

Etiology

7. The differential diagnosis of hyponatremia is wide.²³ Possible causes include medications (Table 2) and various diseases and conditions including SIADH, heart failure, renal failure, liver cirrhosis, hypovolemia (e.g., due to diarrhea), psychogenic polydipsia, and adrenal insufficiency. Appendix 1 lists several potential non-medication causes of hyponatremia grouped by volume status and laboratory findings. Evidence is limited in terms of which causes might be more common in a primary care setting.^{1,24}

Table 2. Medications That Can Cause Hyponatremia^{6,25,26}

Class	Mechanism
Diuretics: <ul style="list-style-type: none"> Thiazide (e.g., indapamide, chlorthalidone, hydrochlorothiazide). Refer to Info point 8. Loop (e.g., furosemide, bumetanide), especially when combined with ACE inhibitor/angiotensin receptor blocker (ARB) or spironolactone. 	Renal sodium loss
Anticonvulsants (e.g., carbamazepine, oxcarbazepine, phenytoin, sodium valproate, lamotrigine).	ADH release or action stimulus (SIADH)
Opiates (e.g., morphine, tramadol).	
Chemotherapy (e.g., vinblastine, carboplatin, cisplatin, cyclophosphamide).	
Antipsychotics (e.g., clozapine, fluphenazine, haloperidol, risperidone, thioridazine).	
Antidepressants (e.g., citalopram, sertraline, fluoxetine, paroxetine, venlafaxine, amitriptyline). <ul style="list-style-type: none"> SSRIs, particularly citalopram, have the greatest risk of inducing SIADH (incidence rate ratio 7.8). 	
Dopamine antagonists (e.g., metoclopramide, domperidone).	
ACE inhibitors, ARBs (e.g., ramipril, perindopril, lisinopril, losartan, olmesartan).	
Proton pump inhibitors (e.g., lansoprazole, omeprazole, pantoprazole).	Loss of ADH inhibition (SIADH)
NSAIDs, COX-2 inhibitors, especially when combined with thiazides or in CHF (e.g., ibuprofen, diclofenac, naproxen, celecoxib).	
ADH analogues (e.g., desmopressin).	ADH analogue

8. Thiazide diuretics are a particularly common cause of hyponatremia.⁶ A primary care study found that approximately 14% of 951 thiazide-treated outpatients had hyponatremia.²⁷
- Thiazide-induced hyponatremia presents as euvolemic hyponatremia. It usually occurs within 3 months of medication initiation but may also develop years later, especially during intercurrent illness.²⁸
 - Older age, female sex, and lower body weight are associated with increased risk of thiazide-induced hyponatremia; however, there is no current method of predicting which individuals will be affected.²⁹
 - Thiazide diuretics should not be used in people with a history of thiazide-induced hyponatremia.

Assessment and Management of Hyponatremia (Appendices 1, 2)

9. The assessment and management of hyponatremia is based on patient symptoms, volume status, and acuity.

Step 1. Consider Initial Management Approaches

10. Severe and/or acute hyponatremia can cause brain edema, seizures, and death. Patients with severe hyponatremia (sodium level < 125) should be strongly considered for hospital evaluation, especially if the finding is new.^{9,11,12} Many patients will require IV fluid administration and careful monitoring of sodium levels, as rapid correction of the sodium level can lead to osmotic demyelination.²⁶
11. Patients with any concerning symptoms (e.g., agitation, ataxia, seizures, stupor, respiratory depression, and/or decreased level of consciousness) require urgent transfer to hospital regardless of their sodium level. Patients with no or mild symptoms of hyponatremia may be managed in primary care, at least initially. Outpatient management is generally aimed toward treating the underlying cause.²⁶