SIADH & Diabetes Insipidus

The ADH axis · Too much or too little — the diagnosis is made on paired osmolalities

PAIRED OSMOLALITIES
serum + urine, same sample time

ONE HORMONE, TWO FAILURES *ADH holds water back — everything follows from that*

WHAT ADH DOES

Antidiuretic hormone inserts aquaporin-2 channels in the collecting duct, reabsorbing **water without sodium**. So ADH moves **water, not salt**. Excess ADH therefore **dilutes** the plasma and **concentrates** the urine; absent ADH does the reverse.

TOO MUCH — SIADH

Retained water lowers the sodium while the urine stays inappropriately concentrated. The patient is **clinically euvolemic** — not edematous, not dry — which is the single most useful bedside discriminator from heart failure, cirrhosis and hypovolemia.

TOO LITTLE — DI

Water is lost as dilute urine, so the sodium **rises** if the patient cannot drink. Renamed in 2022 to **AVP-deficiency** (formerly cranial or central DI) and **AVP-resistance** (formerly nephrogenic DI), to stop the fatal confusion with diabetes mellitus.

DIAGNOSE SIADH *it is a diagnosis of exclusion with hard criteria*

Criterion	Detail and why it matters
Hypotonic hyponatremia	**Serum osmolality < 275 mOsm/kg** with a low sodium. **Confirm the hyponatremia is genuinely hypotonic first** — marked hyperglycemia, mannitol and severe hyperlipidemia or paraproteinemia produce a low sodium with a normal or high osmolality and need no water restriction at all.
Urine osmolality > 100	The kidney should dilute maximally (< 100 mOsm/kg) when the plasma is dilute. **Failure to do so means ADH is acting.** A truly suppressed, dilute urine points instead to **primary polydipsia, beer potomania or low solute intake**.
Urine sodium > 30–40 mmol/L	Shows the kidney is **not** avidly conserving sodium, which argues against hypovolemia and against the edematous states. **Recent diuretics invalidate this number entirely** — interpret it only off diuretics.
Clinical euvolemia	**No edema, no ascites, no postural drop, no dry axillae.** This is the criterion most often assumed rather than examined, and getting it wrong sends the patient down the opposite treatment path.
Exclude the mimics	**Check thyroid function and a morning cortisol or short Synacthen test. Hypothyroidism and adrenal insufficiency reproduce SIADH exactly** and are corrected by hormone replacement, not fluid restriction. Also exclude renal failure and current diuretics before applying the label.

WHY IS ADH HIGH? *find the driver or the sodium will keep coming back*

Group	Examples and the action they demand
Drugs	**The commonest reversible cause and the first thing to review. SSRIs and SNRIs, carbamazepine and oxcarbazepine, antipsychotics, cyclophosphamide, PPIs, NSAIDs, opioids and MDMA.** Stopping the drug frequently fixes the problem.
Pulmonary	**Pneumonia, tuberculosis, empyema, and positive-pressure ventilation.** Often the sodium is simply a marker of the chest disease and corrects as it treats.
Central nervous system	**Subarachnoid hemorrhage, stroke, meningitis, trauma and tumor.** In subarachnoid hemorrhage **do not fluid restrict reflexively** — distinguish cerebral salt wasting, where the patient is hypovolemic and needs salt and volume.
Malignancy	**Small cell lung cancer classically**, plus head and neck and others. **Unexplained SIADH in a smoker warrants imaging of the chest** — the hyponatremia can precede the diagnosis.
Pain, nausea, surgery	**Powerful non-osmotic stimuli to ADH release.** A postoperative patient given hypotonic fluid on top of surgical ADH release is the classic avoidable severe hyponatremia. **Use isotonic maintenance fluid.**

DIAGNOSE AND SUBTYPE DI *the polyuria workup*

1. **Confirm true polyuria first** — more than about **3 L or 50 mL/kg in 24 hours** — and separate it from urinary frequency. **Exclude an osmotic diuresis**: check glucose, and consider recovering acute kidney injury, post-obstructive diuresis and high urea.
2. **Send paired serum and urine osmolality with electrolytes.** A **dilute urine (< 300 mOsm/kg) with a high-normal or raised serum sodium** is the signature of DI. **A high serum sodium with dilute urine effectively makes the diagnosis** without further provocation.
3. **Distinguish DI from primary polydipsia**, where the serum sodium sits **low-normal** because drinking drives the polyuria. Historically by water deprivation testing; **stimulated copeptin** (a stable surrogate for ADH) is now the more accurate test and is replacing it where available.
4. **Then separate deficiency from resistance with desmopressin. AVP-deficiency concentrates the urine in response; AVP-resistance does not**, because the defect is at the kidney.
5. **Treat by subtype. AVP-deficiency: desmopressin**, with a deliberate break in dosing to allow a dilute urine and avoid iatrogenic hyponatremia. **AVP-resistance: remove the cause** — most often **lithium**, hypercalcemia or hypokalemia — plus thiazide, amiloride and a low-solute diet. **Free access to water is the priority in both.** Image the pituitary in new central disease.

TRAPS ON BOTH SIDES *the errors that cause harm*

CORRECTING TOO FAST

Chronic hyponatremia corrected quickly causes osmotic demyelination, which is irreversible and can appear days later. **Cap the rise at about 8 mmol/L in 24 hours**, and less in the high-risk patient: **alcohol use, malnutrition, liver disease, hypokalemia, sodium below 105**. Watch for the **auto-correction brisk diuresis** once the ADH stimulus is removed, and be ready to re-lower with desmopressin and dextrose.

MISSING THE POSTOPERATIVE PITUITARY

After **pituitary surgery or head injury**, expect a **triphasic response**: early DI, then a phase of **SIADH-like hyponatremia** as stored hormone is released, then permanent DI. **Continuing desmopressin blindly through the middle phase produces severe hyponatremia.** Monitor sodium and urine output closely, and remember these patients also need **glucocorticoid cover** — unreplaced cortisol deficiency both mimics SIADH and masks DI.

PEARLS & PITFALLS

- **Send serum and urine osmolality with urine sodium before any fluid.** One dose of saline destroys the diagnostic information.
- **Assess volume status properly.** Euvolemia is a criterion for SIADH, not an assumption, and it decides restriction versus resuscitation.
- **Always exclude adrenal insufficiency and hypothyroidism** before labelling SIADH — both copy it precisely and both are treated differently.
- **Review the drug chart.** An SSRI or carbamazepine is a commoner cause of SIADH than any tumor.
- **Diabetes insipidus is not diabetes mellitus.** The 2022 renaming to AVP-deficiency and AVP-resistance exists because that confusion has killed patients.
- **Never restrict fluid in a hyponatremic subarachnoid patient** without excluding cerebral salt wasting — volume depletion worsens vasospasm.

References: European clinical practice guideline on the diagnosis and treatment of hyponatremia · US expert panel recommendations on hyponatremia · Working Group for Renaming Diabetes Insipidus (2022) · copeptin-based diagnostic studies of the polyuria-polydipsia syndrome.