

# Syndrome of Inappropriate Antidiuretic Hormone

Hyponatremia is defined by a serum sodium less than 135mEq/L, and it occurs frequently in hospitalized patients with cancer. The syndrome of inappropriate antidiuretic hormone (SIADH) is the most common cause for hyponatremia in cancer patients. SIADH is most frequently associated with small cell lung cancer but it can occur in a broad range of solid tumors and hematologic malignancies. SIADH is associated with increased mortality and other poor outcomes.

## Pathophysiology and Causes of SIADH

**Normal Physiology:** Serum osmolality increases or circulating blood volume decreases → Posterior pituitary secretes ADH to increase free water uptake in the renal collecting duct.

**SIADH from Ectopic Production of ADH:** Tumor cells produce ADH resulting in water retention even when plasma osmolality falls.

### Other causes of SIADH in patients with cancer:

- Medications: Vincristine, cyclophosphamide, opiates, antidepressants
- Intracranial pathology: Brain metastases
- Nausea, pain, stress

Rapid overcorrection can lead to osmotic demyelination syndrome and **permanent neurologic deficits**.

## Clinical Presentation and Diagnosis

Symptoms may be non-specific and include nausea, vomiting, confusion, headache, and generalized malaise. However, life-threatening symptoms such as **seizures** or **coma** may develop due to cerebral edema.

For all patients presenting with hyponatremia, volume status, serum osmolality, urine osmolality, and urine sodium should be quickly determined.

### Hallmarks of SIADH

- Hypo-osmolality: Serum Na < 275mOsm/kg
- Euvolemia on exam
- Normal urine sodium: >30mEq/L
- Normal urine osmolality: >100mOsm/kg
- Normal thyroid and adrenal function

### Hypovolemic Hyponatremia

- **Causes:**
  - Renal losses: Diuretics
  - Extrarenal losses: Nausea, vomiting, diarrhea, dehydration
- **Lab Findings:**
  - Urine Na <20-30mEq/L for extra-renal losses but >30mEq/L for renal losses
  - Urine osmolality >100mOsm/L

### Euvolemic Hyponatremia

- **Causes:**
  - SIADH, hypothyroidism, adrenal insufficiency, psychogenic polydipsia
- **Lab findings:**
  - Urine Na >30mEq/L, except for psychogenic polydipsia (<20mEq/L)
  - Urine osmolality >100mEq/L, except for psychogenic polydipsia (<100mOsm/L)

### Hypervolemic Hyponatremia

- **Causes:**
  - CHF, cirrhosis, renal failure
- **Lab Findings:**
  - Urine Na <20-30mEq/L except for renal failure (>30mEq/L)
  - Urine osmolality >100mOsm/L

## Management

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### Is the patient severely symptomatic?:

- Dangerous symptoms include altered level of consciousness and seizures → **Give hypertonic (3%) saline**
- Initial bolus = 150mL over 15-20 min
- Repeat boluses until Na increases by 5mmol/L. If the symptoms do not improve with this, consider another diagnosis
- Urgent Nephrology consult

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### Is this acute hyponatremia (onset < 48hrs)?

- Risk of overcorrection is much less with acute hyponatremia. **However, most patients with SIADH will have chronic hyponatremia.**
- Stop medications or IV fluids that could be contributing (i.e., thiazide diuretics, D5W)
- If acute decrease in Na >10mmol/L, consider 3% saline 150mL IV x 1 (even without significant symptoms)
- Consider Nephrology consult

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### Treatment for SIADH:

- 1st line = Fluid restriction (1-1.5L/day)
- 2nd line = Urea or salt tabs +/- furosemide

Tolvaptan can be considered as 2nd line option as well but should not be given with any other therapies. Risk of overcorrection may be increased.

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### How to Manage Overcorrection:

- **Na should not be allowed to increase by >8mmol/24h** due to risk of osmotic demyelination → Patients with co-existing liver disease, hypokalemia, alcohol misuse, or malnutrition are at higher risk.
- Consult Nephrology for guidance
- Stop current therapy and start intervention to re-lower serum Na
- Treatment options include IV dextrose solutions that do not contain sodium, desmopressin 2-4mcg IV or both