PLEASE CHECK Editing file BEFORE!

Electrolytes Imbalance I

(Sodium & water)

★ **Objectives:**

1. Recognize the systems that control body sodium and water contents.
2. Understand the difference between body volume status and serum Sodium concentration.
3. Recognize the different types of intravenous fluids used at bedside.
4. Know the workup for Hyponatremia.
5. Know how to calculate the water deficit in Hypernatremia.

★ **Resources Used in This lecture:** Slides and Davidson's

Extra Explanation

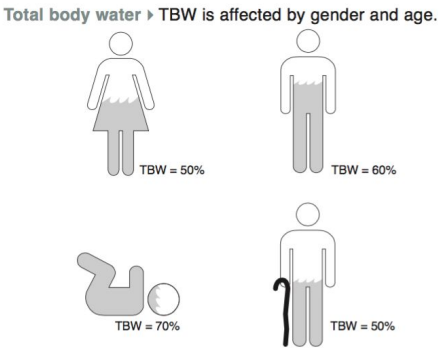
Done by: Mohammad Alkharraz
Revised by: Nouf Almasoud

Contact us at: InternalMedicineTeam434@gmail.com

In this lecture, our goal is to understand sodium and water disorders. The key to unlocking this subject is clearly distinguishing between total body sodium and serum sodium concentration First we will brush on the concepts of body fluids and osmolarity and other basic principles.

★ Body Fluids

- Total body water (TBW)=
  - 60% of weight in males
  - 50% of weight in females
  - It decreases as we increase in age (babies have more TBW than the elderly)
- TBW is divided into
  - ICF (⅔ of TBW)
  - ECF (⅓ of TBW). ECF is divided into
    - Interstitial fluid (¾ of ECF)
    - Plasma (¼ of ECF)



★ Osmosis

- **What is osmosis?**
  - It is the movement of WATER from an area of LOW osmolarity to an area of HIGH osmolarity
- **What is osmolarity?**
  - It depends on the amount of solutes in the liquid
- Listen I am a medical student not a chemistry student please get to the point
  - OK

Our plasma has a certain osmolarity. This osmolarity depends on two things: the solutes in the plasma, and the amount of water in it. The major electrolyte in the plasma is sodium. **Therefore, the plasma osmolarity mainly depends on the concentration of sodium in the plasma**.

Here is the full formula to appreciate what is going on:

Plasma osmolarity = 2[Na+] + [Glucose]/18 + [BUN]/2.8

*Where [Glucose] and [BUN] are measured in mg/dL.

[Na+]	**[Na+] means the concentration of sodium, which depends on two things: 1- the amount of sodium in the serum and 2- the amount of water in the serum.**
[Glucose]	Also note that glucose is divided by 18, meaning it is negligible in normal situations. Normal glucose 100mg/dl → 100/18= 5.5, which can be ignored. This becomes important in case of hyperglycemia. Type II diabetics might get a condition called hyperosmolar hyperglycemia where the concentration of glucose is so high that it caused an increase in the plasma osmolarity.
[BUN]	Regarding BUN, it normally diffuses through membranes and it is therefore not important.

- **We can approximate the osmolarity by ignoring the other solutes (glucose and BUN) and just multiply the serum sodium concentration by 2**
    a) Patient serum concentration is 140 → osmolarity is approximately 280
- **Why is it that we multiply sodium by 2?**
    a) Because there are anions (Chloride) present with it that we can't measure.

The bottom line of all what we have just said is:

- Plasma osmolarity depends on sodium **CONCENTRATION** in the plasma.
- Concentration means that it depends on the **amount of sodium** in the plasma and the **amount of water** in the plasma.

Example: if I have TOO much ADH→ ADH will go to my kidneys and retain all of the WATER that it can (it doesn't do anything to sodium). This then increases the amount of water in the plasma. Sodium concentration= Na^+ in plasma/ water in plasma → this means that there will be HYPONATREMIA. Notice that although we have hyponatremia, the amount of sodium in the body did not change.

SO WHAT? Why is it a problem if the osmolarity changed?

- Because of the law of osmosis

The law of osmosis says that WATER will move from the area of low osmolarity to the area of high osmolarity
Let us assume that I have poured pure water into the bloodstream (this is impossible and has many complications but just imagine). The osmolarity of the blood would drop. Now the ECF has a lower osmolarity than the ICF. WATER will start moving from the ECF into the ICF. The problem is in the brain. As water moves into the cells of the brain, they will start swelling and the brain is inside the cranium which cannot stretch → CNS symptoms, seizures, and possible herniation of the brain.

The brain, if given enough time, has the ability to fix this problem by changing its osmolarity to avoid this water movement. This is why in cases of slow and chronic lowering of the sodium concentration, the brain accommodates and the patient might be asymptomatic. And this is also why we correct sodium disorders very slowly; because we want to give the brain the opportunity to fix the osmolarity issue.

ADH mechanism quick review of normal physiology *control over osmolarity*:

- If your plasma Na^+ concentration increases → ADH will increase → reabsorb water from the kidneys → Na^+ concentration goes back to normal
- If you drink too much water → Na^+ concentration decreases → ADH will decrease → ↑ water excretion from the kidneys→ Na^+ concentration back to normal

Therefore the main stimulus for ADH is the *osmolarity*!

- There are other minor stimuli for ADH release, I will mention one example for completeness:
    - Severe hypotension: patients with heart failure who have low plasma Na^+ concentration (hyponatremia) have a poor prognosis[1]. This means that the condition is so bad that ADH was released and reabsorbed water from the kidney → hyponatremia

Take home message:

1) **Serum osmolarity depends mainly on sodium concentration**
2) **Remember that concentration means that it depends on two things: (water and sodium)**
3) **The problem is that if there is a disturbance in the osmolarity: WATER will start moving between the ICF and ECF → CNS problems**

Tonicity & Fluids

Tonicity compares the osmolarity of two different fluids

- Compared to the blood stream, fluids might be:
    - Isotonic (have the *same* osmolarity)
    - Hypotonic (have a *lower* osmolarity)
    - Hyperosmotic (have a *higher* osmolarity)

The topic of IV fluids was discussed intensively in surgery and this lecture covers the same concepts...

D5W (5% dextrose in water):

- The only extra piece of information is that D5W consists of 5% dextrose and water. As it is infused, the dextrose gives this solution osmolarity; so at the beginning it is isotonic. After a while, the cells will metabolize the dextrose, and then there will only be water remaining, so the fluid would become hypotonic.

Blood Pressure Control

After discussing ADH, you should have it clear in mind that ADH is mainly responsible of the serum osmolarity because it only manipulates water.

- However, in cases of hypovolemia, we need to maintain BP[2], so the body activates the Renin Angiotensin Aldosterone System (RAAS) and starts reabsorbing SODIUM from the kidney.

It is important to talk about hypovolemia, hypervolemia, and euvolemia. These all depend on the **TOTAL AMOUNT of sodium in the body**.

---

[1] https://www.uptodate.com/contents/hyponatremia-in-patients-with-heart-failure#H3

[2] Remember if a patient is hypotensive you always want to give normal saline to restore BP. Because it is isotonic and would stay in the ECF, supporting the plasma volume and BP.

In hypovolemia, there is decreased total body sodium. This causes the ECF volume to decrease, leading to a decrease in the amount of sodium in the plasma → hypotension.
In hypervolemia, the opposite occurs.

★ Clinical Features of Volume Disorders:

	Hypovolemia	Hypervolemia
Symptoms	• Thirst • Dizziness on standing • Weakness	• Ankle swelling • Abdominal swelling • Breathlessness
Signs	• Low JVP • Postural hypotension • Tachycardia • Dry mouth • Reduced skin turgor • Weight loss • Confusion, stupor	• Raised JVP • Hypertension (sometimes) • Peripheral edema • Pulmonary crepitations • Pleural effusion • Weight gain • Ascites

Notice that all of the indicators of volume status depend on clinical findings. There is no lab test to measure the volume status.

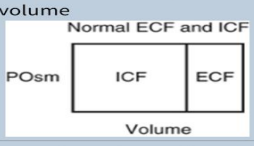
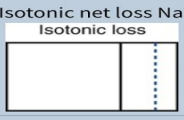
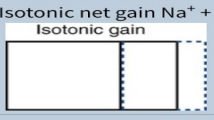
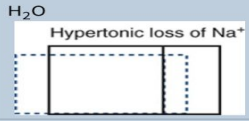
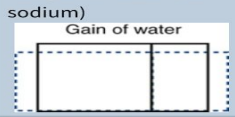
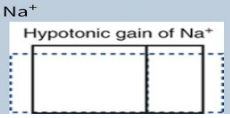
At this point of the lecture, the most important thing is to clearly distinguish between serum sodium concentration (which would lead to hyponatremia/ hypernatremia) and total body sodium (which would lead to hypovolemia/hypervolemia).

To help you with that, we will perform some exercises. It might be useful to think of it this way: Serum Na^+ concentration = Total body Na^+ / Total Body water

	How will serum Na^+ concentration change?	Will the volume status change?
A normal person was infused with Normal Saline	*It will not change.* Normal saline is iso-osmotic (same osmolarity as the plasma) because it contains almost equal amounts of sodium " = 154 mmol/L". No change in serum sodium concentration.	Since normal saline contains sodium, the total body sodium will increase, and the patient would become *hypervolemic*.
A patient has Inappropriate ADH Secretion	Since we increased water, the sodium will be diluted → decreased = *hyponatremia*	ADH will only be reabsorbing fluids → no change in total body volume → NO CHANGE IN VOLUME STATUS → *Euvolemia*

I infuse a normal person with ½ normal saline (hypotonic fluid)	It will be decreased = *hyponatremia*, because I am increasing the body water more that the body sodium ↑ Total body sodium/ ↑ ↑ Total body water → ↓ serum sodium concentration (think about it mathematically)	Since this solution contains sodium, the total body sodium would be increased → *hypervolemia*
I infuse a normal person with 2 normal saline (hypertonic fluid)	*Increased = hypernatremia*	*Hypervolemic*
Person is sweating profusely (hint: sweat is hypotonic- contains more water than salt)	*Hypernatremia*	*Hypovolemic*

For more examples, navigate through the following table[3]

COMPARTMENT ALTERATION	POsm/Na^+	ECF VOLUME	ICF VOLUME	CONDITIONS
Normal ECF and ICF volume 	Normal	Normal	Normal	Normal hydration
Isotonic net loss $Na^+ + H_2O$ 	Normal ↓TBNa^+/↓TBW	Contracted	Normal	**Hypovolemic normonatremia** Adult diarrhea (secretory type; e.g., cholera)
Isotonic net gain $Na^+ + H_2O$ 	Normal ↑TBNa^+/↑TBW	Expanded	Normal	**Hypervolemic normonatremia** Infusion of excessive isotonic saline
Net loss Na^+ in excess of H_2O 	Decreased ↓↓TBNa^+/↓TBW	Contracted	Expanded	**Hypovolemic hyponatremia** Loop diuretics Addison disease 21-Hydroxylase deficiency
Net gain in water (no sodium) 	Decreased TBNa^+/↑↑TBW	Expanded	Expanded	**Euvolemic hyponatremia** SIADH Compulsive water drinker
Net gain in H_2O in excess of Na^+ 	Decreased ↑TBNa^+/↑↑TBW	Expanded Starling forces alteration	Expanded	**Hypervolemic hyponatremia** RHF Cirrhosis Nephrotic syndrome

[3] From Goljan Rapid Review Pathology

Sodium and water and how are they different.

Sodium is much better than water in maintaining BP. This is because if we add pure water (without Na^+)into the ECF it will equilibrate between the ECF and ICF. This means that ⅔ of that water will go to the ICF and we are only left with ⅓ for the ECF. In contrast, when we put isotonic fluid (Normal Saline), all of it would stay in the ECF (no osmosis between ECF and ICF because it is isotonic). Therefore, sodium is what preserves BP. Our body knows this. Therefore, the RAAS which eventually releases aldosterone is responsible for maintaining BP. ADH plays a minor, negligible role. ADH is mainly concerned with osmolarity (as previously discussed).

The clinical implications of this are very important:

1) If patient has hypotension (hypovolemic), we want to correct this with normal saline which is an isotonic solution that contains sodium instead of pure water. If you get diarrhea, you should drink something that contains salt (بطاطا مع ملح على قولة الدكتور) water is not enough.
2) Patients with too much aldosterone (primary hyperaldosteronism) get HTN. While patients with too much ADH do not get HTN (SIADH diagnostic criteria requires the patients to be euvolemic)

★ Effective Arterial Blood volume (EABV)

If you go back to the table of hypovolemia and hypervolemia, which is taken from the lecture slides, you will notice that there is the word (sometimes) beside hypertension in hypervolemia. We will now expand on this thought using the concept of EABV

- When a patient has hypervolemia, that means that there is an increase in total body sodium; which is mostly in the ECF (distributed between the interstitial fluid and the plasma)
- Therefore, when I have increased total body sodium (when I am hypervolemic), sodium will equilibrate through the ECF. That is, it will go into the interstitial space (possibly giving edema) and to the plasma (increasing by blood pressure).
- The amount in the plasma can be either in the veins or in the arteries.

Remember that only the amount of fluid in the arteries is what maintains the blood pressure and is responsible for perfusing organs (this is what is called effective arterial blood volume)

This is important because patients with heart failure have a failing heart which cannot pump the blood effectively into the arterial tree. Blood pools in the venous side and these patients have hypervolemia as evidenced by their edema, high JVP, etc. Whereas their EABV is decreased and there is decreased perfusion of the kidneys. The kidneys sense a decrease in perfusion and starts activating RAAS which worsens the problem. That is why ACE inhibitors are given in HFrEF (Heart Failure with reduced Ejection Fraction)

- **RECALL:**
  - TBW is divided into
    - ICF (⅔ of TBW)
    - ECF (⅓ of TBW). ECF is divided into
      - Interstitial fluid (¾ of ECF)
      - Plasma (¼ of ECF): fluid might be in the veins or in EABV

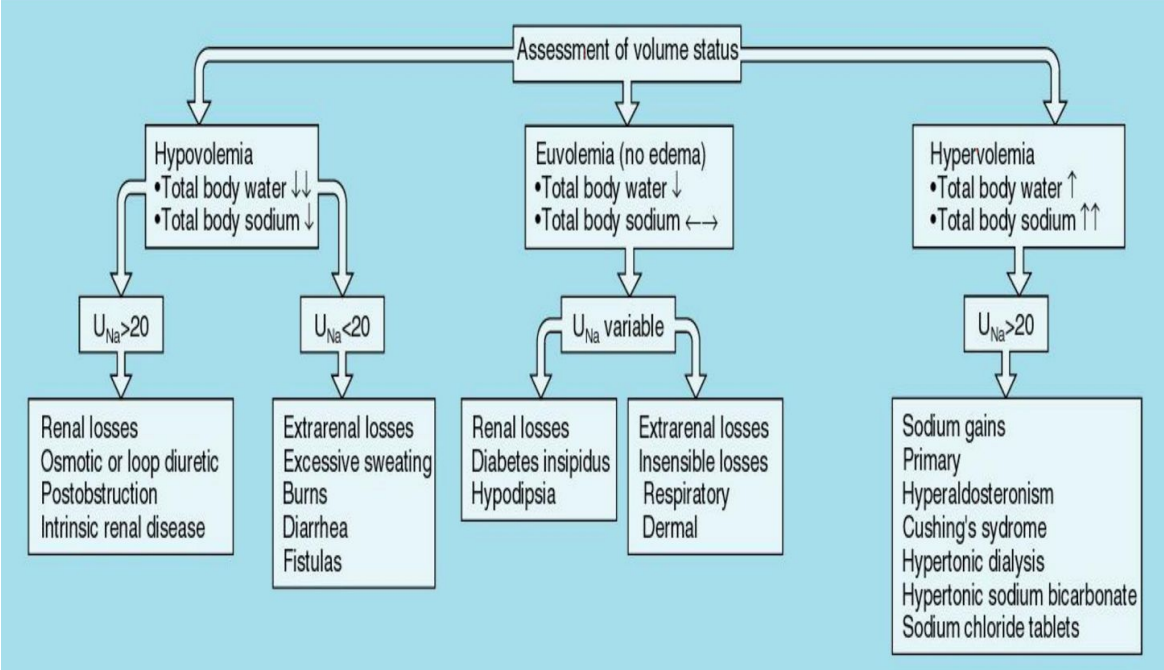
Movements Across Membranes:

The last thing to mention before moving on to the disorders is what governs movements across membranes:

- We have already described osmolarity and its importance in movement between ECF and ICF. Remember the CNS symptoms secondary to cerebral edema in cases of low plasma osmolarity.
- However, fluid movement across the capillaries between the plasma and and interstitium depends on the Starling forces (hydrostatic pressure and oncotic pressure - and all that crap we learned in physiology). That is why in nephrotic syndrome we get increased filtration into the interstitial space and get edema (low plasma oncotic pressure). It is also why when we infuse a patient with normal saline, the hydrostatic pressure increases favoring filtration → edema.

★ Sodium Disorders ★

❑ Hypernatremia "Plasma Na concentration > 145 mmol/L"



1. Hypovolemic hypernatremia: we have lost more water than sodium (lost a hypotonic solution) **→ next step measure the urine sodium**	
High urine sodium (>20) →	The kidney is the problem: Osmotic and loop diuretics lose more water that sodium
Low urine sodium (<20) →	The kidney is doing its job, so external losse: 1) Excessive sweating: sweat is hypotonic (it has more water than sodium) 2) Diarrhea, fistulas, burns, respiratory losses.

2. Euvolemic Hypernatremia decrease in total body water (normal total body sodium, euvolemic)	
Diabetes insipidus ADH is not working, can be:	**Nephrogenic DI** → ADH normal but kidney isn't responding **Central DI:** kidneys are normal but ADH is not produced

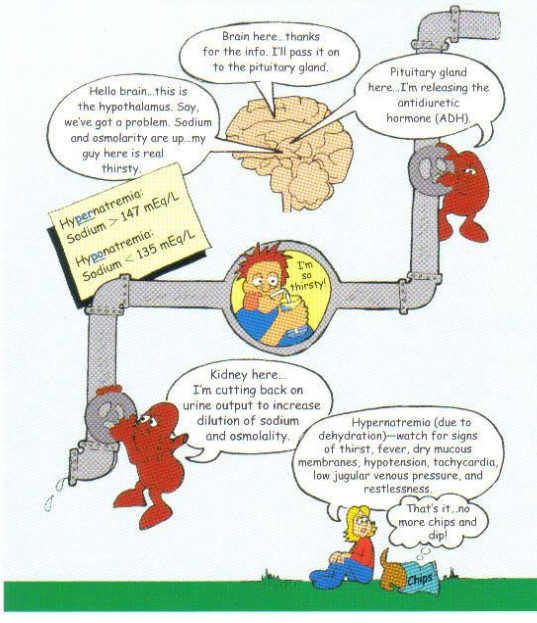
We differentiate between the two causes of diabetes insipidus by using the water deprivation test. First the patient is asked to stop drinking water. A normal kidney should start concentrating the urine because there is no water intake. After the patient has stopped drinking water for sometime (4-18 hours), we first go and measure the urine osmolarity. If it is high (concentrated urine) this means that there is no problem with ADH and you should think of other causes. For example, the patient might have primary polydipsia which means that he/she just loves to drink too much water and came to the doctor complaining of increased urination. On the other hand if we measure the urine osmolarity is low (dilute urine), then we know there is problem with ADH because a normal kidney should suck all of the water from the urine if there is no water intake. After that we infuse the patient with desmopressin (which works like ADH). If the kidney starts concentrating the urine after desmopressin administration → nephrogenic DI; because the kidney is normal and there is no ADH to concentrate the urine. However if desmopressin fails to concentrate the urine → nephrogenic DI.

Central DI is treated with desmopressin. Nephrogenic DI is treated with thiazide diuretics (why would you give a diuretic to someone who is peeing a lot?!) actually thiazides interfere with the kidney's ability to dilute urine→ NDI patients will pass concentrated urine.

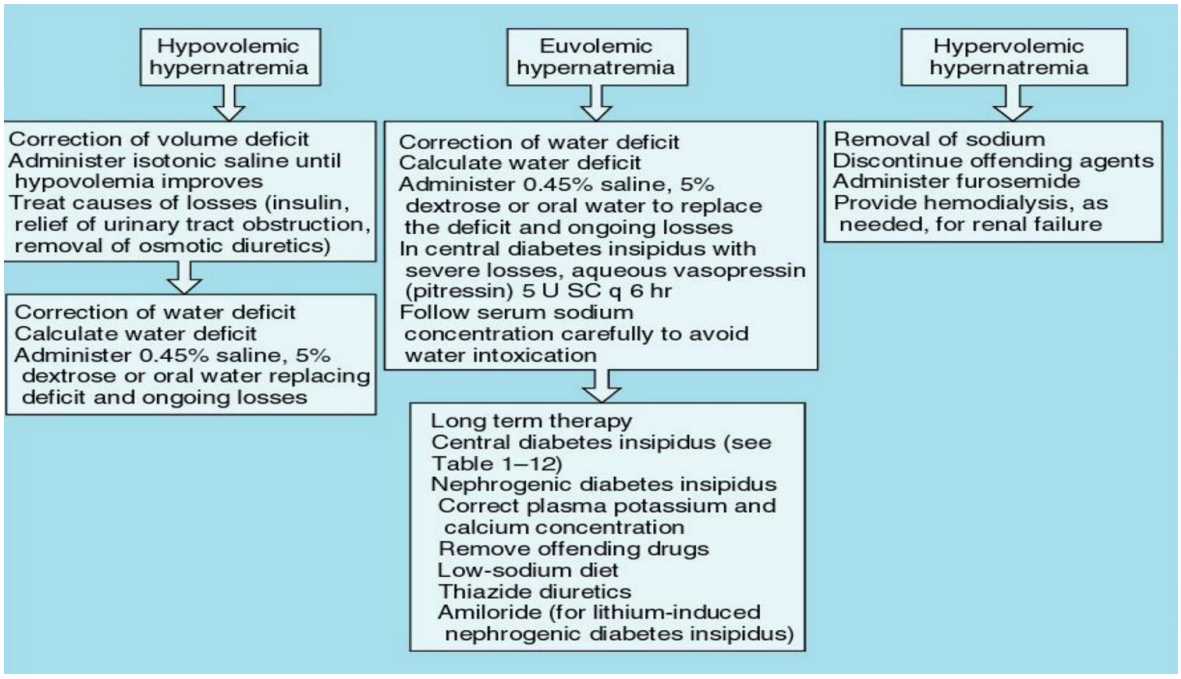
3. Hypervolemic hypernatremia gained more sodium than water (a hypertonic solution)	
Possible causes :	• Primary hyperaldosteronism • Hypertonic saline infusion (iatrogenic) • Exogenous glucocorticosteroids • Cushing syndrome

❑ Clinical Features of Hypernatremia:

- ○ Neurogenic symptoms predominate (Remember CCNS SSoduim)
  - ■ Altered mental status, restlessness, weakness focal neurologic deficits.
  - ■ Can lead to confusion, seizures, coma.
- ❑ Tissues and mucus membrane are dry; salivation decreases.



❑ Treatment of Hypernatremia



- Treat the underlying cause
- **In hypervolemic hypernatremia:** give diuretics (furosemide) and D5W to remove excess sodium. Dialyze patients with renal failure.

- **In hypovolemic hypernatremia:** patient is hypovolemic! Stabilize him with NS ⇒ after that correct the hyponatremia by replacing the free water deficit*.

- **In euvolemic hypernatremia:** replace the free water deficit* and patients with central diabetes insipidus require desmopressin.

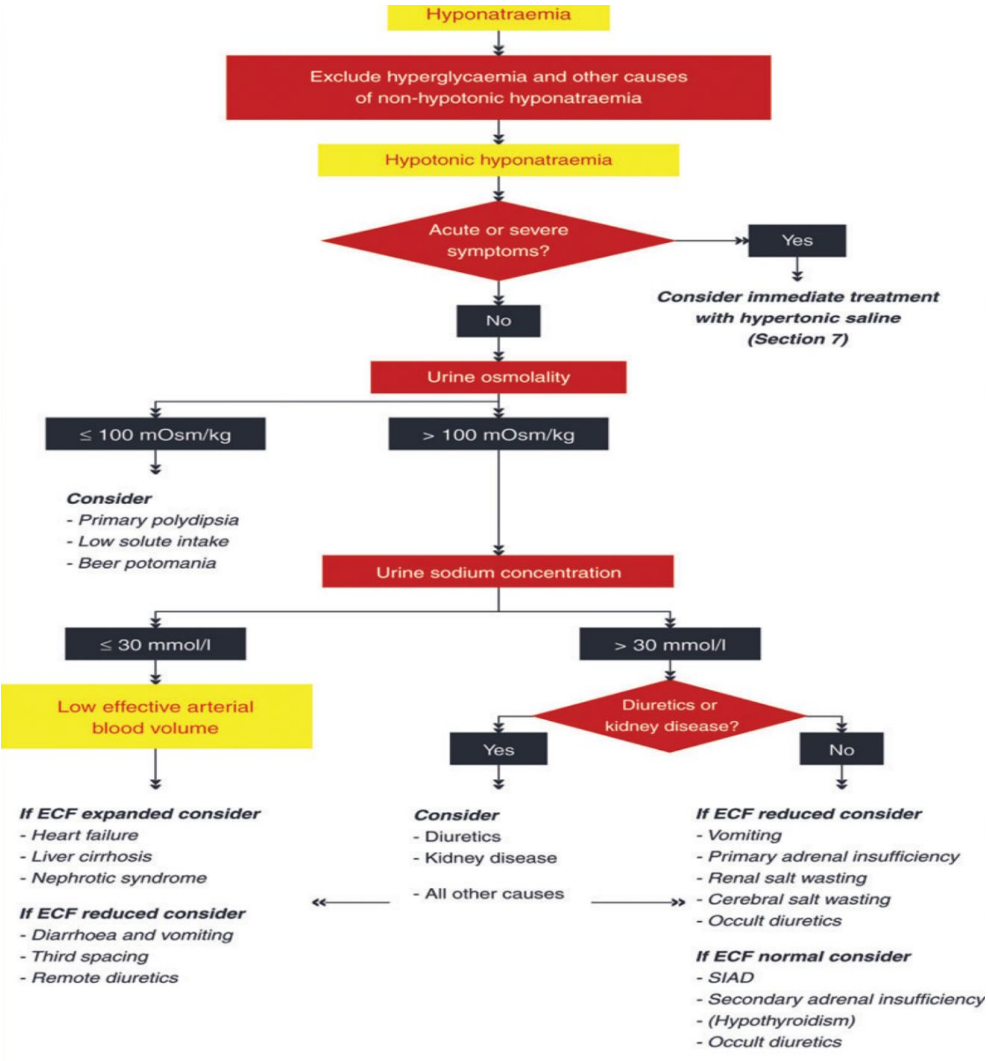
*** The water deficit should be calculated.** That is the amount of water the patient needs to go back to normal sodium concentration. If you ever need to know this for the care of your patient (when you become a resident), you can use your smartphone and put the patient's weight and serum sodium concentration and the application can tell you the answer. :)

Free water deficit= 0.6x current weight (kg) x (current sodium concentration/140 -1)

According to Uptodate, this equation is not accurate and you need to closely monitor the patient and frequently order serum sodium levels. You can then adjust your therapy according to how the patient is responding.

In short, this is too advanced and I recommend that you forget about it. (I only put this in here because it is in the objectives)

❑ Hyponatremia "Plasma Na concentration < 135 mmol/L"

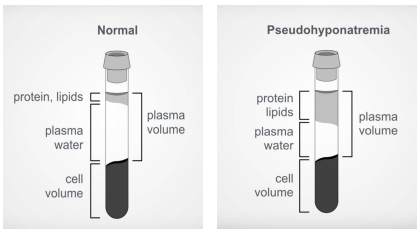


Note: although this graph looks scary, it is is extremely beautiful once you get to know it.

1. False Hyponatremias:

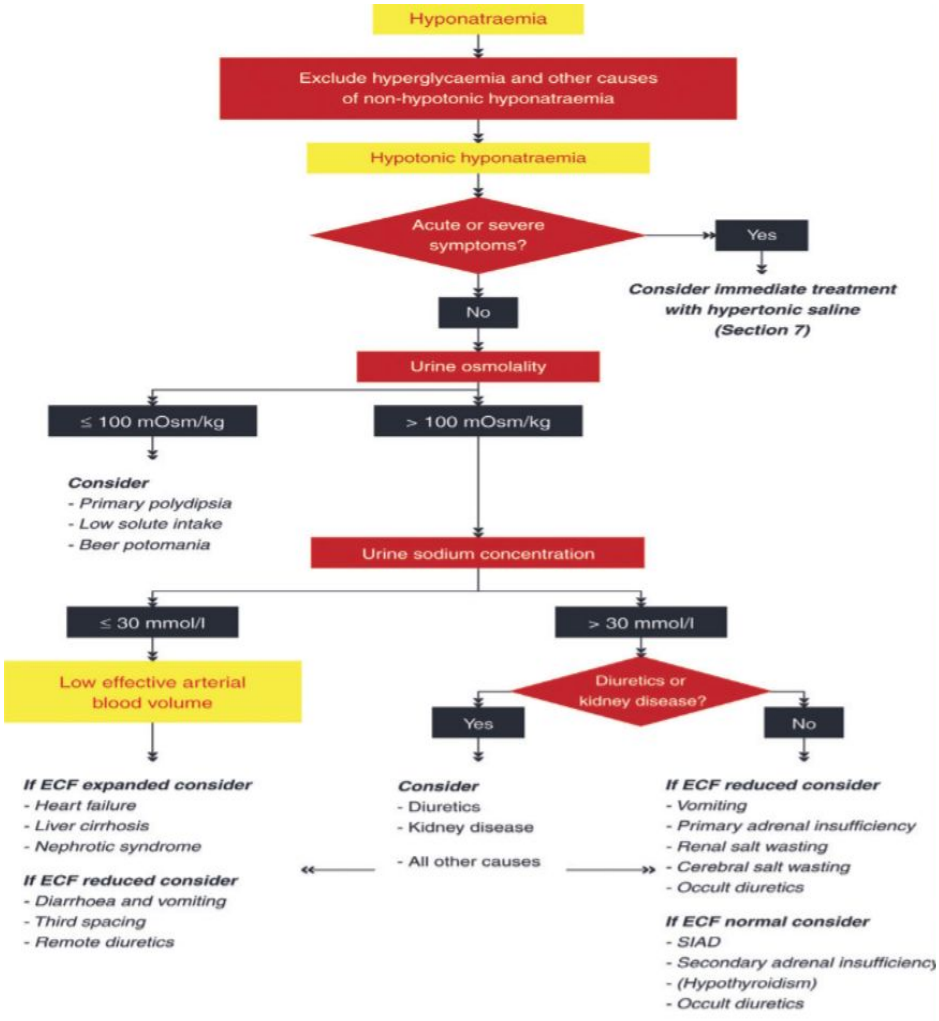
A. Isotonic hyponatremia "Pseudohyponatremia" (where water doesn't move at all)

About 97% of plasma is fluid/water "where sodium is" while the rest is solids (proteins and lipids) and cells, so lab machines measures the amount of sodium in plasma water factored in the total plasma volume, so when there are **high concentrations of solids proteins (example: IgG proteins in multiple myeloma) or lipids (hyperlipidemia)**, in this case the amount of sodium will be factored in the total plasma volume which is *high* giving a false impression of hyponatremia; now modern lab equipment with direct ion detection are not susceptible to this error



B. **Hypertonic hyponatremia "Factitious hyponatremia"**(where water moves out of the cells)

- The first thing that should be done when working up hyponatremia is to exclude hyperglycemia. Because in this case, the Na^+ is completely normal and it is a victim of what is going on with glucose.
    - If there is hyperglycemia, glucose molecules will suck water into the plasma (vai osmosis) and this will dilute the sodium. Therefore, sodium concentration appears to be decreased when in fact everything is normal (normal total body sodium, normal total body water).
    - In this cases, if the plasma osmolarity were to be measured, the osmolarity would be high; because glucose would be very high.
        - If you don't get it plug a very high glucose (5000) in here and look what happens to plasma osmolarity
        - Plasma osmolarity= 2[Na+] + [Glucose]/18 + [BUN]/2.8
    - In case of hyperglycemia → hypertonic hyponatremia



Again take a look at the graph and continue reading the true hyponatremia....

<table>
<tr><th colspan="2">2. True Hyponatremia:</th></tr>
<tr><th colspan="2">Hypotonic hyponatremia</th></tr>
<tr><td colspan="2">If we have a true hyponatremia, which is decreased plasma sodium concentration, there must be a decrease in the plasma osmolarity because Na^+ is the primary cation responsible for plasma osmolarity.
(remember we said that 2x Na^+ is almost the plasma osmolarity)
● After we have made sure that this is hypotonic hyponatremia (a true sodium concentration problem), we must first ask is the patient severely affected? I the answer is yes we need to treat quickly. We might use hypertonic saline to quickly raise the plasma sodium concentration.

● If the patient is stable we can continue with the graph and look at the urine for answers:</td></tr>
<tr><td>If the urine has a low osmolarity (<100) (dilute urine) → the kidney is doing its job;</td><td>because the patient is hyponatremic, the osmolarity is low, ADH will be inhibited, and the urine should be dilute. We want to pee more water to raise the Na^+ concentration
● The problem here is that this patient might be drinking TOO much water which caused hyponatremia→ psychogenic polydipsia</td></tr>
<tr><td>If the urine osmolarity is high (concentrated urine) then we need to know why is the kidney doing that ?</td><td>look at the urinary sodium!

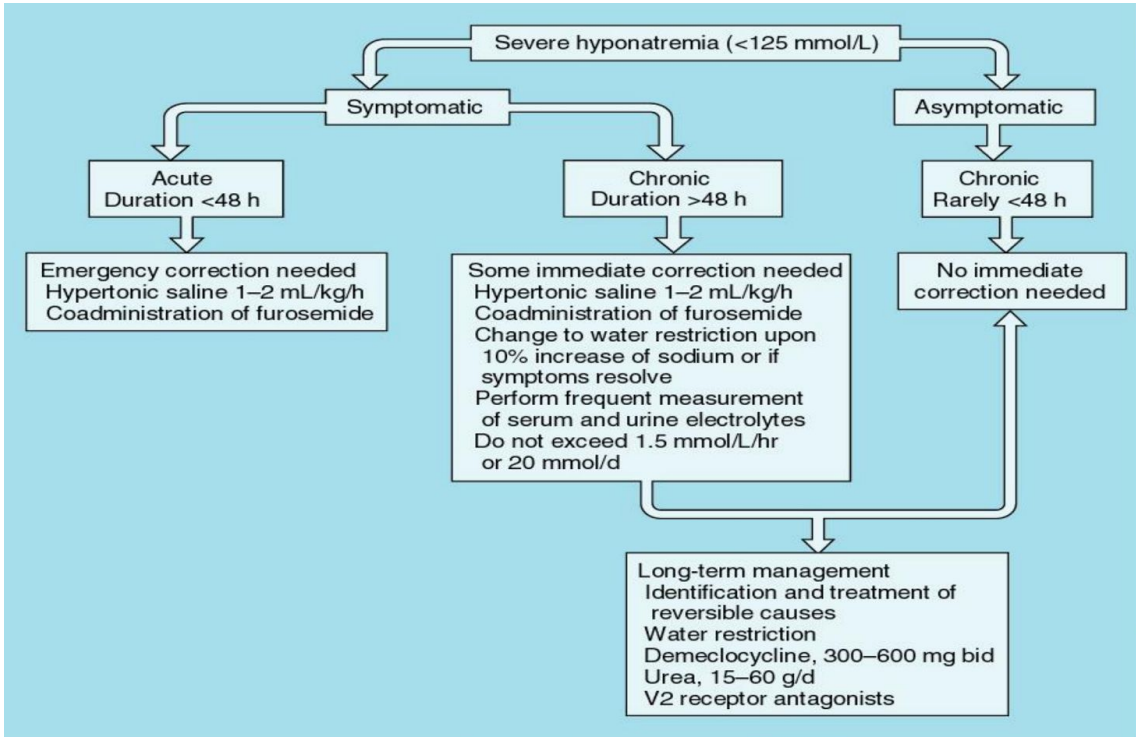
*If there is low sodium (<30) → the kidney is preserving sodium
There must be something causing decreased perfusion of the kidney
● If the patient is hypervolemic → heart failure, cirrhosis, nephrotic
● If the patient is hypovolemic → diarrhea

*If the urine sodium is high (>30)
● Euvolemic → SIADH
● Hypovolemic → primary adrenal insufficiency (destruction of the adrenal glands), renal salt wasting, etc.</td></tr>
</table>

❑ Clinical Features of Hyponatremia: All symptoms that can be signs of *cerebral edema* should be considered as severe or moderate symptom:

Moderately Severe	Severe
● Nausea without vomiting ● Confusion ● Headache	● Vomiting ● Cardiorespiratory distress ● Abnormal and deep somnolence ● Seizures ● Coma

❑ Treatment of Hyponatremia



- If symptomatic, consider hypertonic saline
- If asymptomatic, correct slowly, and treat the underlying cause

★ Remember that if you quickly correct hyponatremia you can damage the CNS (central pontine myelinolysis)

- Do not exceed 9 mEq/L in 24 hours (Uptodate)