### Background Information

- Most common electrolyte disorder.
- Higher in females, elderly & hospitalized patients.
- 30% of elderly patients in nursing homes.
- 30% of depressed patients on antidepressants.
- **Common causes:**
  - Diuretic use
  - Diarrhea
  - Heart failure
  - Renal disease

### Causes

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypovolemic hyponatremia</strong> (Decreased TBW and Na, with a relatively greater decrease in Na)</td>
<td>GI losses *</td>
<td>Diarrhea, Vomiting</td>
</tr>
<tr>
<td></td>
<td>3rd-space losses *</td>
<td>Burns, Pancreatitis, Peritonitis, Rhabdomyolysis, Small-bowel obstruction</td>
</tr>
<tr>
<td></td>
<td>Renal losses</td>
<td>Diuretics, Mineralocorticoid deficiency, Osmotic diuresis (glucose, urea, mannitol), Salt-losing nephropathies (e.g. interstitial nephritis, medullary cystic disease, partial urinary tract obstruction, and polycystic kidney disease)</td>
</tr>
<tr>
<td><strong>Euvolemic hyponatremia</strong> (Increased TBW with near normal total body Na)</td>
<td>Drugs</td>
<td>Diuretics, barbiturates, carbamazepine, chlorpropamide, clofibrate, opioids, tolbutamide, vincristine Possibly cyclophosphamide, NSAIDS, oxytocin</td>
</tr>
<tr>
<td></td>
<td>Disorders</td>
<td>Adrenal insufficiency as in Addison’s disease Hypothyroidism Syndrome of inappropriate ADH secretion</td>
</tr>
<tr>
<td></td>
<td>Increased intake of fluids</td>
<td>Primary polydipsia</td>
</tr>
<tr>
<td></td>
<td>States that increase non-osmotic release of ADH</td>
<td>Emotional stress, Pain, Postoperative states</td>
</tr>
<tr>
<td><strong>Hypervolemic hyponatremia</strong> (Increased total body Na with a relatively greater increase in TBW)</td>
<td>Extrarenal disorders</td>
<td>Cirrhosis, Heart failure</td>
</tr>
<tr>
<td></td>
<td>Renal disorders</td>
<td>Acute kidney dysfunction, Chronic kidney disease, Nephrotic syndrome</td>
</tr>
</tbody>
</table>

TBW = total body water

* GI and 3rd-space losses cause hyponatremia if replacement fluids are hypotonic compared to losses.
Signs/Symptoms of Hyponatremia

- Primarily neurologic (due to an osmotic shift of water into brain cells causing edema, especially in acute hyponatremia)
- Include headache, confusion, and stupor; seizures & coma may occur.
- Symptoms can be mild as changes in mental status, including altered personality, lethargy & confusion.
- Others symptoms: Nausea, vomiting, headache, confusion, lethargy, fatigue, appetite loss, restlessness/irritability, muscle weakness, spasms, or cramps, seizures, and decreased consciousness or coma.
- Symptoms generally occur when the effective plasma osmolality falls to < 240 mOsm/kg.
- Older chronically ill patients with hyponatremia develop more symptoms than younger otherwise healthy patients.

Extrarenal fluid losses

- Losses of Na-containing fluids as in protracted vomiting, severe diarrhea, or sequestration of fluids in a 3rd space can cause hyponatremia typically when losses are replaced by ingesting plain water or liquids low in Na or by hypotonic IV fluid.
- Significant ECF fluid losses also cause release of ADH, causing water retention by the kidneys, which can maintain or worsen hyponatremia.
- In extrarenal causes of hypovolemia, because the normal renal response to volume loss is Na conservation, urine Na concentration is typically < 10 mEq/L.

Renal fluid losses

- Renal causes of hypovolemic hyponatremia can usually be differentiated from extrarenal causes by the history of renal diseases.
- Distinguished from patients with extrarenal fluid losses because the urine Na concentration is inappropriately high (> 20 mEq/L), except in metabolic alkalosis (as occurs with protracted vomiting) is present & large amounts of HCO₃ are spilled in the urine, obligating the excretion of Na to maintain electrical neutrality.
- In metabolic alkalosis, urine Cl concentration frequently differentiates renal from extrarenal sources of volume depletion.

Euvolemic hyponatremia

- Total body Na & thus ECF volume are normal or near-normal; however, TBW is increased.
- Result from excessive water intake in the presence of Addison's disease, hypothyroidism, or non-osmotic ADH release.
- Cyclophosphamides, NSAID, chlorpropamide potentiate the renal effect of ADH whereas drugs like oxytocin have a direct ADH-like effect on the kidneys.
- A deficiency in water excretion is common in all these conditions.
- Diuretics can cause or contribute to euvolemic hyponatremia if another factor causes water retention or excessive water intake.
Hypervolemic hyponatremia

- Characterized by an increase in both total body Na (and thus ECF volume) & TBW with a relatively greater increase in TBW.
- Various edematous disorders, including heart failure & cirrhosis, cause hypervolemic hyponatremia.
- Rarely, hyponatremia occurs in nephrotic syndrome, although pseudo-hyponatremia may be due to interference with Na measurement by elevated lipids.
- In each of these disorders, a decrease in effective circulating volume results in the release of ADH and angiotensin II.

Hypovolemic hyponatremia

- Deficiencies in both TBW & total body Na exist, although proportionally more Na than water has been lost; the Na deficit produces hypovolemia.
- In hypovolemic hyponatremia, both serum osmolality & blood volume decrease.
- ADH secretion increases despite a decrease in osmolality to maintain blood volume.
- The resulting water retention increases plasma dilution & hyponatremia.

Diagnosis

- Serum Na.
- Serum & urine electrolytes & osmolality help determine the cause.
- Hyponatremia is occasionally suspected in patients who have neurologic abnormalities & are at risk.
- However, because findings are nonspecific, hyponatremia is often recognized incidentally only after serum electrolyte measurement.

Diagnostic algorithm
Treatment

- Restricting water intake
- Promoting water loss
- Replacing any Na deficit
- Treating the cause.
- When hypovolemic - 0.9% saline
- When hypervolemic - fluid restriction & sometimes a diuretic
- When euvoletic - treatment of cause
- Rarely, cautious correction with hypertonic (3%) saline

Treatment - Severe hyponatremia

- Hypertonic (3%) saline (containing 513 mEq Na/L) may be used, but only with frequent (q 2 to 4 h) electrolyte determinations.
- For patients with seizures or coma, ≤ 100 mL/h may be administered over 4 - 6 h in amounts sufficient to raise the serum Na 4 - 6 mEq/L.
- This amount (in mEq) may be calculated using the Na deficit formula.
Sodium Deficit Formula

- (Desired change in Na) × TBW
- TBW is 0.6 × body weight in kg in men and 0.5 × body weight in kg in women.

Example: The amount of Na needed to raise the Na from 106 to 112 in a 70-kg man can be calculated as follows:

\[(112 \text{ mEq/L} - 106 \text{ mEq/L}) \times (0.6 \text{ L/kg} \times 70 \text{ kg}) = 252 \text{ mEq}\]

I.V. Fluid

Initial $\Delta N_{\text{Serum per L infusate}} = \frac{N_{\text{infusate}} - N_{\text{serum}}}{\text{TBW} + 1}$

Where TBW = 0.6 x IBW (x 0.85 if female and x 0.85 if elderly)

Example: 1 L hypertonic saline (513 mEq/L) given to 70 kg (IBW) man with Na = 110 mEq/L will $\uparrow N_{\text{serum}}$ by 9.4 mEq (assuming full retention and no output of Na or H2O). Note: If patient is euvoletic as in SIADH, infused Na will be excreted therefore normal saline can worsen hyponatremia secondary to SIADH if $U_{\text{Osm}} > I_{\text{infusate Osm}}$

What happens if we correct too fast?

Rate of $\uparrow$Na should not exceed 10 – 12 mEq/L to avoid osmotic demyelination syndrome (Pontine & extrapontine areas), or central pontine myelinolysis (spastic/flaccid quadriplegia, dysarthria, dysphagia)

T2 weighted magnetic resonance scan image showing bilaterally symmetrical hyperintensities in Caudate nucleus (small, thin arrow), Putamen (long arrow), with sparing of Globus Pallidus (broad arrow), suggestive of Extrapontine myelinolysis.
Review Questions – Cause & Symptom

What are the common causes of hyponatremia?

• Volume depletion, edema states, SIADH, psychogenic polydipsia, diuretics

What are the symptoms and why do they occur?

• Headache, N/V, lethargy, confusion, seizures, coma.
• The lower osmolality of the ECF causes water to shift into cells resulting in cerebral edema.

Review Questions - Physiology

What’s the mathematical relationship between hyperglycemia and serum Na?

• Each 100 mg/dL elevation of serum glucose above normal decreases serum Na by ~1.6 mEq/L (translocational hyponatremia => ↑serum osmolality leads to water movement into intravascular space)

How is serum or Posm calculated?

• Posm = 2 * Na + Glucose / 18 + BUN / 2.8

Review Questions - Treatment

What is the first step in management?

• Determining volume status

How do you treat hyponatremia with:

Hypovolemia?

• Administration of normal saline IV

Hypervolemia?

• Diuretics & fluid restriction

Euvolemia (SIADH)?

• Fluid restriction. If patient is symptomatic, correction of s. Na with hypertonic saline may be indicated

What are the indications for hypertonic saline +/- diuretics?

S. Na < 120 mEq/L, particularly when CNS symptoms are present

Reivew Questions

What is the appropriate rate for administration of IV NaCl in the treatment of hyponatremia?

• Rate is calculated as that necessary to increase serum Na by 0.5 – 1.0 mEq/L per hour (ex: raise serum Na from 115 to 125 mEq/L over 24 hours)

What can result from rapid correction of hyponatremia?

• Osmotic demyelination syndrome with spastic/flaccid quadriplegia or other neurological symptoms