Case B: Elderly Woman with Hyponatremia and Confusion

A Case-Based Approach to Hyponatremia: Applying the Expert Panel Recommendations to Clinical Practice

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Three Questions

1. What is the etiology of hyponatremia?
2. What should the initial therapy be?
3. How should the patient be managed once the presenting symptoms improve?
Case: History

- 71-year-old woman with hypertension brought to emergency room by family after several days of worsening headache, nausea, vomiting, lethargy, and confusion
- Medications: HCTZ 25 mg (added by PCP 1 month earlier), amlodipine 10 mg, metoprolol 50 mg two times per day, alprazolam 0.5 mg every day, as needed
- Retired high school principal
- Nonsmoker
- Occasional glass of wine
- Lives with husband
Case: Physical Exam

• HR - 84 beats per minute (bpm)
• BP - 108/64 mmHg, Weight - 85 kg
• Jugular veins flat
• Clear chest
• Normal cardiac exam
• No edema
• Arousalable but lethargic
• Follows simple commands
• No focal neurologic deficit
Case: Hospital Course and Lab Findings - I

• 08:00 (0 hours)
  – Brought from triage into emergency room
  – Given 500 mL bolus of isotonic saline followed by infusion at 250 mL/h
  – Nothing by mouth
Case: Hospital Course and Lab Findings - II

- 09:00 (1 hour)
  - Lab studies from 08:00 return:
    - $[\text{Na}^+]$ 109 mmol/L, $[\text{K}^+]$ 3.5 mmol/L, $[\text{tCO}_2]$ 26 mmol/L, $[\text{Cl}^-]$ 78 mmol/L, BUN 11 mg/dL, creatinine 1.1 mg/dL, glucose 88 mg/dL, hemoglobin 13.1 gm/dL

- 09:15 (1:15 h)
  - HR - 85 bpm, BP - 115/66 mmHg
  - Isotonic saline stopped
  - Begun on 3% saline at 170 mL/h (2 mL/kg/h) with goal of increasing serum $[\text{Na}^+]$ by 4 to 6 mmol/L
  - Repeat basic labs and confirmatory labs drawn
Case: Hospital Course and Lab Findings - III

- **10:00 (2:00 h)**
  - HR - 79 bpm, BP - 118/70 mmHg
  - Serum $[Na^+]$ 110 mmol/L, $[K^+]$ 3.2 mmol/L
  - Serum osmolality 235 mOsm/kg, urine osmolality 405 mOsm/kg, urine $[Na^+]$ 18 mmol/L
  - Transferred to ICU
  - Repeat electrolytes ordered for 11:00 (03:00 h) and every 4 hours thereafter
# Etiology of Hyponatremia

<table>
<thead>
<tr>
<th>Criteria for Diagnosing SIADH&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased effective osmolality of the ECF ($P_{osm} &lt; 275 \text{ mOsm/kg H}_2\text{O}$)</td>
</tr>
<tr>
<td>Inappropriate urinary concentration ($U_{osm} &gt; 100 \text{ mOsm/kg H}_2\text{O}$ with normal renal function) at some level of plasma hypo-osmolality</td>
</tr>
<tr>
<td>Clinical euvolemia—absence of signs of hypovolemia (orthostasis, tachycardia, decreased skin turgor, dry mucous membranes) or hypervolemia (subcutaneous edema, ascites)</td>
</tr>
<tr>
<td>Elevated urinary sodium excretion (&gt; 20–30 mmol/L) while on normal salt and water intake</td>
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<tr>
<td>Absence of other potential causes of euvolemic hypo-osmolality: severe hypothyroidism, hypocortisolism (glucocorticoid insufficiency), and thiazide diuretic use</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Key Features in This Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotensive at presentation</td>
</tr>
<tr>
<td>$U_{osm}$ 405 mOsm/kg</td>
</tr>
<tr>
<td>$U_{Na^+}$ 18 mmol/L</td>
</tr>
<tr>
<td>HCTZ</td>
</tr>
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</table>

AVP, arginine vasopressin; ECF, extracellular fluid; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

Case: Hospital Course and Lab Findings - IV

**• 12:00 (04:00 h)**

- HR - 76 bpm, BP - 117/70 mmHg
- Lethargic but easier to arouse; some spontaneous conversation with family and hospital staff
- Placed on 1 L fluid restriction
- Repeat labs from 11:00 (03:00 h) return:
  - Serum [Na⁺] 114 mmol/L; 3% saline stopped
  - Begun on 0.45% saline with 40 mmol KCl per L added at 100 mL/h
Life-Threatening Hyponatremia

- Cerebral edema
  - Seizures
  - Brain herniation
  - Non-cardiogenic pulmonary edema
- Factors that increase the risk of brain injury from hyponatremia itself
  - Female sex
  - Hypoxia

Recommended Treatment of Severely Symptomatic Hyponatremia

Seizures or coma, regardless of known chronicity:

- 100 mL of 3% NaCl over 10 minutes x 3, as needed
- Front-load the initial day’s correction

Indications:
- Self-induced acute water intoxication (eg, psychiatric diseases such as acute psychosis or schizophrenia, endurance exercise, “ecstasy” use);
- Known duration of hyponatremia <24 to 48 hours (eg, postoperative);
- Intracranial pathology or increased intracranial pressure;
- Seizures or coma, regardless of known chronicity.

Goal:
- Urgent correction by 4-6 mmol/L to prevent brain herniation and neurological damage from cerebral ischemia.
Recommended Treatment of Severely Symptomatic Hyponatremia

Seizures or coma, regardless of known chronicity:

- 100 mL of 3% NaCl over 10 minutes x 3, as needed
- Front-load the initial day’s correction

Recommended Treatment:
- For severe symptoms, 100 mL of 3% NaCl infused intravenously over 10 minutes x 3 as needed;
- For mild to moderate symptoms with a low risk of herniation, 3% NaCl infused at 0.5 to 2 mL/kg/h;
- The rate of correction need not be restricted in patients with true acute hyponatremia, nor is readjustment of excessive corrections indicated (Figure 3); however, if there is any uncertainty as to whether the hyponatremia is chronic versus acute, then the limits for correction of chronic hyponatremia should be followed (see section: Current Recommendations for Rate of Correction of Hyponatremia).
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Patients at High Risk of Osmotic Demyelination Syndrome (ODS)

<table>
<thead>
<tr>
<th>Risk Factors for ODS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum sodium concentration $\leq 105$ mmol/L</td>
</tr>
<tr>
<td>Hypokalemia$^a$</td>
</tr>
<tr>
<td>Alcoholism$^a$</td>
</tr>
<tr>
<td>Malnutrition$^a$</td>
</tr>
<tr>
<td>Advanced liver disease$^a$</td>
</tr>
</tbody>
</table>

$^a$ Unlike the rate of increase in serum sodium concentration, neither the precise level of the serum potassium concentration nor the degree of alcoholism, malnutrition, or liver disease that alters the brain’s tolerance to an acute osmotic stress have been rigorously defined.
Diuretic-induced hyponatremia is always a chronic hyponatremia
- Current limits for rate of correction for chronic hyponatremias should be observed

Thiazides interfere with urinary dilution
- Discontinuation of thiazides and correction of volume deficits may be followed by a rapid, spontaneous water diuresis that can raise serum [Na⁺] very quickly
- Numerous cases of osmotic demyelination syndrome have been reported after correction of severe thiazide-induced hyponatremia

Desmopressin to Reverse Overcorrection

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DDAVP, desmopressin acetate; D5W, 5% dextrose in water; NS, normal saline.
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Combined Therapy: Desmopressin and 3% NaCl

![Graph showing the effect of combined therapy on serum sodium levels over time.](image)

- **Desmopressin**
- **3% NaCl**

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Combined Desmopressin and 3% NaCl

- Desmopressin 1 to 2 µg every 6 to 8 hours
  - Started before 3% NaCl
  - Iatrogenic SIADH
- 3% NaCl to achieve desired rate
  - 100 mL bolus for severe symptoms
  - 0.3 mL/kg/h average dose in most patients
  - 400 mM KCl can substitute for 3% NaCl
- No cases of overcorrection
  - 25 patients with serum [Na⁺] < 120 mmol/L

How should the patient be managed after presenting symptoms improve?

- Patient has chronic hyponatremia
- Risk of ODS exceeds risk of hyponatremia itself
- Remain well below therapeutic limits
- Careful monitoring of serum [Na\(^+\)]
  - Autocorrection may occur with spontaneous water diuresis once volume stimulus to arginine AVP release resolves
  - Be prepared to employ measures to retard correction
Case: Hospital Course and Lab Findings - V

- **16:00 (8:00 h)**
  Mental status unchanged,
  HR - 72 bpm, BP - 120/70 mmHg

- **Labs from 15:00 return:**
  Urine output 400 mL over preceding hour
  Urine studies repeated

<table>
<thead>
<tr>
<th>Clock Time</th>
<th>Elapsed Time, h</th>
<th>[$\text{Na}^+\text{]}$ (mmol/L)]</th>
<th>$\Delta[\text{Na}^+]$ (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:00</td>
<td>00:00</td>
<td>109</td>
<td></td>
</tr>
<tr>
<td>09:15</td>
<td>01:15</td>
<td>110</td>
<td>1</td>
</tr>
<tr>
<td>11:00</td>
<td>03:00</td>
<td>114</td>
<td>5</td>
</tr>
<tr>
<td>15:00</td>
<td>07:00</td>
<td>116</td>
<td>7</td>
</tr>
</tbody>
</table>

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Case: Hospital Course and Lab Findings - VI

• 17:00 (09:00 h)
  – HR - 73 bpm, BP - 119/68 mm Hg
  – Urine osmolality from 16:00 reported at 100 mOsm/kg
  – Desmopressin 2 µg IV given
  – Fluid restriction discontinued; patient encouraged to drink
  – IV fluid changed to 0.45% saline
  – Potassium given in periodic doses of 20 mmol in 50 mL 0.9% saline
### Case: Hospital Course and Lab Findings - VII

<table>
<thead>
<tr>
<th>Clock Time</th>
<th>Elapsed Time, h</th>
<th>$[\text{Na}^+]$, mmol/L</th>
<th>$\Delta [\text{Na}^+]$, mmol/L</th>
<th>Comment</th>
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<tbody>
<tr>
<td>19:00</td>
<td>11:00</td>
<td>116</td>
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<td>Urine output 75 mL/h</td>
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<tr>
<td>23:00</td>
<td>15:00</td>
<td>114</td>
<td>5</td>
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**Hospital Day 2**

<table>
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<tr>
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<th>Elapsed Time, h</th>
<th>$[\text{Na}^+]$, mmol/L</th>
<th>$\Delta [\text{Na}^+]$, mmol/L</th>
<th>Comment</th>
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</thead>
<tbody>
<tr>
<td>03:00</td>
<td>19:00</td>
<td>117</td>
<td>8</td>
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</tr>
<tr>
<td>07:00</td>
<td>23:00</td>
<td>118</td>
<td>9</td>
<td>$[\text{K}^+]$ 3.6 mmol/L</td>
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<tr>
<td>11:00</td>
<td>27:00</td>
<td>120</td>
<td>11</td>
<td>Supplemental potassium stopped</td>
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<tr>
<td>15:00</td>
<td>31:00</td>
<td>122</td>
<td>13</td>
<td>Urine output 500 mL/h Desmopressin 2 µg IV given</td>
</tr>
<tr>
<td>19:00</td>
<td>35:00</td>
<td>120</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>23:00</td>
<td>39:00</td>
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**Hospital Day 3**

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<th>Clock Time</th>
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<th>$[\text{Na}^+]$, mmol/L</th>
<th>$\Delta [\text{Na}^+]$, mmol/L</th>
<th>Comment</th>
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<tbody>
<tr>
<td>03:00</td>
<td>43:00</td>
<td>119</td>
<td>10</td>
<td></td>
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</tbody>
</table>
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**Case: Hospital Course Graphic**

- **Serum Na⁺, mmol/L**
- **Elapsed Time from ER Presentation, h**

Graph shows the progression of serum sodium levels over time, with the administration of DDAVP at 2 µg indicated. The levels increase with time, reaching a peak at 21 hours after ER presentation, with values at specific times marked (e.g., 9, 12).
Relowering $[\text{Na}^+]$ After Over-rapid Correction

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![Diagram showing change in serum sodium concentration in first 24 hours.](https://example.com/diagram.png)

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Relowering \([\text{Na}^+]\) After Over-rapid Correction
(Cont’d)

• Administer desmopressin to prevent further water losses
  – 2 to 4 \(\mu\)g every 8 hours parenterally
• Replace water enterally or IV as D5W at 3 mL/kg/h
• Measure \([\text{Na}^+]\) hourly and continue water administration until target reached
  – Unpredictable how much serum \([\text{Na}^+]\) will be lowered