HYPONATREMIC PATIENTS AT RISK FOR NEUROLOGIC COMPLICATIONS

Complication	Persons at Risk
Acute cerebral edema	Postoperative menstruant females
	Elderly women taking thiazides
	Children
	Psychiatric polydipsic patients
	Hypoxemic patients
Osmotic demyelination syndrome	Alcoholics
	Malnourished patients
	Hypokalemic patients
	Burn victims
	Elderly women taking thiazide diuretics

FIGURE 1-22

Hyponatremic patients at risk for neurologic complications. Those at risk for cerebral edema include postoperative menstruant women, elderly women taking thiazide diuretics, children, psychiatric patients with polydipsia, and hypoxic patients. In women, and, in particular, menstruant ones, the risk for developing neurologic complications is 25 times greater than that for nonmenstruant women or men. The increased risk was independent of the rate of development, or the magnitude of the hyponatremia [21]. The osmotic demyelination syndrome or central pontine myelinolysis seems to occur when there is rapid correction of low osmolality (hyponatremia) in a brain already chronically adapted (more than 72 to 96 hours). It is rarely seen in patients with a serum sodium value greater than 120 mEq/L or in those who have hyponatremia of less than 48 hours' duration [20,21]. (*Adapted from* Lauriat and Berl [21]; with permission.)

SYMPTOMS OF CENTRAL PONTINE MYELINOLYSIS

Initial symptoms
Mutism
Dysarthria
Lethargy and affective changes

Classic symptoms
Spastic quadriparesis
Pseudobulbar palsy

Lesions in the midbrain, medulla oblongata, and pontine tegmentum
Pupillary and oculomotor abnormalities
  Altered sensorium
  Cranial neuropathies
Extrapontine myelinolysis
  Ataxia
  Behavioral abnormalities
  Parkinsonism
  Dystonia

FIGURE 1-23

Symptoms of central pontine myelinolysis. This condition has been described all over the world, in all age groups, and can follow correction of hyponatremia of any cause. The risk for development of central pontine myelinolysis is related to the severity and chronicity of the hyponatremia. Initial symptoms include mutism and dysarthria. More than 90% of patients exhibit the classic symptoms of myelinolysis (*ie*, spastic quadriparesis and pseudobulbar palsy), reflecting damage to the corticospinal and corticobulbar tracts in the basis pontis. Other symptoms occur on account of extension of the lesion to other parts of the midbrain. This syndrome follows a biphasic course. Initially, a generalized encephalopathy, associated with a rapid rise in serum sodium, occurs. This is followed by the classic symptoms 2 to 3 days after correction of hyponatremia, however, this pattern does not always occur [22]. (*Adapted from* Laureno and Karp [22]; with permission.)

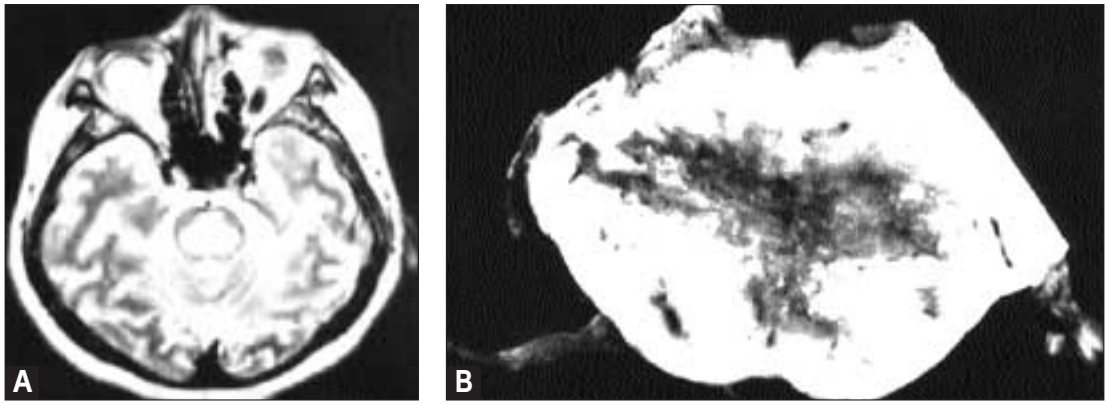

FIGURE 1-24

A, Imaging of central pontine myelinolysis. Brain imaging is the most useful diagnostic technique for central pontine myelinolysis. Magnetic resonance imaging (MRI) is more sensitive than computed tomography (CT). On CT, central pontine and extrapontine lesions appear as symmetric areas of hypodensity (not shown). On T2 images of MRI, the lesions appear as hyperintense and on T1 images, hypointense. These lesions do not enhance with gadolinium. They may not be apparent on imaging until 2 weeks into the illness. Other diagnostic tests are brainstem auditory evoked potentials, electroencephalography, and cerebrospinal fluid protein and myelin basic proteins [22]. **B**, Gross appearance of the pons in central pontine myelinolysis. (*From* Laureno and Karp [22]; with permission.)

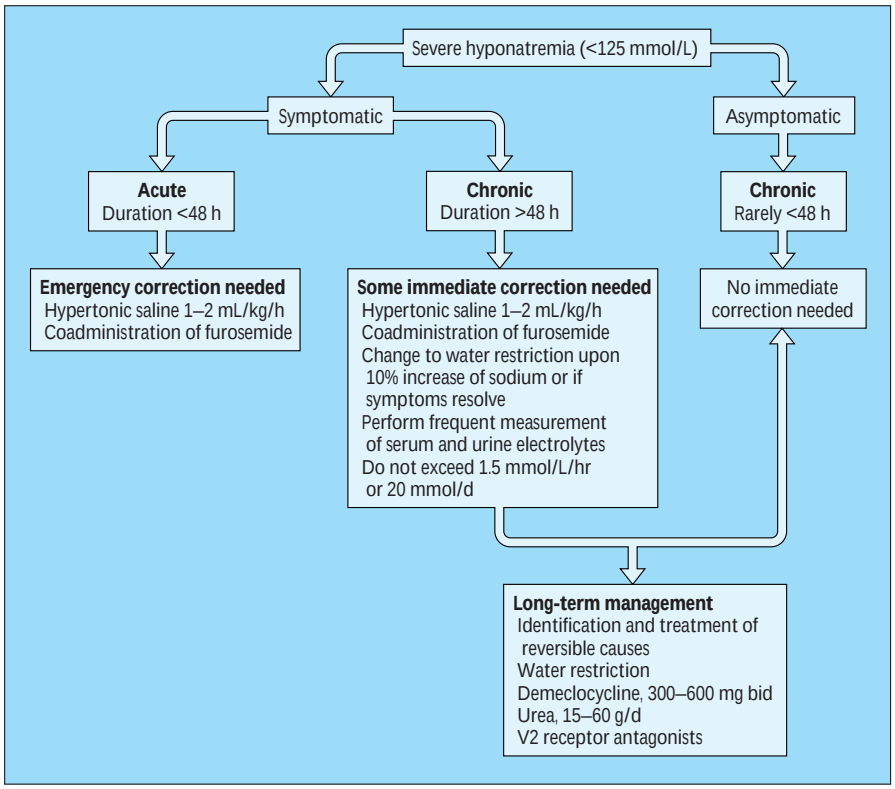

FIGURE 1-25

Treatment of severe euvolemic hyponatremia (<125 mmol/L). The evaluation of a hyponatremic patient involves an assessment of whether the patient is symptomatic, and if so, the duration of hyponatremia should be ascertained. The therapeutic approach to the hyponatremic patient is determined more by the presence or absence of symptoms than by the absolute level of serum sodium. Acutely hyponatremic patients are at great risk for permanent neurologic sequelae from cerebral edema if the hyponatremia is not promptly corrected. On the other hand, chronic hyponatremia carries the risk of osmotic demyelination syndrome if corrected too rapidly. The next step involves a determination of whether the patient has any risk factors for development of neurologic complications.

The commonest setting for acute, symptomatic hyponatremia is hospitalized, postoperative patients who are receiving hypotonic fluids. In these patients, the risk of cerebral edema outweighs the risk for osmotic demyelination. In the presence of seizures, obtundation, and coma, rapid infusion of 3% sodium chloride (4 to 6 mL/kg/h) or even 50 mL of 29.2% sodium chloride has been used safely. Ongoing careful neurologic monitoring is imperative [20].

A. GENERAL GUIDELINES FOR THE TREATMENT OF SYMPTOMATIC HYPONATREMIA*

Acute hyponatremia (duration < 48 hrs)

Increase serum sodium rapidly by approximately 2 mmol/L/h until symptoms resolve

Full correction probably safe but not necessary

Chronic hyponatremia (duration > 48 hrs)

Initial increase in serum sodium by 10% or 10 mmol/L

Perform frequent neurologic evaluations; correction rate may be reduced with improvement in symptoms

At no time should correction exceed rate of 1.5 mmol/L/h, or increments of 15 mmol/d

Measure serum and urine electrolytes every 1–2 h

*The sum of urinary cations ($U_{Na} + U_K$) should be less than the concentration of infused sodium, to ensure excretion of electrolyte-free water.

B. TREATMENT OF CHRONIC SYMPTOMATIC HYPONATREMIA

Calculate the net water loss needed to raise the serum sodium (S_{Na}) from 110 mEq/L to 120 mEq/L in a 50 kg person.

Example

Current $S_{Na} \times$ Total body water (TBW) = Desired $S_{Na} \times$ New TBW

Assume that TBW = 60% of body weight

Therefore TBW of patient = $50 \times 0.6 = 30$ L

$$\text{New TBW} = \frac{110 \text{ mEq/L} \times 30 \text{ L}}{120 \text{ mEq/L}} = 27.5 \text{ L}$$

Thus the electrolyte-free water loss needed to raise the S_{Na} to 120 mEq/L = Present TBW − New TBW = 2.5 L

Calculate the time course in which to achieve the desired correction (1 mEq/h)—in this case, 250 mL/h

Administer furosemide, monitor urine output, and replace sodium, potassium, and excess free water lost in the urine

Continue to monitor urine output and replace sodium, potassium, and excess free water lost in the urine

FIGURE 1-26

General guidelines for the treatment of symptomatic hyponatremia, **A**. Included herein are general guidelines for treatment of patients with acute and chronic symptomatic hyponatremia. In the treatment of chronic symptomatic hyponatremia, since cerebral water is increased by approximately 10%, a prompt increase in serum sodium by 10% or 10 mEq/L is permissible. Thereafter, the patient's fluids should be restricted. The total correction rate should not exceed 1.0 to 1.5 mEq/L/h, and the total increment in 24 hours should not exceed 15 mmol/d [12]. A specific example as to how to increase a patient's serum sodium is illustrated in **B**.

MANAGEMENT OPTIONS FOR CHRONIC ASYMPTOMATIC HYPONATREMIA

Treatment	Mechanism of Action	Dose	Advantages	Limitations
Fluid restriction	Decreases availability of free water	Variable	Effective and inexpensive	Noncompliance
Pharmacologic inhibition of antidiuretic hormone action				
Lithium	Inhibits the kidney's response to antidiuretic hormone	900–1200 mg/d	Unrestricted water intake	Polyuria, narrow therapeutic range, neurotoxicity
Demeclocycline	Inhibits the kidney's response to antidiurectic hormone	1200 mg/d initially; then, 300–900 mg/d	Effective; unrestricted water intake	Neurotoxicity, polyuria, photosensitivity, nephrotoxicity
V2-receptor antagonist	Antagonizes vasopressin action		Ongoing trials	
Increased solute intake				
Furosemide	Increases free water clearance	Titrate to optimal dose; coadminister 2–3 g sodium chloride	Effective	Ototoxicity, K^+ and Mg^{2+} depletion
Urea	Osmotic diuresis	30–60 g/d	Effective; unrestricted water intake	Polyuria, unpalatable gastrointestinal symptoms

FIGURE 1-27

Management options for patients with chronic asymptomatic hyponatremia. If the patient has chronic hyponatremia and is asymptomatic, treatment need not be intensive or emergent. Careful scrutiny of likely causes should be followed by treatment. If the cause is determined to be the syndrome of inappropriate antidiuretic hormone (ADH) secretion, it must be treated as a chronic disorder. As summarized here, the treatment strategies involve fluid restriction, pharmacologic inhibition of ADH action, and increased solute intake. Fluid restriction is frequently successful in normalizing serum sodium and preventing symptoms [23].

MANAGEMENT OF NONEUVOLEMIC HYPONATREMIA

Hypovolemic hyponatremia

Volume restoration with isotonic saline

Identify and correct causes of water and sodium losses

Hypervolemic hyponatremia

Water restriction

Sodium restriction

Substitiute loop diuretics for thiazide diurectics

Treatment of timulus for sodium and water retention

V2-receptor antagonist

FIGURE 1-28

Management of noneuvolemic hyponatremia. Hypovolemic hyponatremia results from the loss of both water and solute, with relatively greater loss of solute. The nonosmotic release of antidiuretic hormone stimulated by decreased arterial circulating blood volume causes antidiuresis and perpetuates the hyponatremia. Most of these patients are asymptomatic. The keystone of therapy is isotonic saline administration, which corrects the hypovolemia and removes the stimulus of antidiuretic hormone to retain fluid. Hypervolemic hyponatremia occurs when both solute and water are increased, but water more than solute. This occurs with heart failure, cirrhosis and nephrotic syndrome. The cornerstones of treatment include fluid restriction, salt restriction, and loop diuretics [20]. (*Adapted from* Lauriat and Berl [20]; with permission.)