Water Balance Made Easier

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The non-cognitive approach

May lead you astray to the incorrect etiology, incorrect therapy, and poor outcome.
Humans regulate ECF volume mainly by regulating body sodium content.

Several major systems work together to balance sodium content.

We’ll first divide these into the
1. Affector (sensing) systems
2. Effector systems

Affector systems

Baroreceptors
Aortic arch
Carotid arteries
Atria
Brain, liver, kidney

“Osmostat”
Hypothalamus
### Effector systems

**Renin-Angiotensin-Aldosterone System (RAAS)**

- Ang II $\rightarrow$ peripheral arterial vasoconstrictor
- Aldosterone $\rightarrow$ Na and water retention

**Vasopressin (VP)** = Anti-diuretic hormone (ADH)
- Systemic vasoconstrictor
- Water retention

### Vasopressin (VP)

**Stimuli for vasopressin release:**
- Elevated serum osmolality (via the osmostat)
- Decreased baroreceptor stretch
- Nausea
- Pain

$\rightarrow$ If VP is present and all of these “appropriate” stimuli are absent, then the diagnosis of SIADH can be made!
VP action at the kidney

- Can produce urine with osmolality ranging from 50 to 1,200 mosm/kg.
- Urine at the end of the DCT is maximally diluted. (Always 50-100 mosm/kg).
- As the urine travels down the collecting duct one of two things can happen:
  - If VP is absent:
    - Large amount of dilute urine produced
      (Maximally dilute urine = 50 mosm/kg)
  - If VP is present:
    - Small amount of concentrated urine produced
      (Maximally concentrated = 1,200 mosm/kg)
So, how do we know if VP is being secreted?

<table>
<thead>
<tr>
<th>Urine osmolality</th>
</tr>
</thead>
<tbody>
<tr>
<td>For a young person with healthy kidneys</td>
</tr>
<tr>
<td>&gt; 100 VP is present</td>
</tr>
<tr>
<td>≤ 100 VP is absent</td>
</tr>
<tr>
<td>For an older patient or patient with kidney dz</td>
</tr>
<tr>
<td>&gt; 300 VP is present</td>
</tr>
<tr>
<td>≤ 300 VP is absent</td>
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</tbody>
</table>

The classical RAS pathway
Stimuli for renin release

- Decreased delivery of Na\(^+\) to the macula densa  
  (eg volume depletion)
- Decreased stretch of the afferent arteriole  
  (eg low arterial pressure)
- Increased sympathetic tone  
  (beta-adrenergic stimulation)

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Fig. 1: Outline of the renin-angiotensin system. ACE, angiotensin converting enzyme. Not shown is the metabolism of Ang I by aminopeptidase A to form Ang(1–7), which may then be metabolized by ACE or serine proteases to form Ang II. Renin cleaves between Leu\(^{\text{30}}\) and Val\(^{\text{31}}\) of the human angiotensinogen sequence. Of the several alternate pathways of metabolism, the bold, black and dashed arrows indicate pathways of decreasing contribution, although the minor pathways can assume major importance when the main pathway is inhibited.

How can we determine if the RAAS has been activated?

<table>
<thead>
<tr>
<th>Urine sodium measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10 RAAS is active</td>
</tr>
<tr>
<td>&gt; 10 RAAS is inactive</td>
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</tbody>
</table>

Interplay of afferent and efferent systems

- Osmostat (↑ serum osm) → VP (ADH) secreted
- Baroreceptors (inadequate stretch) → RAAS activated
What data are we taught to gather in evaluating a patient with an abnormal serum sodium?

- Serum osmolality
- Patient’s volume status
- Urine sodium
- Urine osmolality

Here is what these data are really telling us?

<table>
<thead>
<tr>
<th>Data</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum osmolality</td>
<td>What the osmostat is sensing</td>
</tr>
<tr>
<td>Patient’s volume status</td>
<td>What the baroreceptors are sensing</td>
</tr>
<tr>
<td>Urine sodium</td>
<td>Is the RAAS on or off</td>
</tr>
<tr>
<td>Urine osmolality</td>
<td>Is VP being produced <em>and</em> having an effect at the kidney</td>
</tr>
</tbody>
</table>
By interpreting these data within the context of the history and physical exam we can better understand why a patient has developed hypo- or hypernatremia.

Let us not be led astray by mindlessly following a flow chart.

For each patient we must ponder:
1. What the afferent systems are sensing
2. What the efferent systems are doing in response

Integration of normal water balance mechanisms

• Starting with a euvolemic “normal” person with normal electrolytes and Posm…
Integration of normal water balance mechanisms

- Starting with a euvolemic “normal” person with normal electrolytes and Posm...

- What happens when the person drinks a water load? (For example 2 Liters over 30 minutes).

NL response to a water load

- Water is absorbed from the gut.
- Serum sodium and serum osm are reduced.
- VP release is suppressed (via osmostat).
- Collecting ducts become impermeable to water.
- Large output of maximally diluted urine occurs.
### Integration of normal water balance mechanisms

- What happens when the person is deprived of water for several hours?

<table>
<thead>
<tr>
<th>NL response to water restriction</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Insensible losses are ongoing (breath &amp; sweat).</td>
</tr>
<tr>
<td>• Serum sodium and serum osm increase.</td>
</tr>
<tr>
<td>• VP is released when a threshold serum osm is reached.</td>
</tr>
<tr>
<td>• Collecting ducts become permeable to water.</td>
</tr>
<tr>
<td>• Smaller output of more concentrated urine occurs.</td>
</tr>
</tbody>
</table>
NL response to water restriction

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>If no water is taken in, eventually serum osmolality will rise to the threshold that causes thirst.</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Thirst prompts person to drink water.</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Serum sodium and serum osm are reduced toward normal.</strong></td>
<td></td>
</tr>
</tbody>
</table>

Clinical approach to hyponatremia

When hyponatremia is detected:
1. Repeat serum electrolytes
2. Take a directed history
3. Perform a directed physical exam (focus on volume status)
4. Initial labs as discussed previously (Serum osm, urine Na, urine osm)
Hyponatremia case #1

- Young adult
- 3 days of nausea, vomiting, & diarrhea
- Told by nurse to drink plenty of liquids
- Sweaty, pale, dry mucus membranes
- Tachycardic, mildly hypotensive

Labs

- Serum Na 128 meq/L
- Serum osm 270 mosm/kg
- Urine osm 1100 mosm/kg
- Urine Na < 10 meq/L
### Your assessment

1. Estimated volume status: **Low**
2. Status of each effector system:
   - Catecholamines? Active
   - RAAS? Active
   - VP system? Active
3. Explain why each effector system is active or inactive, and whether this is appropriate given the clinical situation.
4. Explain why the patient is hyponatremic.
5. What is your treatment strategy?

### Hyponatremia case #2

- 60 y/o male with known ASCAD
- History consistent with MI ~2 weeks earlier
- Sweaty, pale, and nervous
- Neck veins distended
- S3 & S4 present
- Crackles ½ way up on lung exam
- 2+ pitting edema
Your assessment

1. Estimated volume status: High
2. Status of each effector system:
   - Catecholamines? Active
   - RAAS? Active
   - VP system? Active
3. Explain why each effector system is active or inactive, and whether this is appropriate given the clinical situation.
4. Explain why the patient is hyponatremic.
5. What is your treatment strategy?

Labs

- Serum Na 128 meq/L
- Serum osm 270 mosm/kg
- Urine osm 1100 mosm/kg
- Urine Na < 10 meq/L
Labs

- Serum Na 128 meq/L
- Serum osm 270 mosm/kg
- Urine osm 1100 mosm/kg
- Urine Na < 10 meq/L

What is the difference between these labs and the first patient’s labs?

Hyponatremia case #3

- 60 y/o male, 80 pack-year smoking history
- Presents with viral gastroenteritis x 2-3 days → Anorexia, limited water/food intake
- ROS: Cough, hemoptysis, 20-lb weight loss
- No medications
- Exam: Appears tired and ill, otherwise NL exam
- 2 Liters normal saline given IV in clinic
- CXR: Large perihilar mass c/w lung CA
Labs: before and after 2 Liters IV normal saline

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After 2 Liters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Na</td>
<td>120 meq/L</td>
<td>120 meq/L</td>
</tr>
<tr>
<td>Serum osm</td>
<td>250 mosm/kg</td>
<td>250 mosm/kg</td>
</tr>
<tr>
<td>Urine osm</td>
<td>600 mosm/kg</td>
<td>600 mosm/kg</td>
</tr>
<tr>
<td>Urine Na</td>
<td>12 meq/L</td>
<td>40 meq/L</td>
</tr>
</tbody>
</table>

Your assessment

1. Estimated volume status: **Euvolemic, by exam**
2. Status of each effector system:
   - Catecholamines? Inactive
   - RAAS? Active initially, inactive post NS
   - VP system? Active
3. Explain why each effector system is active or inactive, and whether this is appropriate given the clinical situation.
4. Explain why the patient is hyponatremic.
5. What is your treatment strategy?
Will this patient’s hyponatremia get better or worse with further normal saline infusion?

Clinical approach to hypernatremia

- Think of hypernatremia and hyponatremia as disturbances of water balance along a continuum.
- Assess the affector/efferctor systems the same way we did for hyponatremia.
- You need to ask patients two key questions:
  1. Are you thirsty?
  2. Are you urinating a little or a lot?
### Hypernatremia case #1

- 72 y/o male in nursing home s/p hip fracture
- Confined to bed
- Alert, oriented
- Thin, wasted
- Dry mucous membranes, no edema

### Labs

- Serum Na 150 meq/L
- Serum osm 310 mosm/kg
- Urine osm 850 mosm/kg
- Urine Na 16 meq/L
Clinical approach to hypernatremia

1. Are you thirsty?
2. Are you urinating a little or a lot?

His answers:
1. Yes, quite thirsty.
2. Urinating a little.

Your assessment

1. Estimated volume status: Low
2. Status of each effector system:
   - Catecholamines? +/-
   - RAAS? Active
   - VP system? Active
3. Explain why each effector system is active or inactive, and whether this is appropriate given the clinical situation.
4. Explain why the patient is hypernatremic.
5. What is your treatment strategy?
Some finer points

- Shouldn’t the urine osm be 1100 or 1200?
- 850 is likely the maximum concentration that the patient’s elderly kidney can achieve.
- Shouldn’t the urine sodium be lower (<10)?
- Again, the age of the patient must be taken into account. The elderly kidney may not be able to achieve a lower urine sodium.

Hypernatremia

- Not thirsty, urinating only a little
  → Check for damage to thirst center
- Thirsty, urinating a lot
  → DI, psychogenic polydypsia
  → Water deprivation test
Summary

The requirements for maintaining normal water balance are:
1. Functioning baroreceptors and osmostat
2. Normal VP production and release.
3. A kidney that responds normally to VP and the RAAS
4. Normal thirst and water intake

Summary

• Use the labs to determine what the affector systems are sensing and what the effector systems are doing.
• To reverse the hypo- or hypernatremia, aim your treatment at the underlying problem.
• Don’t give every patient with hyponatremia normal saline unless you understand the underlying cause of the hyponatremia.