (in the vascular and ISF compartment) --> wake up with puffy eyes, due to the water increasing in the ISF due to the salty chips and increase in Na⁺ in the ECF.

Outline:

1. General comments
2. Fluid Compartments
3. Water permeability and Solutes
4. Movement of water between compartments
5. Clinical Aspects

What happens to ICF and ECF volumes if we drink water (alone)?

- Water is absorbed from gut into the ECF, lowers ECF sodium concentration and osmolality

but the cell membrane can't tolerate a gradient in solute concentration so water moves from ECF to the ICF.

- **Water moves** from ECF to ICF

- **Both the ECF and ICF volumes increase**

women who is running and drank the water, the same thing happens!

If this happens in cells of her brain, shit goes down man

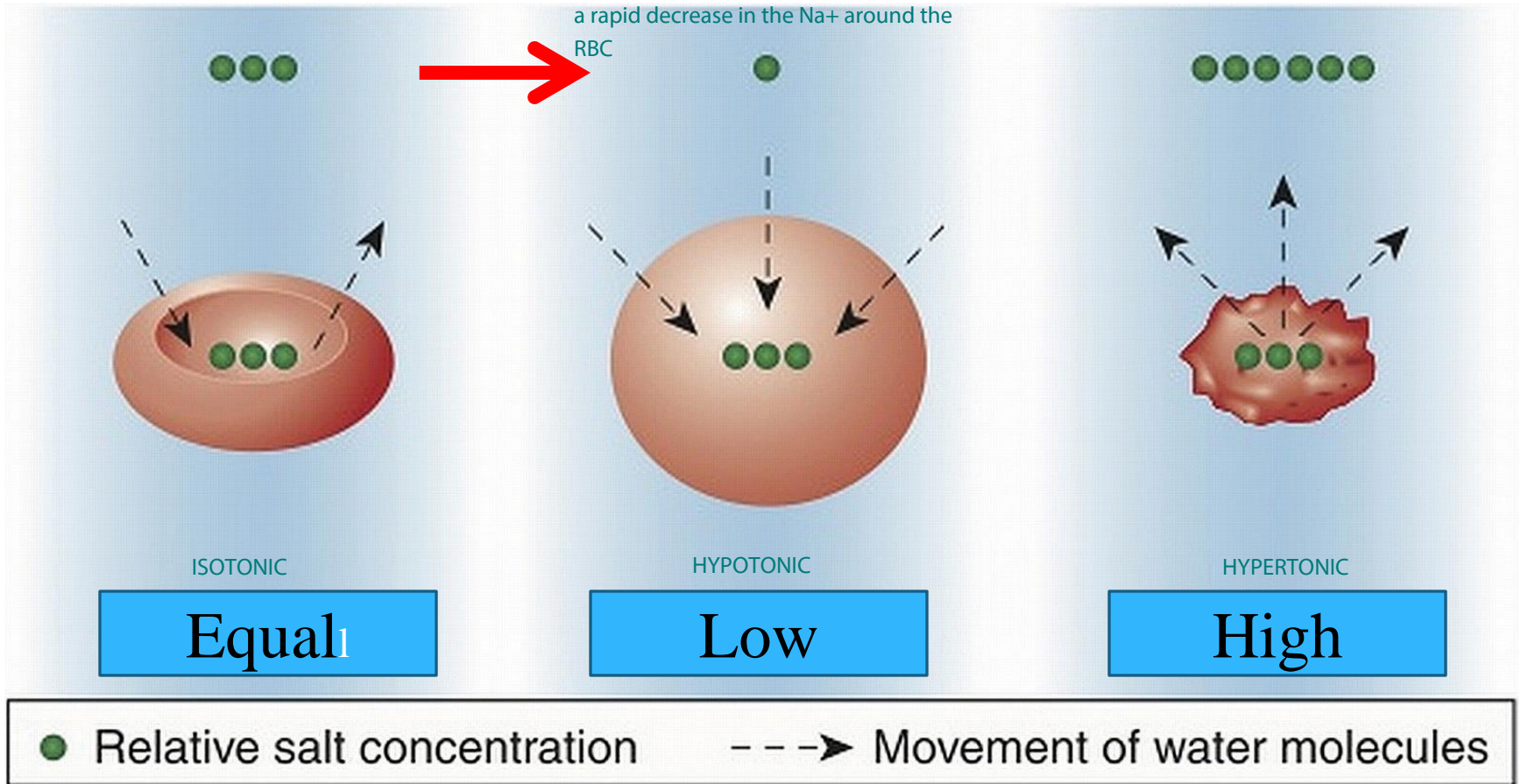
THIS IS WHAT HAPPENED IN THE MARATHON RUNNER - the brain cells are what can be greatly impacted by this action

Drink water

equilibrium! The solute concentration is equal

hydrated - dilue solute conc

RBC gets big and swell and lyse due to a rapid decrease in the Na⁺ around the RBC

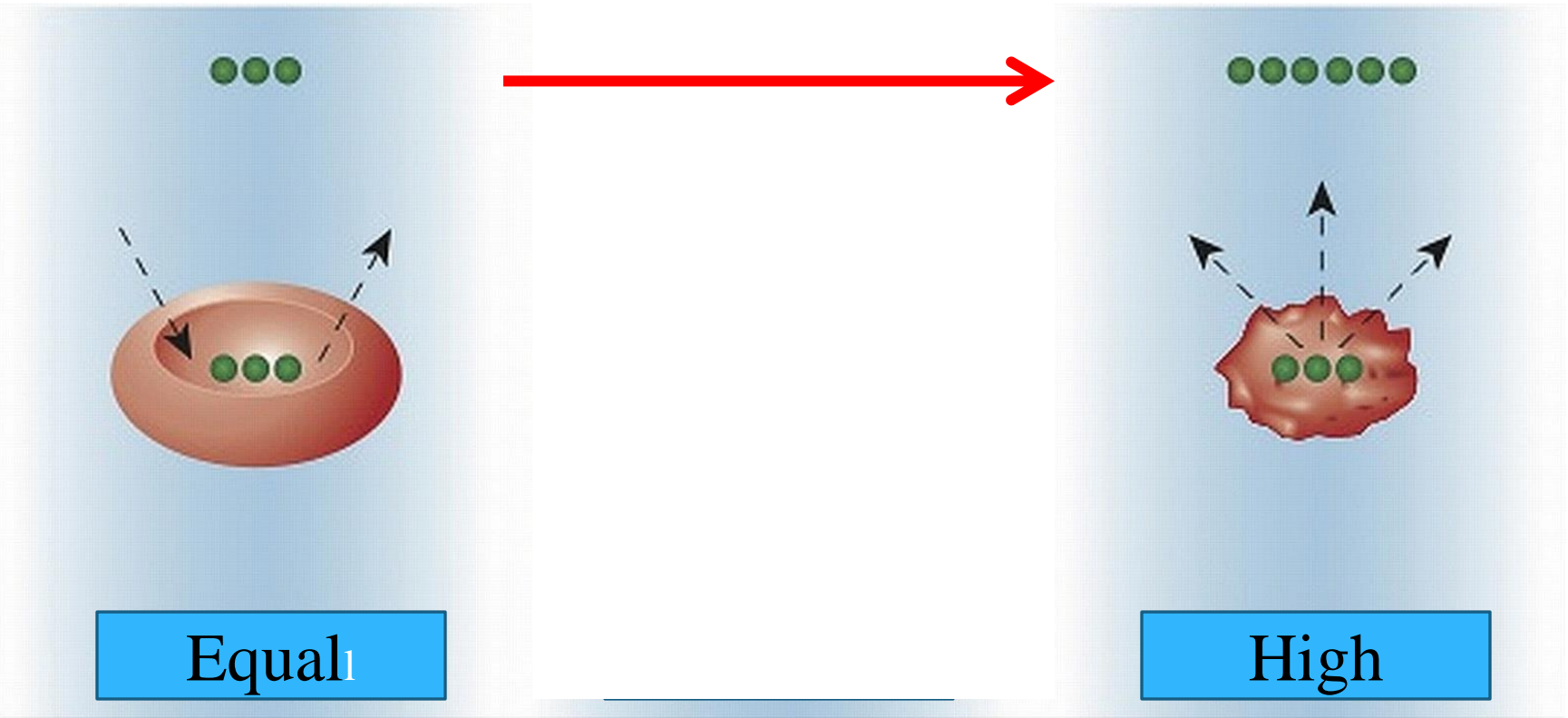


What happens to the ECF and ICF volumes if we eat salt (NaCl)?

- Increase in ECF sodium content and concentration
(**sodium stays in ECF**) stays outside the cell, if it got inside the cell it would be pumped out by the Na⁺/K⁺ ATPase
- This leads to an increase in ECF osmolality
- Water moves from ICF to ECF to equilibrate the solute conc cells cant tolerate a different in solute concentration due to being permeable to water
- There is a **decrease** in ICF volume and **increase** in ECF volume and **cells shrink** NOT WHAT HAPPENED IN THE RUNNER

Eat sodium

Added Na⁺ to the ECF, so osmolality increases outside and so water moves out and the cell shrinks
This is one of the ways the body has chosen to regulate water balance and how it tells the kidney to keep or get rid of water



● Relative salt concentration - - -> Movement of water molecules

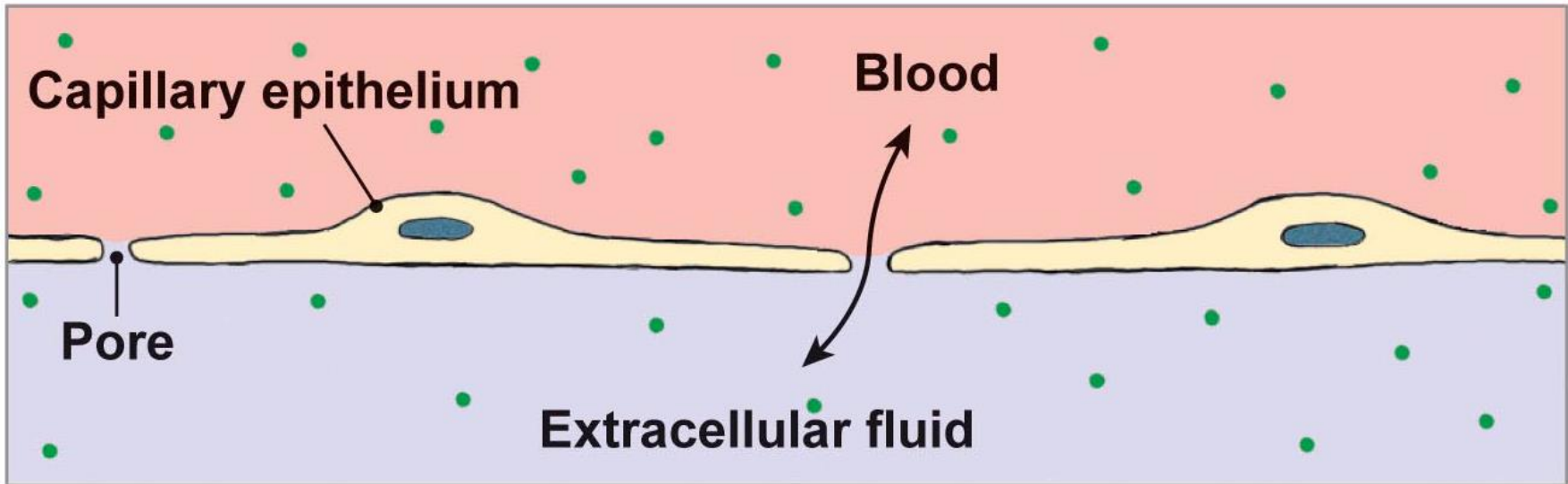
**To this point we have just considered
The ICF and the ECF ... which are
separated by a cell membrane**

What determines the movement of water between the interstitium and the plasma compartments?

Key differences: separated by a leaky water permeable capillary and two opposing physical forces

think about water exchange between vascular and ISF compartment

Capillary:



sodium is the same everywhere and so is the osmolality - so it doesnt govern movement of water

(a) Leaky exchange epithelium allows movement through gaps between the cells. Water moves across to equalize the concentrations of solutes in the plasma and interstitial space

ECF Compartments: Plasma Volume vs Interstitial Volume

- Water flux determined by Starling forces:

this pressure is in both capillary and the interstitium

- Hydrostatic pressure gradient heart generates this within the vascular compartment, to push water out of capillaries

this pressure is both in the capillary and interstitium

- Oncotic pressure gradient liver makes albumin which resides within the vascular compartment to create force to draw fluid in

due to diff in conc of large ass molecules

due to diff in conc of small molecules

(Oncotic pressure is an osmotic force due to charged proteins (mainly albumin))

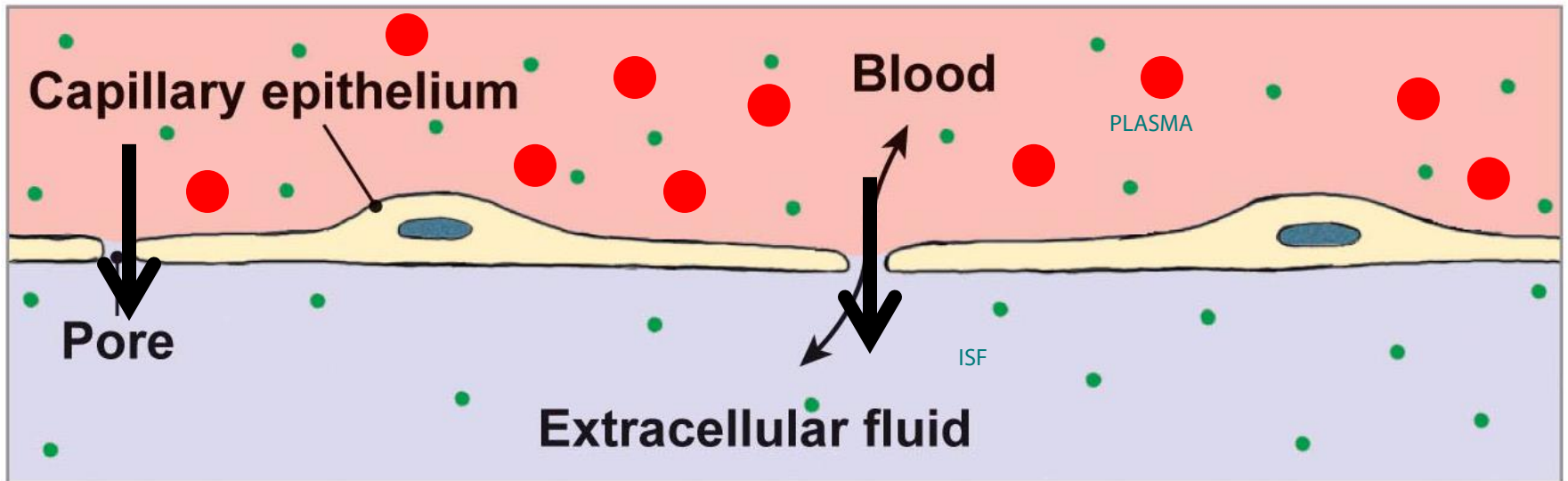
Albumin:

- The **main protein in plasma**: 40 g/L in plasma but low in the interstitium Albumin is restricted mainly to the plasma
- **Molecular weight of ~ 68,000** Large, unlike sodium
- **Capillaries have limited permeability to albumin** most albumin is within the capillaries to provide that oncotic pressure
- Provides **oncotic pressure** in **plasma > ISF**

Capillary Hydrostatic Pressure

pushes fluid out

RECALL THAT THIS IS GENERATED BY THE HEART!

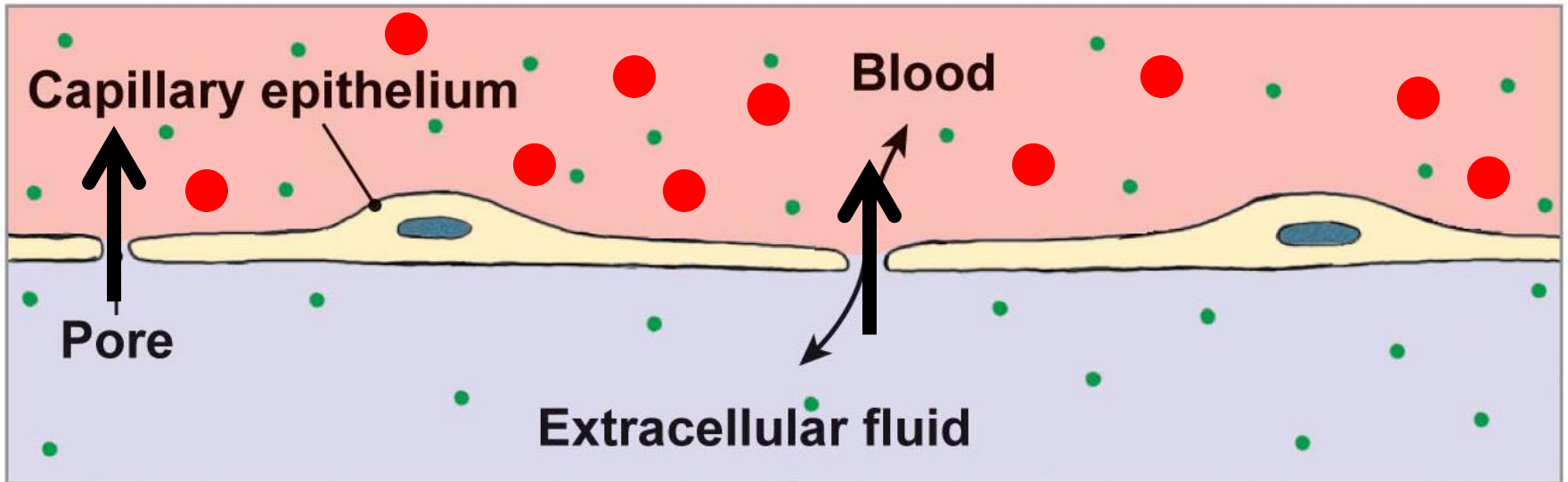


(a) Leaky exchange epithelium allows movement through gaps between the cells.

changes in starling forces aka the hydrostatic and oncotic pressure will influence the movement of water from the interstitium to the vascular compartment and vice versa.

Capillary Oncotic Pressure

pull fluid in



(a) Leaky exchange epithelium allows movement through gaps between the cells.

Copyright © 2009 Pearson Education, Inc.

This is why our fingers get crinkly when we have a bath., There is hydrostatic pressure on the interstitial compartment, pushing water into capillaries.

regulation of filtration of kidney require and depend on these starling forces

Fluid Movement Across Capillaries:

- Fluid flux = permeability x (^{generated by the heart} hydrostatic pressure gradient - oncotic pressure gradient)
generated by albumin synthesized by liver

- $J_v = K_f(\Delta P - \Delta\pi)$
filtration coefficient

- Hydrostatic pressure generated within capillaries
by pumping action of heart

2. Which of the following statements about Na K ATPase are correct?

Ubiquitously expressed in human cells.

Maintains high intracellular sodium concentrations and low intracellular potassium concentrations. opposite

Energy-requiring.

Establishes an osmotic gradient across cell membranes. due to aquaporins establishes different solute concentrations.

Contributes to movement of water out of the capillary compartment and into the interstitial compartment shift of water is due to Starling forces which is dependent on heart and liver function

Outline:

1. General comments
2. Fluid Compartments
3. Water permeability and Solutes
4. Movement of water between compartments
5. Clinical Aspects

Case of the Day: The Seizing Marathoner

A 45 year old woman runs her first marathon after 6 months training. Finished in 5 hours. Rehydrated with water

Complained of headache

symptoms are mostly neurological symptoms

as a result of increased electrical activity

Felt nauseated, vomited then had a seizure and taken to medical area

she overhydrated with water, which lowered the osmolality in the ECF, causing water to move into ICF of cells including the brain cells

Case of the Day: Seizing Marathon Runner

Severe, acute, ^{hyponatremia} **decrease in [sodium]** (122 mmole/L vs usually 140-150 mmole/L in the ECF) **the normal concentration of 140 mmol/L)** osmolality fell and so water moved into the cells including the brain cells swelling

Water **crosses cell membranes** from ECF to ICF

Brain cells swell, intracranial pressure rises –causes seizures, coma, death

brain is contained within a fixed volume due to the bony cranium.

Case of the Day: Seizing Marathon Runner:

Due to **excessive water intake** relative to losses if she breathed more and sweated more

Commonest in **women with slow pace** MORE TIME TO DRINK WATER average women has 2/3 of muscle mass of an average man less muscle you have, the greater the effect of water on osmolality

Treatment: rapid **intravenous infusion of a concentrated** high concentration **saline solution** to move water out of brain cells contain Na+

Na+ stays in the ECF and draws water outside the cells, her brain cells reduce in size and so decreases the intracranial pressure and her neurological function improves.

2-3 milli increments per litre

SUMMARY: Key Points

- TBW = 50-60% BODY WEIGHT: 2/3 ICF, 1/3 ECF

- RULES:

Sodium stays in ECF

Water crosses cell membranes (osmolality)

Plasma vs interstitial volume depends on the balance between oncotic pressure and hydrostatic pressure

For the next lecture ...

Text Book Links:

Anatomy: Pages 591-594

Filtration: Pages 596-602

Case of the Day: Kidney Disease

- **A 55 year old woman has a longstanding history of diabetes mellitus.**
- **Recently underwent a checkup**
- **Serum creatinine is 160 $\mu\text{mol/L}$ (normal value: 80 $\mu\text{mol/L}$)**
- **Found to have 500 mg of albumin in a 24 hour urine collection**

Is there a problem?