Hyponatremia

I. Definitions
   a. Na <135 mmol/L
   b. Plasma osmolality is major determinant of total body water homeostasis (# of solute particles) 2 x [sodium] + [urea] + [glucose]
   c. Osmolality: contribution to osmolality of solutes such as sodium and glucose that cannot freely move across cell membranes → shifts in water.
   d. Any increase in total body sodium → increased tonicity → stimulate thirst center → ADH secretion which acts on V2 receptors in renal tubules to increase water reabsorption
   e. Any decrease in total body sodium → decreased tonicity → inhibit thirst center → decrease ADH secretion resulting in decreased reabsorption → diuresis

II. Measure:
   a. Serum Osmolality- determines tonicity of ECF
   b. Urine Sodium Concentration- used with volume status to determine hypovolemic vs. euvoeemic.
   c. Urine Osmolality- determines whether renal water excretion in impaired

III. Causes of Hyponatremia
   a. Elimination of total body water decreases: Renal excretion impairment
   b. Excessive water intake

IV. Evaluating Impaired Renal excretion
   a. Assessment of Volume Status (ECFV)
      i. : expanded, normal/near-normal, contracted (insert table)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Volume of extracellular fluid</th>
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<tbody>
<tr>
<td>Causes</td>
<td>Contracted</td>
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<tr>
<td>Diarrhea; vomiting; excessive sweating; poor water intake; diuretic use</td>
<td>Syndrome of inappropriate secretion of antidiuretic hormone; hypothyroidism; adrenal insufficiency</td>
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<tr>
<td>Serum osmolality</td>
<td>Low</td>
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<tr>
<td>Urine osmolality, mOsm/L†</td>
<td>&gt; 500</td>
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<tr>
<td>Urine volume</td>
<td>Usually decreased</td>
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<tr>
<td>Urine sodium concentration, mmol/L</td>
<td>&lt; 20‡</td>
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<tr>
<td>Response to 0.9% saline infusion</td>
<td>Clinical and biochemical improvement</td>
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</table>

*For simplicity, conditions such as central salt wasting† and “isotonic osmostat”‡ have been omitted.
†Values less than 100 imply an appropriate pituitary and renal response to hyponatremia, as would be expected with psychogenic polydipsia. The variability in urine osmolality results in low sensitivity and specificity for causes of hyponatremia in which the osmolality is greater than 100 mOsm/L.
‡May be greater than 20 with diuretic use.

b. Hypovolemic (edematous)
   i. Increased total body water (increased volume of ECFV) > \( \uparrow \) in total Na
   ii. CHF, liver cirrhosis, renal diseases such as renal failure and nephrotic syndrome, pregnancy.
   iii. Kidneys can’t differentiate between low effective circulating volume and ECF contraction. So will retain water and Na
   iv. Urine Na <20 (higher if on diuretics)

c. Hypovolemic: (volume depleted)
   i. Decrease in total body sodium > Decreased total body water (decreased volume of ECFV)
   ii. Stimulates release of ADH to defend ECFV, water reabsorbed and retain sodium
   iii. Urine Sodium (<30mmol/L)
      1. Renal sodium loss
         a. Diuretic agents
         b. Osmotic diuresis, adrenal insufficiency, salt wasting nephropathy, bicarbonauria, ketonuria
      2. Extra-renal sodium loss
         a. Diarrhea, vomiting, blood loss, excessive sweating
      3. Fluid sequestration
         a. Bowel obstruction, peritonitis, Pancreatitis, burns, muscle trauma

d. Euvolemic (essentially normal volume of ECFV)
   i. ADH release or renal tubular responsiveness to ADH is unrelated to serum tonicity or volume contraction.
   ii. Urine Na > 40
   iii. Decrease in total body water with unchanged total body sodium
   iv. Etiologies
      1. Thiazides
      2. Hypothyroid
      3. Adrenal Insufficiency
      4. SIADH
      5. Decreased intake: beer potomania, tea and toast diet.

V. Serum Osmolality
   a. High serum osmolality (>300 mmol/kg)
      i. Severe hyperglycemia- glucose exerts osmotic force, drawing h20 in ECF with diluting effect
   b. Normal serum osmolality (280- 300 mmol/kg)
      i. Psuedohyponatremia- \( \uparrow \) % of large molecular particles (proteins/fats) causing relative Na concentration to decrease with overall osmolality unchanged (hypertriglyceridmeia and hyperproteinemia)
      ii. Posttransurethral prostatic resection syndrome
   c. Low serum osmolality (<280 mmol/kg)
      i. Urine Na low (<30 mmol/L) (Hypovolemic)
         1. Severe burns
         2. GI losses from vomiting/diarrhea

3. Acute water overload
   ii. Urine sodium high (>30 mmol/L) (Euvolemic)
      1. Renal disorders,
         a. Na losing nephropathy from CKD
         b. Renal ischemia
      2. Endocrine deficiencies
         a. Hypothyroidism
         b. Mineralocorticoid deficiency
         c. Reset osmostat syndrome
            i. Threshold for ADH secretion is reset downwards
      3. SIADH
         a. ADH secretion independent of body’s need to conserve water
         b. Excess water retention in face of sodium losses.
         c. Diagnosis of exclusion
         d. Urine is hyperosmolar when compared with plasma
         e. Any cerebral insult from tumors/infections
         f. Chest disorders: Pneumonia, Empyema,
         g. Ectopic: Bronchogenic carcinoma/small cell carcinoma
         h. MS, Guillan Barre syndrome
         i. Tegretol, amiodarone, theophylline, ssri, tricyclics

4. Drugs
   a. Diuretics
   b. Tegretol
   c. Thorazine
   d. Vasopressin analogs
   e. Indapamide
   f. SSRI
   g. Theophylline
   h. Amiodarone
   i. Ecstasy

VI. Signs/Symptoms
   a. Most are asymptomatic
   b. Usually occur <120meq/L
   c. Nonspecific: ha, lethargy, nausea, vomiting, muscle cramps, depressed reflexes
   d. Rapid decrease can cause symptoms
   e. Severe hyponatremia (115meq/L): neurologic and GI symptoms predominate,
      cerebral edema, seizure, coma, brain damage, respiratory arrest, herniation, death

VII. Physical Exam/History
   a. Elicit symptoms of hyponatremia
   b. Exclude causes such as chf, liver/renal impairment, malignancy, hypothyroid,
      Addison’s, gi losses, psych, drug ingestions, surgery, ivf

VIII. Treatment
   a. Acute vs. Chronic
   b. Immediate vs. Non Immediate
c. Symptoms, degree of hyponatremia, acuteness, hypotension

  d. Acute severe hyponatremia (<48h): Hypertonic Na, treat urgently 2/2 risk of cerebral edema and encephalopathy. 1-2 mmol/L/hour

  e. Chronic hyponatremia (>48h): NS or hypertonic, 0.5mmol/L/hour, avoid rapid correction 2/2 Central pontine myelinolysis (symptoms occur 1-6 days after correction) and often irreversible

  f. Normal/Near Normal ECF : r/o thyroid, adrenal, SIADH treated with water restriction and/or demeclocycline

  g. Contracted ECF

      i. ECF volume contraction treated with NS, which increases ECF thereby inhibiting ADH release.

  h. Expanded ECF

      i. fluid restrict, diuretics, treat underlying etiology

**Table 2. Formulas for Use in Managing Hyponatremia and Characteristics of Infusates.**

<table>
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<th><strong>Formula</strong></th>
<th><strong>Clinical Use</strong></th>
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<td>1. Change in serum Na(^+) = (\frac{\text{infuse Na}^+ - \text{serum Na}^+}{\text{total body water}} + 1)</td>
<td>Estimate the effect of 1 liter of any infusate on serum Na(^+)</td>
</tr>
<tr>
<td>2. Change in serum Na(^+) = (\frac{(\text{infuse Na}^+ + \text{infuse K}^+) - \text{serum Na}^+}{\text{total body water}} + 1)</td>
<td>Estimate the effect of 1 liter of any infusate containing Na(^+) and K(^+) on serum Na(^+)</td>
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**Infusate** | **Infusate Na\(^+\) (mmol per liter)** | **Extracellular-fluid distribution (%)**
---|---|---
5% Sodium chloride in water | 855 | 100†
3% Sodium chloride in water | 513 | 100†
0.9% Sodium chloride in water | 154 | 100
Ringer’s lactate solution | 130 | 97
0.45% Sodium chloride in water | 77 | 73
0.2% Sodium chloride in 5% dextrose in water | 54 | 55
5% Dextrose in water | 0 | 40

*The numerator in formula 1 is a simplification of the expression \((\text{infuse Na}^+ - \text{serum Na}^+) \times 1\) liter, with the value yielded by the equation in millimoles per liter. The estimated total body water (in liters) is calculated as a fraction of body weight. The fraction is 0.6 in children; 0.6 and 0.5 in nonelderly men and women, respectively; and 0.5 and 0.45 in elderly men and women, respectively. Normally, extracellular and intracellular fluids account for 40 and 60 percent of total body water, respectively.

†In addition to its complete distribution in the extracellular compartment, this infusate induces osmotic removal of water from the intracellular compartment.