

HYPONATREMIA

DEFINITION: Serum sodium concentration $[\text{Na}^+]$ less than 135 mEq/L.

INCIDENCE IN CRITICAL ILLNESS: 30%. (The most common electrolyte abnormality encountered in clinical medicine.)

ETIOLOGY:

- **Hypo-osmolar hyponatremia:** Serum osmolality is low (< 280 mOsm/kg H_2O).
 - **Hypovolemic:** Total body water deficit + greater degree of total body sodium deficit.
 - **Renal losses** (urine $[\text{Na}^+] > 20$ mmol/L): Diuretic excess; mineralocorticoid deficiency; cerebral salt wasting; bicarbonaturia (renal tubular acidosis and metabolic alkalosis); ketonuria; osmotic diuresis.
 - **Extrarenal losses** (urine $[\text{Na}^+] < 20$ mmol/L): Vomiting; diarrhea; “third spacing” (burns, pancreatitis, trauma).
 - **Euvolemic:** Total body water excess + normal total body sodium.
 - **The most common subcategory of hyponatremia.**
 - Includes **dilutional hyponatremia**. Excess of water relative to sodium; serum chloride concentration is usually normal.
 - Includes **SIADH**: Diagnosis of exclusion. Inclusion criteria are plasma osmolality < 270 mOsm/kg H_2O ; urine osmolality > 100 mOsm/kg H_2O ; euvolemia; urine $[\text{Na}^+]$ elevated; adrenal, thyroid, pituitary, renal insufficiency absent; diuretic use absent.
 - Urine $[\text{Na}^+]$ is typically > 20 mmol/L.
 - Glucocorticoid deficiency; hypothyroidism; stress; medications (vasopressin analogs, drugs that enhance vasopressin release, drugs that potentiate renal action of vasopressin, haloperidol, amitriptyline, other psychotropic medications).
 - **Hypervolemic:** Total body water excess \gggg total body sodium excess.
 - Urine $[\text{Na}^+] > 20$ mmol/L: Renal failure.
 - Urine $[\text{Na}^+] < 20$ mmol/L: Nephrotic syndrome (hypoalbuminemia); hepatic cirrhosis (peripheral vasodilatation); cardiac failure (diminished cardiac output). Decreased effective arterial blood volume \rightarrow increased angiotensin II; increased ADH; increased sympathetic stimulation \rightarrow renal sodium and water retention.
- **Iso-osmolar hyponatremia:** Serum osmolality is normal (280-320 mOsm/kg H_2O).
 - **Pseudohyponatremia:** Hyperlipidemia and hyperproteinemia; an increase in plasma lipids of 4.6 g/L or plasma protein concentrations greater than 10 g/dL decreases the $[\text{Na}^+]$ by 1 mEq/L.
- **Hyper-osmolar hyponatremia:** Serum osmolality is high (> 320 mOsm/kg H_2O).
 - **Translocational hyponatremia:** Hyperglycemia; hypertonic sodium-free solutions (mannitol, glycine, maltose); for every 100 mg/dL increase in plasma glucose concentration, $[\text{Na}^+]$ decreases by 1.6 mEq/L; for plasma glucose concentrations > 500 mg/dL, the correction factor is 2.4.

CLINICAL MANIFESTATIONS:

- **Hypo-osmolar hypovolemic hyponatremia:** Volume depletion (tachycardia, orthostatic hypotension, flattened neck veins, dry mucous membranes, decreased skin turgor).
- **Hypo-osmolar euvolemic hyponatremia:** Edema is absent.
- **Hypo-osmolar hypervolemic hyponatremia:** Edema is present.
- **Neurological manifestations:** Cerebral edema \rightarrow nausea; emesis; lethargy; confusion; coma; seizures; cerebral herniation; death.

TREATMENT (NEUROLOGICALLY ASYMPTOMATIC PATIENTS):

- **Hypo-osmolar hypovolemic hyponatremia:** Treatment of the underlying cause of fluid loss; **volume resuscitation with isotonic fluid**.
- **Hypo-osmolar euvolemic hyponatremia:** Treatment of the underlying cause. **Free water restriction**. If urine osmolality is high, loop diuretic or demeclocycline and +/- administration of additional salt.
 - **Vaptans (conivaptan; tolvaptan)** induce a dose-dependent electrolyte-sparing **aquaresis**, thereby increasing serum $[Na^+]$, free water clearance, urine flow and plasma osmolality. **Experience with vaptans in critically ill patients is not well established**.
- **Hypo-osmolar hypervolemic hyponatremia:** Treatment of the underlying cause. **Salt and water restriction**. Loop diuretics in some patients.
 - **Vaptans** may be of benefit in selected and closely monitored patients, but **experience in critically ill patients is not well established**.

TREATMENT (NEUROLOGICALLY SYMPTOMATIC PATIENTS):

- **Sodium repletion:**
 - **Sodium Deficit = $0.5 \times \text{Lean Body Weight} \times (120 - \text{Measured } [Na^+])$**
 - **3% NaCl infusion.**
 - Central line required.
 - ICU or step-down unit monitoring (depending on institutional policy).
 - Check serum electrolytes every 4-6 hours.
 - Frequent neurological examinations.
 - **Acute symptomatic hyponatremia (develops in < 48 hours):**
 - Rate of correction is less than or equal to 2 mEq/L/hour and less than or equal to 15 mEq/L in the first 24 hours.
 - **Chronic symptomatic hyponatremia (develops in > 48 hours):**
 - Rate of correction is less than or equal to 1.5 mEq/L/hour and less than or equal to 12 mEq/L in the first 24 hours.
 - **Loop diuretic:** If urine osmolality is high; especially in dilutional hyponatremia.
- **Treat with caution and utilize close monitoring.**
- **Osmotic demyelination syndrome (central demyelination syndrome, central pontine demyelination syndrome, central pontine myelinolysis):** Most likely to occur with therapy for chronic hyponatremia that is too aggressive and rapid ($> 12-15$ mEq/L/24 hours or $> 1-2$ mEq/L/hour). Alcoholics; protein-calorie malnutrition; hypokalemia; thermal injury; elderly women taking thiazide diuretics. Generalized encephalopathy followed by classic symptoms 2-3 days after the $[Na^+]$ is corrected: behavioral changes, cranial nerve palsies, quadriplegia. Diagnostic lesions on MRI may not occur for two weeks after onset of symptoms.

KEY REFERENCES:

- Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: Expert panel recommendations. *Am J Med* 2013;126:S1-S42.
- Sterns RH, Riggs JE, Schochet SS. Osmotic demyelination syndrome following correction of hyponatremia. *New Engl J Med* 1986;314:1535-1542.
- Sterns RH, Cappuccino JD, Silver SM, et al. Neurologic sequelae after treatment of severe hyponatremia: A multicenter perspective. *J Am Soc Nephrol* 1994;4:1522-1530.