Syndrome of inappropriate antidiuretic hormone (SIADH)

Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is characterized by **hypotonic hyponatremia** and **euvolemia** due to the **continued, unregulated release or action of antidiuretic hormone (ADH)** . This leads to **excessive water reabsorption** , dilutional hyponatremia, and suppressed renin-aldosterone activity.

Normal Physiology of ADH

- **ADH (vasopressin)** is synthesized in the **hypothalamus** and stored in the **posterior pituitary** .
- It acts on **V2 receptors in the renal collecting ducts** , promoting **free water reabsorption** without sodium.
- ADH secretion is normally regulated by **serum osmolality** and **plasma volume** .

Pathophysiology of SIADH

In SIADH:

- **ADH secretion is inappropriate** , independent of serum osmolality or volume status.
- This causes **excess water retention** , **dilution of serum sodium** , and **decreased serum osmolality** .
- **Suppression of renin and aldosterone** leads to further **natriuresis** (urinary sodium loss).
- **Volume receptors activate natriuretic peptides** , promoting sodium excretion despite hyponatremia.

Result:

- **Hypotonic hyponatremia with low plasma osmolality and high urine osmolality** .

Causes of SIADH

Category	Examples
Malignancies	Small cell lung carcinoma (most common), pancreatic, prostate, lymphoma
CNS Disorders	Stroke, trauma, meningitis, encephalitis, subarachnoid hemorrhage
Pulmonary Diseases	Pneumonia, tuberculosis, COPD, asthma
Drugs	SSRIs, TCAs, carbamazepine, vincristine, cyclophosphamide, opiates, NSAIDs
Surgery & Stress	Post-operative state, pain, nausea
Idiopathic	Especially in elderly

Clinical Features

Symptoms correlate with the **severity and rapidity of hyponatremia** :

- **Mild (<130 mEq/L)** : Nausea, anorexia, fatigue, headache
- **Moderate (<125 mEq/L)** : Muscle cramps, irritability, confusion
- **Severe (<120 mEq/L)** :
  - Seizures
  - Altered mental status
  - **Cerebral edema**
  - **Coma**
  - Respiratory arrest

Diagnostic Criteria (Bartter-Schwartz Criteria)

1. **Serum hyponatremia** (<135 mEq/L) and **hypo-osmolality** (<275 mOsm/kg)
2. **Urine osmolality >100 mOsm/kg** (inappropriately concentrated)
3. **Urine sodium >40 mEq/L**
4. **Euvolemia** : No signs of dehydration, edema, or volume overload
5. **Normal renal, adrenal, and thyroid function**
6. **Correction of hyponatremia with fluid restriction**

Investigations

- **Serum sodium** , osmolality
- **Urine sodium** and **urine osmolality**
- **Serum cortisol** , TSH to rule out other causes
- **ADH levels** (confirmatory but not always practical)
- **Water loading test** (historical use; rarely done today)

Management

General Principles

- **Identify and treat underlying cause**
- Discontinue offending drugs

Treatment by Severity

Severity	Management
Mild/Chronic	- **Fluid restriction** (800–1000 mL/day) - Salt and protein supplementation
Moderate	- Oral salt tablets - **Loop diuretics** with saline to promote free water excretion
Severe/Symptomatic	- **Hypertonic saline (3%)** , administered slowly - Monitor for **osmotic demyelination**
Refractory/Chronic SIADH	- **Demeclocycline** (induces nephrogenic DI)

Severity	Management
	- **Vaptans** (ADH receptor antagonists: conivaptan, tolvaptan)

Complications

- **Cerebral edema** (acute, severe hyponatremia)
- **Seizures** , coma
- **Osmotic demyelination syndrome (ODS)** or **central pontine myelinolysis** :
  - Risk when **serum sodium is corrected too rapidly**
  - Presents with **quadriplegia, pseudobulbar palsy, locked-in syndrome**
- **Non-cardiogenic pulmonary edema**

High-Yield Points

- SIADH is **euvolemic hyponatremia** with **inappropriately concentrated urine** .
- Most common causes: **small cell lung cancer** , **CNS disorders** , and **SSRIs** .
- **Fluid restriction** is first-line in asymptomatic or mild cases.
- Correct sodium **slowly** (<8–10 mEq/L/day) to prevent **ODS** .
- **Hypertonic saline** is reserved for **symptomatic/severe** cases.

Mnemonic: “S-I-A-D-H”

- **S** odium low
- **I** ncreased ADH
- **A** bsent dehydration (euvolemic)
- **D** ilutional hyponatremia
- **H** igh urine osmolality