Med 341 Course: Water Disorders (Dysnatremia) & Sodium Disorders (Dysvolemia)

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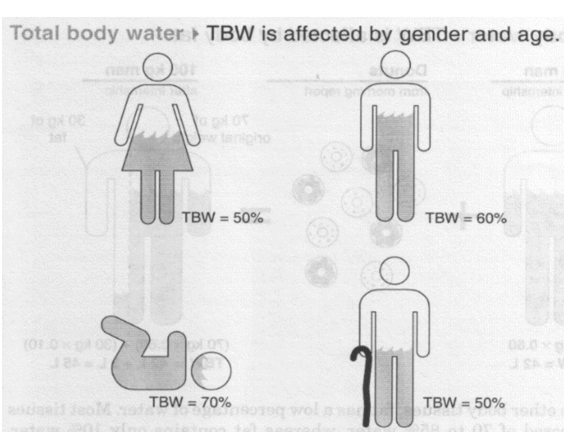
- ***Objectives:***
  1. Composition of the fluid compartments
  2. Mechanisms regulating fluid and sodium balance
  3. Disorders of sodium balance
  4. Disorders of water balance

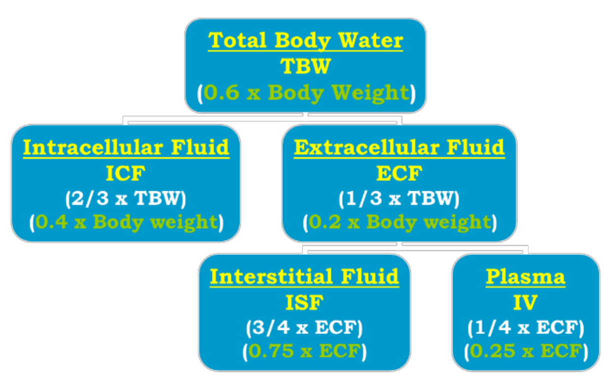
- ***Intended Learning Outcomes:*** By the end of this lecture the student should be able to:
  1. Recognize the systems that control body sodium and water contents
  2. Differentiate between total body sodium content (volume status) and serum sodium concentration (Hypo- and Hypernatremia)
  3. Use the appropriate type of IV fluids in clinical practice
  4. Calculate the water deficit in Hypernatremia
  5. Explain the workup of Hyponatremia

- ***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.

(Accessed November 4, 2020 from https://www.britannica.com/science/homeostasis)

- ***Total Body Fluid & Compartments:***





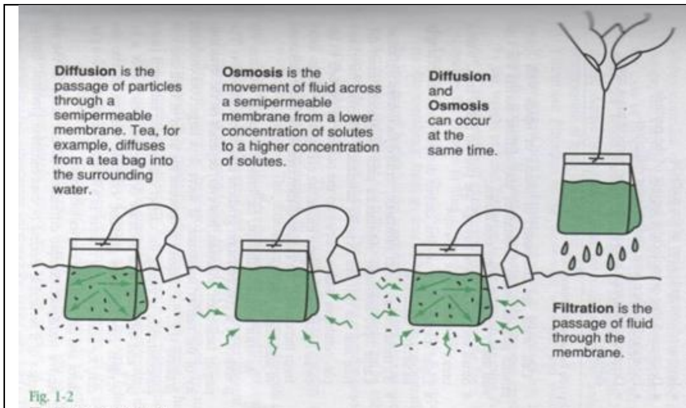
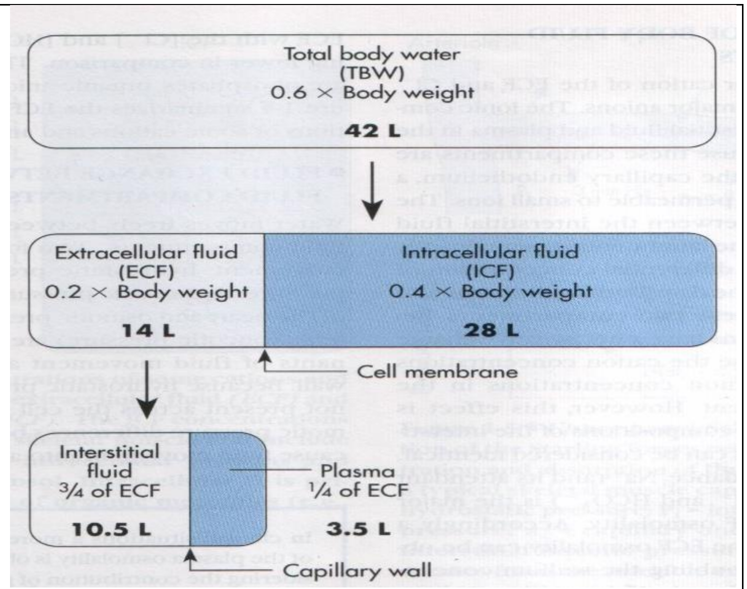


Fig. 1-2
Transport processes.



- Electrolytes are substances dissolved in solutions and dissociated into particles called ions
  1. *Cations:* Positively charged ions
  2. *Anions:* Negatively charged ions

- **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)

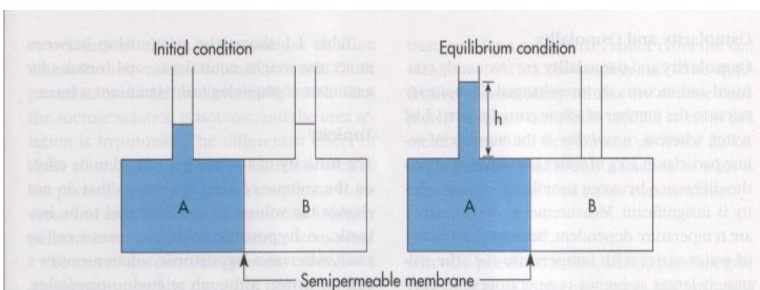
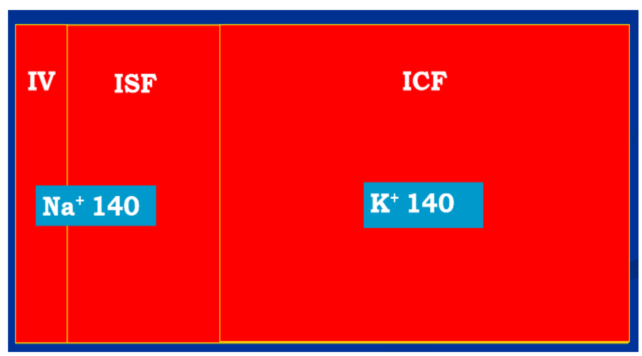


Figure 1-1 **Schematic representation of osmotic water movement and the generation of an osmotic pressure. The solute particles in compartment *A* cause water to move by osmosis from compartment *B* across the semipermeable membrane into compartment *A*. The water column in compartment A will rise until 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**



- **Osmolality & Osmolarity:**

  - **OsmolaLity:** Osmoles in Kg of water (mOsm/kg water) (**measured**)
    - ✓ Normal measured serum osmolality: 283-292 mOsm/kg plasma water

- ❑ **<u>OsmolaRity:</u>** Osmoles in Liter of <u>solution [= Plasma]</u> (mOsm/L) (**calculated**)
- ❑ For $[Na^+]$, $[K^+]$ and $[Cl^-]$: 1 mEq/L = 1 mmol/L = 1 mOsm/L
- ❑ Calculated Posm (mOsm/L) = (**2 x serum $[Na^+]$**) + blood urea (mmol/L) + glucose (mmol/L)

- ❑ **Osmol Gap = Measured Osmolality – Calculated Osmolarity (up to 10 mOsm/kg)**

■ ***<u>Regulation Mechanisms of Fluid and Electrolytes:</u>***

- ✓ **To make one liter of plasma = one liter of water + 140 mmol of $[Na^+]$**

- ✓ <u>The regulation of **plasma volume**</u> occurs through neurological and renal mechanisms
  - o **Volume Receptors: The stretch receptors** (sensing volume status)
    - ✓ **The Natriuretic peptides** (increase urine sodium excretion)
    - ✓ **The Renin-Angiotension-Aldosterone System** (increase vasoconstriction and Na reabsorption = sodium preservation)
    - ✓ **Antidiuretic hormone (vasopressin)**
  - o Kinins & Prostaglandins

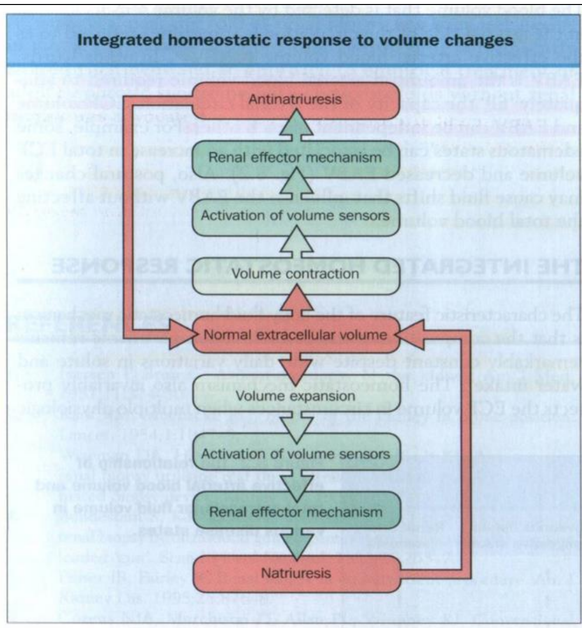


Figure 8.3 A general overview of the integrated homeostatic response system regulating extracellular fluid volume during volume contraction and expansion.

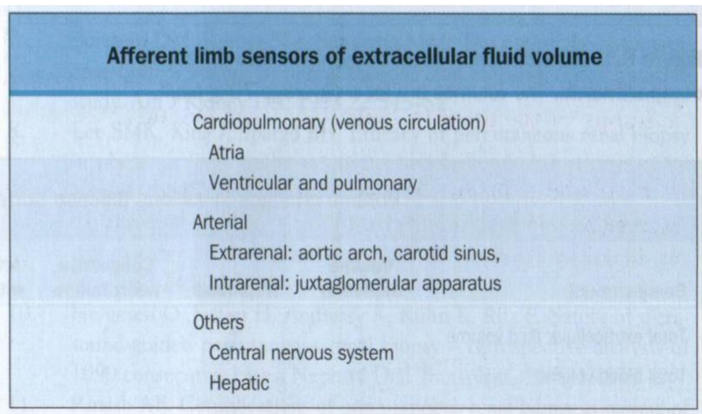
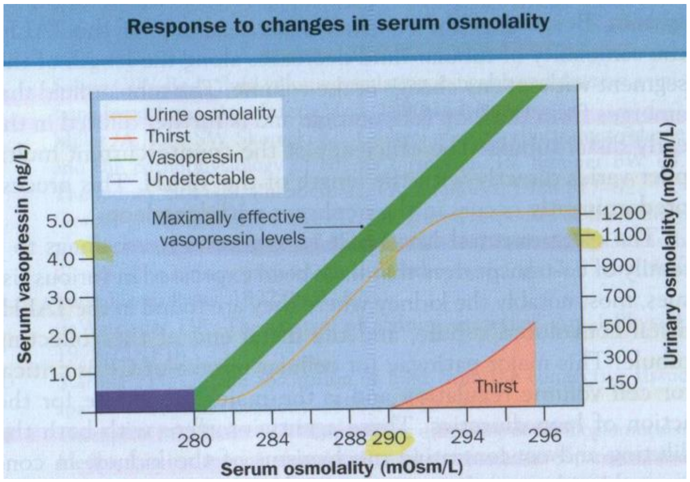
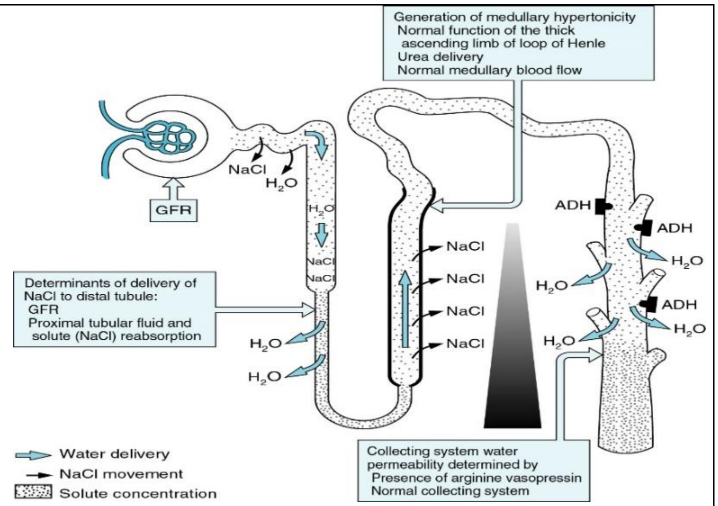
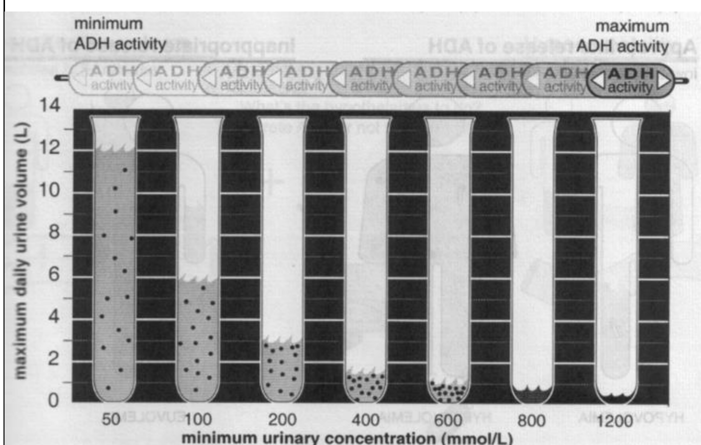


Figure 8.4 The afferent limb (volume sensors) of the integrated homeostatic response system for extracellular volume.

- ✓ <u>The regulation of **plasma osmolality**</u> is achieved through **Osmoreceptors**
    - ✓ **Thirst** (increase water intake)
    - ✓ **Antidiuretic hormone** (vasopressin) (preserve body water = decrease water loss into the urine)
- ✓ ***Volume is more important than osmolality*** (survival = holding water in during hypovolemic state even in the face of hypoosmolality state [hyponatremia])





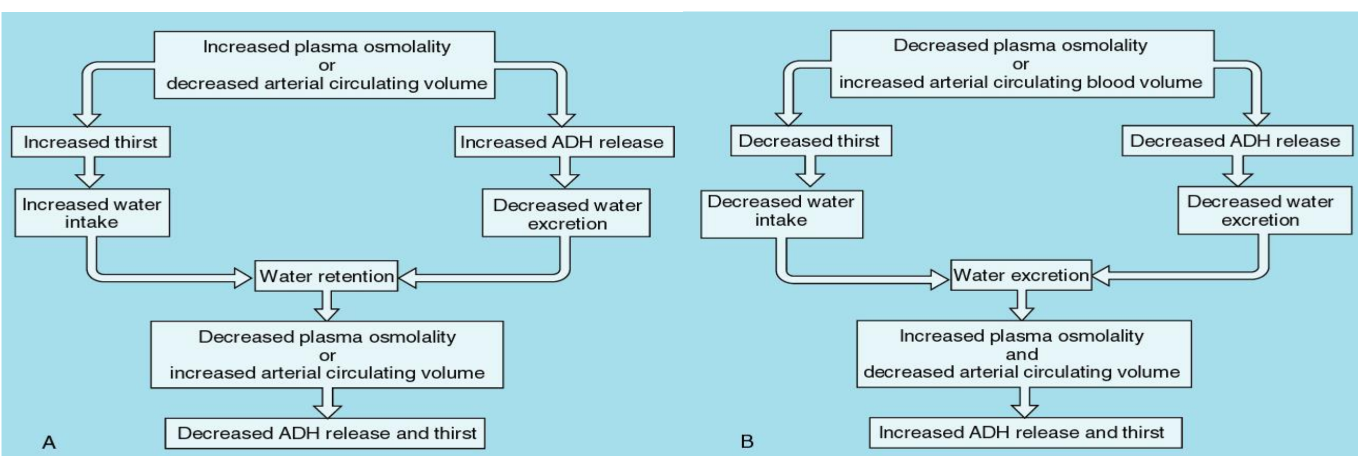


The graph shows the maximum daily urine volume for several values of the minimum urinary concentration (50 to 1200 mmol/L), assuming a daily solute load of 600 mmol/day.

Urine Output & Daily Solute Load

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

The Linear Relationship Between Urine Specific Gravity and Uosm



■ *Clinical features of Hypovolemia & Hypervolemia (Davidson's Principles & Practice of Medicine)*

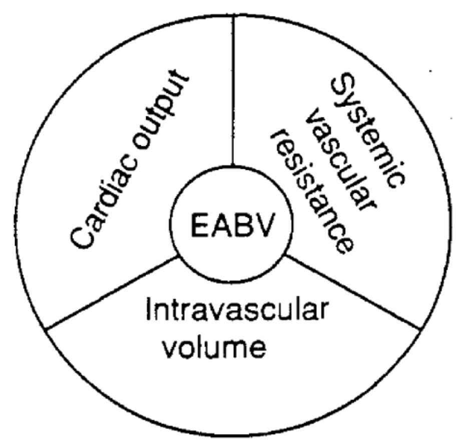
	Hypovolemia	Hypervolemia
Symptoms	Thirst	Ankle swelling
	Dizziness on standing	Abdominal swelling
	Weakness	Breathlessness
Signs	Low JVP	Raised JVP
	Postural hypotension	Peripheral edema
	Tachycardia	Pulmonary crepitations
	Dry mouth	Pleural effusion
	Reduced skin turgor	Ascites
	Reduced urine output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

■ *Effective Arterial Blood Volume (EABV):*

- 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

- ↓ **EABV:**
  - ↑ CO
  - ↑ SVR
  - ↑ Renal Na retention

- ↑ **EABV:**
  - ↓ CO
  - ↓ SVR
  - ↓ Renal Na retention



- **EABV is the amount of arterial blood volume required to adequately 'fill' the capacity of the arterial circulation: Best assessed by spot urine [Na^+] to reflect RAAS activation**

- ECF volume and EABV can be independent of each other
  - Edematous states: increase in total ECF volume with decreased EABV
  - Postural changes may cause shifts that influence the EABV without affecting the total blood volume

■ *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****
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
Water will move from ECF into ICF	It will remain in the ECF	Water will move from ICF to ECF
Distilled Water 0.45% NaCl (1/2) 0.33% NaCl (1/3)	NS (0.9% NaCl) Ringers Lactate 2/3 DW-1/3 NS 5% Dextrose in Water (D5W)	3% NaCl 10%-50% Dextrose D5W-1/2 NS D5NS Amino acid solution

*** see comment of the next table.**

■ *Intravenous Solutions: Crystalloids* vs *Colloids*

- *Crystalloids* are intravenous solutions that contain solutes that readily cross the capillary membrane
  - Dextrose and electrolyte solutions
- *Colloids* are intravenous solutions that DO NOT readily cross the capillary membrane
  - Blood, albumin, plasma

Solution	***Gluc***	***Na^+***	***K^+***	***Ca^{+2}***	***Cl^-***	***Lactate***	***mOsm/L****
D5W	50	0	0	0	0	0	253
D10W	100	0	0	0	0	0	506
NS	0	154	0	0	154	0	308
½ NS	0	77	0	0	77	0	154
D5 NS	50	154	0	0	154	0	561
D5 ½ NS	50	77	0	0	77	0	407
2/3-1/3	33	50	0	0	50	0	285
Ringer's Lactate	0	130	4	3	109	28	274

*** 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"**

D5W: 5 g dextrose/100 mL (50 g/L)

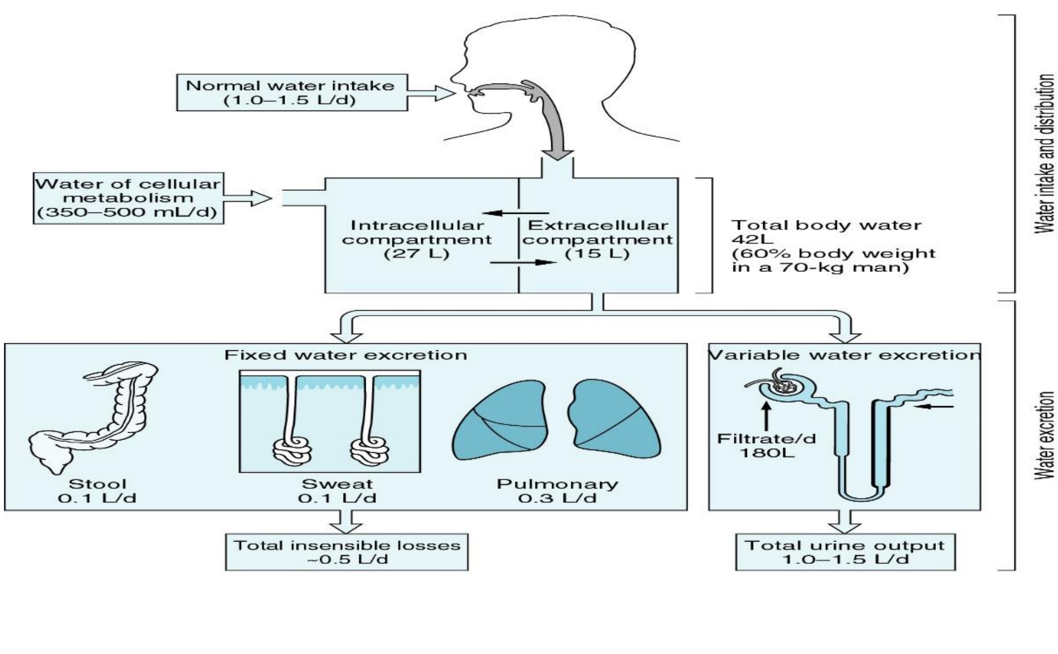
D10W: 10 g dextrose/100 mL (100 g/L)

NS (0.9% NS): 0.9 g NaCl/100 mL (9 g/L)

½ NS (0.45% NS): 0.45 g NaCl/100 mL (4.5 g/L)

2/3-1/3: 2/3 D5W (33 g/L) + 1/3 NS (0.33 g NaCl/100mL or 3.3 g NaCl/L)

Distribution of IV fluid in a normal person*			
Parenteral Fluid	***ECF (1/3 TBW)***		***ICF (2/3 TBW)***
	IV (1/4 ECF)	***ISF (3/4 ECF)***	
1000 ml D_5W	80 ml	250 ml	670 ml
1000 ml NS	250 ml	750 ml	---
Colloids (PRBC)	300 ml	---	---
1000 ml ½ NS:			
(500 ml NS)	125 ml	375 ml	---
(500ml water)	40 ml	125 ml	335 ml
Total	165 ml	500 ml	335 ml
1000 ml D_5½NS	165 ml	500 ml	335 ml
1000 ml $D_{10}W$	80 ml	250 ml	670 ml
1000 ml D_5NS	250 ml	750 ml	---
*** assuming normal capillary wall function (no capillary leak syndrome)**			



■ ***Basal Requirements:***

- Basal Water:
  - 1st 10 kg: 4 ml/kg/h +
  - 2nd 10 kg: 2 ml/kg/h +
  - > 20 kg: 1 ml/kg/h
- Insensible water loss:
  - Stool, breath, sweat: 800 ml/d
  - Increases by 100-150 ml/d for each degree of body temperature above 37 C
- Electrolytes:
  - Na: 50-150 mmol/d
  - Cl: 50-150 mmol/d
  - K: 20-60 mmol/d
- Carbohydrates:
  - Dextrose: 100-150 g/d
- **IV Dextrose minimizes protein catabolism and prevents starvation ketoacidosis**

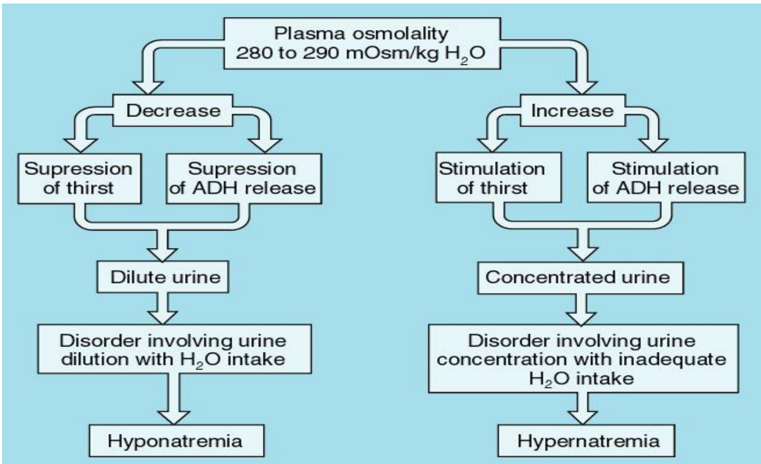
■ ***Sodium and Water Disorders:***

- **ECF volume** = ***Absolute*** amounts of **Sodium** (and water)

- **Plasma [Na^+]** = ***Ratio*** between the amounts of Sodium and water (Concentration)

- **Dysnatremia = Water Disorder/Tonicity Disorder**
  - Hyponatremia = Relative Water Excess
  - Hypernatremia = Relative Water Deficit

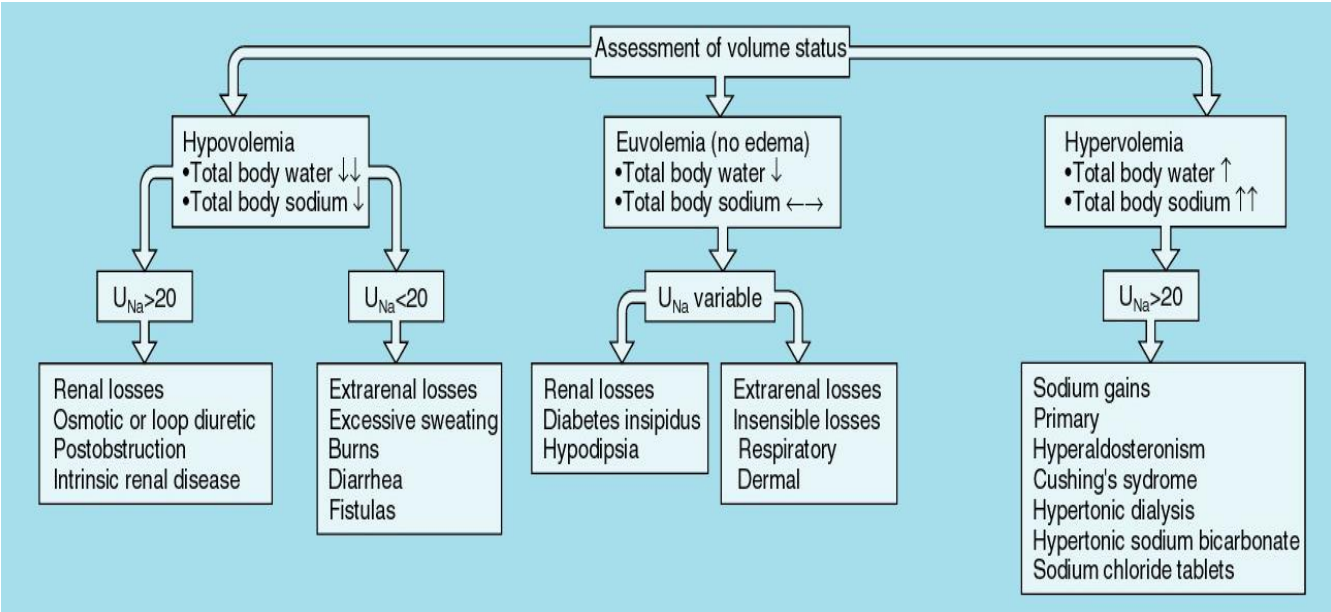
- **Dysvolemia = Sodium Disorder**
  - Hypervolemia = Sodium Excess (“Edema”)
  - Hypovolemia = Sodium Deficit (“Dehydration”)



- ***Dysnatremia and dysvolemia combination clinical cases:***

Sodium Balance	Relative Water Balance (Na and Water losses/gains comparing to plasma ratio) (= 140 mmol Na per 1 L water)		
	Hyponatremia	*Normonatremia*	*Hypernatremia*
Hypovolemia (Sodium Deficit)	Hemorrhagic Shock with good oral water intake	Pure GI bleeding	Diarrhea in Children and Seniors
	Isotonic fluid loss with only water intake (Na loss > Water loss)	Isotonic fluid loss (Na loss = Water loss)	Hypotonic fluid loss with no water intake (Na loss < Water loss)
Euvolemia	SIADH	Normal State	Diabetes Insipidus (DI)
	(Pure Water Gain)	(Homeostasis)	(Pure Water Deficit)
Hypervolemia (Sodium Excess)	Advanced Congestive Heart Failure Advanced Cirrhosis	Heart Failure Cirrhosis Nephrotic Syndrome	Hemodialysis Patient after 3% Saline injection for cramps
	Hypotonic fluid gain (Na gain < Water gain)	Isotonic fluid gain (Na gain = Water gain)	Hypertonic fluid gain (Na gain > Water gain)

■ ***Hypernatremia:***



■ ***Hypernatremia: Water Deficit Calculation***

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

2) Since Serum [Na^+] = Intracellular [K^+] → Total body cations = Current TBW x Current [Na^+]

3) Assuming no other intake or loss:

   ➢ **Current TBW x Current [Na^+] = Target TBW x Target [Na^+]**

4) Target TBW – Current TBW = Water Deficit

5) Consider ongoing water loss (insensitive and other losses)

6) Decide about IVF/PO fluid: type and rate

7) 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?**

✓ Current TBW = 70 x 0.6 = 42 L

✓ Current Total Body Cations = 42 x 170 = New TBW x 140 → New TBW = 51 L

✓ So his total water deficit is 51 – 42 = 9 L. It can be given IV or PO depending in his condition

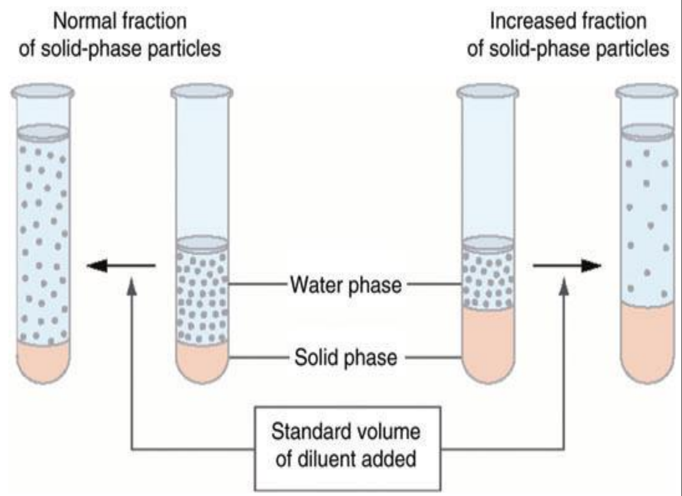
- **_Hyponatremia:_**

1) **_Normotonic or Isotonic Hyponatremia_**

- ***Factitious Hyponatremia***
- ***Pseudohyponatremia***

- Results from laboratory artifact due to high concentrations of proteins or lipids

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



- **Normal Measured SNa^+ = 153 mmol/L of 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**

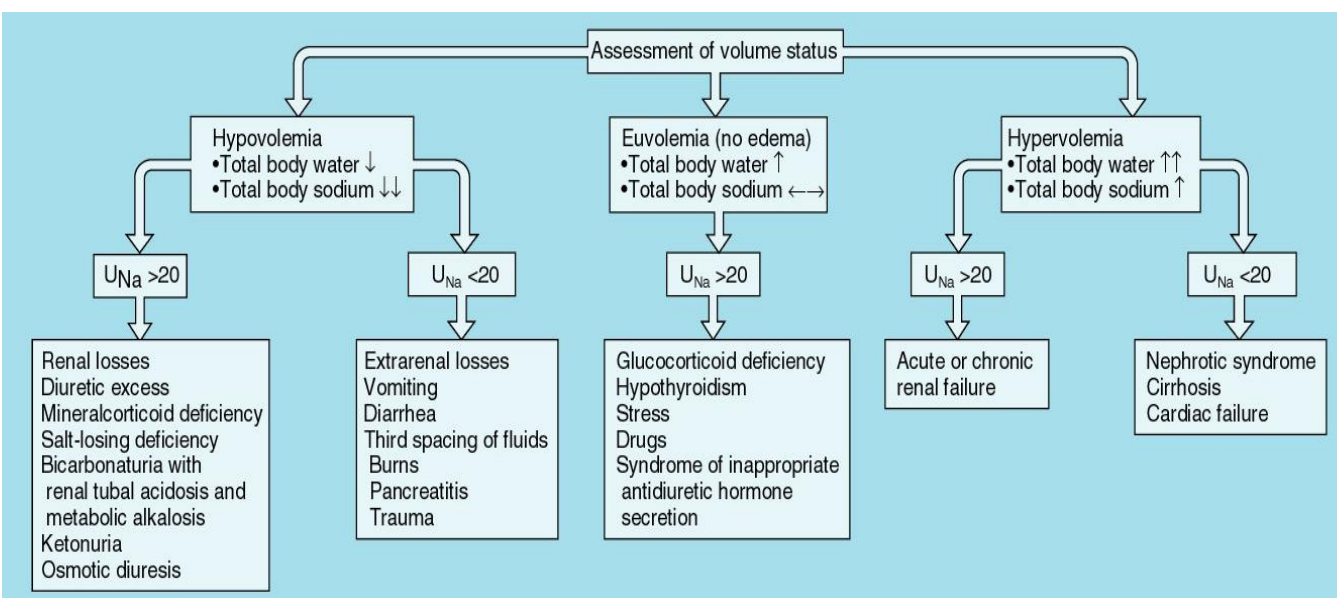
- If water phase decreases due to increased solid phase (high protein or lipids) then:
  - Example: Water phase is 84% now due to myeloma
  - Reported Serum Na^+ = **153** x 0.84 = 129 mmol/L of Plasma

2) **_Hypertonic or Hyperosmolar Hyponatremia_**

- ***Translocational Hyponatremia = Dilutional hyponatremia = True hyponatremia***
- Results from non-Na osmoles in the serum (often glucose or mannitol) drawing Na-free H_2O from cells
- $[Na^+]$ declines by ~2.4 mEq/L for each 100 mg/dL [5.5 mmol/L] increase in serum glucose

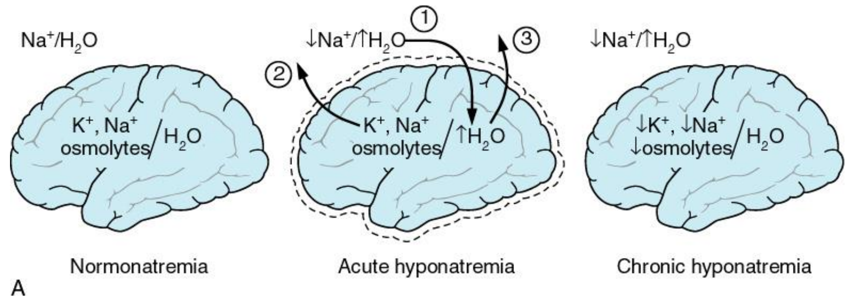
3) **_Hypotonic or Hypoosmolar Hyponatremia_**

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



■ ***Classification of Symptoms of Hyponatremia***

- All symptoms that can be signs of cerebral edema should be considered as moderate or severe symptoms that can be caused by hyponatremia
- **Moderately Severe**
  - Nausea without vomiting
  - Confusion
  - Headache
- **Severe**
  - Vomiting
  - Cardiorespiratory distress
  - Abnormal and deep somnolence
  - Seizures
  - Coma (Glasgow Coma Scale ≤8)



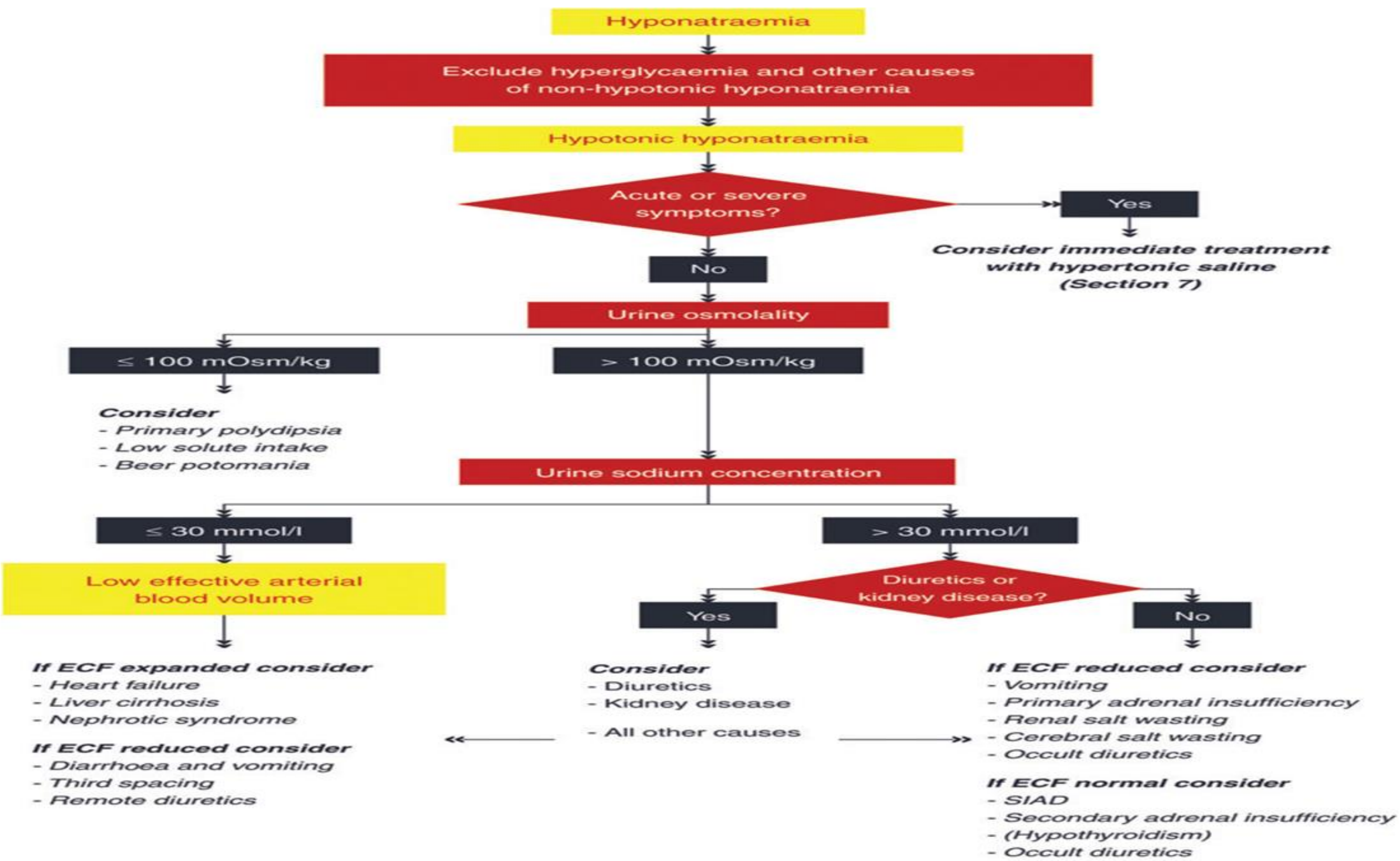
■ ***General Management of Hyponatremia:***

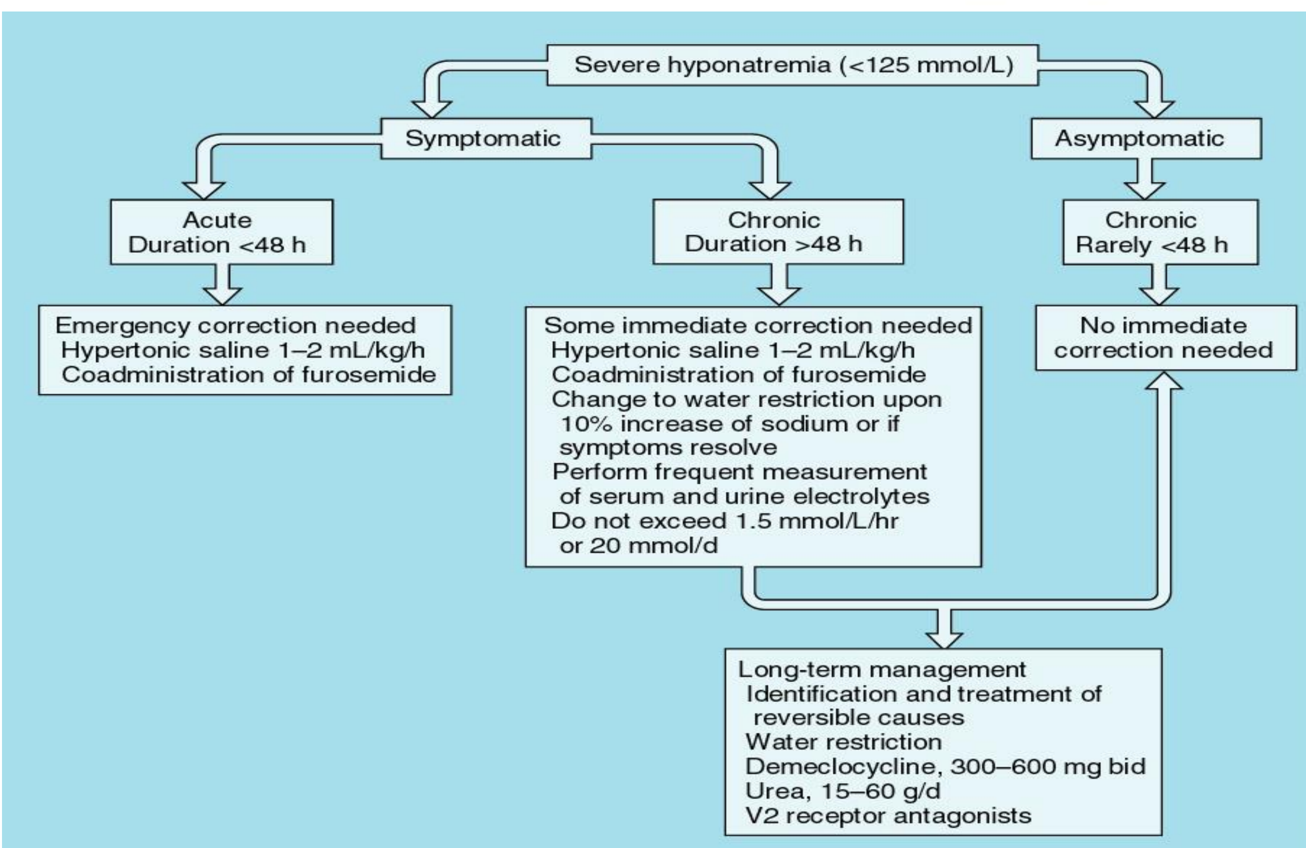
1) Symptoms & Signs
   - Assess acuity of development
   - Volume Status
   - Comorbidities
2) Serum:
   - Measured serum Osmolality
   - TSH, FT4, Serum Cortisol (@ 8 AM)
   - Albumin, Total Proteins, Uric Acid
3) Spot Urine: (even on weekends and holidays)
   - Urine Electrolytes (Na, K, Cl): Spot urine [Na^+] to assess effective arterial blood volume
   - Urine Urea Nitrogen
   - Urine creatinine (to calculate FENa if AKI)
   - Urine Osmolality
   - 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

■ ***Diagnostic Criteria for SIADH*** **("HIVE"): (Be careful: SIADH is a Diagnosis of Exclusion!)**

- ✓ **H:** Hypoosmolar Hyponatremia (Posm <275 mOsm/Kg H_2O)
- ✓ **I:** Inappropriate urine concentration (Uosm >100 mOsm/Kg H_2O)
- ✓ **V:** Euvolemia, No diuretic use
- ✓ **E:** Endocrine = normal Thyroid, adrenal and renal function
- ✓ Hypouricemia (<238 mcmol/L) and low Urea (<3.5 mmol/L)


Hyponatraemia
Exclude hyperglycaemia and other causes of non-hypotonic hyponatraemia
Hypotonic hyponatraemia
Acute or severe symptoms?
Yes
Consider immediate treatment with hypertonic saline (Section 7)
No
Urine osmolality
≤ 100 mOsm/kg
> 100 mOsm/kg
Consider
- Primary polydipsia
- Low solute intake
- Beer potomania
Urine sodium concentration
≤ 30 mmol/l
> 30 mmol/l
Low effective arterial blood volume
Diuretics or kidney disease?
Yes
No
If ECF expanded consider
- Heart failure
- Liver cirrhosis
- Nephrotic syndrome
If ECF reduced consider
- Diarrhoea and vomiting
- Third spacing
- Remote diuretics
Consider
- Diuretics
- Kidney disease
- All other causes
If ECF reduced consider
- Vomiting
- Primary adrenal insufficiency
- Renal salt wasting
- Cerebral salt wasting
- Occult diuretics
If ECF normal consider
- SIAD
- Secondary adrenal insufficiency
- (Hypothyroidism)
- Occult diuretics


Severe hyponatremia (<125 mmol/L)
Symptomatic
Asymptomatic
Acute Duration <48 h
Chronic Duration >48 h
Chronic Rarely <48 h
Emergency correction needed Hypertonic saline 1–2 mL/kg/h Coadministration of furosemide
Some immediate correction needed Hypertonic saline 1–2 mL/kg/h Coadministration of furosemide Change to water restriction upon 10% increase of sodium or if symptoms resolve Perform frequent measurement of serum and urine electrolytes Do not exceed 1.5 mmol/L/hr or 20 mmol/d
No immediate correction needed
Long-term management Identification and treatment of reversible causes Water restriction Demeclocycline, 300–600 mg bid Urea, 15–60 g/d V2 receptor antagonists

■ ***Chronic Hypervolemic Hyponatremia: Water Excess Calculation***

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

2) Since Serum [Na^+] = Intracellular [K^+] → Total body cations = Current TBW x Current [Na^+]

3) Assuming no other intake or loss:

   ✓ **Current TBW x Current [Na^+] = Target TBW x Target [Na^+]**

4) Current TBW – Target TBW = Water Excess

5) Both salt and water restrictions

6) Treat excess volume with loop diuretics (Furosemide):
   ✓ Diuretic use = increase hypotonic urine (U[Na^+] ~ 70-100 mmol/L): Na loss < water loss

7) Always reassess clinically and with lab results

8) 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?**

✓ Current TBW = 90 x 0.6 = 54 L.

✓ Current Total Body Cations = 54 x 110 = New TBW x 140 → New TBW = 42.5 L.

✓ So his total water excess is 54 – 42.5 = 11.5 L.

■ ***Symptomatic Euvolemic Hyponatremia: Sodium Deficit Calculation***

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

2) 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)
   ✓ Sodium deficit = TBW x 4

3) 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

4) Always reassess clinically and with lab results.

5) 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!

■ **<u>Example:</u> 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?**

- ✓ Current TBW = 60 x 0.6 = 36 L.
- ✓ Sodium deficit = 36 x 4 = 144 mmol.
- ✓ So 3% saline = 144 x 2 = 290 ml to be given IV push. Repeat lab right after the infusion.
- ✓ Watch urine output with Foley catheter

■ **<u>Suggested Reading:</u>**

1. Alluru Reddi. Fluid, Electrolyte and Acid-Base Disorders: Clinical Evaluation and Management. (Download free from KSU domain). http://www.springer.com/gp/book/9781461490821

2. John A. Myburgh and Michael G. Mythen. Resuscitation Fluids. N Engl J Med 2013;369:1243-51. DOI: 10.1056/NEJMra1208627

3. Fluid Management in Adults and Children: Core Curriculum 2014. AJKD. http://dx.doi.org/10.1053/j.ajkd.2013.10.044

4. Clinical practice guideline on diagnosis and treatment of hyponatremia. EJE. http://www.eje-online.org/content/170/3/G1.full.pdf+html

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