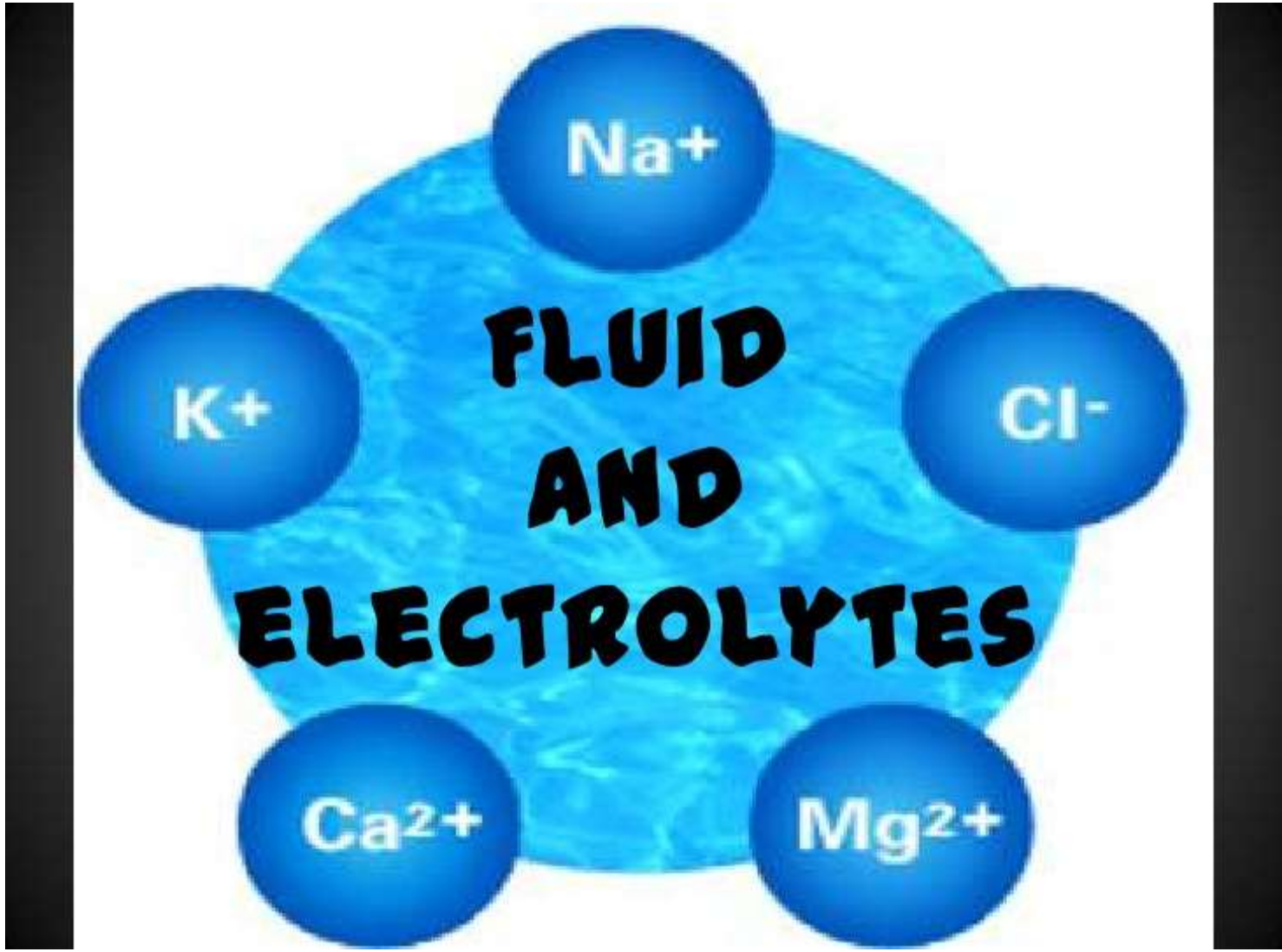
Sodium and Water Balance

February 2021



Objectives

01

Understand how water and Na+ are distributed in the body and how water follows solute.

02

Understand how intake, renal filtration, and renal reabsorption of Na+ determines Na+ balance and ECF volume.

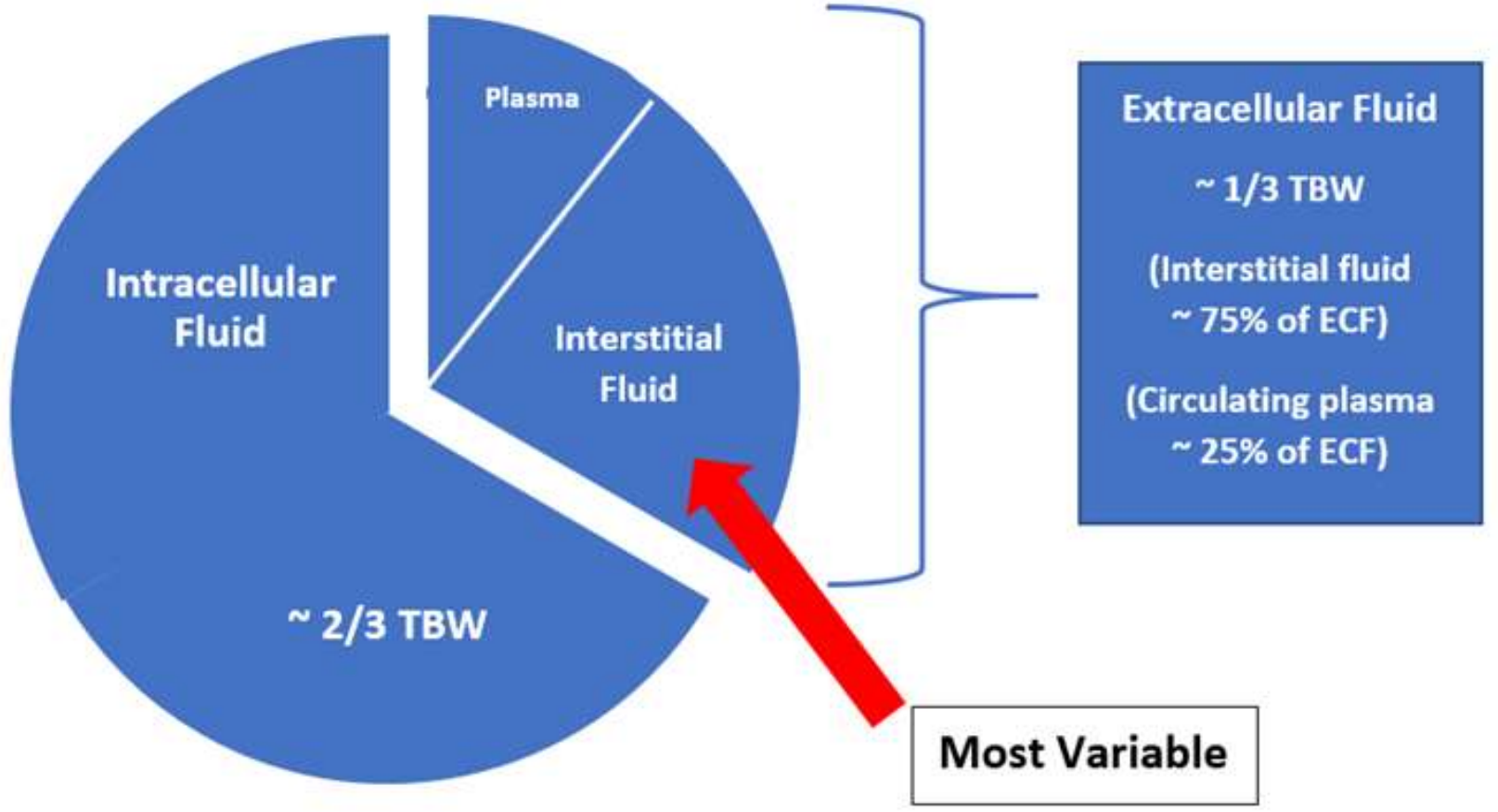
03

Understand how ADH mechanisms regulate free water balance.

04

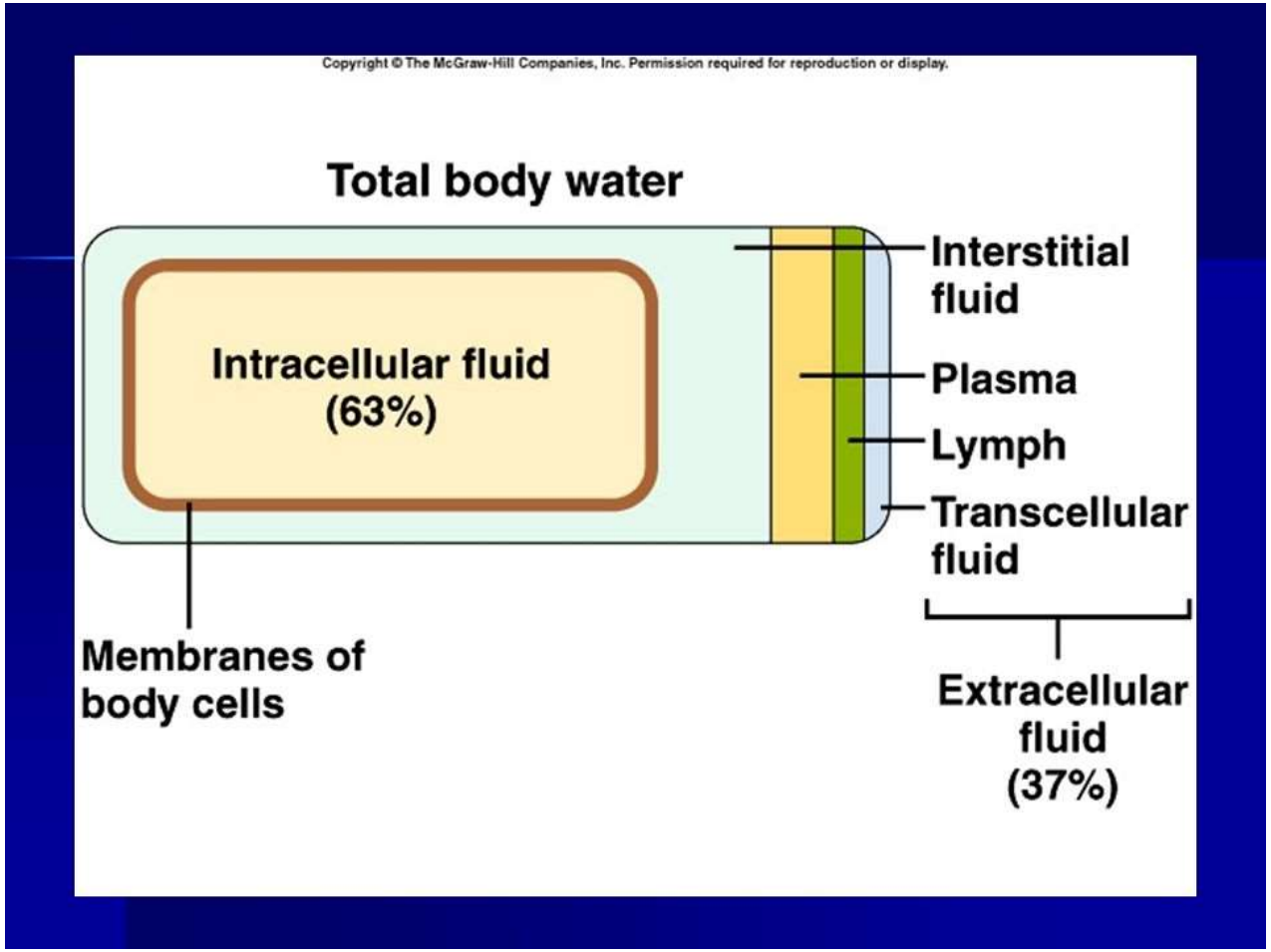
Interpret bedside and laboratory information to assess ECF volume and water balance.

Distribution of Total Body Water



Total Body Water Distribution- Another View

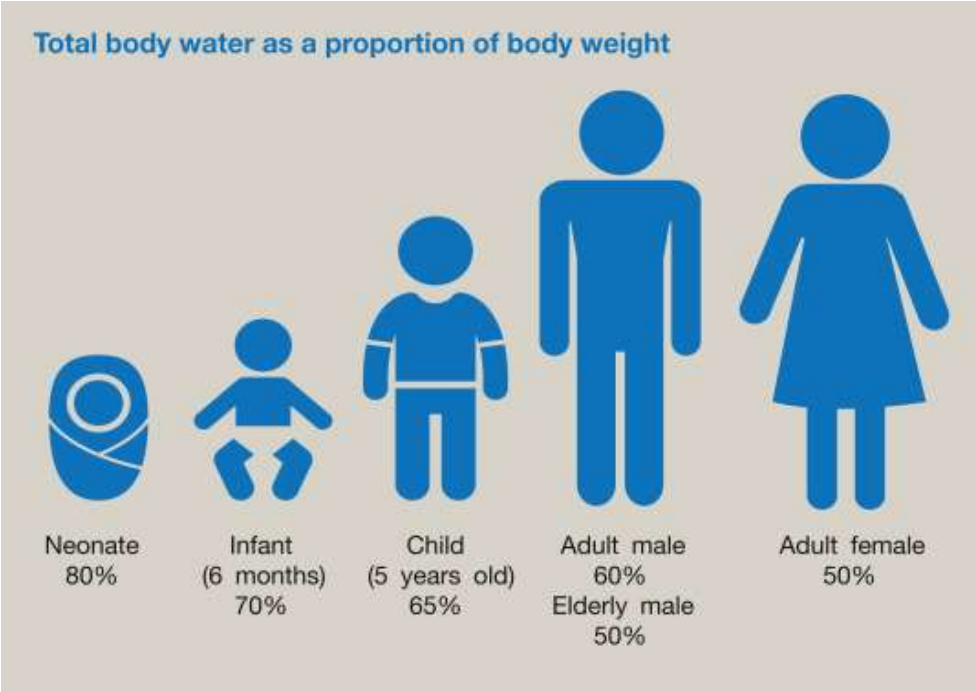
- **TBW= 0.5-0.6 L/kg**
- **ICF= ~2/3 TBW (63%)**
  - Regulated by osmolality
- **ECF= ~1/3 TBW (37%)**
  - Regulated by sodium balance
  - Interstitial Fluid= ¾ ECF
  - Intravascular Fluid (plasma)= ¼ ECF

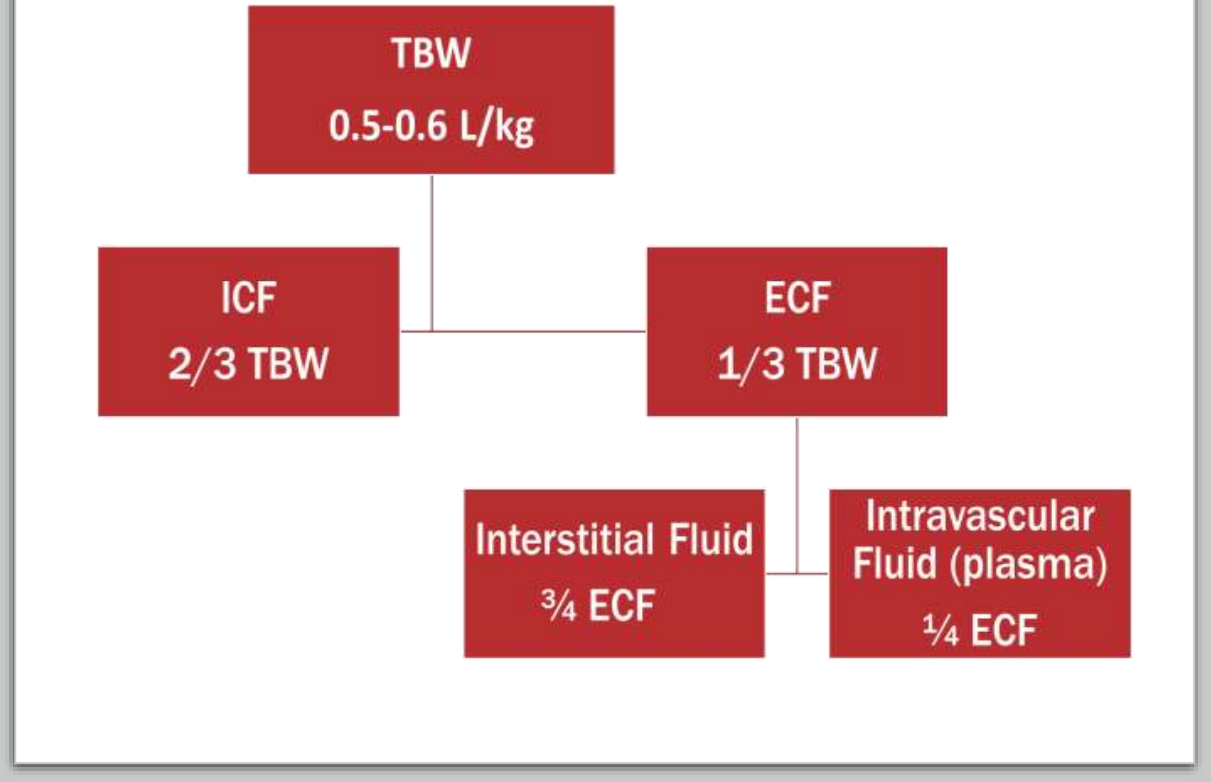


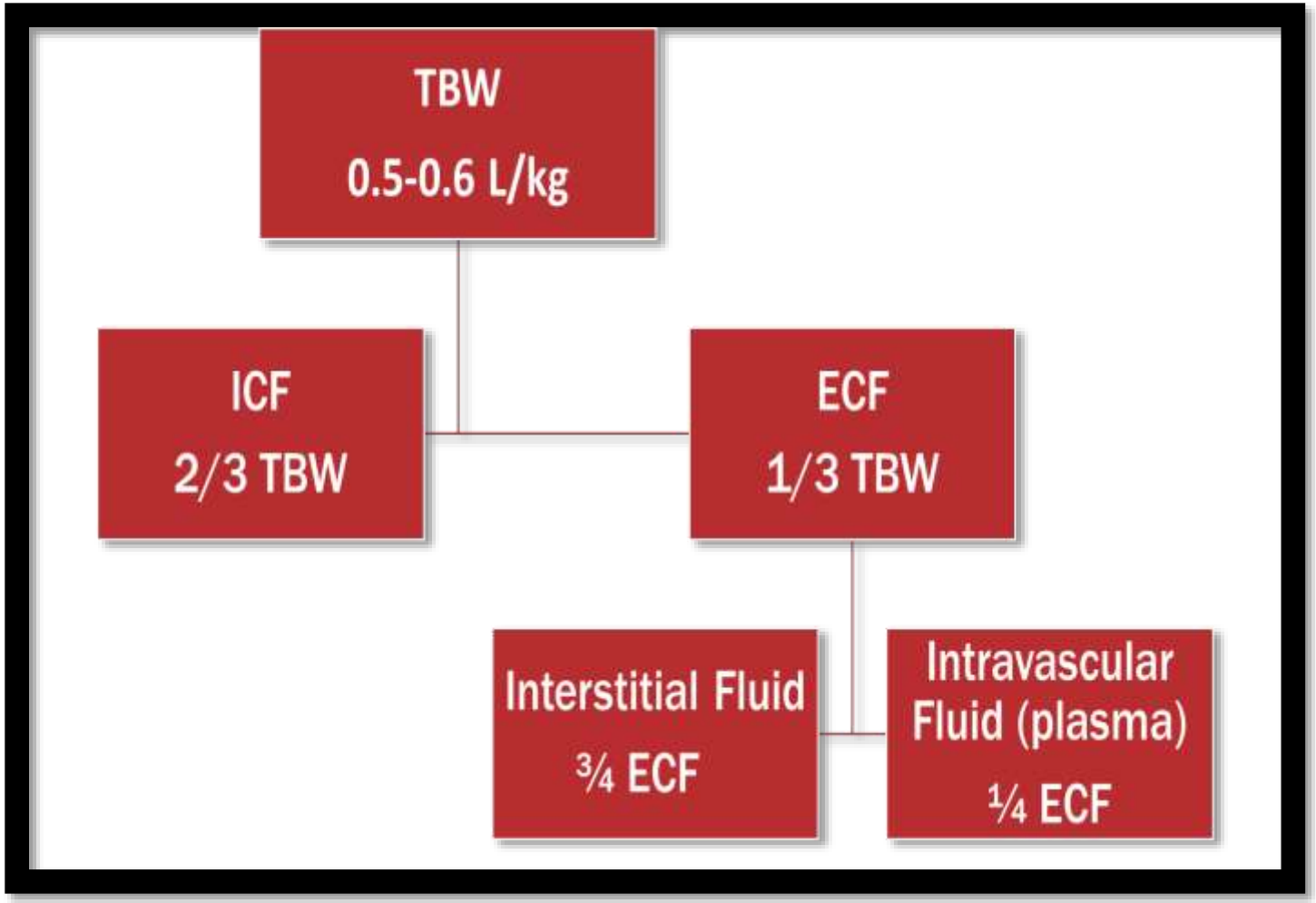
Clinical Correlates:

The estimated TBW in a physically fit 30 yo Caucasian female is 30.9L.

What is her estimated ICF and ECF volumes?







Clinical Correlates:

The estimated TBW in a physically fit 30 yo Caucasian female is 30.9L.

What is her estimated ICF and ECF volumes?

Answer:

ICF ~19.5L and ECF ~11.4 L

Homeostasis

- Water and electrolytes must be balanced to achieve homeostasis
- Water balance: total water intake = total water output
- Electrolyte balance: quantities of electrolytes gained = those lost
- When electrolyte concentrations are altered, water concentrations are also altered by adding or removing solutes.

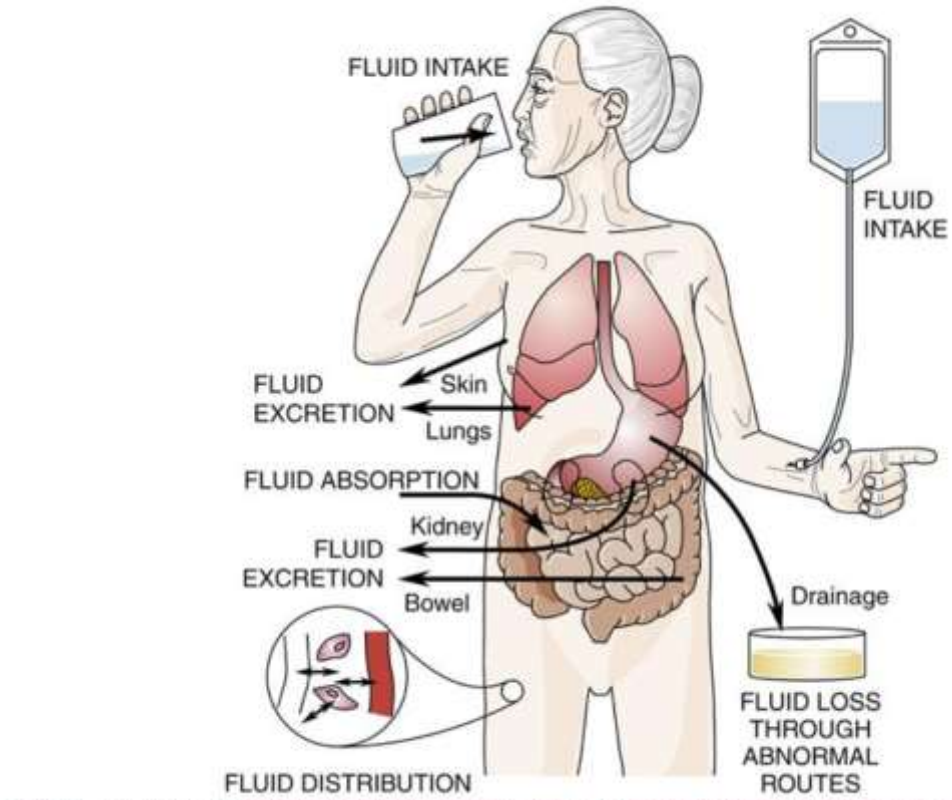
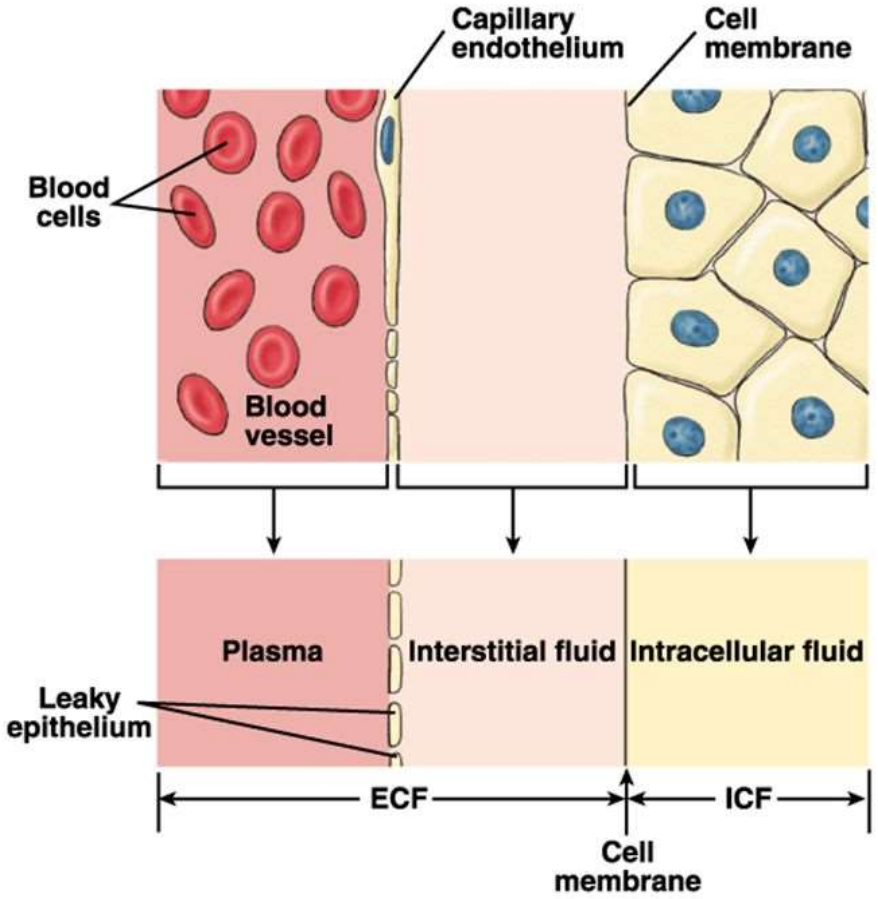
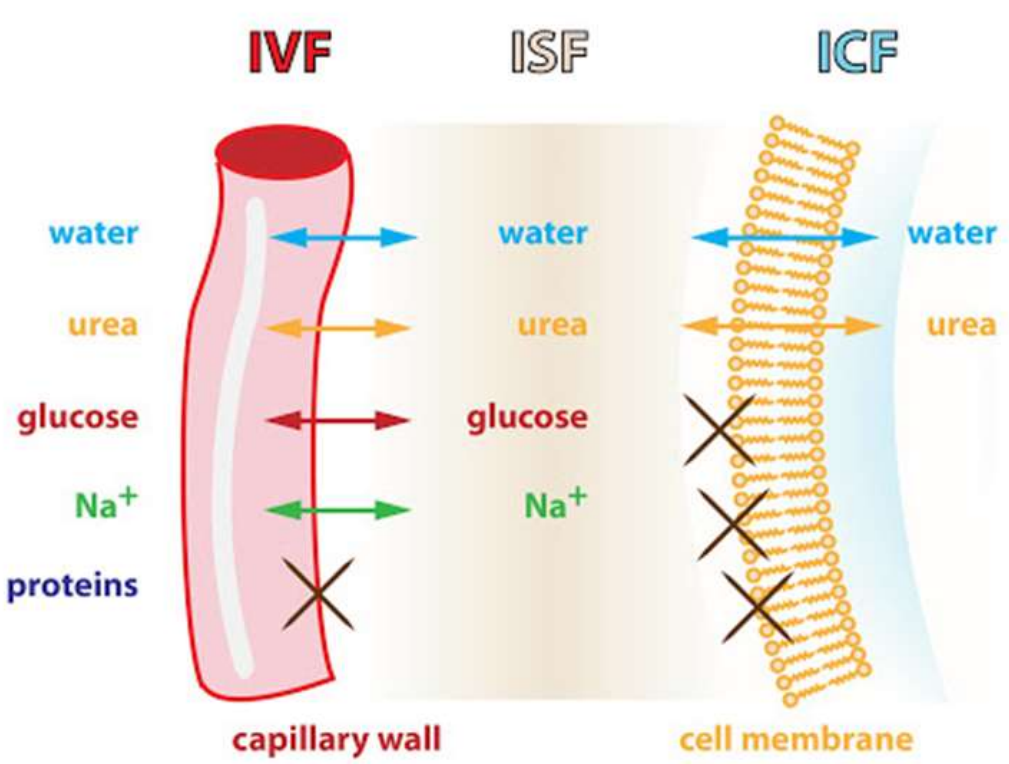


FIGURE 24-3 Fluid homeostasis. Fluid homeostasis is the interplay of fluid intake and absorption, fluid distribution, fluid excretion, and fluid loss through abnormal routes.

Chemistry and Physiology Refresher





Homeostasis-General Principles

1. ***Both blood volume and plasma osmolality are tightly regulated in the body.***

2. ***Osmolality ~ equal among plasma, interstitial fluid and intracellular fluid.***

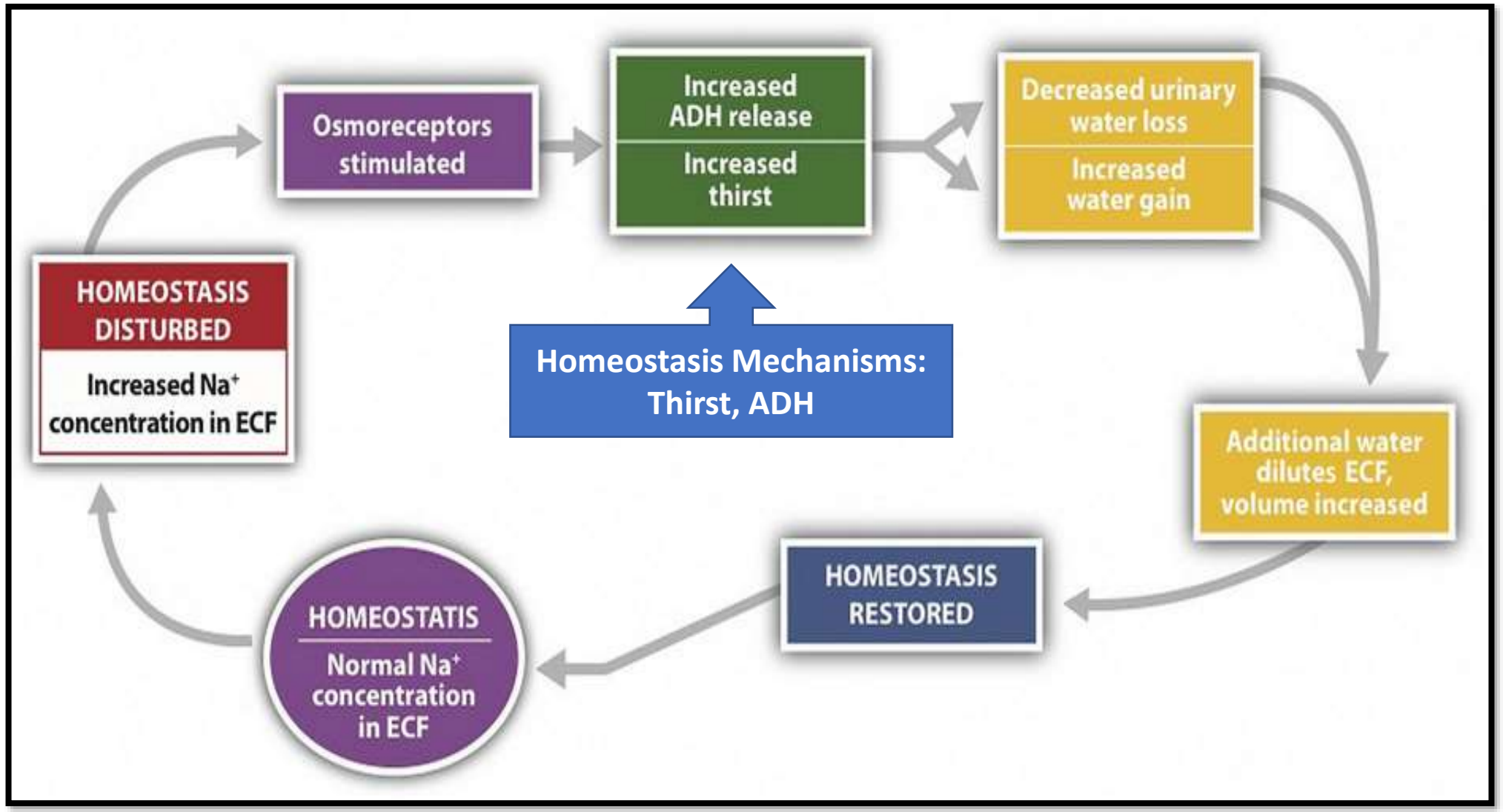
3. ***ICF volume is determined by plasma osmolality.***
   - Water exchange between ICF and ECF depends on osmotic gradients
     - Water moves from areas of low to higher solute concentration by diffusion (osmosis)
   - ***Osmolality is determined by solute concentration (sodium) in plasma!***

4. ***Water balance determines serum sodium concentration and sodium balance determines volume status.***
   - Homeostatic mechanisms that regulate *plasma (or ECF) volume* (RAAS) focus on controlling *sodium balance*
   - Homeostatic mechanisms that *control ICF volume* (thirst, ADH) focus on controlling osmolality (or *free water balance)*

General Principles: Water Balance

1. Daily water intake is maintained through thirst.
2. Water concentration (osmolality) is equal in all body fluids (except in the kidney).
   - 280-300 mOsm/kg
3. Water follows sodium (except in the kidneys).
   - Volume in a compartment will change with changes in sodium balance.
4. Serum Na+ concentration and osmolality are indicators of water balance relative to Na+.

Water Balance Continued

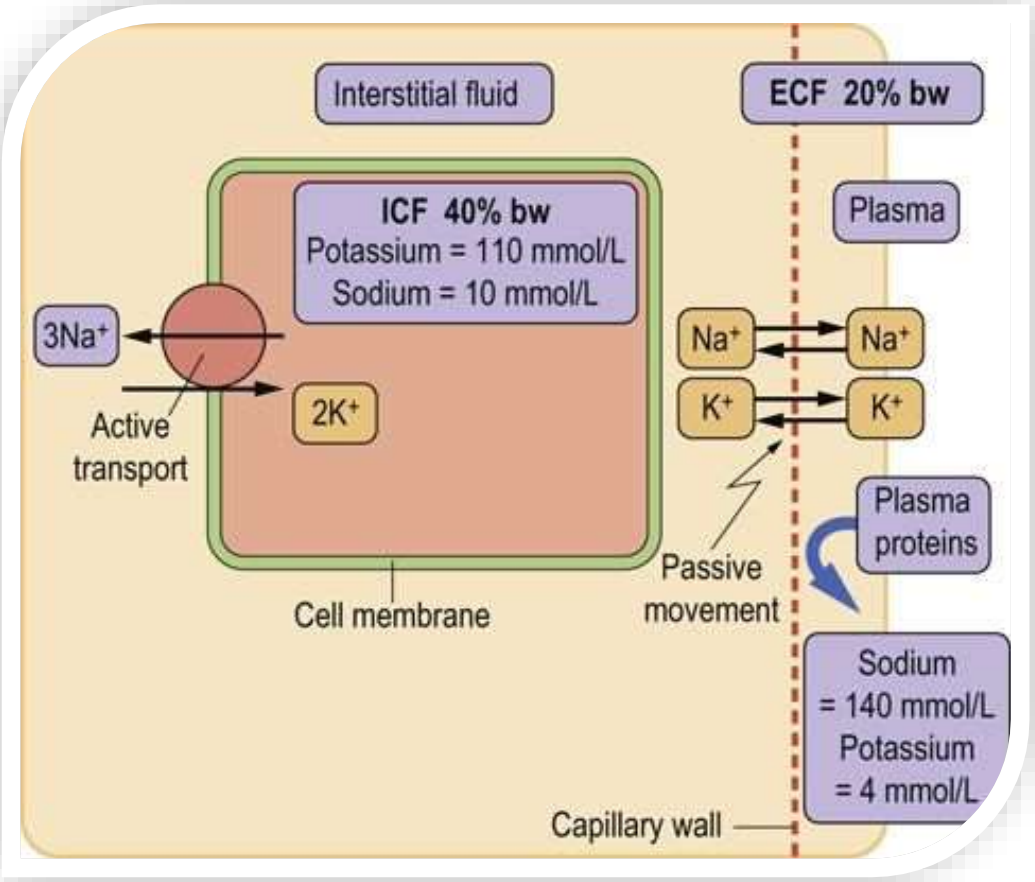


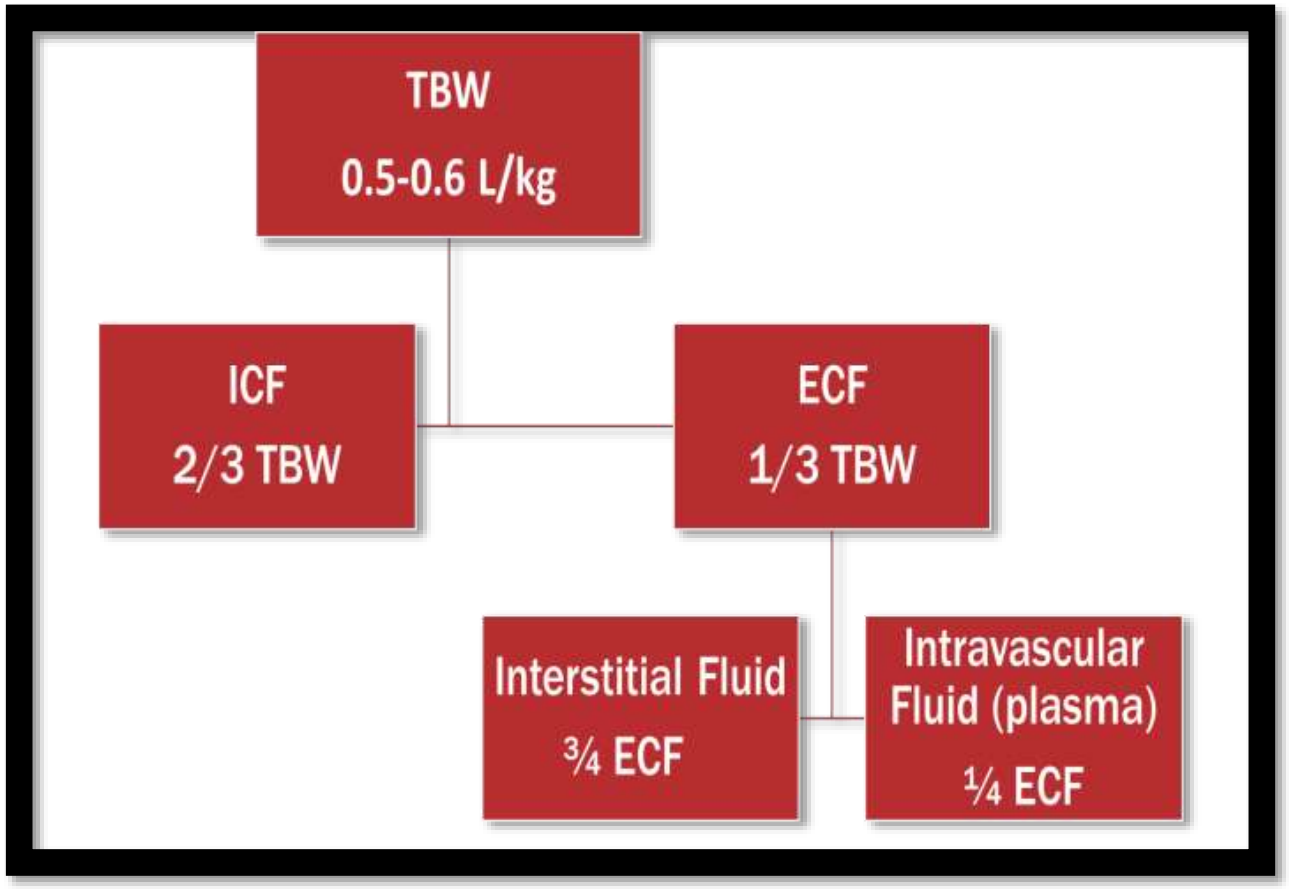
General Principles: Sodium Balance

1. **Sodium represents 90% of ECF solute and total osmolality of ECF**
   - ECF volume is regulated via Na+ balance
2. **Sodium serum concentration is tightly regulated- varies by NMT 2-3%**
   - Directly controlled by RAAS
   - Indirectly controlled by mechanisms that control blood volume and plasma osmolality (ADH, thirst)
3. **Normally daily excretion = daily intake**
   - Most adults in US have intake > 140 mEq/day (>3400 mg/day)
   - IOM (2013) recommended intake of 65-100 mEq/day (<2300 mg/day)
4. **Excretion is result of renal filtration and reabsorption**

Electrolytes: Plasma vs ICF

Ions	Plasma (mEq/L)	Intracellular (mEq/L)
Cations		
Sodium	142	12
Potassium	4.4	140
Ionized Calcium	2.5	4
Ionized Magnesium	1.1	34
Total Cations	**150**	**190**
Anions		
Chloride	104	4
Bicarbonate	24	12
Inorganic Phosphate	2	40
Proteins	14	50
Other Anions	6	84
Total Anions	**150**	**190**

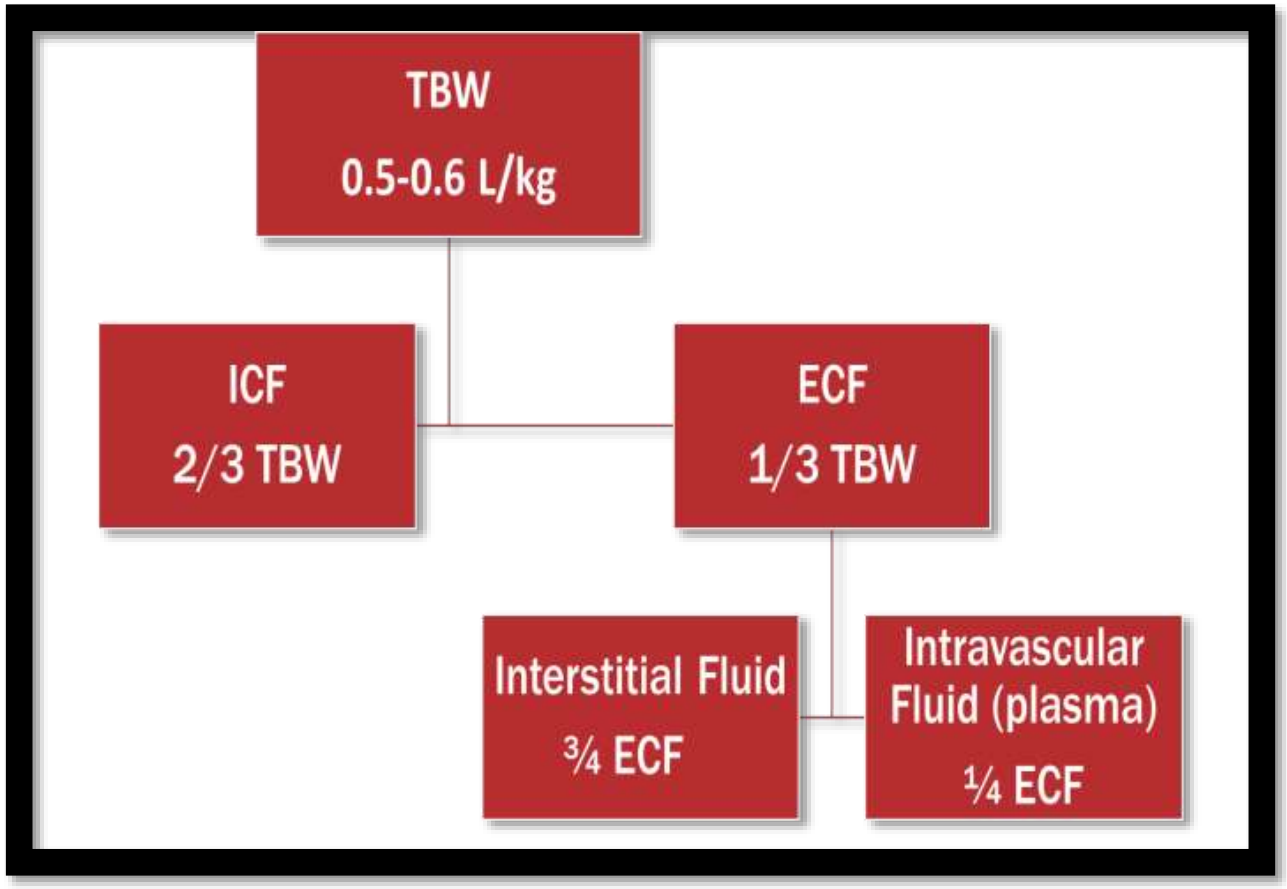




Clinical Correlates:

The estimated TBW in a physically fit 30 yo Caucasian female is 30.9L.

What is her estimated ICF and ECF distribution of body sodium and potassium?



Clinical Correlates:

The estimated TBW in a physically fit 30 yo Caucasian female is 30.9L.

What is her estimated ICF and ECF distribution of body sodium and potassium?

Answer:

ICF ~19.5L = Na+ ~ 230 mMol, K+ ~ 2700 mMol

ECF ~11.4 L = Na+ ~ 1600 mMol, K+ ~ 50 mMol

Objectives

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Sodium Reabsorption and Excretion

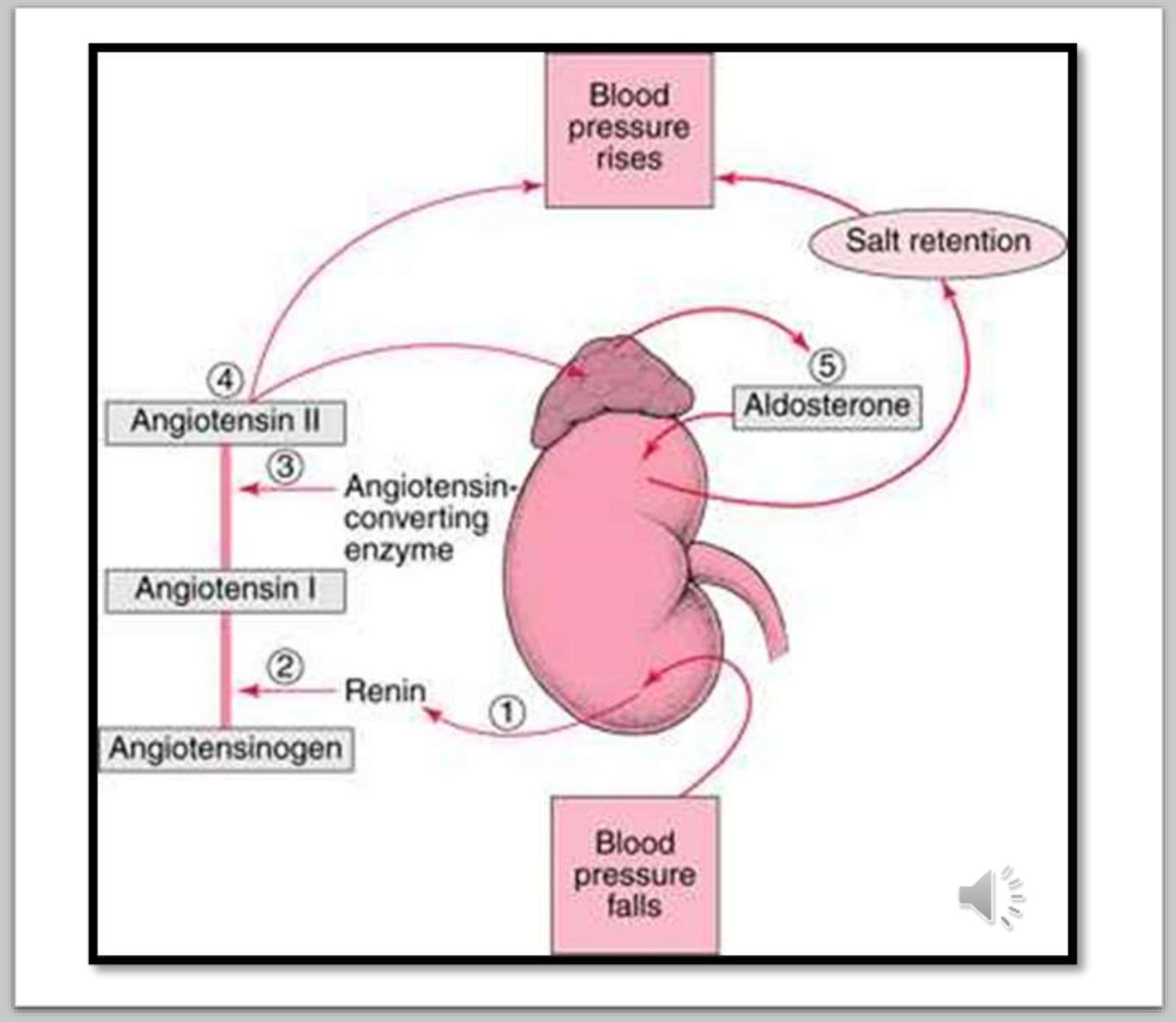
- **Glomerular filtrate rate** –
  - % of filtered sodium reabsorbed remains constant.
  - Change in GFR will result in proportional change in Na+ excretion.
    - Renal blood flow
    - Renal function
  - Example: reduced renal perfusion causes reduced GFR, leading to reduced Na+ excretion.

Daily Work Performed by Kidneys with GFR = 100 ml/min

Substance	Filtered	Excreted	% Reabsorbed
Water	180 L	0.5-3 L	98-99
Sodium	26,000 mMol	100-250 mMol	> 99
Chloride	21,000 mMol	100-250 mMol	> 99
Bicarbonate	4800 mMol	0	100
Potassium	800 mMol	40-120 mMol	85-95
Urea	54 g	27-32 g	40-50

Anatomic Distribution and Determinants of NaCl Reabsorption

Tubule Segment	% NaCl Reabsorbed	Determinants of Reabsorption
Proximal Tubule	70	Na/H exchange (carbonic anhydrase) Na/Glucose cotransport AT II Norepinephrine (β1) Peritubular capillaries
Loop of Henle	20	Flow-Dependent (Na/K/Cl transporter)
Distal Tubule	5	Flow-Dependent (Na/Cl transporter)
Collecting Tubule	4	Aldosterone (+) Natriuretic Peptide (-) (Na/K ATPase and apical Na Channels)

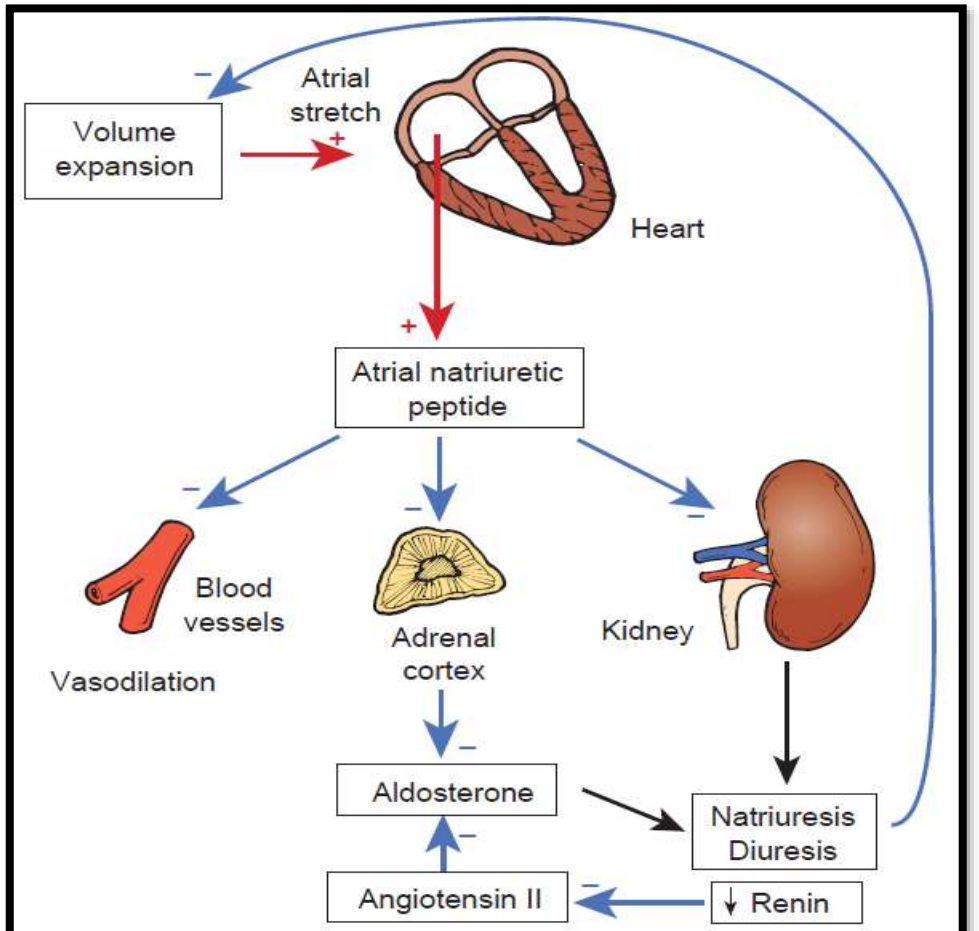


Sodium Reabsorption and Excretion Continued

- **Renin Angiotensin Aldosterone System (RAAS)**
  - Decrease renal perfusion or BP will cause renin release and produce ATII
  - AT II increases aldosterone secretion and increases Na+ reabsorption in proximal tubule
  - Aldosterone increases Na+ in exchange for potassium in collecting tubule and collecting duct
  - Decrease renin: AT II, Na+, increase renal perfusion

Sodium Reabsorption and Excretion Continued

- **Natriuretic Peptides**
  - 3 types (A,B,C)- secretion associated with pressures and volumes in circulation
  - Vasodilation, natriuresis, diuresis, increase GFR, decrease RAAS
  - Roles in Na and blood pressure homeostasis
  - Associated drugs:
    - Nesiritide- recombinant type B; vasodilator
    - Sacubitril- inhibits neprilysin degradation of natriuretic peptides



Atrial natriuretic peptide (ANP) and its actions. ANP release from the cardiac atria is stimulated by blood volume expansion, which stretches the atria. ANP produces effects that bring blood volume back toward normal, such as increased Na^+ excretion.

Source : Medical physiology - principles for clinical medicine, Rodney A. Rhoades

Anatomic Distribution and Determinants of NaCl Reabsorption- Drug Targets

Tubule Segment	% NaCl Reabsorbed	Determinants of Reabsorption
Proximal Tubule	70	Na/H exchange (carbonic anhydrase) **Na/Glucose cotransport** **AT II** **Norepinephrine (β1)** Peritubular capillaries
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Collecting Tubule	4	**Aldosterone (+)** **Natriuretic Peptide (-)** (Na/K ATPase and apical Na Channels)

CA Inh

SGLT-2 Inh

ACEI
ARB
BB

Loop diuretics

Thiazide diuretics

Spironolactone

Neprilysin inhibitor

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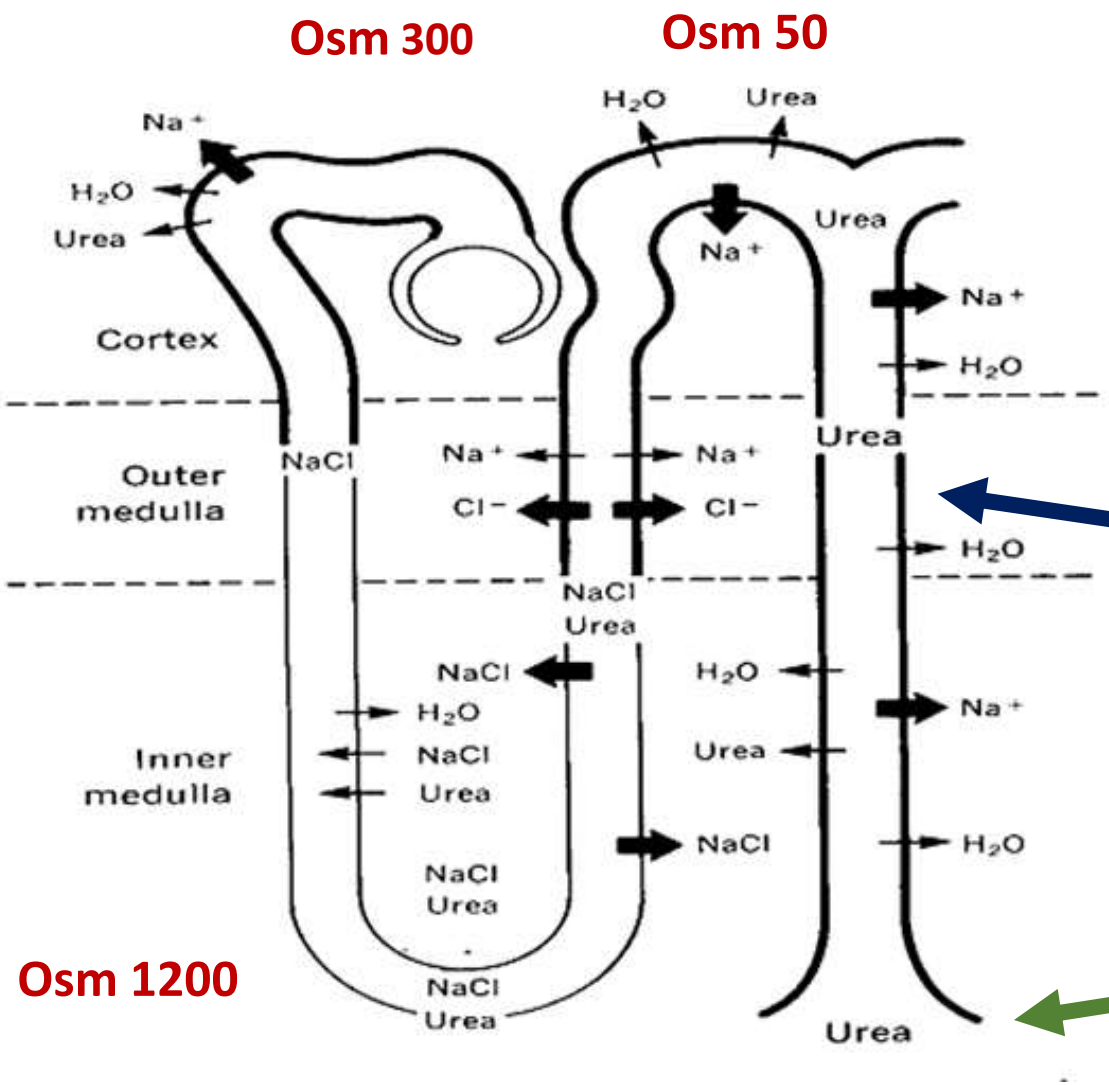
The Urinary Concentrating Mechanism

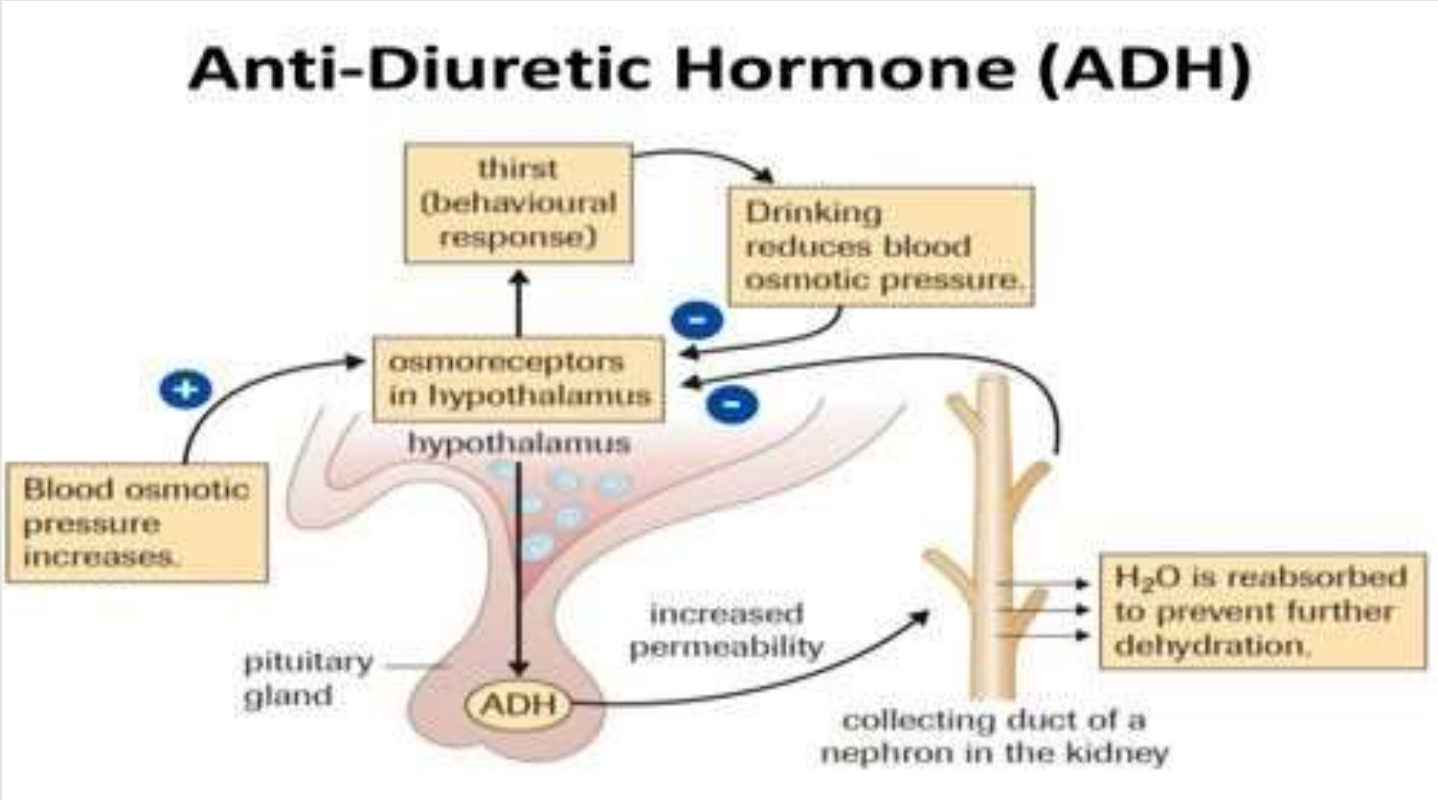


The kidneys can separate solute and water; therefore, water does not follow sodium (free water)!

ADH-dependent permeability to water

Urine volume 25-900 mL/hr

Vasopressin (ADH)



- ADH activates vasopressin V_2 receptors on renal collecting tubules
  - Causes insertion of aquaporin-2 water channels
  - Makes collecting tubules water-permeable, allowing reabsorption
- Water channels removed quickly in absence of vasopressin
- Water balance (via ADH) is adjusted by kidneys to match Na+ balance, maintaining normal osmolality

Stimuli of ADH Secretion

Osmotic

- Osmolality is the primary stimulus for ADH secretion under normal conditions; minimal ADH secretion at Osm < 280, and maximal antidiuresis at Osm > 295

Non-osmotic

- Reduced circulating volume or blood pressure
- Pain; nausea; acute psychosis; hyperthermia; hypoxia
- Drugs: barbiturates, carbamazepine, nicotine, opiates, chemo (cyclophosphamide, vincristine, vinblastine), general anesthesia
- Stimulation of RAAS

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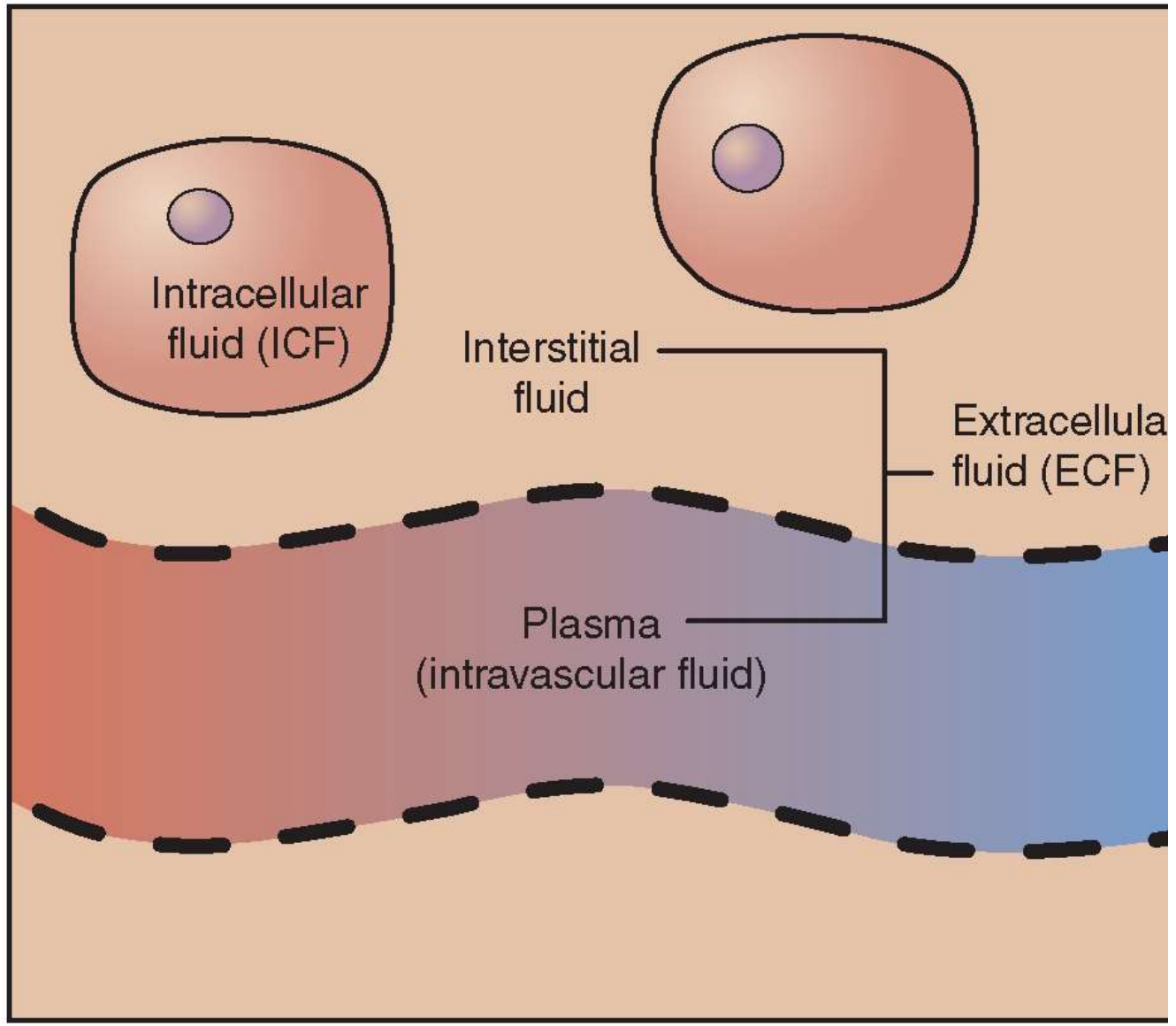
Assessment of Body Fluids

I. Total Body Water

~~II. ICF Volume~~

III. ECF Volume
   A. Interstitial fluid
   B. Intravascular fluid

IV. Free water balance

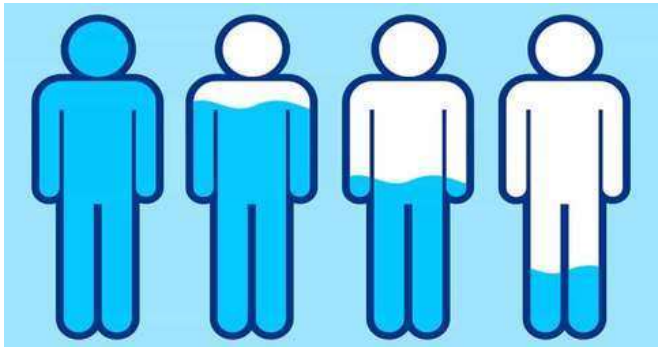


I. Total Body Water

- Body weight changes
  - Changes in total body water (1 liter water ~ 1 Kg)
  - Most sensitive and quantitative measure of short-term fluid imbalance
- Documented I/O
  - Ideally, I=O over 24 hours
  - Intake examples: IV fluids, oral intake, enteral feedings, blood product transfusions
  - Output examples: urine (foley catheter), diarrhea, emesis, wound drainage, gastric contents suctioned, blood loss

III. Extracellular Fluid Volume

- ***ECF status assessed mostly by physical exam***
- Physical findings are not very sensitive
  - An adult may have up to +/- 3 liters changes in ECF without noticeable physical findings
- ***Changes in weight generally reflect changes in ECF if there are no changes in osmolality***
- Hypovolemic, hypervolemic, euvolemic
- Two compartments:
  A. Interstitial fluid
  B. Intravascular fluid

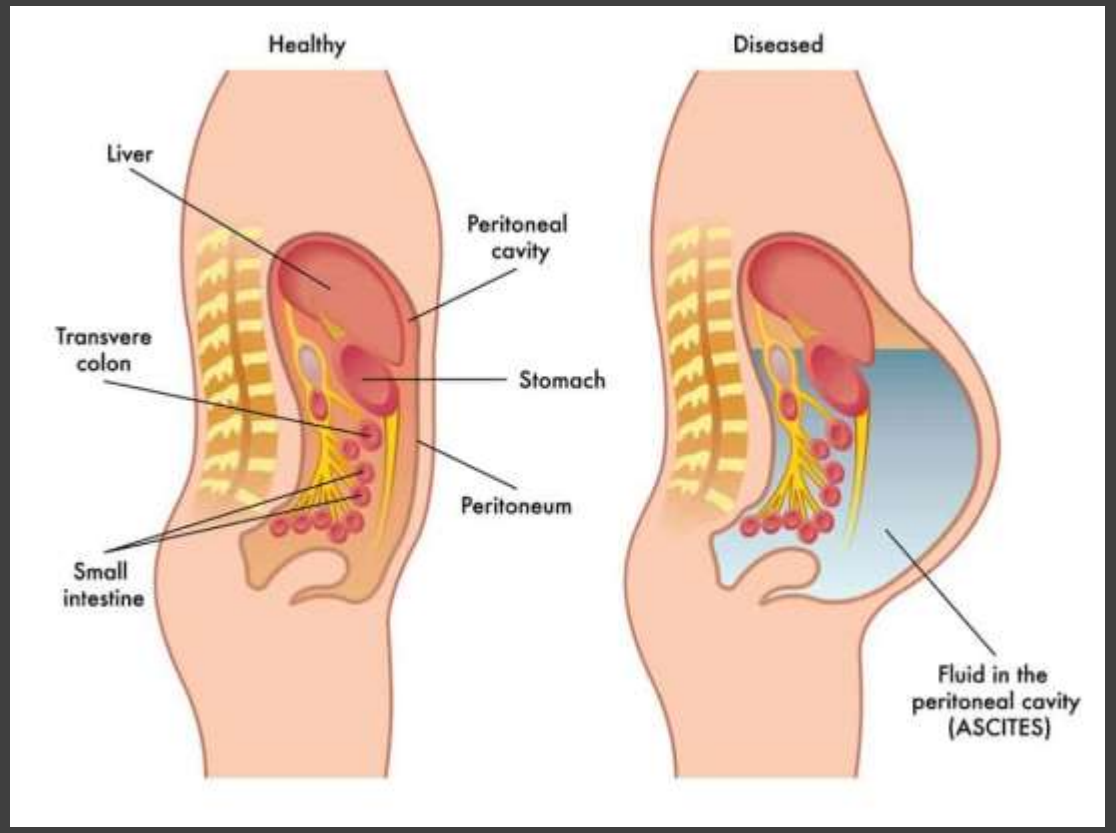


Volume Status

- **Hypovolemia**- defined as an ECF deficit
  - May occur as decrease in water volume with/without electrolyte deficiency
  - Chemical abnormalities reveal ***hypernatremia*** and ***hyper-osmolality***
  - S/sx of ***dehydration:*** thirst, dizziness, postural hypotension (orthostasis), tachycardia
  - Causes: environmental temperatures, vomiting, diarrhea, reduced sodium intake, and medications.
  - Treatment: replace water with goal of regaining sodium homeostasis and serum osmolality.

Volume Status Continued

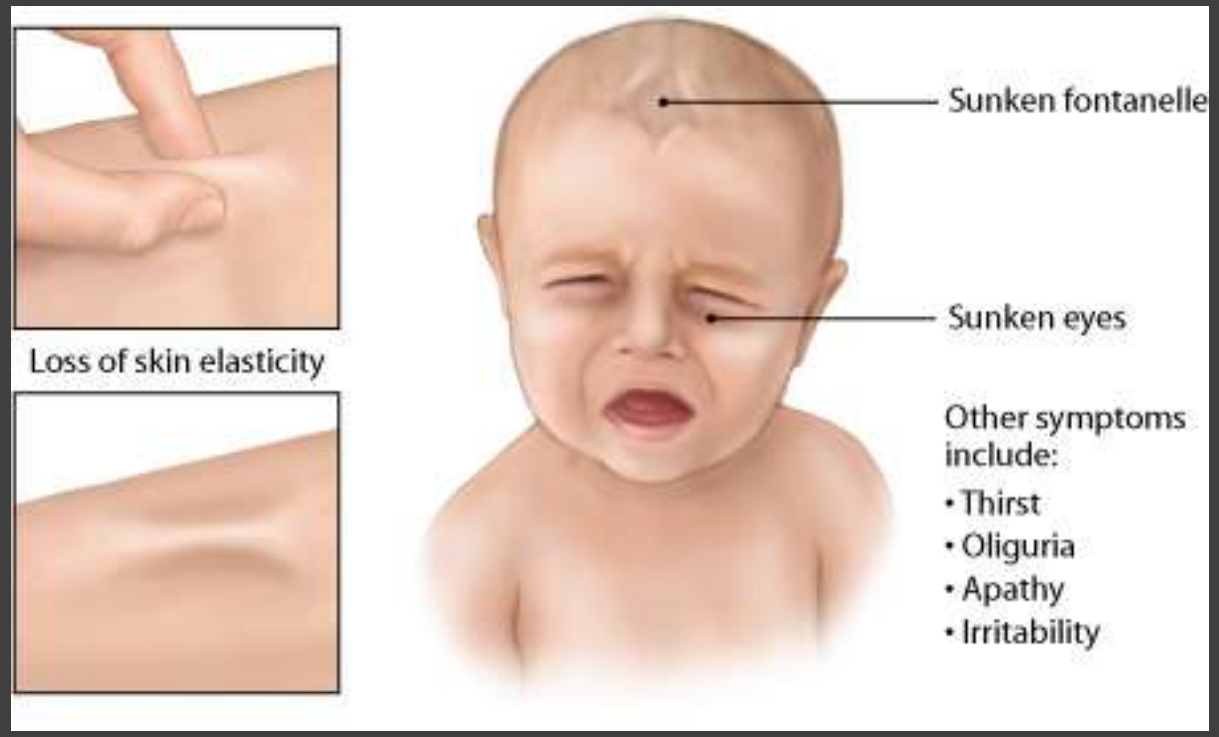
- **Hypervolemia**- defined as ECF volume expansion
  - May occur due to altered renal function, excessive fluid administration, or fluid shift from interstitial to intravascular compartments
  - S/Sx: see next slides
  - Chemical abnormalities: ***hyponatremia*** and ***hypo-osmolality***
  - Treatment: sodium and/or fluid restriction, diuretics
    - ***Usually safe to remove 0.5-1 kg/day of excess ECF***



A. Interstitial Fluid (Extravascular)

Indicators of ***increased*** interstitial fluid:

- Periphery- pitting edema
- Lungs- dyspnea, orthopnea, crackles (rales)
- Abdomen- ascites (or 3rd space fluid)



A. Interstitial Fluid Continued

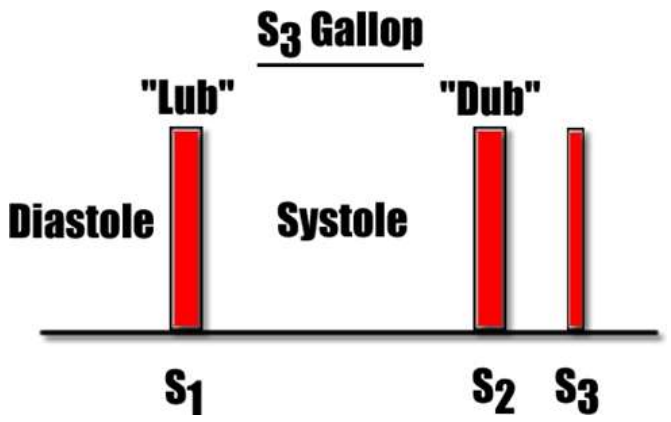
Indicators of ***decreased*** interstitial fluid:

- Skin- decreased turgor, dry axilla
- Oral- dry mucous membranes, fissured (furrowed) tongue
- Sunken eyes, anterior fontanelle

B. Intravascular Fluid Status

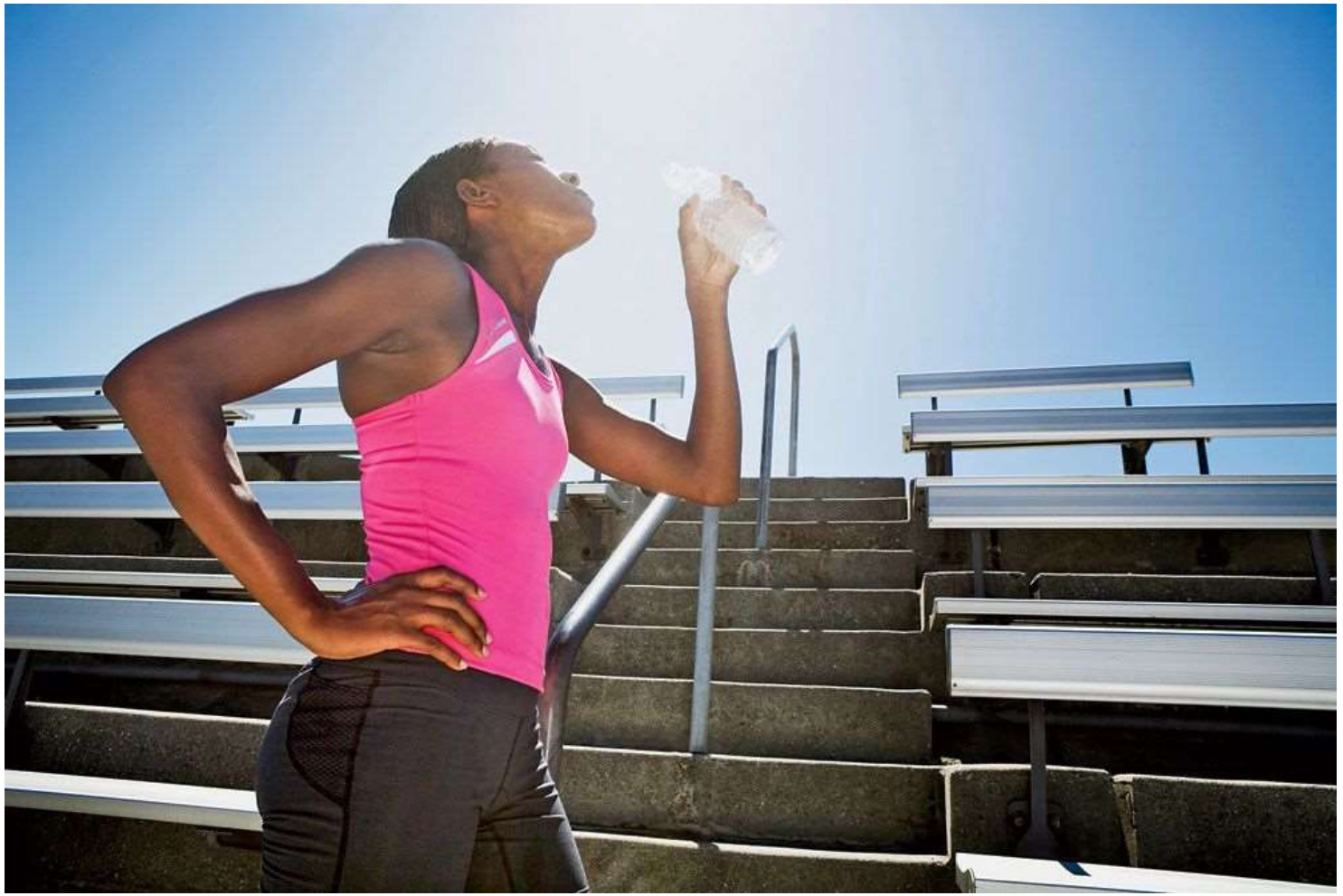
Increased intravascular volume

1. **Increased venous volume/venous return**
   - **Increased CVP**- filling pressure of the right ventricle
     - Normally 1-9 mmHg
   - Jugular venous distension, hepato-jugular reflux
2. **Increased left ventricular filling pressure**
   - S3 heart sound



Key Points: Monitoring Sodium and Water Balance

- Physical findings help to evaluate volume status of ECF compartment
- Status of body sodium is determined from clinical assessment of ECF volume
  - 1 kg = 1 liter ECF
  - 1 liter ECF represents ~ 140 mMol of Na+
- Serum sodium concentration and plasma osmolality are indicators of water balance (or free water)



Sodium and Water Balance

Thank you!

Patient Case Example

- 73 yo male with complaints of SOB, orthopnea, and pitting edema on his legs. He reports a recent weight gain of 5 kg.
- On physical exam, he has a positive hepato-jugular reflux and a S3 heart sound.
- Labs reveal serum sodium of 140 mMol/liter
- Questions:
  - What is this patient's ECF status? Hypovolemic, euvolemic, or hypervolemic
  - What is this patient's total body sodium status? Decreased, normal, or increased

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  - What is this patient's total body sodium status? Decreased, normal, or **increased**

Treatment Strategy

- Based on 5 kg weight gain, he has an excess of ~ 5 liters ECF, containing ~ 700 mMol sodium
- Usually safe to remove excess ECF by 0.5-1 kg/day
- Therefore, he needs to excrete 70-140 mMol sodium/day MORE than his intake
- Treatment Strategies include:
  - Reduce dietary sodium intake
  - Begin diuretic therapy, titrating dose to achieve weight loss
  - Monitor for signs of over-diuresis (orthostasis)