# Approach to the Hypernatremic Patient

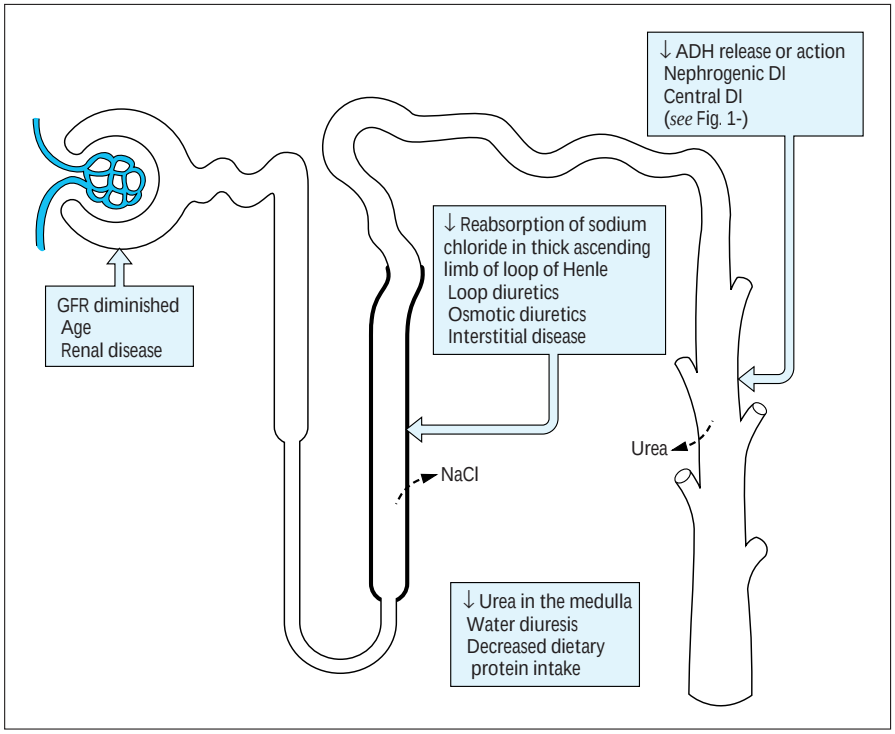


**FIGURE 1-29**

Pathogenesis of hypernatremia. The renal concentrating mechanism is the first line of defense against water depletion and hyperosmolality. When renal concentration is impaired, thirst becomes a very effective mechanism for preventing further increases in serum osmolality. The components of the normal urine concentrating mechanism are shown in Figure 1-2. Hypernatremia results from disturbances in the renal concentrating mechanism. This occurs in interstitial renal disease, with administration of loop and osmotic diuretics, and with protein malnutrition, in which less urea is available to generate the medullary interstitial tonicity.

Hypernatremia usually occurs only when hypotonic fluid losses occur in combination with a disturbance in water intake, typically in elders with altered consciousness, in infants with inadequate access to water, and, rarely, with primary disturbances of thirst [24]. GFR—glomerular filtration rate; ADH—antidiuretic hormone; DI—diabetes insipidus.

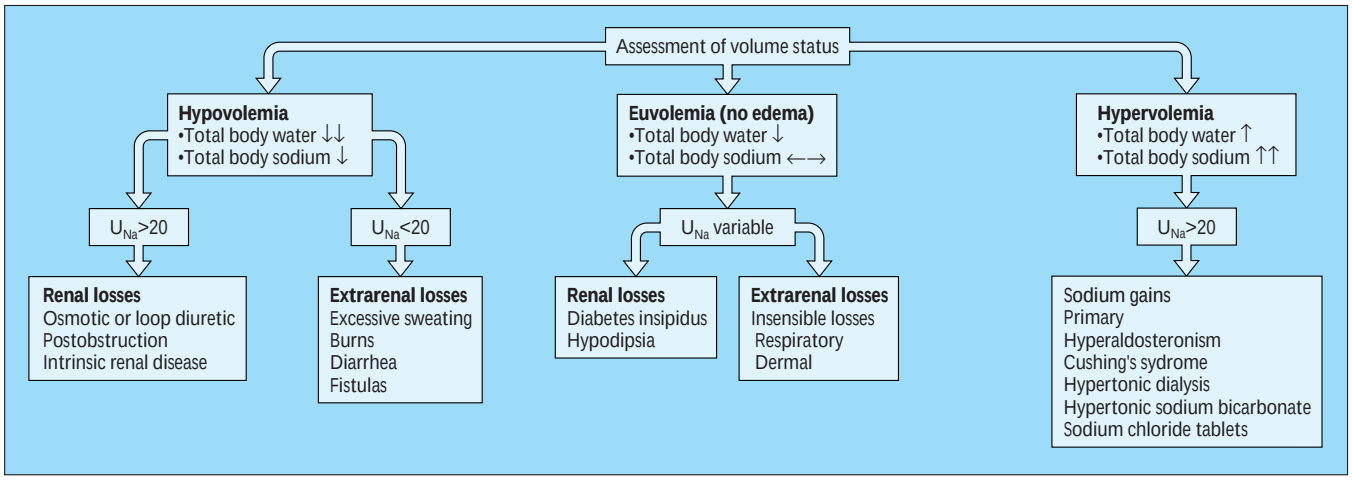


**FIGURE 1-30**

Diagnostic algorithm for hypernatremia. As for hyponatremia, the initial evaluation of the patient with hypernatremia involves assessment of volume status. Patients with hypovolemic hypernatremia lose both sodium and water, but relatively more water. On physical examination, they exhibit signs of hypovolemia. The causes listed reflect principally hypotonic water losses from the kidneys or the gastrointestinal tract.

Euvolemic hyponatremia reflects water losses accompanied by inadequate water intake. Since such hypodipsia is uncommon, hypernatremia usually supervenes in persons who have no access to water or who have a neurologic deficit that impairs thirst perception—the very young and the very old. Extrarenal water loss occurs from the skin and respiratory tract, in febrile or other hypermetabolic states. Very high urine osmolality reflects an intact osmoreceptor–antidiuretic hormone–renal response. Thus, the defense against the development of hyperosmolality requires appropriate stimulation of thirst and the ability to respond by drinking water. The urine sodium ($U_{Na}$) value varies with the sodium intake. The renal water losses that lead to euvolemic hypernatremia are a consequence of either a defect in vasopressin production or release (central diabetes insipidus) or failure of the collecting duct to respond to the hormone (nephrogenic diabetes insipidus) [23]. (*Modified from* Halterman and Berl [12]; with permission.)

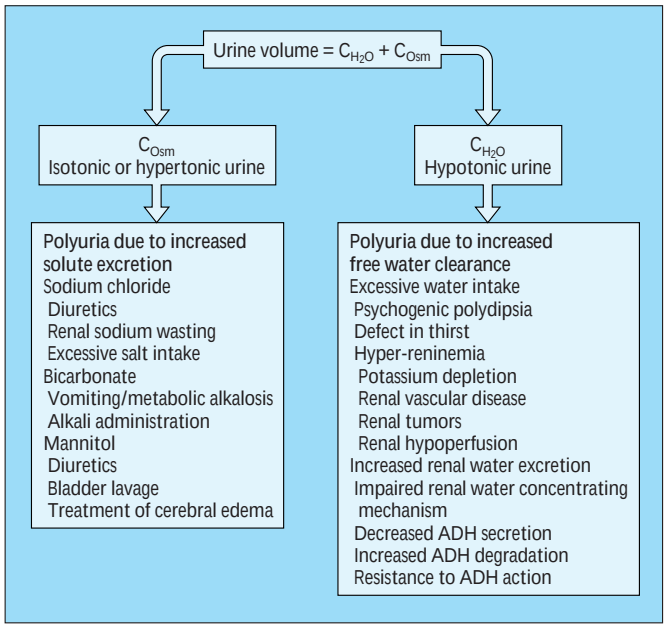


**FIGURE 1-31**

Physiologic approach to polyuric disorders. Among euvolemic hypernatremic patients, those affected by polyuric disorders are an important subcategory. Polyuria is arbitrarily defined as urine output of more than 3 L/d. Urine volume can be conceived of as having two components: the volume needed to excrete solutes at the concentration of solutes in plasma (called the *osmolar clearance*) and the other being the *free water clearance*, which is the volume of solute-free water that has been added to (positive free water clearance [$CH_2O$]) or subtracted (negative $CH_2O$) from the isotonic portion of the urine osmolar clearance (Cosm) to create either a hypotonic or hypertonic urine.

Consumption of an average American diet requires the kidneys to excrete 600 to 800 mOsm of solute each day. The urine volume in which this solute is excreted is determined by fluid intake. If the urine is maximally diluted to 60 mOsm/kg of water, the 600 mOsm will need 10 L of urine for effective osmotic clearance. If the concentrating mechanism is maximally stimulated to 1200 mOsm/kg of water, osmotic clearance will occur in a minimum of 500 mL of urine. This flexibility is affected when drugs or diseases alter the renal concentrating mechanism.

Polyuric disorders can be secondary to an increase in solute clearance, free water clearance, or a combination of both. ADH—antidiuretic hormone.

## WATER DEPRIVATION TEST

| Diagnosis | Urine Osmolality with Water Deprivation (mOsm/kg $H_2O$) | Plasma Arginine Vasopressin (AVP) after Dehydration | Increase in Urine Osmolality with Exogenous AVP |
|---|---|---|---|
| Normal | > 800 | > 2 pg/mL | Little or none |
| Complete central diabetes insipidus | < 300 | Indetectable | Substantial |
| Partial central diabetes insipidus | 300–800 | < 1.5 pg/mL | > 10% of urine osmolality after water deprivation |
| Nephrogenic diabetes insipidus | < 300–500 | > 5 pg/mL | Little or none |
| Primary polydipsia | > 500 | < 5 pg/mL | Little or none |

* Water intake is restricted until the patient loses 3%–5% of weight or until three consecutive hourly determinations of urinary osmolality are within 10% of each other. (Caution must be exercised to ensure that the patient does not become excessively dehydrated.) Aqueous AVP (5 U subcutaneous) is given, and urine osmolality is measured after 60 minutes. The expected responses are given above.

**FIGURE 1-32**

Water deprivation test. Along with nephrogenic diabetes insipidus and primary polydipsia, patients with central diabetes insipius present with polyuria and polydipsia. Differentiating between these entities can be accomplished by measuring vasopressin levels and determining the response to water deprivation followed by vasopressin administration [25]. (*From* Lanese and Teitelbaum [26]; with permission.)

## CLINICAL FEATURES OF DIABETES INSIPIDUS

- Abrupt onset
- Equal frequency in both sexes
- Rare in infancy, usual in second decade of life
- Predilection for cold water
- Polydipsia
- Urine output of 3 to 15 L/d
- Marked nocturia but no diurnal variation
- Sleep deprivation leads to fatigue and irritability
- Severe life-threatening hypernatremia can be associated with illness or water deprivation

**FIGURE 1-33**

Clinical features of diabetes insipidus. Other clinical features can distinguish compulsive water drinkers from patients with central diabetes insipidus. The latter usually has abrupt onset, whereas compulsive water drinkers may give a vague history of the onset. Unlike compulsive water drinkers, patients with central diabetes insipidus have a constant need for water. Compulsive water drinkers exhibit large variations in water intake and urine output. Nocturia is common with central diabetes insipidus and unusual in compulsive water drinkers. Finally, patients with central diabetes insipidus have a predilection for drinking cold water. Plasma osmolality above 295 mOsm/kg suggests central diabetes insipidus and below 270 mOsm/kg suggests compulsive water drinking [23].

## CAUSES OF DIABETES INSIPIDUS

| Central diabetes insipidus | Nephrogenic diabetes insipidus |
|---|---|
| Congenital | Congenital |
| Autosomal-dominant | X-linked |
| Autosomal-recessive | Autosomal-recessive |
| Acquired | Acquired |
| Post-traumatic | Renal diseases (medullary cystic disease, polycystic disease, analgesic nephropathy, sickle cell nephropathy, obstructive uropathy, chronic pyelonephritis, multiple myeloma, amyloidosis, sarcoidosis) |
| Iatrogenic | Hypercalcemia |
| Tumors (metastatic from breast, craniopharyngioma, pinealoma) | Hypokalemia |
| Cysts | Drugs (lithium compounds, demeclocycline, methoxyflurane, amphotericin, foscarnet) |
| Histiocytosis | |
| Granuloma (tuberculosis, sarcoid) | |
| Aneurysms | |
| Meningitis | |
| Encephalitis | |
| Guillain-Barré syndrome | |
| Idiopathic | |

**FIGURE 1-34**
Causes of diabetes insipidus. The causes of diabetes insipidus can be divided into central and nephrogenic. Most (about 50%) of the central causes are idiopathic; the rest are caused by central nervous system involvement with infection, tumors, granuloma, or trauma. The nephrogenic causes can be congenital or acquired [23].

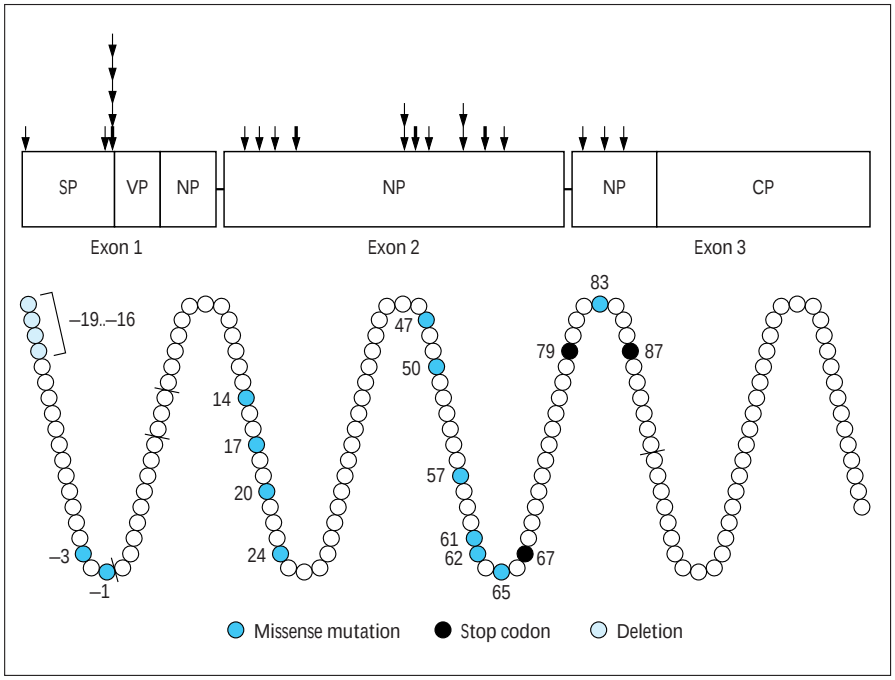


**FIGURE 1-35**
Congenital central diabetes insipidus (DI), autosomal-dominant form. This condition has been described in many families in Europe and North America. It is an autosomal dominant inherited disease associated with marked loss of cells in the supraoptic nuclei. Molecular biology techniques have revealed multiple point mutations in the vasopressin-neurophysin II gene. This condition usually presents early in life [25].
A rare autosomal-recessive form of central DI has been described that is characterized by DI, diabetes mellitus (DM), optic atrophy (OA), and deafness (DIDMOAD or Wolfram's syndrome). This has been linked to a defect in chromosome-4 and involves abnormalities in mitochondrial DNA [27].
SP—signal peptide; VP—vasopressin; NP—neurophysin; GP—glycoprotein.