Approach to Severe Hyponatremia

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Objectives

• Review the role of volume status in the assessment and management of hyponatremia
• Recognize common pitfalls in the management of hyponatremia
• Understand the role of different treatment options for hyponatremia
• Appreciate and understand the risk of overcorrection of hyponatremia

Sodium Disorders
AKA “water disorders”

\[ \text{H}_2\text{O in} \quad \Rightarrow \quad \text{H}_2\text{O out} \quad \Rightarrow \quad \text{Hyponatremia} \]

It’s ALL about Water
Background:
Salt (NaCl) and Water (H₂O)

Sodium
- Primary determinant of serum osmolality
- Primary extracellular electrolyte
- Regulates extracellular volume
  - If total body sodium goes UP -> extracellular volume goes UP
- Hyponatremia, serum Na < 135

Water: Where Does it Go?

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<thead>
<tr>
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<th>Intra-cellular 67% or 2/3</th>
<th>Extra-cellular 33% or 1/3</th>
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<tbody>
<tr>
<td>Intra-cellular</td>
<td>67% or 2/3</td>
<td>33% or 1/3</td>
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<tr>
<td>Interstitial</td>
<td>25% or 3/4</td>
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<tr>
<td>Intravascular</td>
<td>8% or 1/4</td>
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Everywhere!
**Fast Facts: 🌊 & 🌞**
- $H_2O$ can move freely between all compartments
  - All compartments have equal osmolalities
- Salt cannot move freely between all compartments
  - Maintains extracellular (intravascular) volume
- Osmolality determines movement of $H_2O$

**Serum Osmolality**
- Osmolality = Osmoles/kg of water
- What makes up serum osmolality?
  - $2 (Na^+) + \text{Glucose/18 + BUN/2.8}$
- Normal serum osmolality is 285-295
  - Kidney runs a pretty tight ship!

**Maintaining Osmolality**
- High plasma osmolality (osm)
  - $H_2O$ flows OUT of cells and cells shrink
    - i.e. CPM (central pontine myelinolysis)
- Low plasma osm
  - $H_2O$ flows INTO cells and cells swell
    - i.e. cerebral edema
- Both scenarios interfere with cell function
Definitions

**Dehydration**: Too little H2O

**Volume Depletion**: Too little NaCl

**Volume Overload**: Too much NaCl

**Volume Status = Salt Status**

Choosing a fluid...

Ask the question...

- Is this a H2O problem?
- Is this a NaCl problem?
- Is this BOTH a NaCl and H2O problem?

Remember... IVNS (or LR) ALWAYS fluid of choice for volume resuscitation (always a NaCl problem)

Background: IV Fluids

- Solute in a particular IVF determines where the IVF distributes
- For example...
  - DSW distributes to all compartments
  - IVNS (0.9%) - only to the extracellular space
  - LR - only to the extracellular space
  - Plasma expanders (pRBC, FFP, albumin, hetastarch) - only to the intravascular space
Fluid Selection

- Normal Saline (IVNS)
  - Isotonic (308 osm)
    - Sodium: 154 meq/L
    - Chloride: 154 meq/L

- 3% saline
  - Hypertonic (1027 osm)
    - Sodium: 513 meq/L
    - Chloride: 513 meq/L

- Lactated Ringers (LR)
  - Hypotonic (274 osm)
    - Sodium: 130 meq
    - Chloride: 109 meq
    - Calcium: 3 meq
    - Potassium: 4 meq
    - Lactate: 28 meq
    **Lactate metabolized to bicarbonate in the liver**

IV Fluid Examples...

- 1 Liter of D5W
  - 67% or 670 cc to intracellular space
  - 25% or 250 cc to interstitial space
  - 8% or 80 cc to intravascular space

- 1 Liter of IVNS (0.9%)
  - ¾ or 75% or 750 cc to interstitial space
  - ¼ or 25% or 250 cc to intravascular space

Normal Kidney
  (and normal brain)

- Increased total body sodium (hypervolemia)
  - Kidney increases sodium excretion

- Decreased total body sodium (hypovolemia)
  - Kidney decreases sodium excretion

- Normal total body sodium (euvolemia)
  - You pee what you eat
**Normal Volume Regulation**

- Adequate GFR
- Adequate distal delivery of Na\(^+\) and H\(_2\)O to loop of Henle and collecting duct
- Intact tubular function for reabsorption
- Central ADH secretion
- ADH responsiveness in the kidney

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**What about Urine Electrolytes?**

- There is **no** normal value
- Generally speaking...you pee what you eat
- Interpretation of urine electrolytes should be defined as **appropriate or inappropriate NOT normal or abnormal**

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**You pee what you eat...**
Hyponatremia

Remember...

Hyponatremia is *ALWAYS* a H₂O problem and *SOMETIMES* a NaCl problem

Always *too much* H₂O!

Hyponatremia

- True Hyponatremia
  - Hypo-osmolar hyponatremia (*most common*)
    - Hypovolemic
    - Euvolemic
    - Hypervolemic
- Pseudohyponatremia
Pseudohyponatremia
- Hyper-osmolar hyponatremia (less common)
  - Hyperglycemia
    - HIGH measured and calculated osm
    - Na ↓ 1.6 meq/dL for every 100 mg/dL ↑ in glucose > 100
  - Mannitol
    - HIGH measured osm but LOW calculated osm
- Normo-osmolar hyponatremia (very uncommon)
  - Hypertriglyceridemia
  - Hyperproteinemia (MM)
    - NORMAL measured osm but LOW calculated osm

Hyponatremia
- Occurs when H2O in > H2O out
  - Can’t get hyponatremic without water intake
    - Watch for water “hiding” in gtt, flushes, meds, hypotonic fluids...
  - Ingestion of too much H2O with normal kidneys (i.e. psychogenic polydipsia)
    - Increased H2O in
  - Ingestion of “normal” H2O with renal failure
    - Decreased H2O out
  - Ingestion of “normal” water with increased ADH activity
    - Decreased H2O out

Hyponatremia: Signs & Symptoms
- Primarily due to osmotic shifts
- Water flows from hypotonic extra-cellular compartment to relatively hypertonic intracellular compartment -> cerebral edema
- Signs & symptoms primarily neurologic
- For non-neuro patients symptoms depend more on the rate of change NOT the absolute number (chronic > 48 hr)
Hyponatremia: Signs & Symptoms

**ACUTE**
- Severity of symptoms reflects severity of cerebral "overhydration"
- Nonspecific: malaise, nausea, headache, lethargy, obtundation, seizures, coma, respiratory arrest

**CHRONIC**
- May be asymptomatic
- Nonspecific: fatigue, nausea, dizziness, gait disturbance, forgetfulness, confusion, lethargy, muscle cramps

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Hyponatremia

Extracellular (hypotonic) → Intracellular (hypertonic)

H₂O → H₂O

H₂O → H₂O

Cerebral Compensation

- 1st line of "self" defense
  - Increased hydrostatic pressure from cerebral edema causes fluid to shift to CSF, shunted into systemic circulation

- 2nd line of defense
  - Secretion of intracellular solutes (to decrease gradient drawing water into cells) – rapid
  - Secretion of osmolytes (after 24-48hr) - slower
ADH: Antidiuretic Hormone

ADH: Fast Facts

- Produced in posterior pituitary gland
- Primary function -> maintain plasma osmolality
- Secondary function -> volume regulation
- Action via $H_2O$ reabsorption in collecting tubules ($V_2$ receptors)

Osmoreceptors in hypothalamus detect changes in osmolality
Baroreceptors detect hypovolemia
Increase in plasma osmolality stimulates ADH and thirst
- If plasma osm too high
  - ADH and thirst activated
- If plasma osm too low
  - ADH and thirst inactivated
ADH: “Appropriate”
SAADH – syndrome of “appropriate” ADH secretion

- Appropriate ADH secretion
  - Hyperosmolar state (e.g., hypernatremia)
  - Hypovolemic state
- ADH increases H₂O reabsorption in kidney
- ADH is last response to hypovolemia
  - Released after decrease in BP by 10-15mmHg
  - Not very effective for replacing volume
    - REMEMBER only 8% of H₂O stays in intravascular space

Wake UP!!!

Approach to Hyponatremia
Hyponatremia

- **Step 1** - Assess volume status
  - Determine whether it is a **problem,
  - a **problem or both
- **Step 2** - Check urine sodium
  - add urine potassium and osmolality in SIADH

True Hyponatremia

- **Hypovolemic** hyponatremia
  - Too little **too much
- **Euvolemic** hyponatremia
  - Just the right amount of **but too much
- **Hypervolemic** hyponatremia
  - Too much **and too much

Diagnosis: Hyponatremia

- **Hypovolemic**
  - Extra-renal volume loss
    - Low urine Na
    - diarrrhea, fever, vomiting, burns
  - Renal volume loss
    - High urine Na
    - diuretics
    - salt wasting nephropathy
    - cerebral salt wasting
Diagnosis: Hyponatremia

**Euvolemic**

- Low urine Na
  - Psychogenic polydipsia
  - Beer Potomania
- High urine Na
  - Adrenal insufficiency
  - Hypothyroid
  - SIADH

**Hypervolemic**

- Low urine Na
  - CHF right or left sided
  - Pulmonary hypertension
  - Hepatic failure
  - Nephrotic syndrome

**SIADH**

Syndrome of “Inappropriate” ADH Secretion
ADH “Inappropriate” : SIADH

SIADH – syndrome of inappropriate ADH secretion
1st described in 1957
5 criteria:
• Hypotonic hyponatremia (low osmolality), SNa <135
• Euvolemia (not on diuretics)
• Urine Na > 20
• Urine osm > plasma osm
• Rule out adrenal and thyroid dysfunction

ADH “Inappropriate” : SIADH

• Due to excessive ADH release or increased sensitivity to ADH
• Characterized by hyponatremia in the setting of inappropriately concentrated urine
  • *i.e. should have dilute urine with hyponatremia*
• No defect in Na⁺ handling in SIADH
  • High salt intake, high salt output (high urine output)
  • Low salt intake, low salt output (low urine output)

Common Etiologies of SIADH

• CNS disease (CVA, SAH, SDH, trauma, autoimmune, infection...)
• Ectopic (malignancy, classic small cell)
• Medications (TONS...)
• Pulmonary disease
• Stress, nausea, pain
• HIV
Cerebral Salt Wasting (CSW)
Syndrome of “Appropriate” ADH Secretion
“SAADH”

SIADH versus CSW

<table>
<thead>
<tr>
<th>SIADH</th>
<th>CSW</th>
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<tr>
<td>Euvolemic</td>
<td>Hypovolemic</td>
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<tr>
<td>Urine Na⁺ excretion equals urinary sodium intake</td>
<td>Net negative Na⁺ balance</td>
</tr>
<tr>
<td>Treatment: fluid restriction</td>
<td>Treatment: IV saline</td>
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Hyponatremia in a Neuro ICU

- **Most common** electrolyte abnormality in a Neuro ICU
- Differential Diagnosis: consider SIADH, CSW, acute adrenal insufficiency
- Up to 43% of patients with SAH develop hyponatremia
- Hyponatremia after SAH is a risk factor for and predictor of vasospasm and cerebral ischemia
- Hyponatremia potentiates cerebral edema
- Early diagnosis and effective treatment is **critical** for hyponatremic patients with intracranial disease
Wake UP!!!

Hyponatremia: Treatment Considerations

- **Hypovolemic?** – replete volume deficit, rule out adrenal insufficiency
  - Give IVNS
- **Hypervolemic?** – increase free H₂O loss and NaCl loss
  - Give diuretics
- **Euvolemic?**
  - Restrict water intake
  - Increase water loss

? symptomatic
SIADH: Treatment

- Restrict free H₂O intake
  - Calculate Free H₂O Clearance
- Increase free H₂O loss
  - Hypertonic saline + diuretics
    - Fluid osm has to exceed urine osm
  - Vaptans (V₂ antagonists) – pure aquaretis
  - Salt (or urea) tablets + diuretics
- Correct slowly due to possibility of demyelinating syndromes (CPM)

Free H₂O Clearance

Urine volume = Cₑ + CₑF

\[ Cₑ = \frac{U_{Na} + U_K}{S_{Na} + S_K} \]

Example 1: 60 yo woman with metastatic melanoma (to brain)
Serum Na 115, Urine Na 80, Urine K 24, Uosm 500

\[ U_{vol} = (Cₑ) 0.9 (80 + 24) + (CₑF) 0.1 \]

Only 10% of all urine output is free H₂O, 90% is electrolyte clearance

EXAMPLE: IF UOP 1 liter, only 100cc is H₂O. Any H₂O intake > 100cc + insensible losses will cause serum Na⁺ to fall

Example 2: 50 year old woman s/p large hemorrhagic MCA CVA with Serum Na 119, Urine Na 140, Urine K 20, Uosm >700

\[ U_{vol} = (Cₑ) >1 + (CₑF) \]

NONE of urine output is free H₂O, any intake exceeding insensible losses will drop serum Na⁺
Maximum urine volume

Max daily urine vol = daily solute load

minimum urine [ ] → 10mmol x kg

normal ~ 50

Examples: “normal” intake
80 kg man with min urine [ ] of 50 can drink 16 L
80 kg man with min urine [ ] of 400 can drink 2 L
80 kg man with min urine [ ] of 600 can drink 1.3 L

SIADH: Acute Symptomatic Hyponatremia

- Using 3% saline + lasix for SIADH = net aquaresis
  - Goal salt in = salt out (euvolemic to start)
- Replace all Na⁺ lost in the urine with 3%
  - 3% saline Na⁺ content 513 meq/L
  - 1 mL of 3% = approx 0.5 meq of Na⁺
- Example: If urine Na⁺ is 80 meq/L and urine volume is 500cc over 2 hr, 40meq of Na⁺ has been lost and must be replaced with 80cc of 3%

Vaptans

- Provide option for net aquaresis
- Tolvaptan & Conivaptan available in U.S.
- For use in heart failure, cirrhosis, SIADH
- Caution: overly rapid correction is a risk
- Caution: avoid use in hypovolemic patients
- Increased thirst side effect in studies (in absence of hypernatremia)
- Often requires nephrology approval
Why use hypertonic saline?

- To avoid worsening hyponatremia in SIADH, osmolality of fluid must exceed that of urine
- Risk of missing CSW -> increased vasospasm and cerebral ischemia

Example: Urine osm 600 (max ability to dilute)

- 1 liter of IVNS (308 osm)
  - 308 osm/616 osm = 0.5 L UOP (308 osm will be excreted in 500cc of urine or 616 osm urine) and 500cc of water will be retained, SNa will fall
- 1 liter of 3% saline (1026 osm)
  - 1026 osm/616 osm = 1.6 L UOP (1026 osm will be excreted in 1.6L of urine or 616 osm urine) and no water will be retained, SNa will rise

Using 3% Saline for Hyponatremia (SIADH or CSW)

\[
\text{Na}^+ \text{ deficit} = \text{total body water} \times (\text{target Na}^+ - \text{serum Na}^+)
\]
e.g. \((0.6 \times 80\text{kg} \times (130 - 120) = 480\text{ meq})

\[
\text{Rate of infusion (cc/hr)} = \frac{\text{Na}^+ \text{ deficit (meq)} \times 1000}{\text{infusate Na}^+ (\text{meq/L}) \times \text{time (hours)}}
\]
e.g. \((480 \times 1000)/(513 \times 24) = 39\text{cc/hr of 3\% saline})

*Total Body Water
- Women 0.5 x weight in kg (~0.4 in elderly)
- Men 0.6 x weight in kg (~0.5 in elderly)
Treatment: Hyponatremia

\[
\Delta \text{serum Na} = \text{Infusate Na} - \text{Serum Na} \\
\text{Total Body Water} * + 1
\]

- 1 liter 3% saline \[\text{Na}^+\] = 513 meq/L

Example: If SNa 120 and 1 liter 3% given to 80Kg man, Na\(^+\) will rise by 8 meq

*Total Body Water

- Women 0.5 x weight in kg (~0.4 in elderly)
- Men 0.6 x weight in kg (~0.5 in elderly)

CSW: Treatment

1. Avoid Volume Depletion!
2. Treat hypovolemic hyponatremia
   - Calculate & replace deficit (use 3% if symptomatic)
   - Match I's & O's for ongoing losses
   - Urine Na\(^+\) x Urine Volume = meq of ongoing loss

Example of ongoing losses: UNa 150 (meq/L) x 5 L UOP (750 meq) = ~ 4.8L IVNS or 200cc/hr IVNS

CSW vs. SIADH: Treatment

- Response to isotonic saline
  - SIADH - worsening of hyponatremia
    - Lose the salt, hold on to the H\(_2\)O
  - CSW – improvement in hyponatremia (unless coexistence of CSW and SIADH)

- Response to fluid restriction
  - SIADH – appropriate
  - CSW – clinical deterioration, high risk of significant complications
Central Pontine Myelinosis

- Complication of overly rapid correction of hyponatremia
- Caused by severe damage to the myelin sheath in the pons
- Alcoholics, malnourished and elderly females are at highest risk

Hyponatremia: Complications of Rapid Correction

Rate of correction is critical
- Correction not to exceed ~10meq/24 hr
  - On occasion will need to give water back to slow rate of correction
- WATCH OUT for significant increase in urine output with correction of hyponatremia
  - When ADH is “turned off”
- CAUTION: SOMETIMES TREATMENT CAN BE RISKIER THAN THE PROBLEM ITSELF!
It Can Be Complicated...
  • A patient’s condition may change over time
  • Causes of hyponatremia may coexist
  • Treatment of one problem may unmask another (e.g. volume depletion and SIADH)
  • Always go back and reassess volume status, follow urine osm and urine electrolytes
  • Slow correction!!!

Wake UP!!!

Case #1
45 yo alcoholic admitted with AMS after being found at home in his own vomit with multiple empty bottles of beer. SNa 118, UNa 10. HR 110, BP 80/50. Exam: confused, nonfocal, dry MM, no edema, no axillary sweat. Unable to provide any history.
Case #1

What’s the cause of his hyponatremia?

1) Hypovolemic hyponatremia
2) Beer potomania
3) Euvolemic hyponatremia 2/2 SIADH
4) Hypervolemic hyponatremia 2/2 alcoholic cardiomyopathy

Case #1

What’s the treatment?

1) IVNS bolus 1 liter
2) IVNS 125 cc/hr
3) D5 ½ NS 125 cc/hr
4) Fluid restriction
5) Lasix 20mg IV x 1

Case #2

45 yo alchoholic admitted with AMS after being found at home confused with multiple empty bottles of beer. SNa 118, UNa 10. HR 90, BP 100/50. Exam: confused, nonfocal, moist MM, 2+ edema, elevated JVP, rales and S3 on exam. Unable to provide any history.
### Case #2

**What’s the cause of his hyponatremia?**

1) Hypovolemic hyponatremia  
2) Beer potomania  
3) Euvolemic hyponatremia 2/2 SIADH  
4) Hypervolemic hyponatremia 2/2 alcoholic cardiomyopathy

### Case #2

**What’s the treatment?**

1) IVNS bolus 1 liter  
2) IVNS 125 cc/hr  
3) D5 ½ NS 125 cc/hr  
4) Fluid restriction  
5) Lasix 20mg IV x 1

### Case #3

45 yo alchoholic admitted with AMS after being found at home confused with multiple empty bottles of beer. SNa 118, UNa 110. HR 80, BP 120/70. Exam: confused, nonfocal, moist MM, no edema, no elevated JVP, cardiopulm exam without rales or S3. Unable to provide any history.
Case #3

What’s the cause of his hyponatremia?

1) Hypovolemic hyponatremia
2) Beer potomania
3) Euvolemic hyponatremia 2/2 SIADH
4) Hypervolemic hyponatremia 2/2 alcoholic cardiomyopathy

Case #3

What’s the treatment?

1) IVNS bolus 1 liter
2) IVNS 125 cc/hr
3) D5 ½ NS 125 cc/hr
4) Fluid restriction
5) Lasix 20mg IV x 1

Thanks!

Paula.Dennen@ucdenver.edu
1) Hyponatremia is *ALWAYS* a disorder of which of the following?

a) salt  
b) water  
c) neither  
d) both

2) Which condition is characterized by a volume depleted state?

a) Cerebral Salt Wasting (CSW)  
b) SIADH  
c) Neither  
d) Both

3) Which condition is characterized by a euvolemic or "normal" volume state?

a) Cerebral Salt Wasting (CSW)  
b) SIADH  
c) Neither  
d) Both
POST-TEST
4) Water can move freely between the intracellular and extra-cellular space.
   a) True
   b) False

POST-TEST
5) Which of the following is NOT a cause of SIADH?
   a) Medications
   b) Pulmonary disease
   c) CNS disease
   d) Congestive heart failure
   e) Pain

POST-TEST
6) What is a normal urine sodium?
   a) 20
   b) 40
   c) There is no such thing!
   d) 70
7) What is the primary determinant of a person's volume status (i.e. hypovolemia, euvolemia, hypervolemia)?
   a) salt
   b) water
   c) blood pressure
   d) pulse
   e) none of the above

8) What is the risk of rapidly correcting hyponatremia?
   a) cerebral edema
   b) central pontine myelinosis (CPM)
   c) volume overload
   d) none of the above

9) Which of the following is NOT commonly associated with polyuria?
   a) CSW (cerebral salt wasting)
   b) SIADH
   c) Diabetes Insipidus (central or nephrogenic)
   d) Psychogenic polydipsia
POST-TEST

10) Dehydration refers to which of the following

a) too little salt  
b) too little water  
c) neither  
d) both