

## TREATMENT OF CENTRAL DIABETES INSIPIDUS

Condition	Drug	Dose
Complete central DI	dDAVP	10–20 (g intranasally q 12–24 h
Partial central DI	Vasopressin tannate	2–5 U IM q 24–48 h
	Aqueous vasopressin	5–10 U SC q 4–6 h
	Chlorpropamide	250–500 mg/d
	Clofibrate	500 mg tid–qid
	Carbamazepine	400–600 mg/d

FIGURE 1-36

Treatment of central diabetes insipidus (DI). Central DI may be treated with hormone replacement or drugs. In acute settings when renal water losses are extensive, aqueous vasopressin (pitressin) is useful. It has a short duration of action that allows for careful monitoring and avoiding complications like water intoxication. This drug should be used with caution in patients with underlying coronary artery disease and peripheral vascular disease, as it can cause vascular spasm and prolonged vasoconstriction. For the patient with established central DI, desmopressin acetate (dDAVP) is the agent of choice. It has a long half-life and does not have significant vasoconstrictive effects like those of aqueous vasopressin. It can be conveniently administered intranasally every 12 to 24 hours. It is usually tolerated well. It is safe to use in pregnancy and resists degradation by circulating vasopressinase. In patients with partial DI, agents that potentiate release of antidiuretic hormone can be used. These include chlorpropamide, clofibrate, and carbamazepine. They work effectively only if combined with hormone therapy, decreased solute intake, or diuretic administration [23].

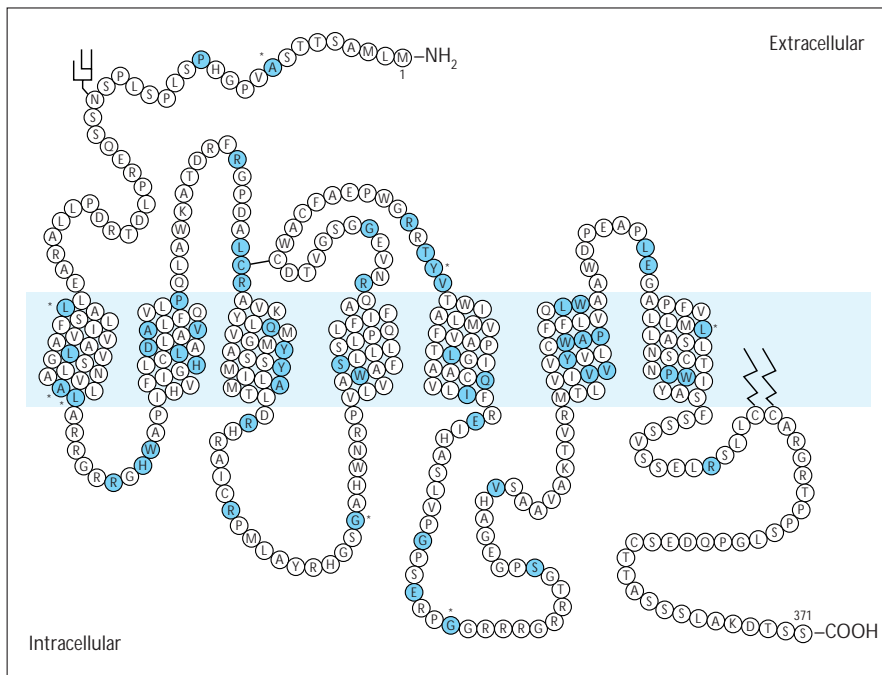
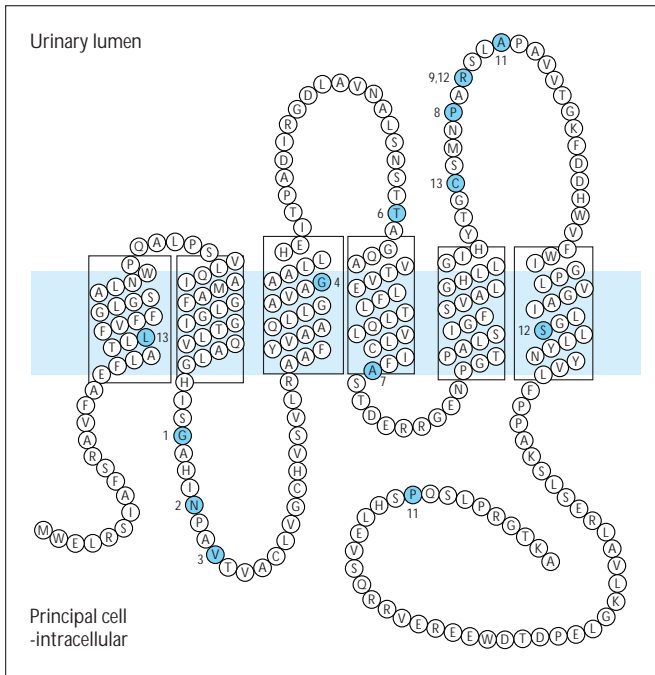


FIGURE 1-37

Congenital nephrogenic diabetes insipidus, X-linked-recessive form. This is a rare disease of male patients who do not concentrate their urine after administration of antidiuretic hormone. The pedigrees of affected families have been linked to a group of Ulster Scots who emigrated to Halifax, Nova Scotia in 1761 aboard the ship called “Hopewell.” According to the Hopewell hypothesis, most North American patients with this disease are descendants of a common ancestor with a single gene defect. Recent studies, however, disproved this hypothesis [28]. The gene defect has now been traced to 87 different mutations in the gene for the vasopressin receptor (AVP-R2) in 106 presumably unrelated families [29]. (From Bichet, *et al.* [29]; with permission.)



**FIGURE 1-38**

Congenital nephrogenic diabetes insipidus (NDI), autosomal-recessive form. In the autosomal recessive form of NDI, mutations have been found in the gene for the antidiuretic hormone (ADH)-sensitive water channel, AQP-2. This form of NDI is exceedingly rare as compared with the X-linked form of NDI [30]. Thus far, a total of 15 AQP-2 mutations have been described in total of 13 families [31]. The acquired form of NDI occurs in various kidney diseases and in association with various drugs, such as lithium and amphotericin B. (From Canfield *et al.* [31]; with permission.)

**ACQUIRED NEPHROGENIC DIABETES INSIPIDUS: CAUSES AND MECHANISMS**

Disease State	Defect in Generation of Medullary Interstitial Tonicity	Defect in cAMP Generation	Downregulation of AQP-2	Other
Chronic renal failure	✓	✓	✓	Downregulation of V <sub>2</sub> receptor message
Hypokalemia	✓	✓	✓	
Hypercalcemia	✓	✓		
Sickle cell disease	✓			
Protein malnutrition	✓		✓	
Demeclocycline		✓		
Lithium		✓	✓	
Pregnancy				Placental secretion of vasopressinase

**FIGURE 1-39**

Causes and mechanisms of acquired nephrogenic diabetes insipidus. Acquired nephrogenic diabetes insipidus occurs in chronic renal failure, electrolyte imbalances, with certain drugs, in sickle cell disease and pregnancy. The exact mechanism involved has been the subject of extensive investigation over the past decade and has now been carefully elucidated for most of the etiologies.

**PATIENT GROUPS AT INCREASED RISK FOR SEVERE HYPERNATREMIA**

- Elders and infants
- Hospitalized patients receiving
  - Hypertonic infusions
  - Tube feedings
  - Osmotic diuretics
  - Lactulose
  - Mechanical ventilation
- Altered mental status
- Uncontrolled diabetes mellitus
- Underlying polyuria

**FIGURE 1-40**

Patient groups at increased risk for severe hypernatremia. Hypernatremia always reflects a hyperosmolar state. It usually occurs in a hospital setting (reported incidence 0.65% to 2.23% of all hospitalized patients) with very high morbidity and mortality (estimates of 42% to over 70%) [12].

### SIGNS AND SYMPTOMS OF HYPERNATREMIA

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**Central Nervous System**

Mild

- Restlessness
- Lethargy
- Altered mental status
- Irritability

Moderate

- Disorientation
- Confusion

Severe

- Stupor
- Coma
- Seizures
- Death

**Respiratory System**

- Labored respiration

**Gastrointestinal System**

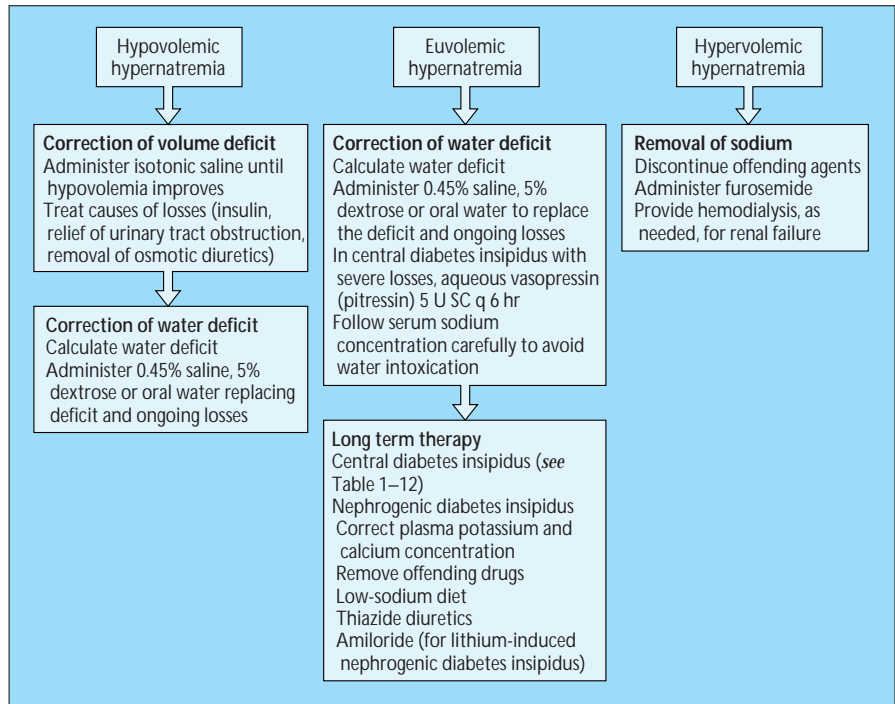
- Intense thirst
- Nausea
- Vomiting

**Musculoskeletal System**

- Muscle twitching
- Spasticity
- Hyperreflexia

**FIGURE 1-41**

Signs and symptoms of hypernatremia. Hypernatremia always reflects a hyperosmolar state; thus, central nervous system symptoms are prominent in affected patients [12].



**FIGURE 1-42**

Management options for patients with hypernatremia. The primary goal in the treatment of hypernatremia is restoration of serum tonicity. Hypovolemic hypernatremia in the context of low total body sodium and orthostatic blood pressure changes should be managed with isotonic saline until blood pressure normalizes. Thereafter, fluid management generally involves administration of 0.45% sodium chloride or 5% dextrose solution. The goal of therapy for hypervolemic hypernatremias is to remove the excess sodium, which is achieved with diuretics plus 5% dextrose. Patients who have renal impairment may need dialysis. In euvolemic hypernatremic patients, water losses far exceed solute losses, and the mainstay of therapy is 5% dextrose. To correct the hypernatremia, the total body water deficit must be estimated. This is based on the serum sodium concentration and on the assumption that 60% of the body weight is water [24]. (Modified from Halterman and Berl [12]; with permission.)

### GUIDELINES FOR THE TREATMENT OF SYMPTOMATIC HYPERNATREMIA\*

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- Correct at a rate of 2 mmol/L/h
- Replace half of the calculated water deficit over the first 12–24 hrs
- Replace the remaining deficit over the next 24–36 hrs
- Perform serial neurologic examinations (prescribed rate of correction can be decreased as symptoms improve)
- Measure serum and urine electrolytes every 1–2 hrs

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\*If  $U_{Na} + U_K$  is less than the concentration of  $P_{Na}$ , then water loss is ongoing and needs to be replaced.

**FIGURE 1-43**

Guidelines for the treatment of symptomatic hypernatremia. Patients with severe symptomatic hypernatremia are at high risk of dying and should be treated aggressively. An initial step is estimating the total body free water deficit, based on the weight (in kilograms) and the serum sodium. During correction of the water deficit, it is important to perform serial neurologic examinations.

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