Lectures 21,22

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Medicine Team
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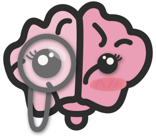

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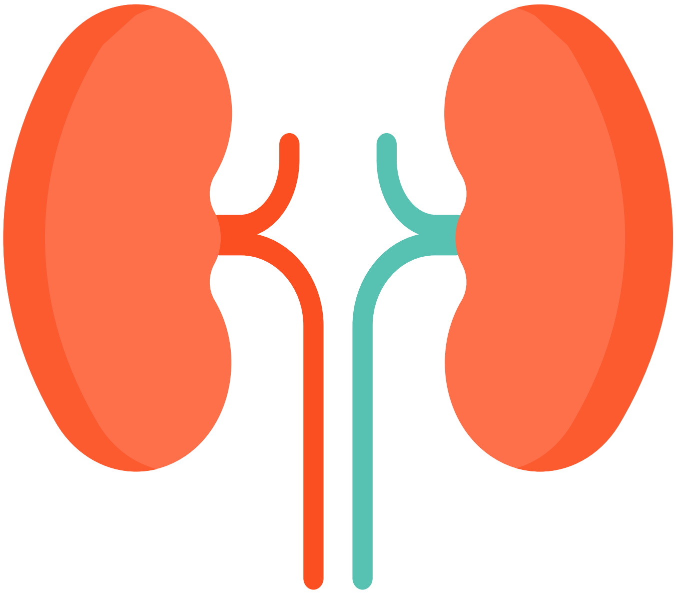


Na & water balance

Objectives:

- Composition of the fluid compartments
- Mechanisms regulating fluid and sodium balance
- Disorders of sodium balance
- Disorders of water balance
- Recognize the systems that control body sodium and water contents
- Differentiate between total body sodium content (volume status) and serum sodium
- concentration (Hypo- and Hypernatremia)
- Use the appropriate type of IV fluids in clinical practice
- Calculate the water deficit in Hypernatremia
- Explain the workup of Hyponatremia

Color index:

Original text Females slides Males slides
Doctor’s notes Text book Important Golden notes Extra

Basic information

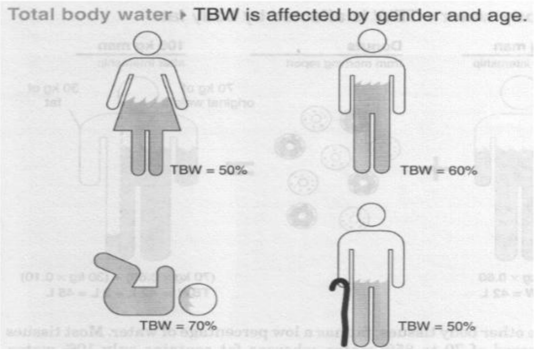
Homeostasis

- Homeostasis, any self-regulating process by which biological systems tend to maintain stability while adjusting to conditions that are optimal for survival.
- If homeostasis is successful, life continues; if unsuccessful, disaster or death ensues.
- The stability attained is actually a dynamic equilibrium, in which continuous change occurs yet relatively uniform conditions prevail.
- A relative constancy in the internal environment of the body, naturally maintained by adaptive responses that promote cell function and survival.

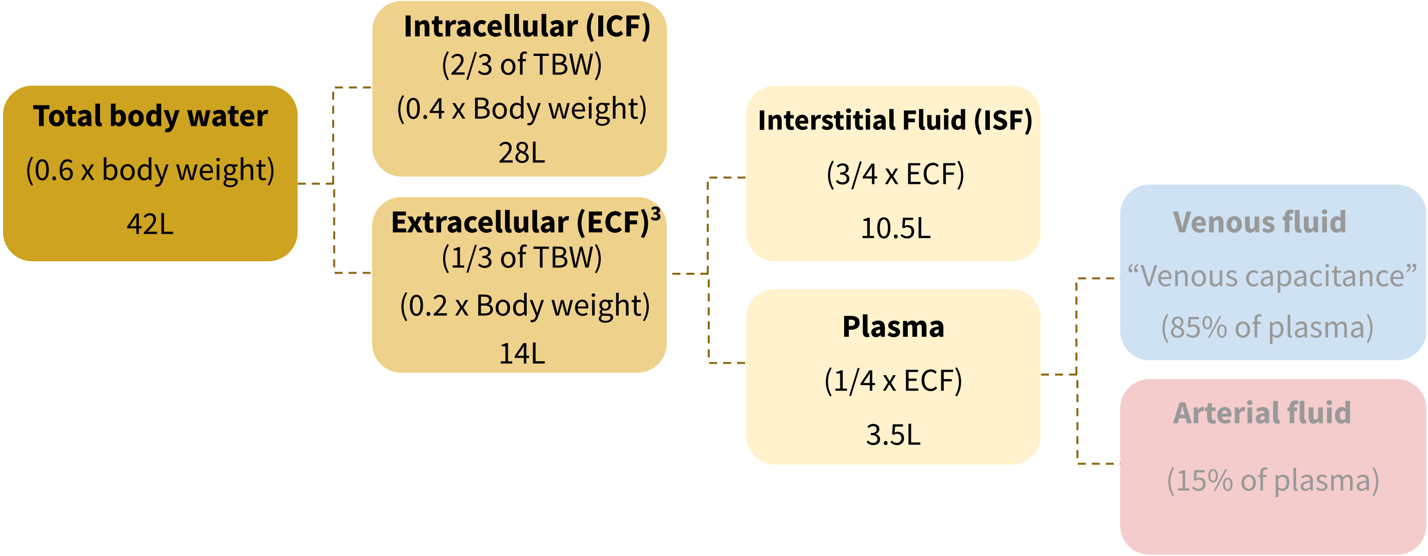
Total Body Water

➔ **Normal TBW[1]:**
  - Men: 60% of body weight
  - Women: 50% of body weight
  - Pediatrics: 70% of body weight
  - Geriatrics: 50% of body weight

➔ **what effects TBW?**
  - **TBW** ↓ with age
  - TBW ↑ with obesity



Distribution of Water[2]



Total body water
(0.6 x body weight)
42L

Intracellular (ICF)
(2/3 of TBW)
(0.4 x Body weight)
28L

Extracellular (ECF)[3]
(1/3 of TBW)
(0.2 x Body weight)
14L

Interstitial Fluid (ISF)
(3/4 x ECF)
10.5L

Plasma
(1/4 x ECF)
3.5L

Venous fluid
"Venous capacitance"
(85% of plasma)

Arterial fluid
(15% of plasma)

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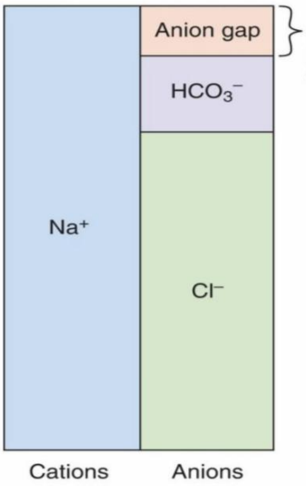
[1] The standard is 60% (in calculations).

[2] Between the ICF and ECF is the cell membrane and water pass by osmosis, and in between the ISF and plasma is the capillary wall and water pass by starling forces: hydrostatic pressure in the capillary and the interstitium, and oncotic pressure in the capillary and interstitium.

[3] In certain diseases ECF fluid distribution will be distorted, e.g. in sepsis there is capillary dilation and increase permeability, and in low albumin there is decrease in oncotic pressure which clinically present as edema.

Electrolytes and anion gap



Unmeasured anions = protein, phosphate, citrate, sulfate

FIGURE 5.25 Serum anion gap.

Electrolytes:

- **Definition:** substances dissolved in solutions and dissociated into particles called ions
- **Types:**
  - Cations: Positively charged ions
  - Anions: Negatively charged ions
- **Anion Gap:** reflects unmeasured anions such as Albumin.

Definitions

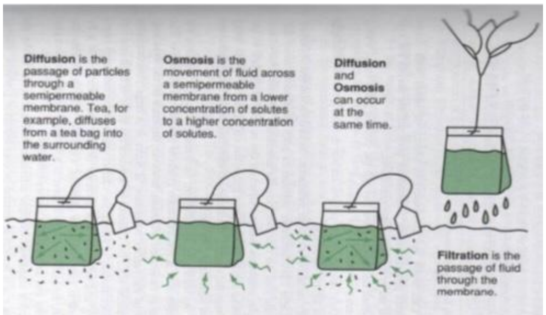
- **Osmosis:** movement of water based on substance osmotic gradient (from low to high)
- **Diffusion:** movement of solutes based on their concentration gradient (from high to low)
- **Filtration:** movement of both solutes and water (solute drag = convection)

What will happen if you put a tea bag is inside a water cup?

1. **Swelling of the tea bag**; why? Because of **osmosis**. Water will move from an area of low osmolarity to an area of high osmolarity.

2. **Diffusion of solutes:** the tea solutes come out (diffusion). Remember that solutes diffuse from an area of high conc to an area of low conc.

3. **Firltration:** What will happen if you lift the teabag? Both water and tea will come out. This is exactly how the glomeruli filter the plasma.



Diffusion is the passage of particles through a semipermeable membrane. Tea, for example, diffuses from a tea bag into the surrounding water.

Osmosis is the movement of fluid across a semipermeable membrane from a lower concentration of solutes to a higher concentration of solutes.

Diffusion and **Osmosis** can occur at the same time.

Filtration is the passage of fluid through the membrane.

Fig. 1-2
Transport processes.

Composition of the fluid compartments

Electrolytes concentration (mmol/L)

Cation	Plasma	Capillary wall	Interstitial fluid	Cell membrane	Intracellular fluid
Na$^+$	**142**		144		10
K$^+$	4		4		**160**
	ECF				ICF

- The dominant Cation in the ICF is potassium (K), while in the extracellular fluid (ECF) it is sodium (Na).
    - The major force maintaining the difference in cation concentration between the ICF and ECF is the **sodium–potassium pump.**

◀ Plasma vs IF

- An important difference between the plasma and interstitial ECF is that **only plasma contains significant concentrations of protein.**
    - **difference in protein content:** maintained by the protein permeability barrier at the capillary wall.
    - This protein concentration gradient contributes to the balance of forces across the capillary wall that favour fluid retention within the capillaries (the colloid osmotic, or oncotic pressure of the plasma) maintaining circulating plasma volume.

Osmolarity vs osmolality

OsmolaLity

- **Definition:** the number of osmoles per kiLo of water (mOsm/kg water). **(measured)**
- Normal osmolality of body fluids: 283-292 (mOsm/kg water) usually measured In the lab.

OsmolaRity

- **Definition:** the number of osmoles per liteR of solution (eg. plasma) (mOsm/L plasma) **(Calculated)**
- The plasma osmolarity (mOsm/L): can be calculated from the plasma concentrations of sodium, urea and glucose, as follows:

Calculated plasma osmolarity = (2 x serum [Na+]) + blood urea + glucose

- **Pink:** **Electrolytes** (multiplied by two to account for the anions).
- **Purple:** **Non-electrolytes** (**blood urea** is around 3 mmol/l and **glucose** is around 5 mmol/l)

Osmolarity vs osmolality[1] *(cont.)*

Osmol Gap

- **(Calculated)**
- Normal osmol gap of body fluids: **up to 10 mOsm/kg**[2]

Osmol Gap = Measured Osmolality – Calculated Osmolarity

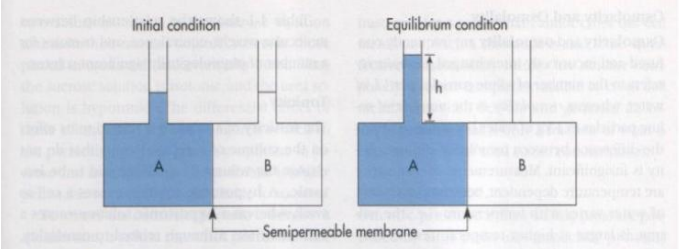
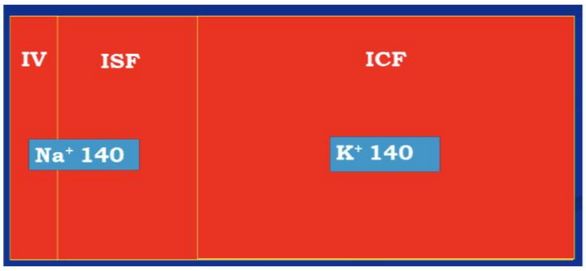


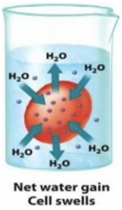
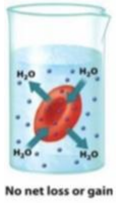
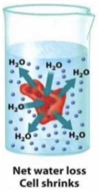
Figure 1-1 ■ **Schematic representation of osmotic water movement and the generation of an osmotic pressure. The solute particles in compartment *A* cause water to move by osmosis from compartment *B* across the semipermeable membrane into compartment *A*. The water column in compartment A will rise until the hydrostatic pressure generated by the water column *(h)* stops the flow of water from compartment *B* into compartment *A*. This hydrostatic pressure is equal to the osmotic pressure generated by the solution in compartment *A*.**

ECF and ICF are in ***osmotic equilibrium***
so **ICFosm = ECFosm = Posm**



◀ Tonicity

- To compare the osmolality of a solution to that of another solution
- In practice Tonicity is used to compare the osmolality of intravenous solutions to that of the plasma:
  - Isotonic or Hypotonic or Hypertonic

	Hypotonic	**Isotonic**	**Hypertonic**
Definition	Solutions have more water than solutes comparing to ECF	Solutions have the same solute concentration as the ECF	Solutions have more solutes than water comparing to ECF
Effect	Water moves ECF → ICF	it will remain in the ECF	Water moves ICF → ECF
examples	- Distilled Water - 0.45% NaCl (½) - 0.33% (⅓)  Net water gain Cell swells	- Normal saline (0.9% NaCl) - Rigers Lactate - 5% dextrose in water (D5W)  No net loss or gain	- 3% NaCl - 10%-50% Dextrose - D5W-½ NS - D5NS - Amino acid solution  Net water loss Cell shrinks

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[1] They are frequently confused and incorrectly interchanged. Osmolarity refers to the number of solutes per 1 l of solvent (volume), whereas osmolality refers to the number of solutes in 1 kg of solvent (weight).

[2] if it's higher than this it indicate that there is high levels of unmeasured osmole usually alcohol.

◀ Regulation mechanisms of fluid and electrolytes

one liter of plasma = one liter of water + 140 mmol of [Na+]

Regulation of plasma volume

- occurs through neurological and renal mechanisms:

Others :

Kinins

Prostaglandins

Volume receptors

stretch receptors
- sensing volume status
- Located in the carotid sinus and in the aortic arch.

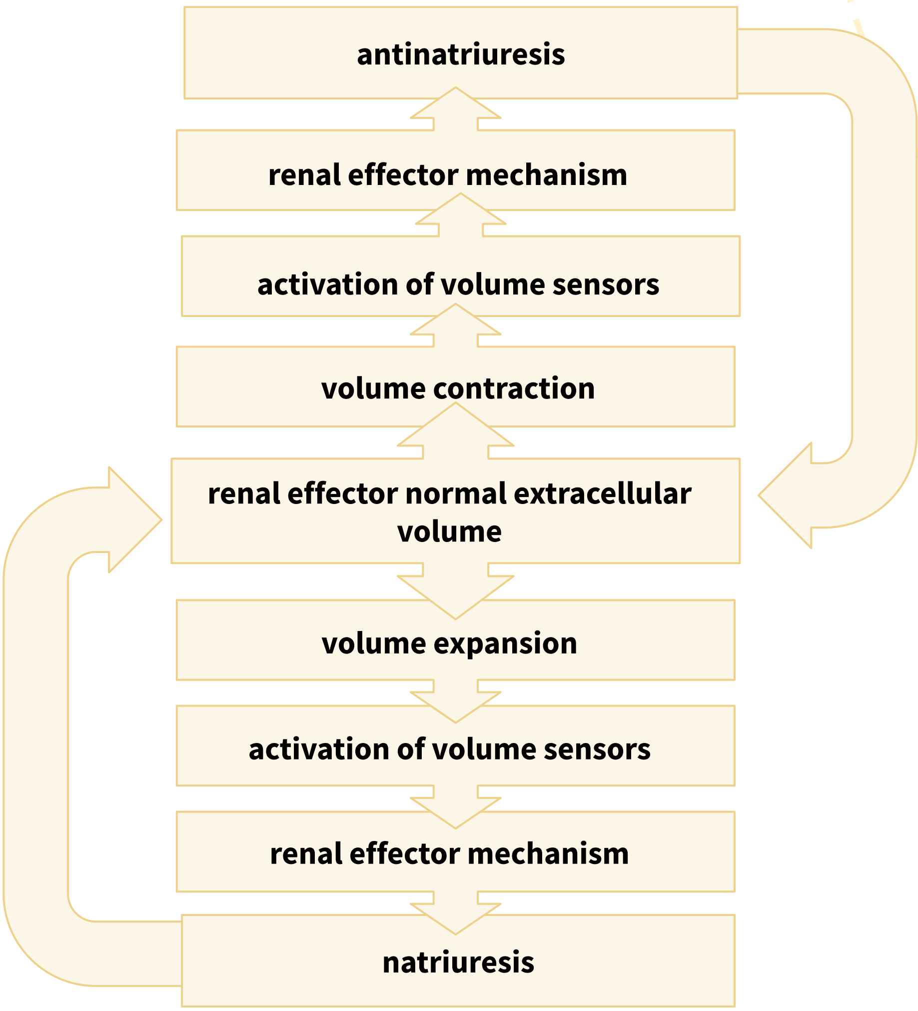
Natriuretic peptides
- increase urine sodium excretion.
- BNP is the one we measure in cardiology 'Heart failure'

The Renin-Angiotensin-Aldosterone System
- increase vasoconstriction and Na reabsorption = sodium preservation)
- RAAS is what mainly dictate volume in the body

Antidiuretic hormone (vasopressin)

Afferent limb sensors of ECF volume:
1. cardiopulmonary (venous circulation), atria, ventricular and pulmonary
2. Arterial: external: aortic arch, carotid sinus. Internal: juxtaglomerular apparatus
3. Others: CNS, hepatic

Integrate homeostatic response to volume change:

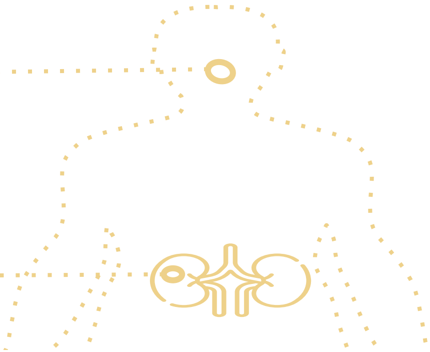


Regulation Mechanisms of Fluid and Electrolytes

Regulation of plasma osmolarity[1]

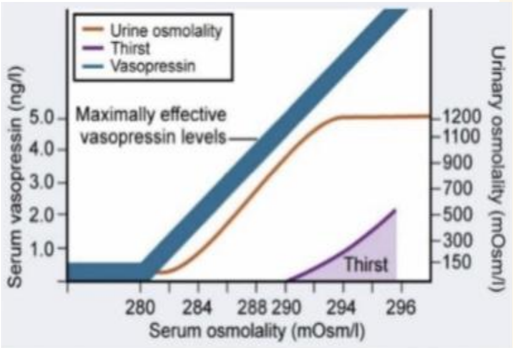
- Achieved through osmoreceptors

Thirst (increase water intake)



Antidiuretic hormone[3] (vasopressin)
(preserve body water = decrease water loss into the urine)

◄ Response to changes in serum osmolality



As soon as the plasma osmolality rise above **280 mOsm/kg** the secretion of ADH increases to preserve water thus urine starts to become concentrated i.e. urine osmolality will increase up to 1200 mOsm/kg but reaches a plateau even with the continuous increase in ADH because it's the maximum capacity, at that time thirst kicks in urine osmolarity and ADH levels have reached the maximum.

- Normal urine Osmolality: 100 – 800 mOsm/kg "in practice"

Bottom line: Volume[2] is more important than osmolality (survival = holding water in during hypovolemic state even in the face of hypoosmolality state [hyponatremia])

◄ The linear relationship between urine specific gravity and uosm (plasma SG ~1.008)

How do we measure the concentration of the urine?

- By checking the urine Osmolarity. Can go as low as 50 mOsmol/L and high as 1200 mOsmol/L. This is done in labs but it's time and effort consuming so we tend to look at the urine specific gravity "SG". This is an indirect way of measuring urine osmolarity.
  - For water, SG is 1.000
  - For plasma SG is 1.010
- So if urine is less than this it means it's diluted, if more than this then it's concentrated.

pure water SG	1.000
plasma SG	1.008
urine SG	**urine osmolality (mOsm/kg H_2O)**
1.010	300-400
1.020	700-800
1.030	1000-1200

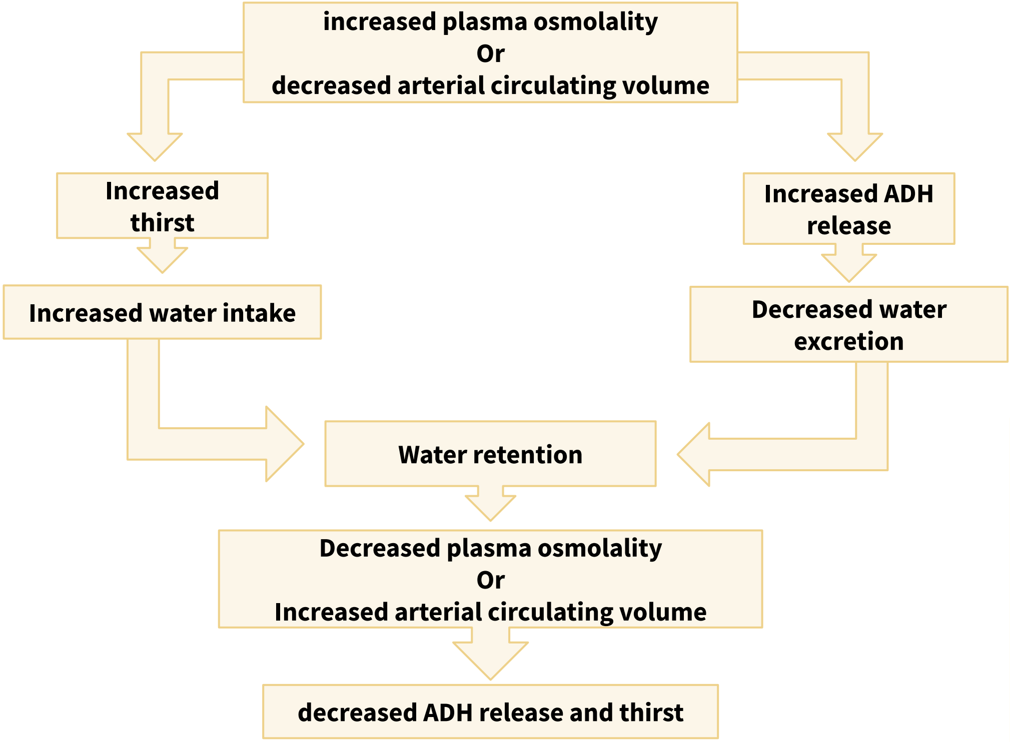
1: Control over serum osmolality is maintained by the intricate feedback loop between the hypothalamus and the juxtaglomerular apparatus in the kidney. Release of **arginine vasopressin** secondary to hyperosmolarity detected by osmoreceptors in the anteroventral hypothalamus leads to upregulation of aquaporin channels in the collecting duct of the kidney. Simultaneously, osmoreceptors in the juxtaglomerular apparatus detect changes in solute (ie, sodium) delivery and volume status and regulate the renin-angiotensin-aldosterone axis to change fluid and sodium retention in renal tubules

2: In hypo/hypervolemia we are not assessing the blood volume directly, we clinically assess the fluid in the interstitium, which reflect the fluids levels intravascularly and intracellularly.

3: Works on the collecting duct, by insertion the aquaporins 'passive movement of water'. It's the last step before excretion of the urine. ADH shares the regulation in BOTH Na & water balance and will be secreted in two conditions (high osmolarity or low volume).

Regulation Mechanisms of Fluid and Electrolytes

◄ Response to↑ plasma osmolality (↓plasma volume)



increased plasma osmolality
Or
decreased arterial circulating volume

Increased thirst

Increased water intake

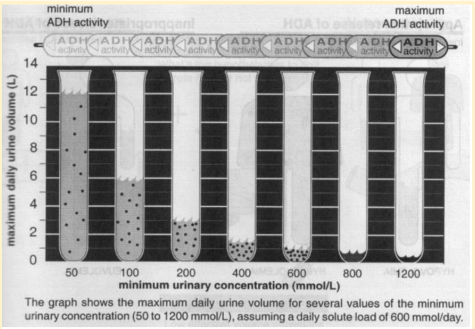
Increased ADH release

Decreased water excretion

Water retention

Decreased plasma osmolality
Or
Increased arterial circulating volume

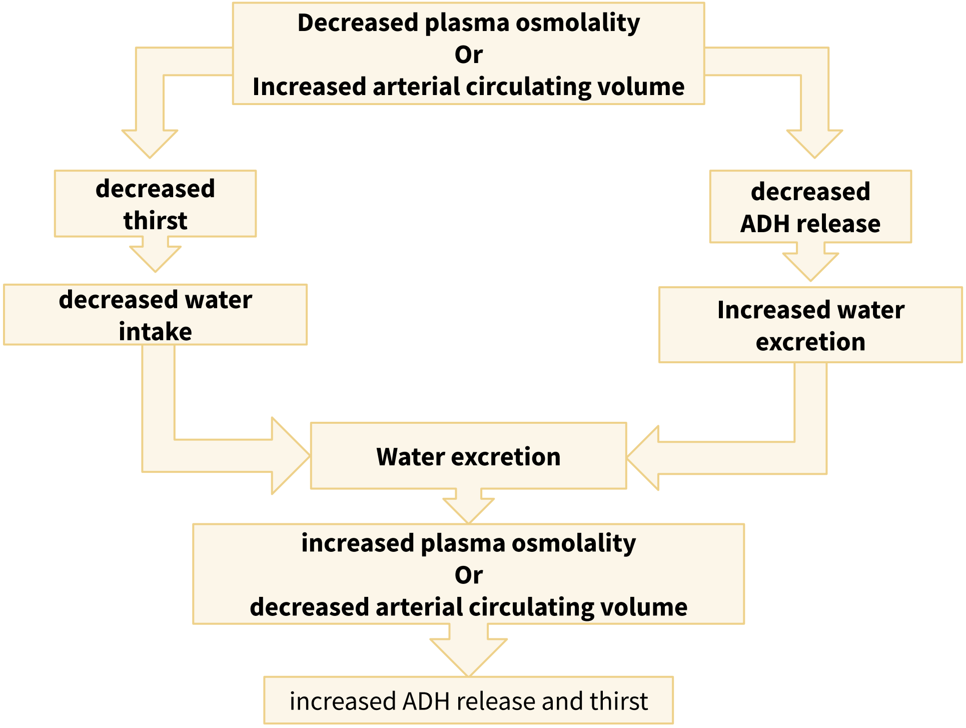
decreased ADH release and thirst



The graph shows the maximum daily urine volume for several values of the minimum urinary concentration (50 to 1200 mmol/L), assuming a daily solute load of 600 mmol/day.

Urine Output & Daily Solute Load

◄ Response to↓ plasma osmolality (↑plasma volume)



Decreased plasma osmolality
Or
Increased arterial circulating volume

decreased thirst

decreased water intake

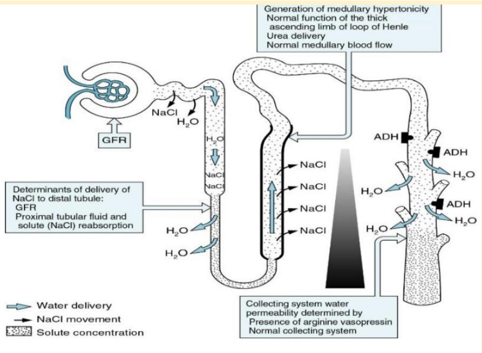
decreased ADH release

Increased water excretion

Water excretion

increased plasma osmolality
Or
decreased arterial circulating volume

increased ADH release and thirst



Effective Arterial Blood Volume (EABV)

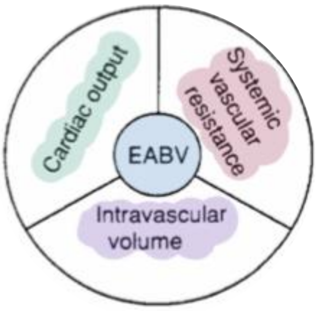
◀ What is EABV[1]

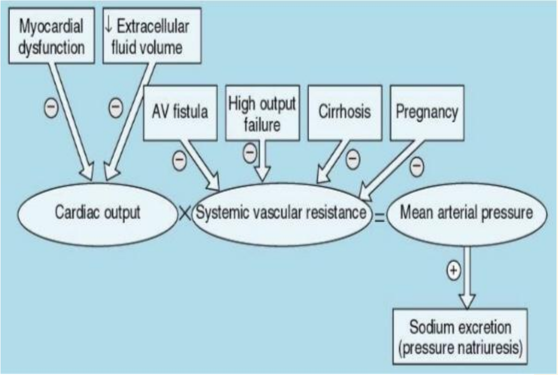
- **Definition:** the amount of arterial blood volume required to adequately “fill” the capacity of the arterial circulation. (also determined by cardiac output and systemic vascular resistance).
- Although the absolute volume of the intravascular space is an important component of circulatory “fullness”, *the adequacy of the circulation* (more commonly called the effective arterial blood volume or EABV) also is determined by cardiac output and systemic vascular resistance
- **Best assessed by spot urine [Na+] to reflect RAAS activation[2]**

◀ Components of EABV

EABV has 3 components:

1. Cardiac output
2. Systemic vascular resistance
3. Intravascular volume





MAP = CO x SVR

CO (cardiac output) = Stroke volume (SV) x Heart rate (HR)

SV → Depends on Ejection fraction (EF) and Preload

- We treat hypertension as well as hypotension by manipulating (EF, preload, HR, and SVR).
- To perfuse the organs we need **good blood pressure** and to have good blood pressure we need **blood volume** i.e preload.

↓ EABV leads to:	↑ EABV leads to :
↑CO ↑Systemic vascular resistance ↑renal Na retention = ↑ volume	↓ CO ↓ Systemic vascular resistance ↓ renal Na retention = ↓ volume

- ECF volume and EABV can be **independent** of each other:
  - Edematous states: increase in total ECF volume and decreased EABV
    - Where there is hypervolemic hyponatremia → TBW is high but it’s mostly in the venous system e.g. Heart failure, cirrhosis and nephrotic syndrome.
  - Postural hypotension: may cause shifts that influence the EABV without affecting the total blood volume.

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[1] It is the primary determinant of renal sodium and water excretion. Thus effective arterial blood volume constitutes effective circulatory volume for the purposes of body fluid homeostasis. The fullness of the arterial compartment depends on a normal ratio between cardiac output and peripheral arterial resistance. Thus, diminished EABV is initiated by a fall in cardiac output or a fall in peripheral arterial resistance. When the EABV is expanded, this in turn leads to an increase in urinary sodium excretion and vice versa.

[2] urine Na <20 reflect **RAAS activation, and if K is increased → aldosterone activation**

I.V Fluids

◀ Type of I.V fluid at the time of infusion

Type of I.V fluid at the time of infusion	What happens after administration of IV?	Example
Hypotonic	Water will move from ECF into ICF	● Distilled Water ● 0.45% NaCl(1/2NS) ● 0.33% NaCl(1/3NS)
Isotonic	It will remain in the ECF	● NS (0.9% NaCl) ● Ringers Lactate 2/3 ● DW-1/3 NS ● 5% Dextrose in Water(D5W)
Hypertonic	Water will move from ICF to ECF	● 3% NaCl ● 10%-50% Dextrose ● D5W-1/2 NS ● D5NS (5%Dextrose in NS) ● Amino acid solution

◀ General rules of IV fluids

- Before giving any type of I.V fluids you have to think of:
  - type of solution
  - amount
  - rate
  - duration
  - You have to reassess the patient to see if you should continue with what you gave or not. etc.
- When your aim to **resuscitate** the patient, then you **look at the blood pressure**. On the other hand, if you want **maintain** the fluid level then you have to **assess the input and output**
- An NPO 40 year old female having a normal blood pressure waiting for a lab call should be given D5 1/2 NS + 20 KCl + 1 cc/kg/hr. K is added to hypotonic fluids

◀ Intravenous solutions (crystalloids vs colloids)

Crystalloids

- Intravenous solutions that contain solutes that readily cross the capillary membrane (electrolytes).
- Examples: Dextrose & electrolyte solutions

Colloids[1] (PRBC)

- Intravenous solutions (IV 300mL) that DO NOT readily cross the capillary membrane **and will stay intravascular** (non-electrolytes large molecules)
- Examples: Blood, albumin[2], plasma.

- **Pure Water CAN'T be given IV, it's a hypotonic fluid thus it will go inside the RBC causing them to swell and burst (hemolysis) and damage the lining of the capillary wall (thrombophlebitis).**

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[1] The use of colloid solutions, as opposed to crystalloids, in the setting of acute resuscitation has been controversial. While they do, in theory, provide intravascular oncotic pressure which saline solutions do not, they have not shown clear benefit in large trials, are expensive, and may cause harm in critically ill and TBI patients due to shift of albumin into the interstitial space. They are currently not the fluid of choice.

[2] only used in ascites and SBP (spontaneous bacterial peritonitis)

The Differences between each Intravenous Solutions

This table is very important, for exam purposes you need to know which fluid is given in a particular scenario.

Distribution in normal person assuming normal capillary wall function (no capillary leak syndrome) (For every 1000mL)

Solution		Components	OsmolaRity (mosm/L)	indication	IV	ISF	ICF
D5W[1]		- Glucose = 5 g/100 mL Or 50 g/L	**253** (Isotonic initially[1])	● **Uses:** ○ prevent ketogenesis *(RBC can't metabolize ketones due to lack of mitochondria)* ○ Hypoglycemia (but not nutritional). ○ dilute powdered medicines ○ used to provide free water (to correct hypernatremia) ● **Cations** ○ **NOT** used for resuscitation: only one-twelfth remains intravascular because it diffuses into the TBW compartment, so not effective in maintaining intravascular volume ○ Use with caution in diabetic patients.	80 mL	250 mL	670 mL
Normal saline (NS) (0.9% NaCl)		Na=154 mEq /L Cl =154 mEq /L 0.9 g NaCl/100 mL (9 g/L)	**308** (154 Na+154 Cl =308) Isotonic	**Resuscitation fluid** (No water shift to the ICF) use with caution in patients with CHF unless the patient needs urgent resuscitation due to true volume depletion	**250**	750	
Half saline (1⁄2 NS) (0.45% NS)	★ **½ NS**	-Na=77 -Cl =77 -0.45 g NaCl/100 mL (4.5 g/L)	**154** (77 Na+77 Cl = 154) Hypotonic	**Maintenance fluid** to match the ongoing loss (urine output) Why not use it for resuscitation? only 165 stay intravenously which does not support blood pressure. Hence why 1⁄2 NS used as a maintenance not for replacing ACUTE volume loss.	125	375	
	½ water				40	125	335
	Total				165 ml	500 ml	335 ml

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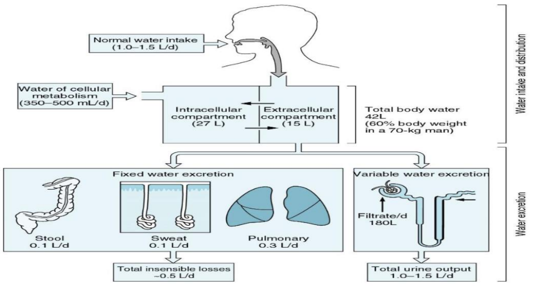
[1] Dextrose gets burned out by insulin so the osmolarity of Dextrose-based solution will eventually decrease. For example, the osmolarity of D5W will become zero so is considered as "free water"

The Differences between each Intravenous Solutions

Distribution in normal person assuming normal capillary wall function (no capillary leak syndrome)
(For every 1000mL)

Solution	**Components**	**OsmolaRity (mosm/L)**	**indication**	**IV**	**ISF**	**ICF**
D_5 ½ NS	Glucose = 50 Na = 77 Cl = 77	**407**	● Before surgery ● Often the standard maintenance fluid, can be used with D5 in diabetics	165 ml	500 ml	335 ml
D_5NS	Glucose = 50 **Na=154** **Cl =154**	**561**		250	750	
D10W	-Glucose = 100 g/L (=10 g dextrose/100 mL)	**506** initially hypertonic, then hypotonic	● continuous hypoglycemia.	**80**	250	**670**
Ringer's lactate[1] **(used by surgeons)**	**Na+ = 130** K = 4 Ca^{+2}= 3 **Cl^-= 109** **Lactate= 28**	**274** **Isotonic**	● With large volumes there is risk of hyperkalemia, hyperlactemia and metabolic alkalosis. ● Excellent for replacement of intravascular volume; it's not a maintenance fluid. It is the most common trauma resuscitation fluid. ● **Benefits:** does not cause hyperchloremic metabolic acidosis like NS. ● **Cautions:** do not use if hyperkalemia is a concern (contains K) ● NOTE: More physiological "balanced" but **BE CAUTIOUS with (AKI & sepsis)**			
⅔-⅓	2/3 D5W (33 g/L glucose) + 1/3 NS (50g/L Na, 50g/L Cl = 0.33 g NaCl/100mL or 3.3 g NaCl/L)					



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[1] Contains Ca for coagulation cascade. Lactate is converted by the liver to HCO3

Total body sodium content (Volume status) & serum sodium concentration (Water disorder)

◀ Basal Requirements:

Basal Water	**Calculation of Maintenance Fluids:** **4/2/1 rule:** (**4** mL/kg for first 10 kg) + (**2** mL/kg for next 10 kg) + (**1** mL/kg for every 1 kg over 20) Example: for a 70 kg man: (**4** x 10 = 40) + (**2** x 10 = 20) + (**1** x 50 = 50) Total = **110 mL/hour.** ● 1st 10 kg: 4 ml/kg/h + ● 2nd 10 kg: 2 ml/kg/h + ● >20kg: 1ml/kg/h
Insensible water loss	- Stool, breath, sweat: 800 ml/d - Increases by 100-150 ml/d for each degree above 37 C.
Electrolytes[1]	- Na: 50-150 mmol/d (NaCl) - Cl: 50-150 mmol/d (NaCl) - K: 20-60 mmol/d (KCl)
Carbohydrates	- Dextrose: 100-150 g/d - IV Dextrose **minimizes protein catabolism** and **prevents starvation ketoacidosis** (enough for ketogenesis suppression not for nutritional use)

◀ sodium and water disorders

- **ECF volume** = absolute amounts of sodium and water.
- **Plasma sodium concentration** = ratio between the amounts of sodium and water (concentration).
- The main determinant of volume is sodium content.
- Na^+ regulation is intimately associated with water homeostasis, yet it is regulated by independent mechanisms. Changes in Na^+ **concentration** are a reflection of water homeostasis, whereas changes in Na^+ **content** (and subsequently, fluid volume) are a reflection of Na^+ homeostasis. Disturbance of Na^+ balance may lead to hypovolemia or hypervolemia, and disturbance of water balance may lead to hyponatremia or hypernatremia.

Dysvolemia = Sodium Disorder	Dysnatremia = Water Disorder/Tonicity Disorder
Hypervolemia = Sodium Excess (Edema) (high volume = high sodium content)	**Hyponatremia** = relative water Excess (Low sodium conc. = high water)
Hypovolemia = Sodium Deficit (Dehydration) (low volume = Low sodium content)	**Hypernatremia** = relative water Deficit (High sodium conc. = low water)

---

[1] equivalent to:
- Na: 1 meq/kg/day = 1 mmol/kg/day = 1 mOsm/kg/day
- Cl: 1 meq/kg/day
- K: 1 meq/kg/day

Disorder in Sodium Balance

◀ Clinical features of Hypovolemia & Hypervolemia

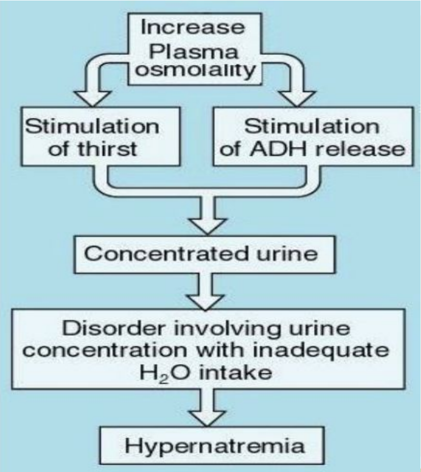
	Hypovolemia	**Hyper**volemia
Symptoms	● Thirst ● Dizziness on standing ● Weakness	- Ankle swelling - Abdominal swelling - Breathlessness
Signs	❖ Low JVP ❖ Postural hypotension ❖ Tachycardia ❖ Dry mouth ❖ Reduced skin turgor ❖ Reduced urine output: either compensatory to conserve fluid or as a manifestation of acute renal failure due to prerenal azotemia ❖ Weight loss ❖ Confusion, stupor Once these symptoms of end-organ damage are present, patient has entered shock and typically has lost 20%-30% of their total blood volume.	❖ Raised JVP ❖ Peripheral edema (usually pitting) ❖ Pulmonary crepitations ❖ Pleural effusion ❖ Ascites ❖ Hypertension (sometimes) ❖ Weight gain Vital signs in some cases may show hypotension and hemodynamic instability (as in decompensated HF) or tachypnea and hypoxia if pulmonary edema is present.

◀ Disorder in Water Balance

Hypernatremia: Water Deficit Calculation. Refers to excess sodium in relation to water; can result from water loss or, rarely, sodium infusion.

General Characteristics

- Defined as a plasma Na+ concentration >145 mmol/L
- Hypernatremia reflects less water in relation to sodium; affected patients may or may not have a concurrent abnormality in sodium balance.
- This is less common than hyponatremia and nearly always indicates a water deficit.



- In hyp**e**rnatremia by default there is high osmolarity.
- In hyp**o**natremia it’s not necessary to have low osmolarity, thus which we have to check serum osmolality:
  - Isotonic hyponatremia
  - Hypertonic hyponatremia
  - Hypotonic hyponatremia

Hypernatremia

◀ Classifications

01 Hypovolemia

02 Euvolemia

03 Hypervolemia

Hypovolemic hypernatremia

Features

↓↓**Total body water**

↓**Total body sodium**
(Na deficit with a relatively greater water deficit)

Causes

01 **Renal losses: Urinary Na > 20**

- **Loop or osmotic diuretic:** during water restriction, it inhibits Na reabsorption & causes water loss
- **Postobstructive diuresis:** copious amounts of salt and water are eliminated after the relief of a urinary tract obstruction
- **Glycosuria**: hyperglycaemic hyperosmolar state
- **Intrinsic renal disease**: renal tubular function is lost → ↓↓ reabsorption of water & Na

02 **Due to Extrarenal losses: Urinary Na < 20**

- Excessive sweating
- Burns
- Diarrhea
- Fistulas

Treatment

➢ **Correction of volume & water deficit:**
  ○ Pt is hypovolemic → Administer isotonic saline till *hypovolemia* improves.
  ○ After that correct the *sodium level* by calculating water deficit accordingly Administer: (**Half saline** or **D5W** or **oral water** replacing the free water deficit & ongoing losses).

➢ **Treat causes of losses:**
(Removal of diuretics, insulin …)

Hypernatremia *(cont.)*

Euvolemic hypernatremia

Features

↓**Total body water**

No change in Total body sodium (water deficit alone)

Causes

01

Due to renal losses: Urinary Na variable

- **Diabetes insipidus** (there's high volume water loss from insufficient ADH)
- Hypodipsia (hypodipsia refers to a partial deficiency of the thirst mechanism → person unable to feel thirsty → ↓ water intake)

02

Due to Extrarenal losses

- Insensible losses: respiratory, dermal

Treatment

- ➢ **Correction of volume & water deficit:** calculate water deficit accordingly Administer (**Half saline** or **D5W** or **oral water** replacing the free water deficit & ongoing losses).
- ➢ **In central diabetes insipidus with severe loss:** give aqueous vasopressin (ADH) "pitressin" but monitor serum Na carefully to avoid water intoxication.
- ➢ **Long term therapy: in nephrogenic diabetes insipidus:** (the causes of nephrogenic diabetes insipidus are: lithium, chronic kidney disease, hypokalemia, hypercalcemia, they make ADH ineffective at kidney tubule) so you have to treat NDI according to the cause: (correct plasma Ca &K conc. give amiloride for lithium induced NDI, remove offending drug)
- ➢ **Long term therapy**: low Na diet

Hypervolemic hypernatremia

Features

↑**Total body water**

↑**Total body sodium**

Causes

01

Sodium Gains: Urinary Na > 20

- **Primary hyperaldosteronism** (because aldosterone causes Na water retention)
- **Cushing's syndrome** (because high Cortisol cause mineralocorticoid effect)
- **Hypertonic dialysis**
- **Iatrogenic:** (hypertonic NaHCO3, NaCl tablets)
- **Chronic kidney disease:** during water restriction.

Treatment

- ➢ Remove Na
- ➢ Discontinue offending agents.
- ➢ Administer furosemide
- ➢ Provide hemodialysis as needed for renal failure.

Hypernatremia *(cont.)*

◀ Principles of Treatment:

- Low volume ⟶ normal saline.
- High volume (high Na) ⟶ loop diuretics. Or dialysis which is much less common.
- Water deficit ⟶ free water (Oral or IV, D5W or half saline)
- Water excess ⟶ water restriction + diuretics.

◀ Water Deficit Calculation

Water deficit: the amount of “water” required to lower the Plasma Na to 140 mmol/L

Water Deficit = Target TBW - Current TBW

Step 1: calculate Current Total Body Water [TBW]:

Current Total Body Water [TBW] (L) = 0.6 x Current Body Weight (kg)

Step 2: calculate total body cations, Since Serum [Na+] = Intracellular [K+]

Total body cations = Current TBW x Current [Na+]

Step 3: Assuming no other intake or loss:

$$\underbrace{\textbf{Current TBW x Current [Na+]}}_{\text{= total body cations (calculated in step 2)}} \textbf{ = Target TBW x Target [Na+]}$$

Step 4: calculate water deficit:

Target TBW – Current TBW = Water Deficit

Then, do not forget to:
- Consider ongoing water loss (insensitive and other losses)
- Decide about IVF/PO fluid: type and rate
- Always reassess clinically and with lab results

Example: 50 year-old male with stroke and tube feeding. S[Na+] = 170 mmol/L. Wt = 70 kg. What is his water deficit to reach normal S[Na+] = 140 mmol/L?

Step 1: calculate Current Total Body Water [TBW]:

Current Total Body Water [TBW] = 0.6 x Current Body Weight
= 0.6 x 70 = **42 L**

Step 2: calculate total body cations, Since Serum [Na+] = Intracellular [K+]

Total body cations = Current TBW x Current [Na+]
= 42 x 170 = **7140**

Step 3: Assuming no other intake or loss:

Current TBW x Current [Na+] = Target TBW x Target [Na+]
7140 = Target TBW x 140
Target TBW= 51 L

Step 4: calculate water deficit:

Target TBW – Current TBW = Water Deficit
51 - 42 = 9L
(Can be given IV or OP depending on the patient’s condition)

Hyponatremia

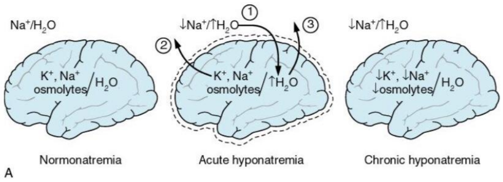
Hyponatremia

General characteristics:

- This refers to too much water in relation to sodium in the serum.
- It is typically defined as a plasma Na+ concentration <135 mmol/L.
- Symptoms usually begin when the Na^+ level falls to <129 mEq/L. An important exception is increased intracranial pressure (ICP) (e.g., after head injury). As ECF osmolality decreases, water shifts into brain cells, further increasing ICP. (Therefore, it is critical to keep serum sodium normal or slightly high in such patients.)

Classification of Symptoms of Hyponatremia

- Symptoms of hyponatremia are dependent on how fast it occurs.
- Sodium means CNS symptoms, whether sodium level above the normal or below it.
- All symptoms that can be signs of cerebral edema[1] should be considered as severe or moderate symptoms that can be caused by hyponatremia:



Moderately Severe	Severe
• Nausea without vomiting • Confusion • Headache	• Vomiting • Cardiorespiratory distress • Abnormal and deep somnolence • Seizures • Coma (Glasgow Coma Scale ≤ 8) For **severe** hyponatremia, Need 3% hypertonic saline as emergency treatment

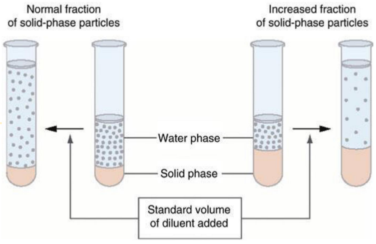
1

Normotonic (Isotonic) Hyponatremia

Also known as:

- Factitious Hyponatremia
- Pseudohyponatremia

Plasma is made of:
- Water phase 93%
- Solid phase 7%



Definition:

Increase in plasma solids lowers the plasma sodium **concentration** . But the **amount** of sodium in plasma is normal (hence, **pseudohyponatremia).** Measure the **plasma osmolarity it will be normal.**

Causes

01 **any condition that leads to elevated protein**
- multiple myeloma

02 any condition that leads to **elevated lipids**
- severe dyslipidemia

1: Neurologic symptoms predominate—caused by "water intoxication"—osmotic water shifts, which leads to increased ICF volume, specifically brain cell swelling or cerebral edema.

Hyponatremia *(cont.)*

Detection method

Measurement of SNa+ by:
- Flame photometric or
- Indirect potentiometry

What is a normal sodium?

Normal Measured SNa+ = 153 mmol/L of Plasma Water

Normal Plasma Water?

Normal Plasma Water Phase = 93% of One liter of Plasma

Reported Serum Na+ = 154 x 0.93 = 143 mmol/L of Plasma solution

Decreases in case of normotonic hyponatremia
(Decreased water phase)

Example: If water phase decreases due to increased solid phase (high protein or lipids) then:

Water phase is 84% now due to myeloma

Reported Serum Na+ = 153 x 0.84 = 129 mmol/L of Plasma

2 Hypertonic (Hyperosmolar) Hyponatremia

Also known as:
- Translocational Hyponatremia
- Dilutional hyponatremia
- True hyponatremia

Causes

- Results from **non-Na osmoles in the serum (often glucose or mannitol) drawing Na-free H2O from cells** (e.g: Diabetes mellitus). In comparison to the hypovolemic hypernatremia that is caused by hyperosmotic hyperosmolar state, transient hyponatraemia occur due to osmotic shifts of water out of cells during hyperosmolar states caused by **acute hyperglycaemia** or by mannitol infusion, but in these cases plasma osmolality is normal.
- [Na+] declines by ~2.4 mEq/L for each 100 mg/dL [5.5 mmol/L] increase in serum glucose

3 Hypotonic (hypoosmolar) Hyponatremia (true Hyponatremia)

True hyponatremia = SIAD = Syndrome of Inappropriate Antidiuresis (Not pure SIADH!)

Hyponatremia *(cont.)*

Classifications

01 Hypovolemia

02 Euvolemia

03 Hypervolemia

Hypovolemic Hyponatremia

Features

↓**Total body water**

↓↓**Total body sodium**
(sodium deficit **exceeds** the water deficit)

Causes

01 **Renal losses: Urinary Na > 20**

- **Diuretic EXCESS**: especially thiazides, over time with excess use of diuretic, it will deplete the body of sodium & water
- **Mineralocorticoid deficiency:** adrenocortical failure, because aldosterone causes Na retention
- **Salt-losing deficiency**
- **Bicarbonate loss:** with RTA and metabolic alkalosis
- **Ketonuria:**↑keto-acid excretion also obligate electrolyte loss

02 **Due to Extrarenal losses: Urinary Na < 20**

- **Diarrhea**
- **Vomiting**
- **Third spacing of fluids** (occurs when too much fluid moves from the intravascular space into the interstitial or "third" space):
  - **Burns, pancreatitis & trauma**

All of these are also causes of hypernatremia; however, they cause hyponatremia if there is chronic replacement with free water. A little sodium and a lot of water are lost in urine, which is then replaced with free water that has no sodium. Over time, this process depletes the body of sodium and the serum sodium level drops.
This is what occurs in cholera patients, they do not vomit but they have severe diarrhea, they will replace the water loss but they do not replace the Na, which may lead to seizures and death. This is also seen marathon runners, they run long distances so they sweat and lose Na, they will drink water but do not replace the Na.

Hyponatremia *(cont.)*

Euvolemic hyponatremia

Features

↑Total body water

No change in Total body sodium (water excess alone)

Causes

Urinary Na > 20:

- **post-operative patient**: there is usually a short period of **oliguria** occurring as a physiological response to surgery.
- **Drugs**
- **Glucocorticoid deficiency**
- **Syndrome of inappropriate ADH** (↑ADH increases water reabsorption)
- **Hypothyroidism** (it induces hyponatremia by inappropriate release of ADH)
- **Primary Polydipsia**.
- **Excessive electrolyte free water infusion:** intravenous dextrose solutions, or by absorption of sodium-free bladder irrigation fluid after prostatectomy
- **Beer potomania:** a specific hypo-osmolality syndrome related to massive consumption of beer

Syndrome of inappropriate ADH

◀ Causes

- **Tumours**
- **Central nervous system disorders:** stroke, trauma, infection, psychosis, porphyria
- **Pulmonary disorders:** pneumonia, tuberculosis, obstructive lung disease
- **Drugs:** anticonvulsants, psychotropics, antidepressants, cytotoxics, oral hypoglycaemic agents, opiates
- **Idiopathic**

◀ Diagnosis

1. **Low plasma sodium concentration (typically < 130 mmol/L)**
2. **Low plasma osmolality (< 275 mOsmol/kg)**
3. Urine osmolality not minimally low (typically > 100 mOsmol/kg)
4. Urine sodium concentration not minimally low (> 30 mmol/L)
5. Low–normal plasma urea, creatinine, uric acid
6. **Clinical euvolaemia**
7. Absence of adrenal, thyroid, pituitary or renal insufficiency
8. No recent use of diuretics
9. Exclusion of other causes of hyponatraemia
10. Appropriate clinical context

Diagnostic criteria for SIADH

“HIVE”

H
H: Hypoosmolar Hyponatremia
(Posm <275 mOsm/Kg H2O)

I
I: Inappropriate urine concentration
(Uosm >100 mOsm/Kg H2O)

V
V: Euvolemia
No diuretic use

E
E: Endocrine
= normal Thyroid, adrenal and renal function

\+ Hypouricemia (<238 mcmol/L) and low Urea (<3.5 mmol/L)
- (Be careful: SIADH is a Diagnosis of Exclusion!)

Hypervolemic hyponatremia

Features

↑↑**Total body water**

↑**Total body sodium**

Causes

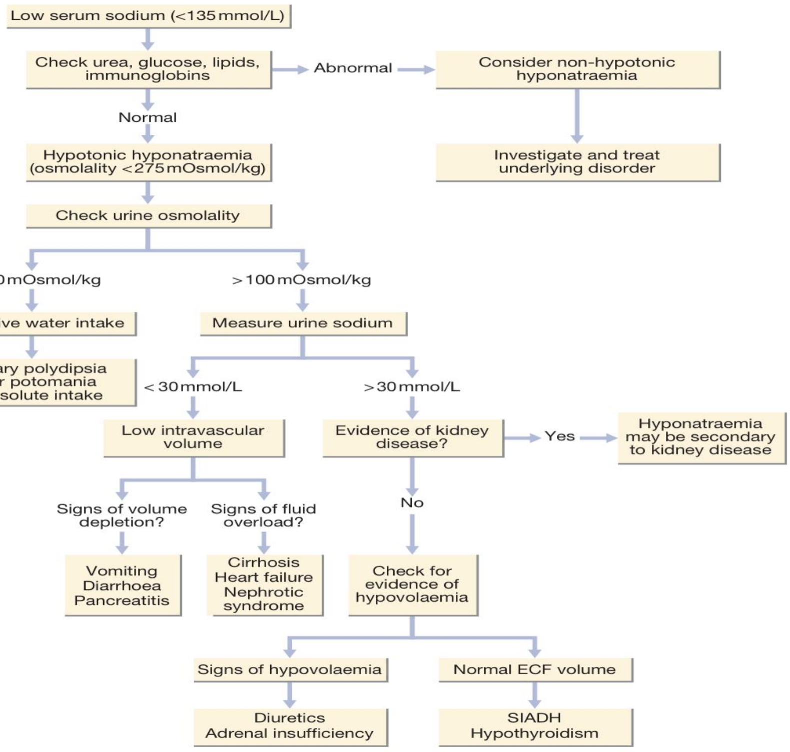
01

Urinary Na > 20
- AKI
- CKD

02

Urinary Na <20
- Nephrotic syndrome
- Cirrhosis
- Heart failure

Investigations algorithm of hyponatremia



Hyponatremia *(cont.)*

◀ General management of hyponatremia

1

Symptoms & Signs

Assess
1. acuity of development
2. Volume Status
3. Comorbidities

2

Serum

1. Measured serum Osmolality
2. TSH
3. FT4
4. Serum Cortisol (@ 8 AM)
5. Albumin
6. Total Proteins
7. Uric Acid

3

Spot Urine (even on weekends and holidays)

1. Urine Electrolytes (Na, K, Cl):
   a. Spot urine [Na+] to assess effective arterial blood volume
2. Urine Urea Nitrogen
3. Urine creatinine (to calculate FENa if AKI)
4. Urine Osmolality
5. Urinalysis (Urine Specific Gravity)

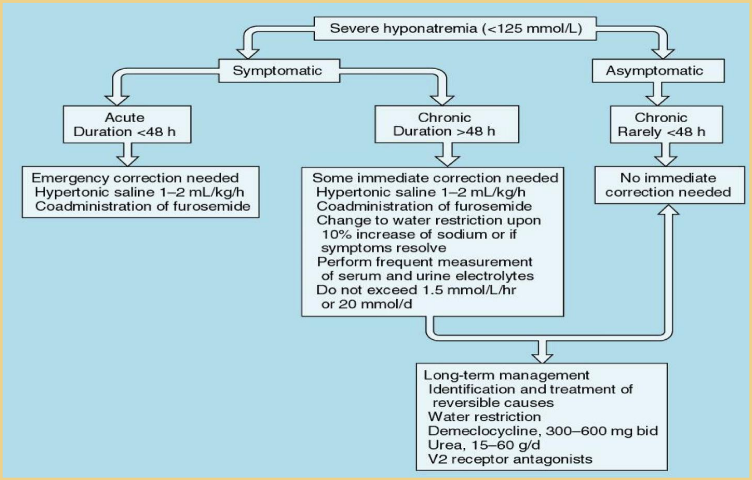
For chronic (>48 h):

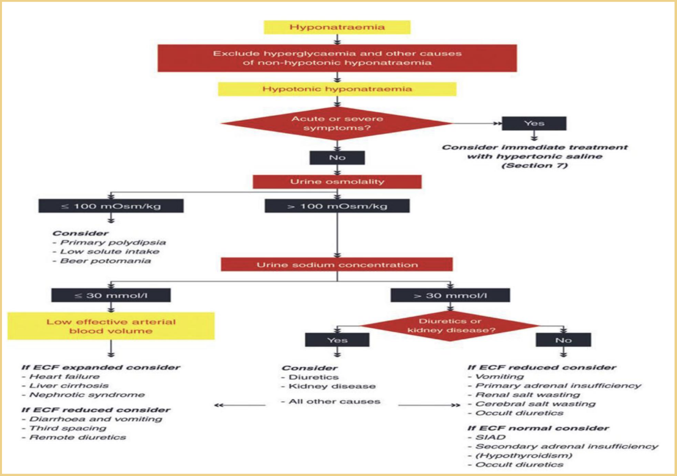
Rate of S[Na+] correction = 0.5 mmol/L/h ~ 6-8 mmol/L/d

Hypovolemia: IV Fluid (Normal Saline or 3% Saline as indicated)

Hypervolemia: Fluid loss with loop diuretic
Decrease total oral fluid intake

◀ Management algorithms





Hyponatremia *(cont.)*

◀ Chronic hypovolemic hyponatremia

Water excess calculations

Step 1: calculate Current Total Body Water [TBW]:

Current Total Body Water [TBW] (L) = 0.6 x Current Body Weight (kg)

Step 2: calculate total body cations, Since Serum [Na+] = Intracellular [K+]

Total body cations = Current TBW x Current [Na+]

Step 3: Assuming no other intake or loss:

$$\underbrace{\textbf{Current TBW x Current [Na+]}}_{\text{= total body cations (calculated in step 2)}} \textbf{ = Target TBW x Target [Na+]}$$

Step 4: calculate water excess :

Current TBW – Target TBW = Water Excess

Do not forget to:

- Both salt and water restrictions
- Treat excess volume with loop diuretics (Furosemide):

Diuretic use = increase hypotonic urine (U[Na+] ~ 70-100 mmol/L): Na loss < water loss

- Always reassess clinically and with lab results
- Watch urine output and volume status

Example: 50 year-old male with decompensated heart failure. S[Na+] = 110 mmol/L. Wt = 90 kg. What is his water excess he needs to lose to reach normal S[Na+] = 140 mmol/L?

Step 1: calculate Current Total Body Water [TBW]:

Current Total Body Water [TBW] = 0.6 x Current Body Weight

= 0.6 x 90 = **54 L**

Step 2: calculate total body cations, Since Serum [Na+] = Intracellular [K+]

Total body cations = Current TBW x Current [Na+]

= 54 x 110 = **5940**

Step 3: Assuming no other intake or loss:

Current TBW x Current [Na+] = Target TBW x Target [Na+]

5940 = Target TBW x 140

Target TBW= 42.5 L

Step 4: calculate water deficit:

Current TBW – Target TBW = Water excess

His total water excess is

54 - 42.5 = 11.5L

Hyponatremia *(cont.)*

◀ Symptomatic euvolemic hyponatremia

Sodium deficit calculation

Step 1: calculate Current Total Body Water [TBW]:

Current Total Body Water [TBW] (L) **= 0.6 x Current Body Weight** (kg)

Step 2: calculate sodium deficit

Sodium deficit = TBW x 4

(We need to **increase S[Na+] by 4 mmol/L** to stop symptoms/seizure = 4 mmol of Na for every one liter of body water))

Treatment: Using 3% Saline (each 1 ml ~ 0.5 mmol of Na+):

Sodium deficit x 2 = amount of 3% saline to be infused

(Consider 3% saline infusion vs bolus per patient condition)

Remember to:

- Always reassess clinically and with lab results.
- Watch urine output (Foley catheter is needed): beware of rapid polyuria with massive urine free water loss due to suppressed ADH, overcorrection of hyponatremia with risk of **osmotic demyelination syndrome!**

Example: 50 year-old male with thiazide-induced hyponatremia has headache and vomiting. S[Na+] = 110 mmol/L. Wt = 60 kg. What is his sodium deficit to reach normal S[Na+] = 114 mmol/L to stop acute symptoms?

Step 1: calculate Current Total Body Water [TBW]:

Current Total Body Water [TBW] = 0.6 x Current Body Weight
= 0.6 x 60 = **36 L**

Step 2: calculate sodium deficit

Sodium deficit = TBW x 4
= 36 x 4 = **144 mmol**

Treatment: Using 3% Saline (each 1 ml ~ 0.5 mmol of Na+):

Sodium deficit x 2 = amount of 3% saline to be infused
144 x 2 = **290 mL** (to be given IV push)

Then:

- Repeat lab right after the infusion.
- Watch urine output with Foley catheter

Dysnatremia & dysvolemia combination clinical cases

	Relative Water Balance (Na and Water losses/gains comparing to plasma ratio) (= 140 mmol Na per 1 L water)		
sodium balance	**hyponatremia**	**normonatremia**	**hypernatremia**
hypovolemia (sodium defect)	**Isotonic fluid loss with only water intake** (Na loss > Water loss) ↓ **Hemorrhagic Shock** (with good oral water intake)	**Isotonic fluid loss** (Na loss = Water loss) ↓ **Pure GI bleeding**	**Hypotonic fluid loss with no water intake** (Na loss < Water loss) ↓ **Diarrhea** (Children and Seniors)
euvolemia	**SIADH** (Pure Water Gain)	**Normal State (Homeostasis)**	**Diabetes Insipidus (DI)** (Pure Water Deficit)
hypervolemia(sodium excess)	**Hypotonic fluid gain** (Na gain < Water gain) ↓ -**Advanced Congestive Heart Failure** -**Advanced Cirrhosis**	**Isotonic fluid gain** (Na gain = Water gain) ↓ -**Heart Failure** -**Cirrhosis** -**Nephrotic Syndrome**	**Hypertonic fluid gain** (Na gain > Water gain) ↓ **Hemodialysis Patient after 3% Saline injection** for cramps

Hyponatremia and hypernatermia in elderly

Causes

1. **Hyponatraemia**: occurs when free water intake continues in the presence of a low dietary salt intake and/or diuretic drugs (particularly thiazides).
2. **Hypernatraemia**: occurs when water intake is inadequate, due to physical restrictions preventing access to drinks and/or blunted thirst.

Both are frequently present in patients with advanced dementia or following a severe stroke. hypernatraemia is aggravated if dietary supplements or medications with a high sodium content (especially effervescent preparations) are administered. Appropriate prescription of fluids is a key part of management.

Predisposing factors

- **Decline in GFR:** older patients are predisposed to both hyponatraemia and hypernatraemia, mainly because, as glomerular filtration rate declines with age, the capacity of the kidney to dilute or concentrate the urine is impaired.
- **Vasopressin release:** water retention is aggravated by any condition that stimulates vasopressin release, especially heart failure. Moreover, the vasopressin response to non-osmotic stimuli may be brisker in older subjects. Appropriate water restriction may be a key part of management.

Summary

IV Fluids:

1. **Hypotonic:** Water will move from ECF into ICF. E.g. Distilled Water, 0.45% NaCl
(1/2NS), 0.33% NaCl (1/3NS)
2. **Isotonic:** It will remain in the ECF. E.g. NS (0.9% NaCl), Ringers Lactate, 2/3 DW-⅓ NS, 5% Dextrose in Water (D5W)
3. **Hypertonic:** Water will move from ICF to ECF. E.g. 3% NaCl , 10%-50% Dextrose, D5W-1/2 NS , D5NS , Amino acid solution
4. **Crystalloids** are intravenous solutions that contain solutes that readily cross the capillary membrane (contents: water + electrolytes). Examples: Dextrose and electrolyte solutions
5. **Colloids** are intravenous solutions that DO NOT readily cross the capillary membrane

Disorders in sodium balance: disturbances in balance affect the volume because sodium is the main.

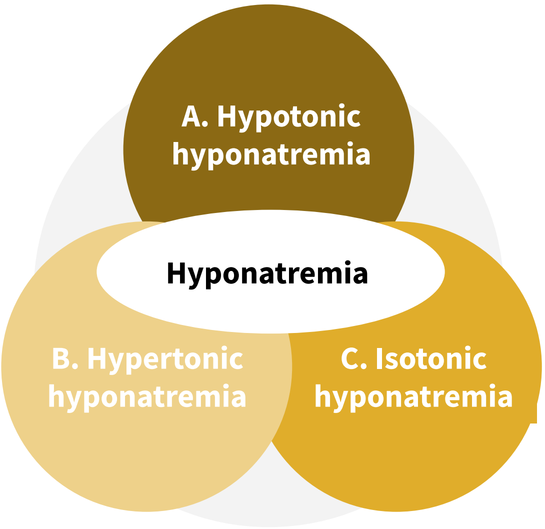
Differentiate between total body sodium content (volume status) and serum sodium concentration (Hypo- and Hypernatremia)

	Sodium Balance Disorders (Determinant of Volume)	
	Hypervolemia	**Hypovolemia**
Signs	Swelling in ankles and abdomen, breathlessness.	Thirst, weakness, dizziness on standing.
Symptoms	High JVP, hypertension, weight gain, peripheral edema and pleural effusion.	Low JVP, postural hypotension, weight loss, reduced urine output and dry mouth.

Disorders in water balance: disturbances in water are related to Na concentration, not Na amount.		
1- *Hypernatremia:* plasma Na+ concentration >145 mmol/L.		
Hypovolemia	**Euvolemia**	**Hypervolemia**
Total body water is decreased more than total body sodium.	Only total body water is decreased.	Total body sodium is increased more than total body water.

Summary

Disorders in water balance: disturbances in water are related to Na concentration, not Na amount.	
2- *Hyponatremia:* plasma Na+ concentration <135 mmol/L.	
Moderately Severe	**Severe**
Nausea without vomiting, confusion, headache.	Vomiting, cardiorespiratory distress, seizures, abnormal & deep somnolence, coma. (Glasgow Coma Scale ≤8)



01 Hypotonic Hyponatremia

- **Hyponatremia with hypovolemia** ⇒ Na deficit with a relatively smaller water deficit.
- **Hyponatremia with euvolemia** ⇒ Increased total body water only.
- **Hyponatremia with hypervolemia** ⇒ Na retention with relatively greater water retention.

02 Hypertonic Hyponatremia

(Translocational Hyponatremia) (Dilutional Hyponatremia) (True not Pseudo)

03 Isotonic Hyponatremia

(Pseudohyponatremia) (Factitious)

Lecture Quiz

Q1: A 33 y/o male marathon runner presented to the ER with dizziness when standing and weakness. On examination, his JVP was low with reduced skin turgor . His HR = 132. Which of the following is the best initial treatment?

A- Administration of Hypertonic saline
B- Administration of Isotonic saline
C- Administration of Hypotonic saline
D- No intervention, only observe the patient

Q2: A 83 y/o patient admitted with heart failure and a sodium level of 113 mEq/L. He is behaving aggressively towards staff and does not recognize family members. When the family expresses concern about his behavior, the doctor would respond most appropriately by stating:

A- He may be suffering from dementia, and the hospitalization has worsened the confusion
B- Most older adults get confused in the hospital
C- His sodium levels are low, and the confusion will resolve as they normalize
D- His sodium levels are high, and his behavior is a result of dehydration.

Q3: A 47 y/o male presented to the ER with 2 days history of diarrhea. His vitals are BP=75/45, HR=113 , RR=23. How would you manage this patient?

A- Normal saline
B- Half normal saline
C- Quarter normal saline
D- 5% Dextrose

Q4: A 27 y/o female patient presented to you with pain in her right forearm associated with redness, warmth of the skin and tissues after she had an IV fluid because of her hypovolemia. What is the most likely cause of her symptoms?

A- Administration of Ringer's lactate
B- Administration of 1/2 Na
C- Administration of pure water
D- Administration of Na

Q5: A nurse would evaluate which of the following patients to be at risk for developing hypernatremia?

A- 50 y/o with pneumonia, diaphoresis and high fever
B- 62 y/o with CHF taking loop diuretics
C- 39 y/o with vomiting and diarrhea
D- 60 y/o with lung cancer and SIADH

Answers: Q1:B | Q2:C | Q3:A | Q4:C | Q5:A |

Answers Explanation File!

THANKS!!

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Send us your feedback:
We are all ears!