

Author(s): Michael Heung, M.D., 2009

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Approach to the Patient with Disorders of Osmoregulation

Michael Heung, M.D.
M2 Renal Sequence

Fall 2008



Objectives

- Know how to calculate plasma osmolality and understand why sodium is a surrogate measure
- Understand the concept of an osmolar gap
- Understand the mechanisms of hypernatremia development and know the differential diagnosis
- Be able to distinguish between various polyuric states
- Know the different types of hyponatremia and develop an approach to determining etiology
- Be able to interpret the urine osmolality in the setting of hyponatremia
- Understand the principles of hypo- and hypernatremia management

Yes, this slide again

- Sodium balance is the critical determinant of fluid compartment size

Therefore, *alterations in **sodium** balance are detected as changes in extracellular **volume***

- Alterations in water balance are critical for the determination of fluid compartment composition

Therefore, *alterations in **water** balance are manifest as changes in plasma **osmolality** and are measured as changes in plasma **sodium concentration***

Further Elaborated

- Although sodium is a determinant of volume, measurement of the plasma sodium concentration reflects a *ratio* of solute and water.
- Therefore, sodium concentration does not correlate with the volume of the extracellular compartment. A *hyponatremic patient may be hypovolemic, euvolemic, or hypervolemic.*

Plasma Osmolality

- The primary solutes that are measured in the clinical lab that contribute to the plasma osmolality are **sodium, glucose and urea**
- Therefore an approximation of the plasma osmolality can be obtained by the following formula:

$$P_{\text{osm}} = (2 \times [\text{Na}^+]) + (\text{glucose}/18) + (\text{urea}/2.8)$$

* Na measured in mEq \equiv mmol; glucose measure in mg/dL; urea measure in mg/dL

- Normal serum osmolality is maintained between 280-290 mosm/kg water
- Under normal conditions the osmolar contributions of glucose and urea are less than 10 mOsm/kg water; thus *plasma sodium is the primary determinant of osmolality*

Measured Plasma Osmolality

- *Measured osmolality* is typically higher than *calculated osmolality* due to the presence of unmeasured osmoles in plasma (e.g. phosphate, sulfate, amino acids, calcium, etc.)
- The difference between the measured and calculated osmolality is termed the *osmolar gap*
 - The osmolar gap is normally $<10\text{mosm/L}$

High Osmolar Gap: A Diagnostic Clue

Effective Osmoles

Mannitol

Glycine

Ineffective Osmoles

Ethanol

Methanol

Ethylene glycol

Isopropyl alcohol



 [Polar Antifreeze](#) by Idiolecter



 [Disinfected Kitty](#)
by Knitty Cent

Normal Values

Basic Panel (Chem 7)

Sodium	140 (135-145) mEq/L
Chloride	100 (95-105) mEq/L
Potassium	4.0 (3.5-4.5) mEq/L
CO2 content (bicarbonate)	28 (24-32) mEq/L
Glucose	65-110 mg/dL
Creatinine	1.0 (M 0.8-1.3, F 0.6-1.1mg/dl)
Urea nitrogen	8-25 mg/dL
Plasma osmolality	280-290 mosm/kg H2O
Urine osmolality	50-1200 mosm/kg H2O

Case 1: Dehydration

A 72 year old male resident of a skilled nursing facility is brought to the emergency department with poor responsiveness. The facility reports that he recently had a urinary tract infection which was being treated with antibiotics. He has also had diarrhea the past few days.

PMHx: Alzheimer's dementia, CAD, HTN

PE: BP 90/60, P 110 reg

HEENT: mucous membranes dry

Chest: clear

CV: RRR, weak peripheral pulses

Ext: no edema

Neuro: minimal responsiveness to voice

Labs: Sodium 162mEq/L, Plasma osm 332mosm/kg,

Urine osm 745mosm/kg



PD-INEL Source Undetermined

What factors contributed to the development of hypernatremia in this patient?

Causes of Hypernatremia

Water loss in excess of sodium

- Insensible losses (skin, respiratory, fever)
- Renal losses (DI, osmotic diuresis)
- Extrarenal losses (diarrhea)

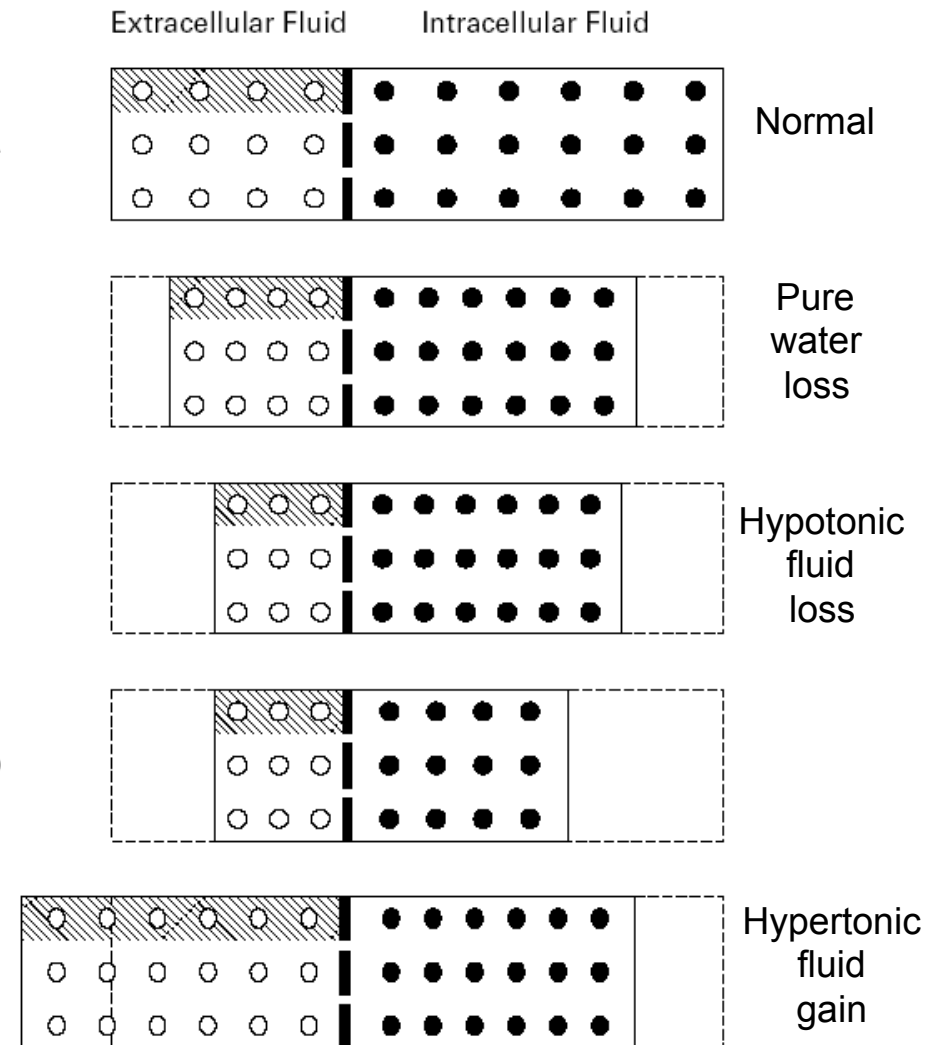
Requires an impairment in the thirst mechanism

Sodium gain in excess of water

- Administration of hypertonic solutions

Most frequently iatrogenic

(Why would we do this?)



Who Develops Hypernatremia?

- An intact thirst mechanism can almost always compensate for water losses, even in the complete absence of ADH
- At-Risk Populations:
 - Impaired thirst sensation
 - Elderly
 - Hypothalamic lesions
 - Psychosis
 - Impaired access to water
 - Dementia, delirium
 - Infants



Case 2: Polyuria

You are asked to evaluate a 24 yr old previously healthy male who was admitted to the orthopedics service following a skiing accident in which he fractured his pelvis. He underwent 6 hours of surgery yesterday. Over the past 24 hrs he has been noted to have a urine output of 4L. The patient is sedated with pain medications, but his girlfriend notes that he “always urinates a lot”.

PE: BP 120/70, P 85, wt 80kg

HEENT: mucous membranes dry

CV: RRR

Ext: no edema

Neuro: somnolent

Labs: Sodium 152mEq/L, Plasma osm 315mosm/kg,

Urine osm 105mosm/kg



What is the diagnosis? Treatment?

Diabetes Insipidus

- Defined by a defect in renal water conservation
 - *diabainein* (Greek): “to pass through”
 - *insipidus* (Latin): “flavorless”

Central DI: Impaired synthesis, transport, storage, or release of ADH from the hypothalamus and pituitary

- Can be hereditary or result from infection, trauma, ischemia, neoplasm or granulomatous disease

Nephrogenic DI: Reduced response to ADH in the collecting tubule

- Hereditary or acquired (eg. renal failure, hypercalcemia, drugs)

How could you distinguish between central and nephrogenic DI?



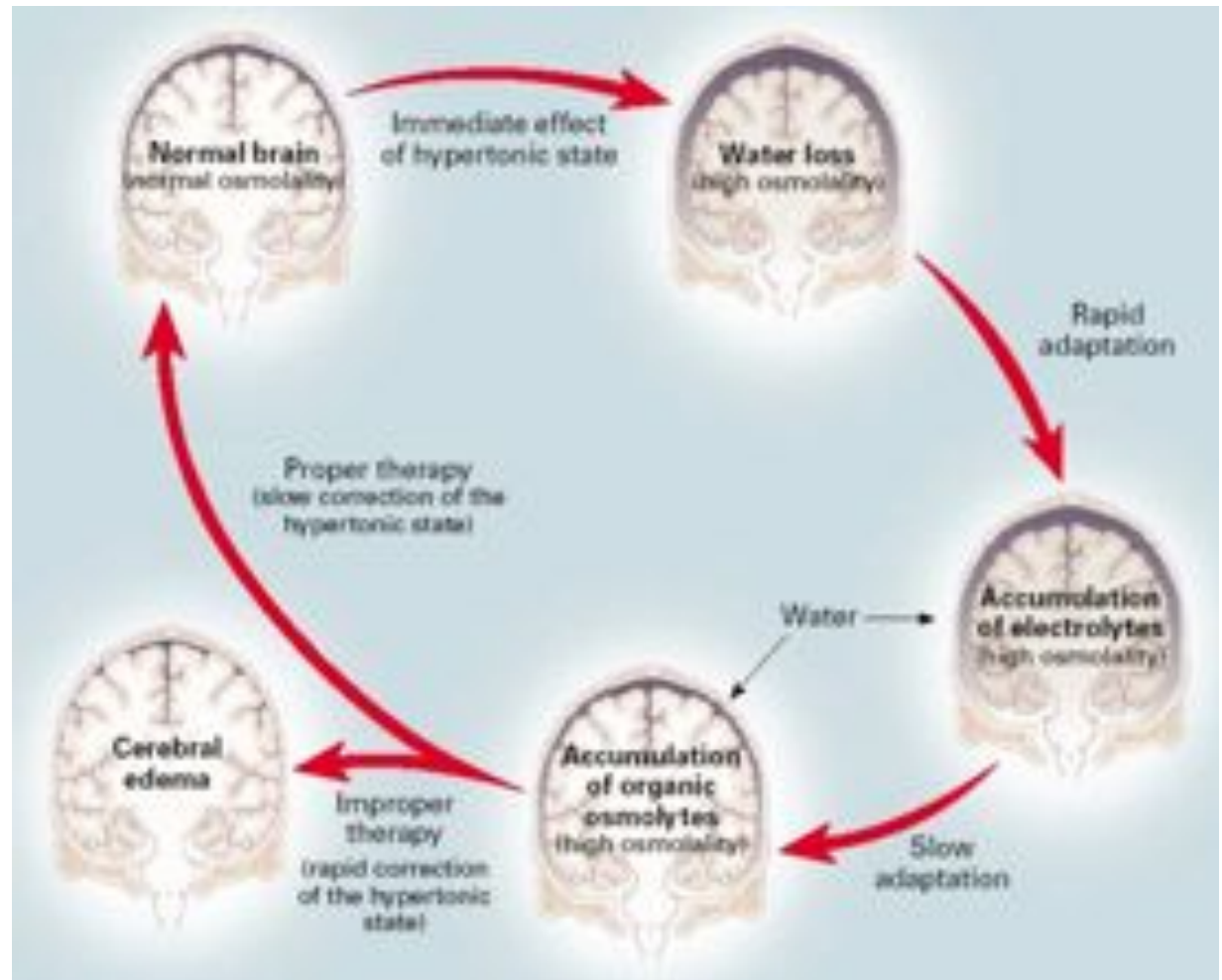
(cc) BY [Peeing Men](#) by gennie catastrophe, Flickr.com

Distinguishing Polyuric States

	Urine osm Following Water Deprivation	Increase in Urine osm with Exogenous ADH
Normal	>800	Little or no increase
Complete central diabetes insipidus	<300	Substantial (>600)
Partial central diabetes insipidus	300-800	>10% following water deprivation
Nephrogenic diabetes insipidus	<300-500	Little or no increase
Primary Polydipsia	>500	Little or no increase

Correction of Hypernatremia

- Over-aggressive correction of hypernatremia can result in cerebral edema and death
- Unless it is acute/symptomatic, correction should occur gradually: 0.5 mEq/L per hour, or 10 mEq/L per day



Correction of Hypernatremia

- Estimating the free water deficit:

$$\text{Current TBW} = (140/[\text{Na}]) \times \text{normal TBW}$$

$$\text{Water deficit} = \text{normal TBW} - \text{current TBW}$$

$$= \underline{0.6 \times \text{weight (kg)} \times (1 - 140/[\text{Na}])}$$

Case 2 Example: Na 152, weight 80kg

$$\text{Water deficit} = 0.6 \times 80\text{kg} \times (1 - 140/152) = 3.8\text{L}$$

Target correction at rate of 0.5mEq/hr = 24hrs

Therefore, need to give 158.3mL of free water/hr
(plus ongoing free water losses!)

- Formula assumptions: - No sodium deficit
 - Total body water distribution
 - Steady state

Correction of Hypernatremia

- Formulas are just an estimate to get you started!
- Clinical Pearls:
 - *Monitor your progress and adjust appropriately*
 - *Err on the side of slow correction*
 - *Account for ongoing losses (eg. urine, insensible)*
 - *Know how much free water you are giving*

Solution	Osm (mosm/L)	Free Water (mL per L solution)
0.9% NS	308	
0.45% NS	154	
D5W	0	

Hyponatremia Basics

- The most common electrolyte disturbance
- Symptoms are primarily neurologic and depend on severity and rapidity of development
 - Acute: confusion, disorientation → seizures, coma, death
 - Chronic: usually asymptomatic until $<125\text{mEq/L}$
- Management depends on underlying etiology

A Systematic Approach

- Three main etiologies (by mechanism):
 1. Non-hypoosmolar: pseudohyponatremia or hyperosmolar
 2. Hypoosmolar hyponatremia with normal renal water excretion
 3. Hypoosmolar hyponatremia with impaired renal water excretion
- Ask 3 questions:
 1. Is the patient hypo-osmolar? ***Serum osm (corrected for urea)***
 3. Are the patient's kidneys responding appropriately to clear free water? ***Urine osm***
 2. Does the patient have an adequate effective intravascular volume? ***Urine Na >20, Physical exam***

Why Not Urea?

$$P_{\text{osm}} = (2 \times [\text{Na}^+]) + (\text{glucose}/18) + (\text{urea}/2.8)$$

In clinical practice:

$$P_{\text{osm}} = (2 \times [\text{Na}^+]) + (\text{glucose}/18)$$

$$\textit{or} = \text{Measured osm} - (\text{urea}/2.8)$$

Urea is an ineffective osmole and therefore does not cause water shifting or contribute to disorders or osmoregulation.

Case 3

An elderly woman with a history of diabetes mellitus presents to her physician with complaints of fatigue and dizziness following a recent bout of the flu. Her food intake has been decreased so she has only taken half of her usual dose of insulin.

Labs: Sodium 128mEq/L Plasma osm 320mosm/kg
Urea 30mg/dL (corrected for urea ~ 310)
Glucose 800mg/dL

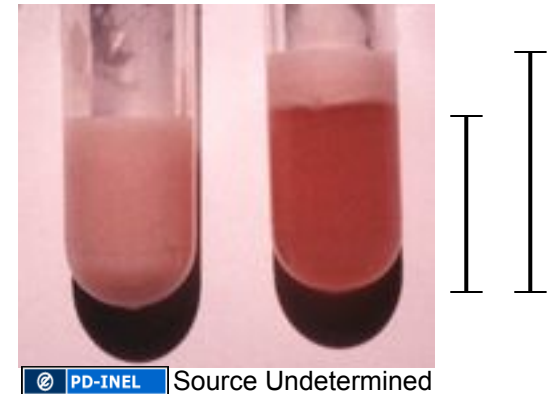
1. Is the patient hypo-osmolar?

Why is she hyperosmolar?

Non-Hypoosmolar Hyponatremia

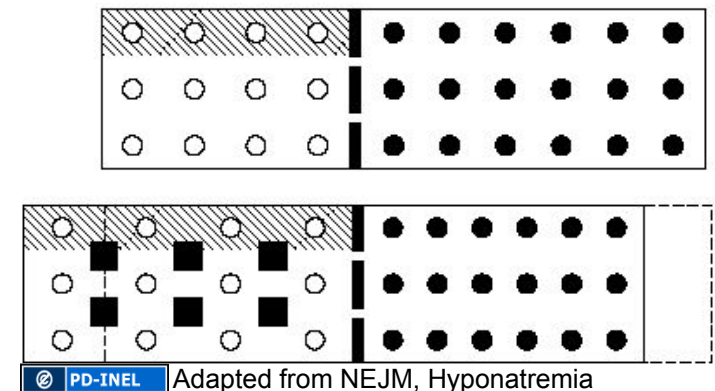
Pseudo-Hyponatremia (Isoosmolar)

- Hyperlipidemia
- Hyperparaproteinemia
- Primarily of historical interest only



Iso- or Hyperosmolar Hyponatremia

- Due to shifting of water from intracellular to extracellular compartments
- Occurs only with effective osmoles
 - Glucose: for every 100mg/dL above 100, [Na] falls by 1.6 mEq/L
 - Mannitol



Case 4

A 35 year old male is admitted to the closed psychiatry ward for auditory and visual hallucinations. He has been on psychotropic drugs for the last 5 years. The renal consultant is called 5 days into the admission when the patient's plasma sodium is noted to be 125 mEq/L on routine chemistries.

Labs: Sodium 125mEq/L
Glucose 90mg/dL
Urea 10mg/dL

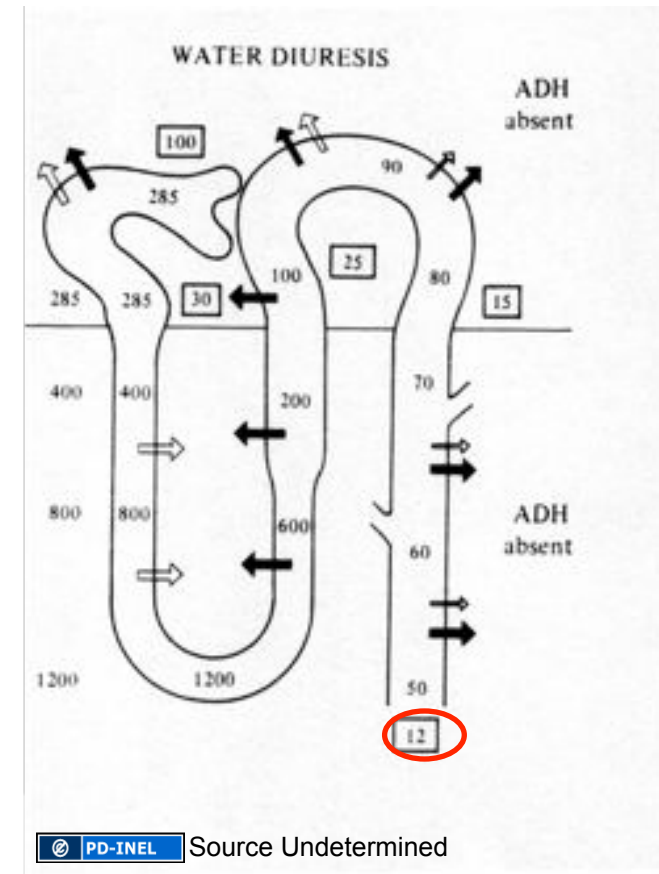
Plasma osm 268mosm/kg
(corrected for urea ~265)
Urine osm 80mosm/kg

1. Is the patient hypo-osmolar?
2. Are the patient's kidneys responding appropriately to clear free water?

What is the best approach to correcting his hyponatremia?

Hyponatremia With Normal Renal Water Excretion

- **Primary Polydipsia:** Water ingestion overcomes the free water clearance capacity of the kidneys
 - Psychogenic polydipsia: thirst defect?
 - Manage with *water restriction*



- **Reset Osmostat:** Normal response to changes in plasma osmolality but at a reduced threshold
 - Sodium is low but stable
 - Seen in malnutrition, psychosis, pregnancy, malignancy
 - Treat underlying cause, *no specific therapy for hyponatremia*

Case 5

A 50 year old woman is newly diagnosed with essential hypertension by her internist. She is placed on hydrochlorothiazide (25 mg/d) and returns one week later with complaints of light-headedness and is found to be orthostatic.

Labs: Sodium 110mEq/L
Glucose 108mg/dL
Urea 10mg/dL

Plasma osm 238mosm/kg
(corrected for urea ~235)
Urine sodium 30mEq/L
Urine osm 300mosm/kg

1. Is the patient hypo-osmolar?
2. Are the patient's kidneys responding appropriately to clear free water?
3. Does the patient have an adequate effective intravascular volume?

Hyponatremia with Impaired Water Excretion

1. ADH Effect

- Appropriate (i.e. low effective circulating volume)
- Inappropriate

2. Advanced Renal Failure

3. Endocrine Disturbances

- Hypothyroidism
- Adrenal insufficiency

Case 6

A 65 year old male with a 10 year history of coronary artery disease presents to his physician with progressive dyspnea on exertion, and difficulty climbing stairs. He notes that he sleeps in a reclining chair and often awakens 2 hours after falling asleep with difficulty breathing.

PE: BP 170/95, P 90 reg, RR 24.

Chest: bibasilar crackles 1/3 up.

CV: JVD to jaw, PMI displaced to post ax line, +S3

Ext: 3+ edema to knees

Labs: Sodium 125mEq/L

Urea 40mg/dL

Glucose 105mg/dL

Plasma osm 265mosm/kg

(corrected for urea ~ 251)

~~Urine sodium <10mEq/L~~

~~Urine osm 350mosm/kg~~

1. Is the patient hypo-osmolar?
2. Are the patient's kidneys responding appropriately to clear free water?
3. Does the patient have an adequate effective intravascular volume?

Hyponatremia Due to “Appropriate” ADH

Low effective intravascular volume leads to ADH release and stimulation of thirst

- Urine sodium can be helpful diagnostically

Total Body Volume Up

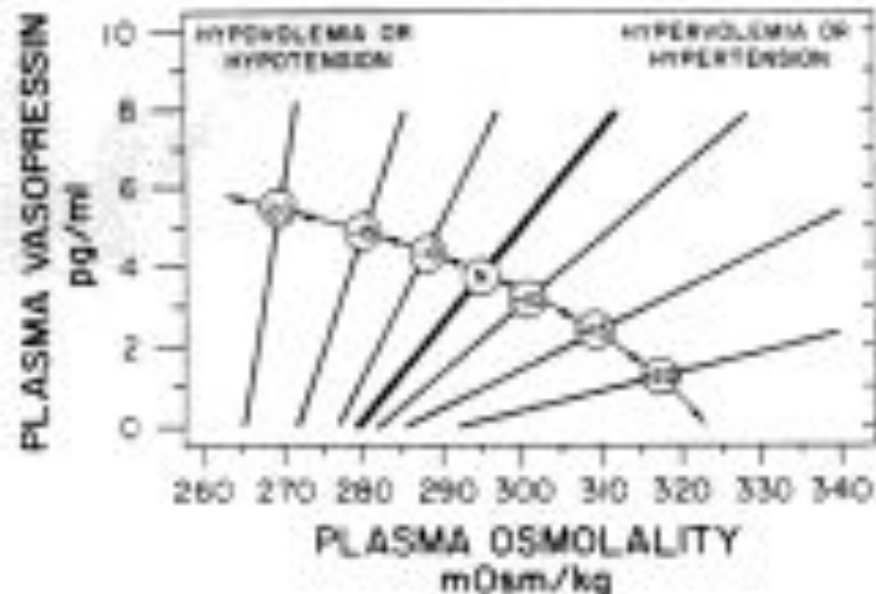
- Edematous states:
 - Congestive heart failure
 - Cirrhosis

Free water restriction

Total Body Volume Down

- Renal Losses
- Extra-renal Losses (GI, skin)

Correction of volume status results in cessation of ADH release



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Case 7

A 52 year old male with a 50 pack-yr smoking history presents to the emergency department for evaluation of hemoptysis. On further questioning, he has unintentionally lost 20 lbs over the past 3 months.

PE: BP 140/90, P 80, no orthostatic changes

HEENT: bitemporal wasting

Chest: diminished breath sounds R upper lobe

Ext: no edema

Labs: Sodium 118mEq/L

Urea 15mg/dL

Glucose 90mg/dL

Plasma osm 250mosm/kg (corr 245)

Urine osm 600mosm/kg

Urine sodium 32mEq/L

CXR: solid mass in R upper lobe

1. Is the patient hypo-osmolar?
2. Are the patient's kidneys responding appropriately to clear free water?
3. Does the patient have an adequate effective intravascular volume?

Syndrome of Inappropriate ADH

Non-physiologic secretion of ADH with resulting impaired water excretion in the setting of normal sodium excretion

- Diagnosis of exclusion

Increased Hypothalamic Production

- CNS disorders (meningitis, CVA, trauma, tumors)
- Pulmonary disease (pneumonia, TB, asthma)
- HIV
- Nausea, pain (post-op)
- Drugs

Ectopic Production

- Small cell lung cancer

ADH Potentiation

- Drugs (carbamazepine, chlorpropamide)
- Psychosis



PD-EXP

The Anatomy of the Nervous System: From the Standpoint of Development and Function by SW Ranson, [Wikipedia](#)



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Source Undetermined

Management of SIADH

- Treat reversible underlying cause(s)
- Free water restriction
- Hypertonic saline (eg. 3% NS, 513mEq/L) +/- furosemide
- Demeclocycline
- V2 receptor antagonists

Giving 0.9% NS (154mEq NaCl/L, 300 mosm/kg) can actually *worsen* the hyponatremia of SIADH. How?

Eg. Na 118, Posm 250, Uosm 600

→ 1L of 0.9% NS contains 308mosm

→ this patient will excrete that solute load in ~500mL of urine

→ the remaining 500mL is kept as free water

General Management of Hyponatremia

Acute and Symptomatic

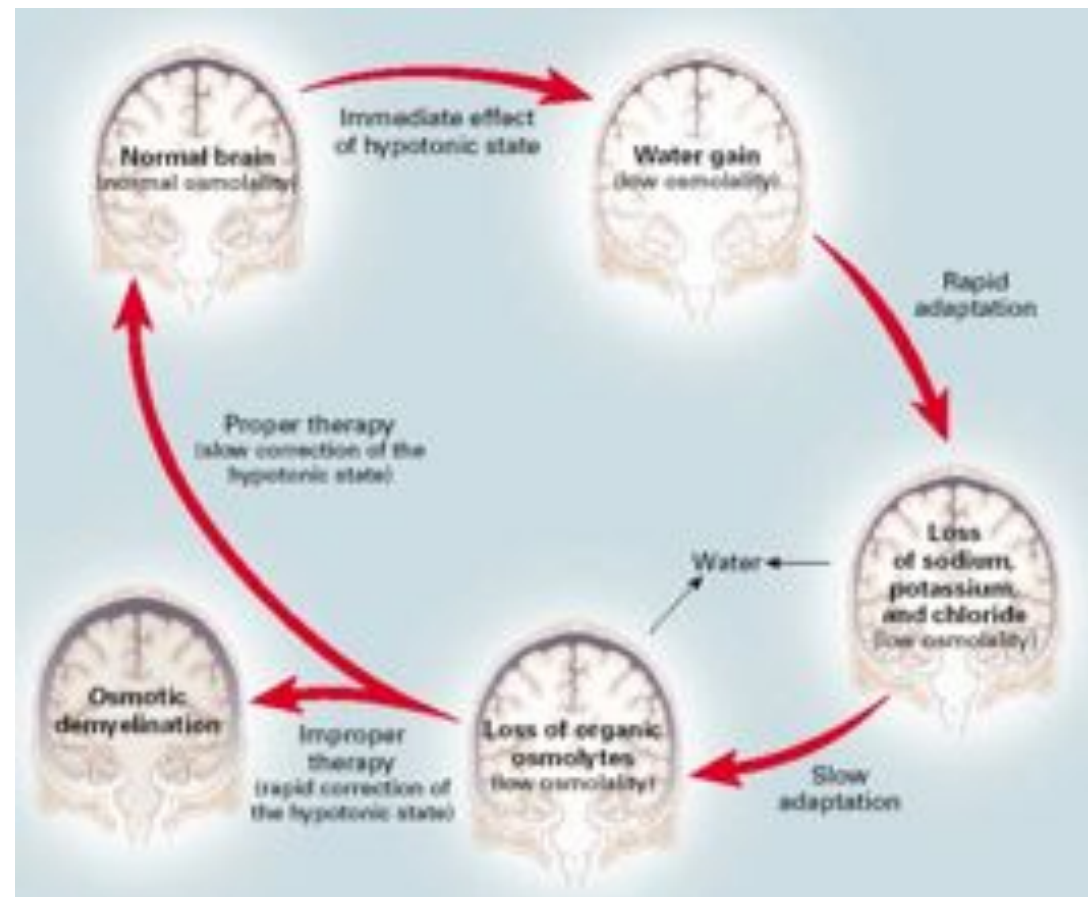
- Correct quickly by up to 5% and then slowly

Chronic

- Limit rate of correction to <math><0.5\text{ mEq/L}</math> per hour or <math><10\text{ mEq/L}</math> per day

Clinical Pearls

- *Know the etiology and treat any reversible processes*
- *Follow your progress and adjust accordingly*
- *Know what's coming out (urine osm)*
- *Err on the side of slow correction*



Summary: Hyponatremia

Type of Hyponatremia	Primary Defect	Serum Osm (mosm/kg water)	Urine Osm (mosm/kg water)	Urine Na (mEq/L)	Volume Status	Therapy
Pseudo Hyperosm	Lab effect Osmotic effect	Normal or High	Varies	>15	Normal	none
Intact renal water clearance	Water intoxication	Low	<100	>15	Normal	Free water restriction
Impaired renal water clearance	ADH	Low	>100	<15	High	Free water restriction
	ADH	Low	>100	<15	Low	Volume repletion
	ADH	Low	>100	>15	Normal	Free water restriction

Low Plasma Sodium

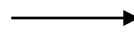


1. Is Patient Hypoosmolar?
(i.e. urea-corrected P osm < 280)

Yes



No (Posm \geq 280)



Iso- or Hyperosm
- Effective osm (glucose, mannitol)

2. Is Renal Water Excretion Intact?

Yes (Uosm<100)

- Primary polydipsia
Water restrict

No (Uosm>100)



3. Is There Adequate Effective Circulating Volume?

Yes (UNa>20)

- SIADH
Water restrict

No (UNa<20, physical exam)

Volume Up
Water restrict

Volume Down
Volume replace

An Algorithmic Approach to Hyponatremia

Pop Quiz

	Na+	K+	Cl-	HCO ₃ ⁻	Glucose	BUN	Posm (corr)	Uosm	UNa
A	125	3.5	80	35	90	30	268	450	5
B	128	4.0	88	28	85	14	310	250	30
C	125	3.8	90	24	90	8	260	90	25
D	120	4.2	90	20	88	14	260	350	40

Which patient has psychogenic polydipsia?

What labs are consistent with SIADH?

Which labs are those of the dehydrated man who has been vomiting?

Who is the cardiac catheterization patient who received mannitol?

Questions?

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