

# SIADH · Syndrome of Inappropriate ADH

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## THE STORY IN ONE SENTENCE

The body releases too much ADH hormone even when it should not, so the kidneys hold extra water and blood salt drops dangerously low.

“SIADH means the kidneys keep too much water even though blood salt is already low. Urine stays concentrated when it should be watery. Fix mild cases by limiting water to 800–1000 mL per day. Severe cases (seizures, confusion, sodium under 120) need 3% hypertonic saline given slowly in the ICU or tolvaptan (a drug that blocks ADH at the kidney). Always hunt for the cause: lung cancer, brain injury, or certain medicines (carbamazepine, SSRIs, cyclophosphamide).”

## Normal anatomy — the body's job

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Normally, special nerve cells in the hypothalamus (a control center deep in the brain) measure how concentrated your blood is. When blood gets too salty or thick, those cells tell the pituitary gland (a pea-sized hormone factory hanging under the brain) to release ADH into the bloodstream. ADH travels to the kidneys and orders the collecting ducts (the final tubes where urine is finished) to pull water back into the blood, making urine more concentrated and blood more dilute. When blood salt drops or gets too watery, the hypothalamus shuts off ADH so the kidneys dump extra water as dilute, pale urine and salt climbs back to normal. This feedback loop keeps sodium between 135 and 145 milliequivalents per liter — the narrow range cells need to work correctly.

**BODY'S JOB**

ADH is the body's water-saver. It keeps just enough water in the blood so cells do not shrivel (if blood is too salty) or swell (if blood is too watery). The hypothalamus and kidneys talk back and forth every minute, adjusting water loss in urine to match what you drink and sweat out, keeping sodium steady so nerves can fire, muscles can squeeze, and every chemical reaction runs at the right speed.

1. Blood flows past sensor cells in the hypothalamus, which measure sodium concentration and total dissolved particles (osmolality).
2. If osmolality climbs above 295 mOsm/kg (blood too thick), the hypothalamus signals the posterior pituitary to release ADH into the bloodstream.
3. ADH reaches the kidney collecting ducts and inserts aquaporin-2 water channels into the duct walls, letting water escape from urine back into blood.
4. Urine becomes concentrated (dark, osmolality over 600 mOsm/kg) and small in volume; blood dilutes and osmolality drops back toward 280–295.
5. When blood osmolality falls below 280 (blood too watery), the hypothalamus shuts off ADH release.
6. Collecting ducts pull aquaporin channels back inside, blocking water reabsorption; urine flows out dilute (pale, osmolality under 100 mOsm/kg) and copious, raising blood sodium back to normal.

**What breaks**

In SIADH, something hijacks ADH release so it keeps flowing even when blood is already too watery and sodium is low. The kidneys obey ADH and hold water they should dump, diluting blood further. The break is not in the kidney or the sodium itself — it is in the control switch that should turn ADH off but does not.

**CLINICAL TERM**

Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH): euvolemic (normal total body water volume) low sodium (hyponatremia) caused by non-osmotic, dysregulated ADH release or action, resulting in impaired free-water excretion and dilutional low sodium despite normal kidney, adrenal, and thyroid function.

**How the body compensates**

The body tries to protect the brain from swelling by pushing sodium and other particles (potassium, organic osmolytes like taurine and glutamate) out of brain cells within hours to

days, letting water follow and shrinking cells back toward normal size. Blood pressure and heart rate often stay normal because total blood volume is only mildly high (euvolemic low sodium (hyponatremia)). These adaptations buy time, but they also set a trap: if you raise sodium too fast during treatment, water rushes out of brain cells faster than osmolytes can return, shrinking cells so hard that the protective myelin sheaths around brainstem nerves tear apart — a disaster called osmotic demyelination syndrome (ODS). The key danger is not the low sodium itself in the first 48 hours — it is fixing it too quickly.

1. {'what': 'Brain cells export potassium, chloride, and organic osmolytes (taurine, glutamate, myoinositol) into the surrounding fluid within 24–48 hours of falling sodium.', 'why': 'Lowering the particle count inside the cell reduces the osmotic pull that draws water in, so cells shrink back toward normal size and swelling eases even though blood sodium is still low. This is why chronic SIADH patients can have sodium of 120 and feel only mildly foggy instead of seizing.'}
2. {'what': 'The kidneys excrete some sodium in the urine (urine sodium often above 40 mEq/L) even though blood sodium is low.', 'why': 'ADH retention of water expands blood volume slightly, triggering atrial natriuretic peptide (ANP) release from the heart, which tells the kidneys to dump sodium. This is counterintuitive — you lose salt while blood salt is already low — but it prevents dangerous fluid overload and high blood pressure.'}
3. {'what': 'Thirst is suppressed or ignored despite falling osmolality.', 'why': 'Low osmolality normally shuts off thirst, so patients do not drink extra. If they do drink (or get IV fluids), low sodium (hyponatremia) accelerates because the kidneys cannot dump the water fast enough against high ADH.'}
4. {'what': 'Blood pressure, pulse, and urine output remain near normal until sodium drops below ~115–120 mEq/L.', 'why': 'SIADH is euvolemic (not dehydrated, not volume-overloaded), so vital signs stay stable and clinicians may miss the diagnosis unless they check a basic metabolic panel. This stable window is the danger zone — it hides a brewing brain emergency.'}
5. {'what': 'Watch for the decompensation point: acute drops below 120 mEq/L or sudden worsening of confusion, vomiting, seizure, or coma.', 'why': 'If sodium falls faster than the brain can adapt (acute SIADH, less than 48 hours), cells cannot export osmolytes in time, swelling overwhelms compensation, intracranial pressure spikes, and herniation or seizure follows. Severe chronic low sodium (hyponatremia) (weeks to months) also decompensates if a new stressor (infection, extra water intake) drops sodium further.'}
6. {'what': 'Track the trend — sodium stable at 128 for days is safer than 132 yesterday and 128 today.', 'why': 'Rate of fall predicts brain risk better than the absolute number. A patient losing 8 mEq/L in 24 hours is headed for seizure even if current sodium is 128; a patient stable at 122 for a month may walk and talk normally because adaptation is complete.'}

## Domino effect

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1. A tumor (small-cell lung cancer), brain injury (meningitis, bleeding (hemorrhage)), lung infection (pneumonia), or drug (SSRI, carbamazepine) keeps ADH pouring into the blood even though plasma osmolality is low (under 280 mOsm/kg). — ADH release is supposed to shut off when blood gets too watery, but the broken control switch — whether it is a rogue tumor making ADH, an injured hypothalamus misfiring, or a drug amplifying ADH signals — ignores the feedback loop and keeps the faucet open.
2. ADH travels to the kidney collecting ducts and forces aquaporin-2 water channels into the cell walls, pulling water out of urine back into the bloodstream. — The kidney obeys the hormone signal. It does not know the signal is inappropriate — it just follows orders. Urine becomes concentrated (osmolality often 300–600 mOsm/kg, higher than plasma) and scanty, even though the body needs to dump water to raise blood sodium.
3. Water retention dilutes the blood, and plasma sodium drops below 135 mEq/L (hyponatremia). Total body water rises slightly, but blood pressure stays normal because the increase is modest and evenly distributed. — You are not adding salt loss (kidneys actually waste some sodium via ANP), you are adding water gain. The math is simple: same amount of salt dissolved in more water equals lower concentration. Clinically, this shows as low serum sodium and low serum osmolality (under 280) on labs.
4. Low blood sodium creates an osmotic gradient: water moves from blood (low particle concentration) into brain cells (higher concentration inside) trying to balance the difference. Brain cells swell. — Cell membranes are leaky to water but not to sodium. Water always flows toward the side with more dissolved particles. When blood sodium falls, the inside of the neuron becomes relatively saltier than the outside, so water rushes in, bloating the cell like a water balloon.
5. Swollen brain cells press against the rigid skull, raising intracranial pressure. Patients develop headache, nausea, vomiting, confusion, trouble walking (ataxia), and in severe cases (sodium under 120, acute drop) seizures or coma. — The skull cannot expand. Swelling compresses neurons and disrupts electrical signaling — that is why thinking gets foggy and muscles misfire. Severe swelling can push the brainstem down through the foramen magnum (herniation), stopping breathing and heart rate — this is the fatal endpoint if untreated.
6. Over 24–48 hours (if the drop is slow), brain cells fight back by pumping potassium, chloride, and organic molecules out, shrinking themselves and easing symptoms even though sodium stays low. — Adaptation buys time and explains why chronic SIADH patients can tolerate sodium of 125 and still walk around. But adaptation is a double-edged sword: if you correct sodium too fast (more than 8–10 mEq/L in 24 hours), water leaves cells faster than osmolytes can return, ripping myelin off brainstem nerves and causing osmotic demyelination syndrome (locked-in state, paralysis, death).

7. Diagnosis requires four findings together: low serum sodium (under 135), low serum osmolality (under 280), urine osmolality inappropriately high (over 100, often over 300), and urine sodium over 40 mEq/L, all in a patient who is euvolemic (normal skin turgor, no swelling (edema), no dehydration) with normal thyroid, adrenal, and kidney function. — Each clue confirms the mechanism. Low serum sodium + low serum osmolality = dilution. High urine osmolality when serum is dilute = kidneys holding water (ADH effect). High urine sodium = ANP wasting salt to prevent volume overload. Euvolemia rules out dehydration (which also raises ADH appropriately) and heart failure or cirrhosis (which cause dilutional low sodium (hyponatremia) by different paths). You must exclude hypothyroidism and adrenal insufficiency because they mimic SIADH but need different treatment.
8. Treatment is find and fix the cause (stop the offending drug, treat the pneumonia, resect the tumor) plus restrict free water to 800–1000 mL per day so kidneys can slowly catch up and urine output exceeds intake, concentrating the blood naturally. — If you keep pouring water in, the kidneys cannot dump it fast enough against high ADH — sodium will keep falling. Fluid restriction lets the body correct itself over days. For severe acute SIADH (sodium under 120, seizures, coma), give 3% hypertonic saline IV in the ICU at a controlled rate (aim to raise sodium 4–6 mEq/L in the first few hours, then stop or slow to avoid overshooting 8 mEq/L in 24 hours) to stop brain herniation. Tolvaptan or conivaptan (V2 receptor antagonists, 'vaptans') block ADH at the kidney and trigger a large water diuresis — useful for refractory cases but risky because sodium can shoot up too fast if not monitored hourly.

## Symptoms · what the patient feels, and why

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- Low sodium in the blood (hyponatremia): The pituitary gland (a tiny organ at the base of the brain) releases too much ADH (a hormone that tells the kidneys to hold onto water). When the kidneys hold onto too much water, the blood gets watered down, so the sodium (a key salt that helps muscles and nerves work) gets diluted and drops too low.
- Nausea and vomiting: When sodium drops too low, brain cells swell because water shifts into them. The swelling bothers the brain's nausea center (the area postrema, a spot near the brainstem that triggers the vomit reflex).
- Headache: Brain cells swell when sodium is low because water moves into the cells. The swelling stretches the skull's lining (the meninges) and the blood vessels around the brain, which makes your head ache.
- Confusion or trouble thinking clearly: The prefrontal cortex (the front part of the brain that handles planning and focus) and the hippocampus (the brain's memory center) work best when sodium levels are just right. When sodium drops, their signals slow down and get scrambled, so thinking gets foggy.

- Muscle cramps or weakness: Muscles need sodium to squeeze and relax. When blood sodium is too low, the nerves that tell muscles to move can't fire correctly, so muscles feel weak or cramp up.
- Seizures: If sodium drops very low very fast, brain cells swell so much that neurons (the brain's message-sending cells) fire chaotically. That runaway electrical storm is a seizure.
- Lethargy or extreme sleepiness: The brainstem's reticular activating system (the network that keeps you awake and alert) slows down when sodium is too low, making it hard to stay awake.
- Concentrated urine (dark or strong-smelling) despite drinking enough water: The kidneys are holding onto water because too much ADH is telling them to, so less water leaves as urine. That makes the urine darker and more concentrated (the waste is packed into less liquid).

## Focused exam

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- Check mental status — confusion, slow thinking, or trouble remembering: Low sodium (below 135 mEq/L) pulls water into brain cells and makes them swell. The brain gets squeezed inside the skull, and thinking gets fuzzy. This is the most common bedside sign in SIADH.
- Ask about headache, nausea, or vomiting: When blood sodium drops, extra water shifts into the brain and gut. The pressure inside the skull goes up (headache) and the gut lining swells (nausea). These symptoms tell you the low sodium is hitting the whole body.
- Look for seizures or sudden change in alertness: When sodium drops very fast (more than 10–12 mEq/L in 24 hours) or falls below 120 mEq/L, brain cells can fire out of control. Seizures mean the brain is in real danger and sodium must be raised carefully right away.
- Check for muscle cramps, weakness, or trouble walking: Low sodium weakens the signals nerves send to muscles. Muscles get wobbly or cramp up. This clue helps you see how far the salt imbalance has spread.
- Measure intake and output — how much the patient drinks versus how much urine comes out: In SIADH, the kidneys hold onto water even when the body already has too much. Urine volume stays low or normal despite drinking a lot. This mismatch is a clue that ADH (the hormone that tells kidneys to save water) is stuck on when it should be off.
- Check volume status — look at skin turgor, mucous membranes, jugular veins, lung sounds, and swelling (edema): SIADH happens when the body is euvolemic (normal fluid volume), not dehydrated and not overloaded. If the patient is dry (dehydrated) or has swelling and wet lungs (volume overload), the low sodium has a different cause — not SIADH. This step rules out heart failure, cirrhosis, and kidney failure.

## Diagnostics · every test answers a question

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- Serum sodium → Is the blood sodium low, and how low is it?
- Serum osmolality → Is the blood dilute (too watery)?
- Urine osmolality → Are the kidneys concentrating urine when they should be diluting it?
- Urine sodium → Are the kidneys leaking sodium into the urine?
- TSH (thyroid-stimulating hormone) → Is thyroid failure causing the low sodium instead of SIADH?
- Morning cortisol or ACTH stimulation test → Is adrenal failure (not enough cortisol) causing the low sodium?
- BUN (blood urea nitrogen) and creatinine → Are the kidneys working normally, and is the patient truly euvolemic?
- Chest X-ray or CT chest → Is there a lung tumor or infection making ADH?

## Treatment logic

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- Fluid restriction to 800–1000 mL per day (all liquids — water, juice, IV fluids, soup) → Cuts the amount of water coming into the body. Because the kidneys can't dump water properly in SIADH (ADH is forcing them to hold it), less water in means blood sodium slowly rises as the body uses and breathes out water. This is safe and works in mild to moderate cases (sodium 125–134 mEq/L, no severe symptoms).
- Treat the underlying cause — remove tumor, stop the triggering medicine (SSRI, carbamazepine, NSAID, cyclophosphamide), or treat lung infection → Stops ADH from being made or released. Once the source is gone, ADH levels drop, the kidneys start dumping water again, and blood sodium climbs back to normal on its own. This is the only true fix.
- 3% hypertonic saline IV, 100 mL bolus over 10 minutes, for severe symptoms (seizure, coma, or sodium below 120 mEq/L) → Very salty IV fluid raises blood sodium fast — about 4–6 mEq/L in the first few hours. This pulls water out of swollen brain cells and stops seizures. Guideline goal: raise sodium by 4–6 mEq/L in the first 6 hours, then slow down. Maximum safe rise is 8 mEq/L in 24 hours to avoid osmotic demyelination syndrome (brain damage from correcting sodium too fast).
- Oral sodium chloride tablets (1–2 grams three times a day) plus loop diuretic (furosemide 20–40 mg once or twice daily) → Salt tablets add sodium directly to the blood. The loop diuretic (a water pill that blocks the kidney's ability to concentrate urine) forces the kidneys to dump dilute urine, which gets rid of extra water but keeps the salt you just gave. Together, blood sodium rises steadily. This combo works when fluid restriction alone is not enough.

- Tolvaptan (a vasopressin V2-receptor antagonist, or 'vaptan') 15 mg once daily, only in hospital → Blocks ADH receptors in the kidney so ADH can't tell the kidneys to hold water. The kidneys dump water (aquaresis — water-only urine) and blood sodium rises without adding extra salt. Works when fluid restriction and salt pills fail. FDA-approved only for euvolemic or hypervolemic low sodium (hyponatremia) in hospitalized patients.
- Urea 15–60 grams per day (powder mixed in juice or water), mainly used in Europe and Canada → Urea pulls water into the kidneys and forces them to make more urine. This gets rid of extra water and raises blood sodium. Cheaper and safer on the liver than vaptans, but tastes bad and can cause stomach upset. Not commonly used in the United States.

## Medications

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### Fluid restriction · Non-pharmacologic cornerstone therapy

Limiting how much someone drinks each day (usually 800–1000 mL, about 3–4 cups) stops the kidneys from diluting the blood any further. Because ADH (the hormone that tells kidneys to hold onto water) is stuck 'on' in SIADH, the body keeps grabbing water from urine and pouring it back into the bloodstream. Drinking less means less water comes in, so over a few days the kidneys can slowly let go of the extra water already trapped inside, and sodium climbs back toward normal.

1. Daily fluid intake is capped at 800–1000 mL (sometimes as low as 500 mL if sodium is very low).
2. Because less water arrives in the stomach and gut, less is absorbed into the bloodstream.
3. Even though ADH is still high and the kidneys are still concentrating urine, there is simply less water available to dilute the blood.
4. Over 24–72 hours, serum sodium begins to rise as the kidneys excrete slightly more water than the person drinks.
5. Fluid restriction works best when urine osmolality is higher than serum osmolality (the hallmark lab pattern of SIADH).

#### SAFETY WATCH

Thirst can be intense and hard to tolerate; clear explanation and support help adherence. · Monitor serum sodium every 1–2 days at first to confirm it is rising and not climbing too fast. · If sodium does not improve after 2–3 days of strict restriction, consider adding medication or rechecking the diagnosis.

## Sodium chloride tablets (salt tabs) · Oral electrolyte supplement

Giving extra salt by mouth raises the amount of sodium in the blood directly. Each salt tablet delivers sodium chloride, which dissolves in the gut and is absorbed into the bloodstream. This adds 'fuel' to push serum sodium up, especially when combined with fluid restriction. Salt tabs are most helpful when sodium is mildly low (125–134 mEq/L) and the person is not having seizures or other emergencies.

1. A typical salt tablet contains 1 gram of sodium chloride (about 17 mEq of sodium).
2. The person swallows 1–3 tablets per day, often split across meals.
3. Sodium is absorbed in the upper small intestine and enters the portal blood, then the general circulation.
4. As serum sodium rises, the osmolality of the blood increases slightly, which can help reduce the gradient that drives water reabsorption in the kidney (though ADH is still high).
5. Salt tabs work best alongside fluid restriction; used alone they may not overcome the diluting effect of excess ADH.

### SAFETY WATCH

Nausea or stomach upset is common; taking tablets with food helps. · Too much salt without enough fluid restriction can backfire—ADH will hold onto the extra water you drink with the tablets. · Check sodium every few days to make sure it is rising steadily and not overshooting. · Not safe as monotherapy if sodium is below 120 mEq/L or if the person has symptoms such as confusion or seizures.

## Tolvaptan · Vasopressin V<sub>2</sub>-receptor antagonist (aquaretic)

Tolvaptan blocks the V<sub>2</sub> receptor on the collecting-duct cells in the kidney—the very dock where ADH normally lands to trigger water reabsorption. With the receptor blocked, ADH floats past without being able to give its 'hold onto water' command. The kidney then lets water leave in the urine (making a large volume of dilute urine), while sodium and other electrolytes stay in the blood. Serum sodium climbs because water is removed without losing salt—this is called a 'pure water diuresis' or aquaresis.

1. Tolvaptan is swallowed as a tablet and absorbed in the gut; it reaches peak blood levels in 2–4 hours.
2. The drug travels to the kidney and binds tightly to V<sub>2</sub> receptors on the basolateral (blood-facing) side of collecting-duct cells.
3. Even though ADH is still high in the blood, it cannot activate those blocked receptors.
4. Without the V<sub>2</sub> signal, the cell does not insert aquaporin-2 water channels into the apical (urine-facing) membrane.

5. Water stays in the tubule and flows out as dilute urine; sodium remains in the blood, so serum sodium rises over 6–24 hours.
6. Urine volume increases markedly (often 3–6 liters per day at first), and urine osmolality drops below serum osmolality.

**SAFETY WATCH**

Risk of severe liver injury (hepatotoxicity)—liver enzymes (AST, ALT, bilirubin) must be checked before starting, at 2 and 4 weeks, then monthly for the first 18 months, and whenever symptoms (nausea, dark urine, yellowing of the skin and eyes (jaundice), fatigue) appear. Stop immediately if ALT rises above 3× normal. · Must start in the hospital so nurses can monitor sodium every 4–6 hours; the rise can be rapid and must not exceed 6–8 mEq/L in 24 hours to avoid osmotic demyelination syndrome (brain-cell damage from sodium climbing too fast). · Intense thirst and large urine output are common—patients need free access to water and should drink to thirst, not on a schedule. · Do not use in people with liver disease, those who cannot sense or respond to thirst, or anyone taking strong CYP3A inhibitors (ketoconazole, clarithromycin, ritonavir) because drug levels can spike. · Expensive; often reserved for chronic SIADH that has not responded to fluid restriction and salt.

**3% hypertonic saline (intravenous) · Hypertonic electrolyte solution (emergency sodium replacement)**

A 3% saline solution is three times saltier than normal blood. Giving it directly into a vein rapidly raises the sodium concentration of the blood. Water shifts out of swollen brain cells (which have taken on extra water because the blood was too dilute) back into the bloodstream, shrinking the cells and relieving pressure inside the skull. This reverses life-threatening symptoms—seizures, coma, difficulty breathing—caused by cerebral swelling (edema) (brain swelling). The goal is to raise sodium just enough and just fast enough to stop the emergency, not to correct it all at once.

1. A 100 mL bolus of 3% saline (which contains 513 mg of sodium per 100 mL, or about 51 mEq) is pushed through an IV over 10 minutes.
2. Serum sodium rises by roughly 2–3 mEq/L per 100 mL bolus.
3. The higher sodium in the blood creates an osmotic gradient; water flows out of brain cells into capillaries.
4. Brain swelling decreases, intracranial pressure drops, and symptoms (confusion, seizure, vomiting) begin to resolve within 15–30 minutes.
5. The bolus can be repeated once or twice if seizures continue or the patient remains unconscious, rechecking sodium after each dose.

6. Target is a rise of 4–6 mEq/L in the first few hours—just enough to stop the crisis—then slower correction (no more than 8 mEq/L total in 24 hours).

**SAFETY WATCH**

Must give through a secure IV, ideally a central line; if it leaks into tissue (extravasation), it causes severe skin damage. · Check sodium every 2–4 hours during active treatment to avoid overshooting; raising sodium faster than 8 mEq/L in 24 hours (or >18 mEq/L in 48 hours) risks osmotic demyelination syndrome—permanent brain injury with locked-in syndrome, paralysis, difficulty speaking, and swallowing problems. · Monitor for fluid overload (the salt pulls water into vessels); watch for rising blood pressure, shortness of breath, and crackling lung sounds, especially in people with heart failure. · Once the emergency is controlled, switch to slower correction with fluid restriction, normal saline, or oral salt.

**Urea (oral powder or tablet) · Osmotic diuretic / osmolyte supplement**

Urea is a natural waste product made when the body breaks down protein; the kidneys filter it out in urine. Giving extra urea by mouth raises the amount in the blood and the kidney tubules. Because urea pulls water along with it (osmotic effect), more water leaves the body in the urine without taking extra sodium or potassium. This gently raises serum sodium over days to weeks. Urea is inexpensive and works even when ADH is high, but it tastes bitter and is hard to find in many countries.

1. The person swallows 15–60 grams of urea per day, often divided into two or three doses and mixed into juice or a flavored drink to mask the taste.
2. Urea is absorbed in the small intestine and enters the bloodstream, raising blood urea nitrogen (BUN) and serum osmolality.
3. The kidneys filter urea freely; it enters the tubule fluid and pulls water with it via osmosis.
4. More water is excreted in the urine (urine volume goes up slightly), but sodium and potassium stay in the blood.
5. Over several days, serum sodium rises gradually and steadily; the effect is milder and slower than tolvaptan.

**SAFETY WATCH**

Bitter, unpleasant taste—many people cannot tolerate it long term; mixing with strong-flavored drinks (cranberry, orange juice) helps. · Can cause nausea and bloating. · Raises BUN lab values, which can be mistaken for kidney failure if not explained to the team. · Not widely available in the United States (more common in Europe and parts of Asia). · Monitor serum sodium every few days; the rise is usually slow and safe, but checking ensures it is working.

## Demeclocycline · Tetracycline antibiotic (off-label use as ADH antagonist)

Demeclocycline is an old antibiotic that, as a side effect, makes the kidney collecting ducts resistant to ADH. It interferes with the kidney cells' ability to respond to the ADH signal, so even though ADH is high, the kidney does not concentrate urine as much. More water leaves in the urine, and serum sodium slowly rises. Because it takes 3–5 days to start working and carries risks (kidney damage, sun sensitivity), it is now rarely used—tolvaptan and fluid restriction have mostly replaced it.

1. The person takes 300–600 mg by mouth twice daily.
2. Demeclocycline accumulates in the kidney over several days.
3. It interferes with cyclic AMP production inside the collecting-duct cells—the second messenger that normally translates the ADH signal into action.
4. With less cAMP, fewer aquaporin-2 water channels are made and inserted, so less water is reabsorbed.
5. Urine becomes more dilute, urine volume increases, and serum sodium climbs gradually over 1–2 weeks.

### SAFETY WATCH

Can cause kidney damage (dose-related nephrotoxicity), especially in people who already have chronic kidney disease or are dehydrated—not safe if eGFR is below 60. · Severe photosensitivity—skin burns easily in the sun; patients must use high-SPF sunscreen and avoid prolonged sun exposure. · Nausea, vomiting, and diarrhea are common. · Takes many days to work, so not appropriate for acute or symptomatic low sodium (hyponatremia). · Check serum sodium, creatinine, and BUN weekly at first; stop the drug if creatinine rises. · Now considered second- or third-line; rarely started in modern practice.

## Red flags

- Seizure (sudden shaking or loss of awareness)
- Severe confusion or not responding when you speak to the person
- Sodium level below 120 mEq/L or dropping very fast (more than 10 points in 24 hours)
- Trouble breathing or very slow breathing
- Coma (cannot be woken up)

## Nursing priorities

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1. Check mental status every 2 to 4 hours using the Glasgow Coma Scale and watch for new confusion, sleepiness, or seizure activity — Low sodium makes brain cells swell with extra water; when sodium drops below 120 mEq/L or falls too fast, brain swelling causes seizures, coma, and death if not caught early
2. Measure and record every drop of fluid the patient drinks and every milliliter of urine output on a strict intake-and-output flowsheet — Fluid restriction to 800-1000 mL per day is the main treatment; tracking intake and output shows if restriction is working and prevents sneaking extra fluids that worsen low sodium
3. Weigh the patient at the same time every morning on the same scale wearing the same clothes — Daily weight shows total body water; patients should lose 0.5 to 1 kg per day on fluid restriction, proving the kidneys are getting rid of extra water and sodium levels are rising
4. Check serum sodium blood levels every 6 to 12 hours during the first 24 hours of treatment — Sodium must rise slowly at 6 to 8 mEq/L per day; fixing sodium too fast causes osmotic demyelination syndrome (brain damage from myelin coating on nerves breaking down), leaving patients paralyzed or unable to speak
5. If giving 3% saline IV for severe symptoms, use a central line or large peripheral IV and check sodium level after every 100 mL bolus — 3% saline is three times saltier than blood and burns small veins; it raises sodium fast in emergencies but requires close monitoring to avoid raising sodium more than 6 to 8 mEq/L in 24 hours
6. Teach the patient which fluids count toward their daily limit, including ice chips, Jello, soup, and IV fluids — Patients often think only water counts and sneak other liquids; ice chips, Jello, and soup all turn to water in the body and must stay within the 800-1000 mL daily limit or sodium stays low
7. Place fall precautions including bed alarm, non-skid socks, and call bell within reach if sodium is below 125 mEq/L — Low sodium causes muscle weakness, confusion, and slow reflexes; patients are at high risk for falls that cause head injury and broken bones
8. Work with the pharmacy to review the medication list and flag any ADH-triggering drugs for the provider to consider stopping — Continuing medicines like SSRIs, carbamazepine, or NSAIDs keeps triggering ADH release; switching these medicines often cures SIADH without needing long-term fluid restriction or tolvaptan

## Sources

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- NEJM 2015 review on SIADH
- Endocrine Society Clinical Practice Guideline on Hyponatremia (2014)
- American Kidney Fund

- UpToDate (Wolters Kluwer clinical decision support)

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