Treatment of hypernatremia in adults

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INTRODUCTION

Hypernatremia is most often due to unreplaced water that is lost from the gastrointestinal tract (vomiting or osmotic diarrhea), skin (sweat), or the urine (arginine vasopressin disorders or an osmotic diuresis due to glycosuria in uncontrolled diabetes mellitus or increased urea excretion resulting from catabolism or recovery from kidney failure) (table 1) [1,2]. Hypernatremia due to water loss is called **dehydration**. This is different from **hypovolemia**, in which both salt and water are lost [3]. (See "General principles of disorders of water balance (hyponatremia and hypernatremia) and sodium balance (hypovolemia and edema)".)

Excessive water loss seldom leads to hypernatremia because the resulting increase in plasma osmolality stimulates thirst (figure 1), which leads to increased intake of fluids that lowers the serum sodium into the normal range. Thus, in patients who have access to water, hypernatremia primarily occurs in those who are unable to sense thirst or respond to thirst normally. This is most commonly seen in infants and in adults with impaired mental status, particularly older adults [4]. Older adult patients may also have a diminished thirst response to osmotic stimulation via an unknown mechanism [5,6]. Adipsia due to hypothalamic disease is rare and usually coexists with arginine vasopressin deficiency; this combination often results in severe hypernatremia [7].

Less commonly, hypernatremia results from the administration of salt in excess of water, as can occur with hypertonic sodium bicarbonate therapy during a cardiac arrest, inadvertent

intravenous administration of hypertonic saline during therapeutic abortion, or salt ingestion. Hypernatremia is also particularly common in critical care units when patients are administered large amounts of fluid, which may be hypertonic relative to their ongoing fluid losses, to correct hypovolemia or hypotension [8,9]. (See "Etiology and evaluation of hypernatremia in adults", section on 'Sodium overload'.)

This topic will focus on the treatment of hypernatremia induced by water loss, which is the most common cause. The treatment of hypernatremia in patients with impaired thirst, with or without arginine vasopressin disorders, and with primary sodium overload will also be reviewed. The causes and evaluation of patients with hypernatremia and the treatment of arginine vasopressin deficiency and resistance are discussed elsewhere:

- (See "Etiology and evaluation of hypernatremia in adults".)
- (See "Arginine vasopressin deficiency (central diabetes insipidus): Treatment".)
- (See "Arginine vasopressin resistance (nephrogenic diabetes insipidus): Treatment".)

The evaluation and management of hypernatremia in children is presented separately. (See "Hypernatremia in children".)

APPROACH TO THERAPY

Correction of hypernatremia requires the administration of dilute fluids to both correct the water deficit and replace ongoing water losses and, also, when appropriate, interventions to limit further water loss.

Patients who present with hypernatremia usually have a serious underlying condition that impairs either their ability to respond to thirst or to experience thirst. As a result, such patients usually require hospitalization to correct the hypernatremia. (See "Etiology and evaluation of hypernatremia in adults", section on 'The importance of thirst'.)

Initial fluid repletion regimen — A detailed and stepwise description of how to calculate the water deficit and devise a fluid repletion regimen is presented later in this topic; those calculations provide the rationale underlying the therapeutic approach. In general, a net positive balance of 3 mL of electrolyte-free water per kilogram of lean body weight will lower the serum sodium by approximately 1 mEq/L [10]. (See 'Rationale for our therapeutic approach' below.)

The therapeutic approach in patients with hypernatremia is presented here (algorithm 1).

Patients with chronic hypernatremia — Hypernatremia is chronic if it has been present for longer than 48 hours. Nearly all patients with hypernatremia will have chronic hypernatremia, even those who present with acute changes in mentation who are discovered to have hypernatremia. The initial regimen in such patients is (algorithm 1):

- Five percent dextrose in water, intravenously, at a rate of (approximately 1.35 mL/hour x patient's weight in kg, up to a maximum of 150 mL/hour) or approximately 70 mL/hour in a 50 kg patient and 100 mL/hour in a 70 kg patient. Hypernatremic patients who are also hypovolemic will require isotonic fluids to expand the extracellular fluid volume. (See 'Treating patients who also have hypovolemia or hypokalemia' below.)

  In clinically stable patients, chronic hypernatremia may also be corrected with oral rehydration (if level of consciousness is normal and the patient can drink adequately) or by administering water through a nasogastric tube. Although no data are available in adult patients with chronic hypernatremia, this approach was found to be safe and effective in children with hypernatremia due to gastroenteritis [11].

- The goal of water repletion in patients with chronic hypernatremia is to lower the serum sodium by approximately 10 mEq/L in 24 hours but to avoid correcting the serum sodium by more than 12 mEq/L in 24 hours. Correction by 12 mEq/L in 24 hours is considered the maximum safe limit in infants; although exceeding this limit in adults has not been proven harmful, it has similarly not been proven beneficial. It is likely that our suggested initial regimen will lower the serum sodium by less than 10 mEq/L in 24 hours as many patients have ongoing free water losses (eg, osmotic diuresis, diarrhea, nasogastric suction) that will reduce the net positive electrolyte-free water balance, thereby slowing the rate of correction. (See 'Rate of correction in chronic hypernatremia' below.)

Patients with acute hypernatremia — Hypernatremia is acute if it has been present for 48 hours or less. Acute hypernatremia is uncommon, occurring in patients with salt poisoning; in patients with arginine vasopressin disorders who acutely lose the ability to replace their water losses (eg, a patient with an arginine vasopressin disorder who undergoes surgery and does not receive adequate intravenous water); and in patients being treated for severe hyperglycemia, whose water losses from glycosuria are not adequately replaced. (See "Etiology and evaluation of hypernatremia in adults", section on 'Salt poisoning' and "Etiology and evaluation of hypernatremia in adults", section on 'Iatrogenic sodium loading' and "Etiology and evaluation of hypernatremia in adults", section on 'AVP deficiency or resistance (central or nephrogenic diabetes insipidus)' and "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Treatment".)

The initial regimen in patients with acute salt poisoning or arginine vasopressin disorders is (algorithm 1):

- Five percent dextrose in water, intravenously, initially at a rate of at least 6 mL/kg/hour.
- The serum sodium and blood glucose should be monitored every one to three hours until the serum sodium is lowered below 145 mEq/L.
- Once the serum sodium concentration has reached 145 mEq/L, the rate of infusion is reduced to 1 mL/kg/hour and continued until a normal serum sodium (140 mEq/L) is restored.
- The goal of this regimen is to rapidly lower the serum sodium in the first few hours (by as much as 8 mEq/L per hour) and to restore a normal serum sodium in less than 24 hours.
- Patients with arginine vasopressin deficiency will also require desmopressin therapy, which is discussed elsewhere. (See "Arginine vasopressin deficiency (central diabetes insipidus): Treatment" and "Arginine vasopressin resistance (nephrogenic diabetes insipidus): Treatment".)
- Hyperglycemia may develop with rapid infusions of 5 percent dextrose; to avoid increased water losses from glycosuria, a slower rate of infusion or a change to 2.5 percent dextrose in water may be required after several hours. (See 'Risk of hyperglycemia' below.)

In patients with both acute hypernatremia and oliguric acute kidney injury, hemodialysis or continuous kidney replacement therapy can be used to correct hypernatremia and avoid volume overload [12,13].

A systemic literature review identified 18 patients who became severely hypernatremic (median serum sodium 180.5 mEq/L; range 167 to 209 mEq/L) over a short period time (less than 12 hours) due to salt poisoning [14]. Salt poisoning was due to self-ingestion in eight patients and iatrogenic sodium administration in ten patients; treatment was initiated within 12 hours from the onset of hypernatremia. Although the small sample size precluded a statistical analysis, correction rates were more rapid in the 13 patients who survived than in the five patients who died. Those who survived typically achieved a serum sodium ≤160 mEq/L within 8 hours, ≤150 mEq/L within 24 hours, and ≤145 mEq/L within 48 hours; the mean maximal correction rate in this group was 7.6 mEq/L per hour. Hyperglycemia due to rapid infusions of 5 percent dextrose in water was a commonly observed, treatment-related, adverse event.

Patients with hypernatremia due to correction of hyperglycemia — As hyperglycemia and hypovolemia are corrected in a patient with diabetic ketoacidosis (DKA) or hyperosmolar

hyperglycemic state, the serum sodium concentration will rise because of an osmotic shift of water from extracellular fluid into cells and because of loss of electrolyte-free water in the urine as excess glucose is excreted. In patients with severe hyperglycemia whose serum sodium concentration is normal or high on presentation, severe hypernatremia is expected to emerge during the course of therapy.

There is no consensus on how this should be managed, and the rationale for our approach is presented below (see 'Rate of correction in hypernatremia associated with severe hyperglycemia' below):

- Cerebral edema has been described in children and young adults (ie, age less than 40 years) who have rapid correction of hyperglycemia and, therefore, hypertonicity. Accordingly, if hypernatremia develops as a consequence of correcting the hyperglycemia in young individuals, our goal is slow correction using the water repletion regimen described for patients with chronic hypernatremia. (See 'Patients with chronic hypernatremia' above.)

- However, cerebral edema has not been described in older individuals during rapid correction of hyperglycemia. Conversely, the relatively sudden onset of hypertonicity in older individuals caused either by severe hyperglycemia (due, for example, to hyperosmolar hyperglycemia) or by acute hypernatremia (due, for example, to salt poisoning) has been associated with osmotic demyelination syndrome [15,16]. Accordingly, if hypernatremia develops as a consequence of correcting the hyperglycemia in older individuals, our goal is rapid correction at the rate described above for patients with acute hypernatremia. (See 'Patients with acute hypernatremia' above.)

  Because most of these patients are hypovolemic and hyperglycemic, with ongoing losses of sodium and water due to glycosuria, free water is usually administered as 0.45 percent saline rather than 5 percent dextrose in water; infusion of 0.45 percent saline at 6 to 12 mL/kg per hour will provide the same amount of electrolyte-free water as 3 to 6 mL/kg per hour of 5 percent dextrose in water.

Because both serum sodium and serum glucose determine tonicity, we also recommend serial calculations of the "effective" serum osmolality (2 x Serum sodium + Serum glucose) to monitor the course in plasma tonicity.

Remeasure the sodium and modify the regimen — The regimen for acute hypernatremia is designed to rapidly lower the serum sodium to normal (ie, 140 mEq/L) in less than 24 hours. During the rapid infusion of 5 percent dextrose in water (or 0.45 percent saline), repeated laboratory measurements are necessary every one to three hours to ensure that serum sodium

concentration is falling at the desired rate, to avoid overshooting the desired endpoint, and to watch for hyperglycemia. In chronic hypernatremia, rapid infusion of free water is not necessary, and, with a slower rate of infusion, the need for frequent monitoring is much less. However, in all cases of hypernatremia, the fluid repletion regimen should be modified, if necessary, based upon the sequential measurements of serum sodium.

For the most commonly encountered patients with **chronic hypernatremia**, we suggest the following approach:

- Remeasure the serum sodium four to six hours after the initial fluid repletion regimen is started.

- If the repeat serum sodium indicates that the target rate of correction has been attained, then the frequency of measurement can be reduced in most patients to every 12 to 24 hours. However, in patients who have large, ongoing water losses due, for example, to hyperglycemia and glycosuria or arginine vasopressin resistance, the serum sodium should be measured approximately every four to six hours during the first day of therapy to ensure that the fluid repletion regimen is adequate.

- If the target rate of correction has not been attained (the rate of correction is either too fast or too slow), then the infusion rate should be modified and the serum sodium should be remeasured four to six hours after the modification has taken place:

  - Most commonly, the rate of correction is too slow (ie, the rate of reduction in serum sodium is less than 0.25 mEq/L per hour) [17]. This usually results from ongoing free water losses due to an osmotic diuresis (eg, hyperglycemia in diabetic patients, urea in patients recovering from azotemia [18]), diarrhea, vomiting, or nasogastric suction, although a higher-than-estimated total body water (TBW) could also contribute. In such cases, the volume of ongoing free water loss should be estimated, and this quantity should be added to the fluid repletion regimen. Estimation of ongoing free water losses is presented below. (See 'Replacing both ongoing water losses and the water deficit' below.)

  - Less commonly, the rate of correction is too fast. In such cases, the infusion can be stopped or slowed (and the infusion rate recalculated using the updated information). Excessively rapid correction of chronic hypernatremia is of greatest concern in infants because rapid correction is common in patients with very small body size and because hypernatremic infants often develop cerebral edema and seizures during overaggressive rehydration. In these patients, it may become necessary to therapeutically increase the serum sodium concentration again to ameliorate

iatrogenic brain swelling [19,20]. Rapid correction of hypernatremia is much less likely to occur in adults than in infants; in adults, cerebral edema as a complication of overaggressive therapy is mostly a theoretical concern, and there is an association between slow correction rates and increased mortality [17,20]. We do not recommend re-raising the serum sodium in adults if the desired maximal correction rate has been exceeded.

Formulas designed to predict the change in serum sodium according to a given fluid regimen do **not** eliminate the need for careful monitoring of the serum sodium during therapy. These formulas often fail because they do not include insensible losses or urinary or gastrointestinal losses of electrolytes and water. Even formulas that include such variables are insufficiently accurate for clinical use because they cannot account for the following factors that impact the serum sodium concentration: rapid changes in fluid and electrolyte losses during therapy, internal exchanges between soluble and bound sodium stores, and shifts of water into and out of cells due to changes in intracellular osmolytes [21]. We discourage the use of these formulas as the sole guide to therapy. They can, however, be useful in providing a rough estimate of the amount of electrolyte-free water that will be needed, and they can help identify unsuspected fluid losses when the actual change in serum sodium concentration deviates markedly from what is predicted.

The regimens presented above and the water deficit formula presented below are based upon an estimate of the TBW, which cannot be measured directly in the clinical setting. As a result, **these equations only provide a guide** to initial therapy, and **serial measurements** of the serum sodium are essential to determine the response to therapy. Limitations to the estimating equations are discussed below. (See 'Initial fluid repletion regimen' above and 'Estimating the water deficit' below.)

Treating patients who also have hypovolemia or hypokalemia — Many hypernatremic patients have concurrent extracellular fluid volume depletion and/or hypokalemia (due, for example, to diarrhea or vomiting). Hypotonic intravenous solutions containing sodium or potassium can be used to simultaneously correct the water and electrolyte deficits. The lowest percentage of sodium chloride in commercially available intravenous solutions is 0.45 percent (often referred to as half-normal saline). Additional dextrose-containing solutions are commercially available, including 2.5 percent dextrose and 0.45 percent sodium chloride, as well as 5 percent dextrose and 0.2 percent sodium.

To avoid hyperglycemia, 0.225 percent sodium chloride (also known as quarter-normal saline) has been previously used to correct hypernatremia. However, it is no longer recommended, because it requires compounding by the pharmacy and can cause hemolysis [22].

Addition of sodium or potassium to the replacement fluid decreases the amount of free water that is being given.

If, for example, one-half isotonic saline (sodium concentration 77 mEq/L) is given, then only half of the solution is free water. In that case, rather than 1.35 mL/hour x patient's weight in kg, which would be the initial prescription if 5 percent dextrose in water were the replacement fluid, the initial fluid repletion regimen would be one-half isotonic saline at a rate of 2.7 mL/hour x patient's weight in kg. If 40 mEq of potassium is added because the patient is hypokalemic, then only one-quarter of the solution is free water. In this setting, the initial fluid repletion regimen would be one-half isotonic saline plus 40 mEq/L of potassium at a rate of 5.4 mL/hour x patient's weight in kg.

An alternative to combining water and sodium (with or without potassium) into one solution is to use two intravenous solutions, one for free water and the other for sodium with or without potassium as an isosmotic solution. The major setting in which this might be important is in a patient with severe hypernatremia who also has clinical signs of marked hypovolemia. In this setting, there is a need for more rapid expansion of the extracellular fluid volume with isotonic saline, but the desired rate of correction of the hypernatremia has not changed. (See 'Application to hypernatremia' below.)

Risk of hyperglycemia — A potential complication of the administration of dextrose-containing intravenous fluids at a rapid rate is the development of hyperglycemia. This is more likely to occur in patients who have diabetes mellitus or who are physiologically stressed, leading to the secretion of hormones that can raise the plasma glucose concentration (eg, epinephrine and cortisol). Hyperglycemia can lead to an osmotic diuresis, which creates electrolyte-free water losses that will limit the reduction in serum sodium. (See 'Replacing both ongoing water losses and the water deficit' below and "Maintenance and replacement fluid therapy in adults", section on 'Dextrose-induced hyperglycemia'.)

In normal individuals (ie, no diabetes, not stressed) receiving high doses of insulin, the maximum rate of glucose metabolism is 10 mg/kg/min [23]. In a patient with a lean body weight of 50 kg, this limit would be attained by administration of 5 percent dextrose in water at 600 mL/hour. Maximum rates of glucose metabolism would be much lower in ill patients with high counterregulatory hormone levels and insulin resistance. Thus, in a patient with a 50 kg lean body weight, prolonged infusion of dextrose in water at rates greater than 250 to 300 mL/hour may result in progressive hyperglycemia.

A 2.5 percent dextrose in water solution can be used in patients who develop hyperglycemia. However, this solution is not available in many hospitals. One option is to dilute 5 percent

dextrose in water with an equal volume of distilled water. An alternative is to simultaneously infuse 5 percent dextrose in water and one-half isotonic saline in a 1:1 ratio through a single intravenous line using a Y-site connector, which will create an infusion that is 2.5 percent dextrose in one-quarter isotonic saline.

RATIONALE FOR OUR THERAPEUTIC APPROACH

The approach to therapy, presented above, is based upon a four-step determination of the water prescription for a patient with hypernatremia:

- Estimate the magnitude of the water deficit. (See 'Estimating the water deficit' below.)
- Determine the appropriate rate of correction since lowering the plasma sodium concentration too rapidly can lead to cerebral edema in chronic hypernatremia and because untreated acute hypernatremia can lead to permanent neurologic injury. (See 'Choosing a rate of correction' below.)
- Use the estimated water deficit, desired rate of correction, and estimation of ongoing free water losses to calculate a fluid repletion regimen. (See 'Designing the fluid repletion regimen' below.)
- Address concurrent volume or potassium deficits. (See 'If concurrent electrolyte replacement is necessary' below.)

Estimating the water deficit — The water deficit in the hypernatremic patient can be estimated from the following formula, the derivation of which is described below [1,2]. (See 'Derivation of the water deficit formula' below.)

$$\text{Water deficit} = \text{Current TBW} \times \left(\frac{\text{Serum [Na]}}{140} - 1\right)$$

Total body water (TBW) refers to the estimated TBW, which is normally approximately 60 and 50 percent of lean body weight in younger males and females, respectively, and approximately 50 and 45 percent of lean body weight in older adult males and females, respectively [2]. However, it is probably reasonable to use values approximately 10 percent lower in hypernatremic patients who are water depleted.

Of note, in a patient with a serum sodium of 141 mEq/L and TBW of approximately 50 percent of lean body weight, then the calculated water deficit using the above formula is approximately 3 mL/kg. This provides the rationale for the estimation, mentioned above, that a net positive balance of 3 mL of electrolyte-free water per kilogram of lean body weight will lower the serum sodium by approximately 1 mEq/L. (See 'Initial fluid repletion regimen' above.)

Thus, in a nonobese, middle-aged, 60 kg female with a serum sodium concentration of 168 mEq/L, TBW is approximately 40 percent of body weight, and the water deficit can be approximated from:

$$\text{Water deficit} = 0.4 \times 60 \times ([168/140] - 1) = 4.8 \text{ liters}$$

The water deficit formula, as well as the equations presented above in the simplified approach, provide a guide to initial therapy. However, they have a number of potential limitations; as a result, the response to therapy must be assessed by remeasuring the serum sodium during therapy, as noted above [21]. (See 'Remeasure the sodium and modify the regimen' above.)

The limitations include:

- The water deficit formula and the simplified approach both require an estimate of TBW. This estimate is based on a percentage of lean body weight, not actual body weight, which includes fat, a tissue containing little water. Even the most precise estimates, based on height, weight, sex, and age, were derived in euvolemic subjects [24], and they will overestimate TBW in hypovolemic patients and underestimate TBW in patients who are edematous [25].

- The formulas estimate the amount of **positive electrolyte-free water balance** that must be attained to lower the serum sodium to a particular goal or at a particular rate. However, ongoing free water losses must also be replaced, including obligatory losses in sweat and stool (approximately 30 to 40 mL/hour) as well as any dilute urinary or gastrointestinal losses. These losses can only be estimated, with the exception of urinary losses in patients with a bladder catheter. The term "dilute" in this context refers to a fluid in which the sodium plus potassium concentration is lower than that in the serum. (See 'Determinants of the plasma sodium concentration' below and "Maintenance and replacement fluid therapy in adults", section on 'Water balance'.)

- The water deficit formula and the simplified approach do not include any isosmotic fluid deficit (ie, volume depletion) that often coexists with the water deficit when both sodium and water have been lost, as occurs with diarrhea or an osmotic diuresis. (See 'Treating

patients who also have hypovolemia or hypokalemia' above and 'If concurrent electrolyte replacement is necessary' below.)

- A substantial portion of body sodium is bound to anionic sites on proteoglycan macromolecules in bone, cartilage, and connective tissue and is not free in solution. Exchanges between bound and free sodium occur and are not accounted for in predictive formulas [8,20,26].

- Cellular accumulation of organic osmolytes, which helps maintain near-normal brain volume in chronic hypernatremia, also occurs in some peripheral tissues. During recovery from hypernatremia, loss of these excess cellular osmolytes would result in a greater fall in serum sodium than predicted by formulas that do not account for changes in intracellular organic osmolytes [8].

Choosing a rate of correction — Overly rapid correction is potentially dangerous in chronic hypernatremia, as it is in chronic hyponatremia, although the risk is not as well defined in hypernatremia [20,27]. (See "Osmotic demyelination syndrome (ODS) and overly rapid correction of hyponatremia".)

Overly rapid correction of hypernatremia causing neurologic symptoms has been described almost exclusively in children who have hypernatremia that is chronic (more than 48 hours in duration) with serum sodium concentrations above 150 mEq/L and usually above 155 mEq/L. In theory, the same principles are applicable to adults. (See "Hypernatremia in children", section on 'Rate of correction'.)

The following sequence has been proposed to explain the adverse effect of overly rapid correction of chronic hypernatremia. The supportive data are presented elsewhere (see "Manifestations of hyponatremia and hypernatremia in adults", section on 'Hypernatremia'):

- The initial response to hypernatremia is osmotic water movement out of brain cells and other cells. The resulting shrinkage of brain cells is thought to be primarily responsible for any early neurologic symptoms (eg, lethargy, seizures, and coma). Severe manifestations of acute hypernatremia are usually seen at serum sodium concentrations above 158 mEq/L.

- Within two to three days, brain volume is largely restored due both to salt and water movement from the cerebrospinal fluid into the brain (thereby increasing the interstitial volume) and to the uptake of osmotically effective solutes by the brain cells (thereby pulling water back into the cells and restoring the cell volume) [1,20,27,28]. At this time,

neurologic symptoms are less likely, and improvement is seen if there were symptoms due to the acute hypernatremia.

- Rapid lowering of the plasma sodium concentration once the cerebral adaptation has occurred causes additional osmotic water movement into brain cells, increasing the brain size above normal. The resulting cerebral edema can lead to an encephalopathy characterized by seizures and, rarely, permanent neurologic damage or death [20,29].

Rate of correction in chronic hypernatremia — Chronic hypernatremia is defined as hypernatremia that has been present for at least 48 hours. There are no definitive clinical trials, but data in children (particularly infants) with chronic hypernatremia suggest that the maximum safe rate at which the serum sodium concentration should be lowered is 12 mEq/L per day. The pediatric studies that provide the rationale for this rate of correction are presented elsewhere. (See "Hypernatremia in children", section on 'Rate of correction'.)

In adults, a maximum safe rate of correction for chronic hypernatremia has not been established, and there have been no published reports of cerebral edema complicating rapid correction of hypernatremia in this population. In one retrospective cohort study of 250 patients with chronic hypernatremia, 30-day mortality rates were similar among those corrected slowly (12 mEq/L or less in 24 hours) compared with those corrected more rapidly (more than 12 mEq/L in 24 hours) [30]. In a subset of 46 patients with chronic hypernatremia who were corrected by more than 12 mEq/L in 24 hours, manual review of medical records failed to identify a case of seizures, cerebral edema, or cerebral injury. However, there is no evidence that a rate of correction slower than 12 mEq/L per 24 hours is harmful, and given a theoretical risk based upon data in children, a goal rate of correction of approximately 10 mEq/L per day is still reasonable. However, if this rate is inadvertently exceeded, we do not recommend that the serum sodium be raised again.

Older adult patients with acute clinical presentations — Many patients with hypernatremia are older adults, often residing in long-term care facilities. Hypernatremia in these patients may present clinically as an acute change in mental status. However, the hypernatremia probably develops gradually in almost all such patients. In the absence of known salt poisoning or known arginine vasopressin disorders, the serum sodium concentration should be corrected slowly (no more than 12 mEq/L per day).

Some data suggest that excessively slow correction (less than 6 mEq/L per day [less than 0.25 mEq/L per hour]) should also be avoided. A single-center, retrospective study of 131 patients (98 percent male, mean age 73 years) admitted to a veterans hospital with a serum sodium concentration greater than or equal to 155 mEq/L found that patients whose hypernatremia

was corrected within 72 hours had significantly lower mortality rates (10 versus 25 percent) [17]. After adjusting for multiple factors, the relative risk for mortality was higher among those whose rate of correction was less than 0.25 mEq/L per hour during the first day of therapy (hazard ratio [HR] 3.10, 95% CI 1.38-6.88). An association between slow rates of correction and mortality was found in another study of 85 hypernatremic patients (serum sodium greater than or equal to 150 mEq/L) presenting to an emergency department; after multivariable adjustment, male sex, lower blood pressure, and slower hypernatremia-correction speed were associated with increased in-hospital mortality [31].

Rate of correction in acute hypernatremia — In patients with acute hypernatremia, the serum sodium should be lowered rapidly to a near-normal level in less than 24 hours. This is because the acute increase in the plasma sodium concentration can lead to irreversible neurologic injury. This injury may be due, in part, to osmotic demyelination [32-35], similar to the injury caused by a rapid elevation in plasma sodium during the treatment of chronic hyponatremia. In addition, neurologic injury in patients with acute hypernatremia may result from cerebral hemorrhage [35].

Patients with acute hypernatremia can be treated with either intravenous dextrose in water or, in patients who also have oliguric acute kidney injury, hemodialysis or continuous venovenous hemofiltration [12,13]. In addition, desmopressin may be necessary in patients with arginine vasopressin deficiency. These issues are discussed elsewhere in detail. (See "Arginine vasopressin deficiency (central diabetes insipidus): Treatment" and "Arginine vasopressin resistance (nephrogenic diabetes insipidus): Treatment" and "Etiology and evaluation of hypernatremia in adults", section on 'Treatment of salt poisoning'.)

Because of the time required for the cerebral adaptation, only patients with hypernatremia for at least 48 hours are at risk for overly rapid correction. The rare patients with known acute hypernatremia (due, for example, to salt poisoning or to surgery without adequate replacement of water losses in patients with arginine vasopressin disorders) have not had time for the cerebral adaptation. These patients may develop severe symptoms of hypernatremia and permanent or fatal brain injury but are **not** likely to be at risk from overly rapid correction. In one case, for example, a 19-year-old male presenting with seizures, coma, and a serum sodium >180 mEq/L after ingesting a quart of soy sauce was treated with 6 L of free water over 30 minutes; he survived neurologically intact without clinical sequelae [36]. (See "Manifestations of hyponatremia and hypernatremia in adults", section on 'Hypernatremia' and "Osmotic demyelination syndrome (ODS) and overly rapid correction of hyponatremia", section on 'Duration of hyponatremia'.)

Rate of correction in hypernatremia associated with severe hyperglycemia — Rapid correction of hypertonicity caused by hyperglycemia can result in cerebral edema. This is an important cause of morbidity and mortality in children and adolescents with diabetic ketoacidosis (DKA) [37,38]. The vast majority of fatal or life-threatening cases of cerebral edema associated with DKA have been reported in patients under the age of 20 years, but there have been a few cases in adults between the ages of 20 and 40 [39-42]. Concerns about this complication have led to recommendations that the decrease in tonicity ("effective osmolality") during correction of hyperglycemia should not be greater than 3 mosmol/kg per hour, that the goal for blood glucose reduction should be 50 to 75 mg/dL per hour [25], and that development of hypernatremia be permitted in order to prevent a decrease in effective osmolality as the blood glucose falls [37,38].

Correction of hyperglycemia and hypovolemia increases the serum sodium concentration because water shifts into cells as hyperglycemia resolves and because water is excreted in urine with excess glucose. In patients with severe hyperglycemia whose serum sodium concentration is normal or high on presentation, severe hypernatremia is likely to emerge during the course of therapy. There is no consensus on how to manage such an increase in serum sodium in adults with nonketotic hyperglycemia. In contrast to the experience in children and young adults with DKA, life-threatening cerebral edema has not been reported after treatment of nonketotic hyperglycemia. However, hyperosmolar hyperglycemia has been associated with osmotic demyelination syndrome, which is thought to result from hypertonic injury to astrocytes [43].

Osmotic demyelination syndrome usually occurs in patients who have overly rapid correction of chronic hyponatremia (ie, a rapid increase in tonicity in hypotonic patients). However, osmotic demyelination syndrome may also result from hyperosmolar hyperglycemia or acute hypernatremia. (See "Osmotic demyelination syndrome (ODS) and overly rapid correction of hyponatremia" and "Etiology and evaluation of hypernatremia in adults", section on 'Sodium overload'.)

In patients who have overly rapid correction of hyponatremia, the appropriate treatment is prompt relowering of the serum sodium to militate against injury to astrocytes and osmotic demyelination [44]. Similarly, it could be argued that the serum sodium concentration should be rapidly relowered with hypotonic fluid as it rises acutely during correction of hyperglycemia. We use this approach in adults with nonketotic hyperglycemia. Although the benefit of this intervention has not been evaluated in either experimental animals or patients, the risk of osmotic demyelination syndrome in this condition likely outweighs the risk of life-threatening cerebral edema.

Designing the fluid repletion regimen — The initial fluid prescription (ignoring ongoing water losses) is based upon the calculated water deficit and the desired rate of correction.

In a patient with acute hypernatremia, the entire deficit is replaced in less than 24 hours, and the hourly infusion rate should exceed the water deficit divided by 24:

$$\text{Hourly infusion rate (mL/hour)} > \text{Water deficit in mL} \div 24 \text{ hours}$$

However, in a patient with chronic hypernatremia, only a fraction of the water deficit is replaced in 24 hours (ie, enough water to lower the serum sodium by 10 mEq/L):

$$\text{Desired water replacement in the first day in mL} = 3 \text{ mL/kg body weight} \times 10$$

$$\text{Hourly infusion rate (mL/hour)} = \text{Desired water replacement in the first day in mL} \div 24 \text{ hours}$$

Replacing both ongoing water losses and the water deficit — The above calculations of hourly infusion rates needed to replace the entire water deficit in acute hypernatremia or a fraction of the water deficit in chronic hypernatremia ignore ongoing water losses. However, patients frequently have ongoing urinary or gastrointestinal water losses and also have obligatory losses from the skin and stool. When ongoing losses are present, an infusion rate based solely upon the water deficit will likely produce a rate of correction substantially less than 10 mEq/L per day. Thus, to achieve the target rate of correction, the fluid repletion regimen must also take into account replacement of ongoing free water losses (algorithm 1). These include:

- Obligatory water output from sweat and stool, which is approximately 30 to 40 mL/hour
- Ongoing urinary and/or gastrointestinal losses that have sodium plus potassium concentrations below the serum sodium concentration

In patients with hypernatremia due to urinary losses, the amount of ongoing water loss that must be replaced **in addition to the existing water deficit** can be calculated using the following equation for the electrolyte-free water clearance, where UV is the urine volume, UNa is the urine sodium concentration, UK is the urine potassium concentration, and SNa is the serum sodium concentration [45]:

$$\text{Urine electrolyte-free water clearance} = UV \times \left(1 - \frac{UNa + UK}{SNa}\right)$$

As an example, the excretion of 100 mL/hour of urine with a sodium plus potassium concentration one-half that of the serum sodium concentration (eg, 84 mEq/L in a patient whose serum sodium is 168 mEq/L) is roughly equivalent to losing 50 mL/hour of electrolyte-free water, regardless of the measured urine osmolality. In addition to replacing the water deficit, the hourly rate of infusion of 5 percent dextrose in water should be increased by 50 mL/hour to account for these urinary losses.

The rationale for using the urine sodium plus potassium concentration to calculate ongoing urinary free water losses, rather than using the urine sodium concentration or the urine osmolality, is discussed below.

In contrast to ongoing urinary losses, measuring ongoing water losses in stool (as in a patient with diarrhea) is usually impractical and not routinely performed. In such patients, the simplest approach is to initiate therapy without accounting for ongoing free water losses, monitor the serum sodium concentration, and increase the rate of fluid administration if it is not falling at the desired rate. (See 'Remeasure the sodium and modify the regimen' above.)

If concurrent electrolyte replacement is necessary — Many patients with hypernatremia have concurrent extracellular fluid volume depletion and/or hypokalemia. Sodium and/or potassium can be added to the intravenous fluid as necessary to simultaneously correct the water and electrolyte deficits. However, the addition of sodium or potassium to the replacement fluid decreases the amount of free water that is being given. An alternative to combining water and sodium (with or without potassium) into one solution is to use two intravenous solutions, one for free water and the other for sodium with or without potassium as an isosmotic solution. This issue is discussed above. (See 'Treating patients who also have hypovolemia or hypokalemia' above.)

DETERMINANTS OF THE PLASMA SODIUM AND DERIVATION OF THE WATER DEFICIT FORMULA

Determinants of the plasma sodium concentration — Understanding the factors that determine the plasma sodium concentration is required to appreciate which fluid losses promote the development of hypernatremia and what the composition of intravenous fluids must be to correct the hypernatremia. As examples:

- How can vomiting or diarrhea, both of which lead to fluid loss that is isosmotic to plasma, induce hypernatremia?

- Why does the addition of potassium salts (usually potassium chloride) to an intravenous solution of 5 percent dextrose in water diminish the degree to which this solution will lower the serum sodium?

Solute concentrations (osmolality) must be equal inside and outside most cells because water moves freely across most cell membranes in response to osmotic forces. Thus, although sodium is largely extracellular and potassium is largely intracellular, the two cations can be thought of as being in a single pool containing sodium, potassium, and water. As such, the sodium concentration in plasma water should equal the amount of sodium plus potassium dissolved in total body water divided by the volume of TBW [20]. This theoretical relationship was validated empirically by measuring the body's content of sodium, potassium, and water using isotopes. A large fraction of the sodium measured isotopically is bound to polyanionic macromolecules (proteoglycans) in bone, cartilage, and connective tissue. Although sodium bound to proteoglycans is not free in solution, it is still exchangeable with the total sodium pool and is therefore measured isotopically. The bound portion of the sodium pool is reflected by an intercept in the equation that relates the plasma sodium concentration to exchangeable sodium plus potassium divided by total body water (TBW). Considering only the ions that are free in solution (and omitting the equation's intercept), the relationship can be described by a simple equation:

$$\text{Plasma [Na]} = (\text{Total body Na} + \text{Total body K}) \div \text{TBW}$$

This relationship applies over a wide range of plasma or serum sodium concentrations (figure 2) [46]. The equation omits glucose and urea, which raise plasma osmolality when their concentrations are markedly elevated:

- Glucose is an **effective** osmole, which, like sodium, alters the distribution of water across cell membranes. The above equation ignores glucose because it is present in a much lower molar concentration than sodium (eg, 5 mmol/L [90 mg/dL] versus 140 mmol/L). In the presence of hyperglycemia, however, the above equation is no longer valid, because glucose osmotically shifts water from cells, which expands the extracellular fluid volume and dilutes the plasma sodium concentration.

- Urea is considered an **ineffective** osmole since it freely equilibrates across the cell membranes. When the plasma concentration of an ineffective osmole like urea changes, the intracellular concentration of the solute changes in parallel, and there is little or no water shift into or out of the cells. Thus, the above equation remains valid regardless of the blood urea concentration.

Application to hypernatremia — Hypernatremia is most often due to unreplaced water loss but can also be caused by the administration of intravenous hypertonic saline or the ingestion of salt. (See "Etiology and evaluation of hypernatremia in adults".)

The importance of sodium plus potassium as a determinant of the plasma sodium concentration has the following applications to the mechanism and treatment of hypernatremia:

- Fluid loss due to diarrhea is isosmotic to plasma, suggesting no direct effect on the plasma sodium concentration. However, the sodium plus potassium concentration in many forms of diarrhea (especially those due to nonsecretory etiologies) is between 40 and 100 mEq/L, with organic solutes, which do not affect the plasma sodium concentration, making up the remaining osmoles [47,48]. Unreplaced losses of this fluid will tend to raise the plasma sodium concentration since water is lost in excess of sodium plus potassium. As an example, this commonly occurs in patients treated with lactulose [49]. By contrast, the sodium plus potassium concentration in secretory diarrheas (eg, cholera, VIPoma) is higher and may be similar to that in the plasma [47,48]. Loss of these fluids will have no direct effect on the plasma sodium concentration. (See "Etiology and evaluation of hypernatremia in adults", section on 'Gastrointestinal losses'.)

- The sodium plus potassium concentration in vomitus and sweat is usually much lower than 140 mEq/L [50-52]. In one study, for example, the sodium plus potassium concentration in gastric fluid averaged approximately 50 to 55 mEq/L [50]. Thus, loss of this fluid will tend to raise the plasma sodium even though the fluid is isosmotic to plasma. Hydrochloric acid accounts for most of the gap between the osmolality of gastric fluid and the contribution of sodium and potassium.

As described above, treatment of hypernatremia consists of correcting the free water deficit. Dextrose in water, which is isosmotic to plasma but electrolyte free, is most effective. In patients without diabetes mellitus, the glucose will usually be metabolized to carbon dioxide and water or stored as glycogen, neither of which contribute to osmolality. Thus, the osmotic effect is similar to the intake of free water.

However, many patients with hypernatremia have a reduced extracellular fluid volume, and some are also potassium depleted (due, for example, to vomiting or diarrhea). The administration of one-quarter or one-half isotonic saline at the same volume will produce a smaller reduction in plasma sodium than dextrose in water. The reduction in plasma sodium will be even less if potassium is added to the saline solution. (See 'Designing the fluid repletion regimen' above.)

Thus, when considering either the etiology or treatment of hypernatremia, it is the **sodium plus potassium** concentration in the fluid lost or the fluid given, **not the osmolality**, that determines the effect on the plasma sodium concentration. In patients who are both hypernatremic and hypokalemic, the addition of potassium to the administered fluid will diminish the amount of electrolyte-free water that is given, thereby limiting the reduction in plasma sodium. (See 'If concurrent electrolyte replacement is necessary' above.)

Derivation of the water deficit formula — The formula for estimating the free water deficit in a hypernatremic patient can be derived from the equation relating the plasma sodium concentration to the body's content of soluble cations (sodium and potassium) and water. (See 'Determinants of the plasma sodium concentration' above.)

$$\text{Serum [Na]} = \text{Total body cations (Na + K)} \div \text{TBW}$$

Thus, the equation for total body cations is:

$$\text{Total body cations} = \text{TBW} \times \text{Serum [Na]}$$

Although sodium is largely limited to the extracellular fluid, the plasma sodium concentration can be used in this equation since the extracellular fluid tonicity is equal to that in the cells in which potassium is the primary cation. (See 'Determinants of the plasma sodium concentration' above.)

If hypernatremia results only from water loss and the body's content of sodium and potassium is unchanged, then:

$$\text{Current total body cations} = \text{Normal total body cations}$$

or, if the normal serum sodium concentration is 140 mEq/L:

$$\text{Current TBW} \times \text{Serum [Na]} = \text{Normal TBW} \times 140$$

If the equation is solved for normal TBW:

$$\text{Normal TBW} = \text{Current TBW} \times \frac{\text{Serum [Na]}}{140}$$

The water deficit can be estimated from:

$$\text{Water deficit} = \text{Normal TBW} - \text{Current TBW}$$

or by substituting from the equation for normal TBW:

$$\text{Water deficit} = \left(\text{Current TBW} \times \frac{\text{Serum [Na]}}{140}\right) - \text{Current TBW}$$

$$= \text{Current TBW} \times \left(\frac{\text{Serum [Na]}}{140} - 1\right)$$

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Fluid and electrolyte disorders in adults".)

SUMMARY AND RECOMMENDATIONS

- **Etiology** – Hypernatremia is most often due to unreplaced water that is lost from the gastrointestinal tract (vomiting or osmotic diarrhea), skin (sweat), or the urine (arginine vasopressin disorders or an osmotic diuresis due to glycosuria in uncontrolled diabetes mellitus or increased urea excretion resulting from catabolism or recovery from kidney failure) (table 1). (See 'Introduction' above.)

  Patients who present with hypernatremia usually have a serious underlying condition that impairs either their ability to respond to thirst or to experience thirst. As a result, such patients usually require hospitalization to correct the hypernatremia. (See 'Approach to therapy' above.)

- **Management** – The therapeutic approach in patients with hypernatremia depends upon the rapidity by which the disorder developed and whether or not it was caused by correction of severe hyperglycemia (algorithm 1) (see 'Initial fluid repletion regimen' above):

  - **Chronic hypernatremia** – Hypernatremia is chronic if it has been present for longer than 48 hours. Nearly all patients with hypernatremia will have chronic hypernatremia,

even those who present with acute changes in mentation who are discovered to have hypernatremia. The initial regimen in such patients is (see 'Patients with chronic hypernatremia' above):

- Five percent dextrose in water, intravenously, at a rate of (approximately 1.35 mL/hour x patient's weight in kg, up to a maximum of 150 mL/hour) or approximately 70 mL/hour in a 50 kg patient and 100 mL/hour in a 70 kg patient.
- The goal of this regimen is to lower the serum sodium by approximately 10 mEq/L in a 24-hour period.
- Patients frequently have ongoing urinary or gastrointestinal water losses and also have obligatory losses from the skin and stool. When ongoing losses are present, an infusion rate based solely upon the water deficit will likely produce a rate of correction substantially less than 10 mEq/L per day. Thus, to achieve the target rate of correction, the fluid repletion regimen must also take into account replacement of ongoing free water losses. (See 'Replacing both ongoing water losses and the water deficit' above.)

- **Acute hypernatremia** – Hypernatremia is acute if it has been present for 48 hours or less. Acute hypernatremia is uncommon, occurring in patients with salt poisoning; in patients with arginine vasopressin disorders who acutely lose the ability to replace their water losses (eg, a patient with an arginine vasopressin disorder who undergoes surgery and does not receive adequate intravenous water); and in patients being treated for severe hyperglycemia, whose water losses from glycosuria are not adequately replaced. The initial regimen in patients with acute salt poisoning or arginine vasopressin disorders is (see 'Patients with acute hypernatremia' above):
  - Five percent dextrose in water, intravenously, initially at a rate of at least 6 mL/kg/hour.
  - The serum sodium and blood glucose should be monitored every two to three hours until the serum sodium is lowered below 145 mEq/L.
  - Once the serum sodium concentration has reached 145 mEq/L, the rate of infusion is reduced to 1 mL/kg per hour and continued until a normal serum sodium (140 mEq/L) is restored.
  - The goal of this regimen is to rapidly lower the serum sodium in the first few hours (by as much as 8 mEq/L per hour) and to restore a normal serum sodium in less

than 24 hours.

- Patients with arginine vasopressin deficiency will also require desmopressin therapy, which is discussed elsewhere. (See "Arginine vasopressin deficiency (central diabetes insipidus): Treatment" and "Arginine vasopressin resistance (nephrogenic diabetes insipidus): Treatment".)

- Hyperglycemia may develop with rapid infusions of 5 percent dextrose; to avoid increased water losses from glycosuria, a slower rate of infusion or a change to 2.5 percent dextrose in water may be required after several hours. (See 'Risk of hyperglycemia' above.)

- **Hypernatremia due to correction of severe hyperglycemia** – As hyperglycemia and hypovolemia are corrected in a patient with diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic state, the serum sodium concentration will rise because of an osmotic shift of water from extracellular fluid into cells and because of loss of electrolyte-free water in the urine as excess glucose is excreted. There is no consensus on how this should be managed; our approach is (see 'Patients with hypernatremia due to correction of hyperglycemia' above):

  - If hypernatremia develops as a consequence of correcting the hyperglycemia in young individuals, our goal is slow correction using the water repletion regimen described above for patients with chronic hypernatremia.

  - If hypernatremia develops as a consequence of correcting the hyperglycemia in older individuals, our goal is rapid correction at the rate described above for patients with acute hypernatremia.

  - Because most of these patients are hypovolemic and hyperglycemic, with ongoing losses of sodium and water due to glycosuria, free water is usually administered as 0.45 percent saline rather than 5 percent dextrose in water; infusion of 0.45 percent saline at 6 to 12 mL/kg per hour will provide the same amount of electrolyte-free water as 3 to 6 mL/kg per hour of 5 percent dextrose in water.

- **Monitoring** – During treatment of acute hypernatremia, repeated laboratory measurements are necessary every one to three hours to ensure that serum sodium concentration is falling at the desired rate, to avoid overshooting the desired endpoint, and to observe for hyperglycemia. During treatment of chronic hypernatremia, the serum sodium should be monitored every four to six hours after the fluid repletion regimen is initiated. If the repeat serum sodium indicates that the target rate of correction has been

attained, then the frequency of measurement can be reduced in most patients to every 12 to 24 hours. However, in patients who have large, ongoing water losses due, for example, to hyperglycemia and glycosuria or arginine vasopressin resistance, the serum sodium should be measured approximately every four hours during the first day of therapy to ensure that the fluid repletion regimen is adequate. The fluid repletion regimen should be modified, if necessary, based upon the sequential measurements of serum sodium. (See 'Remeasure the sodium and modify the regimen' above.)

The above fluid regimens can be altered to accommodate treatment of patients who have concurrent hypovolemia and/or hypokalemia or in those who develop hyperglycemia as a complication of the initial fluid regimen. (See 'Treating patients who also have hypovolemia or hypokalemia' above and 'Risk of hyperglycemia' above and 'If concurrent electrolyte replacement is necessary' above.)

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Topic 2339 Version 36.0

GRAPHICS

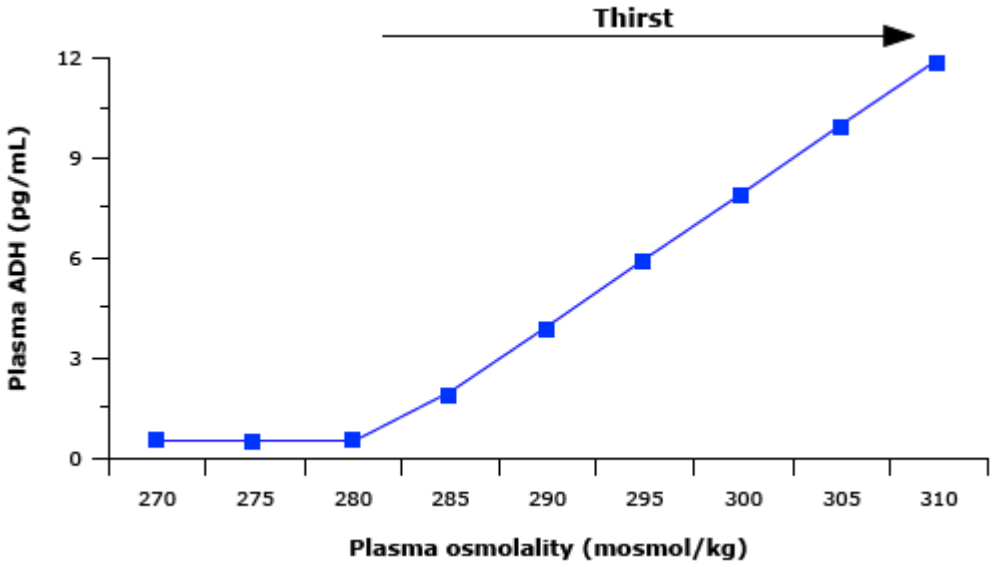
Major causes of hypernatremia

Unreplaced water loss (which requires an impairment in either thirst or access to water)
Insensible and sweat losses
Gastrointestinal losses
Central or nephrogenic diabetes insipidus
Osmotic diuresis
Glucose in uncontrolled diabetes mellitus
Urea in high-protein tube feedings or recovery from azotemia
Mannitol
Hypothalamic lesions impairing thirst or osmoreceptor function
Primary hypodipsia
Reset osmostat in mineralocorticoid excess
Water loss into cells
Severe exercise or seizures
Sodium overload
Intake or administration of hypertonic sodium solutions
ICU-acquired positive solute balance

ICU: intensive care unit.

Graphic 69879 Version 4.0

Osmotic regulation of ADH release and thirst



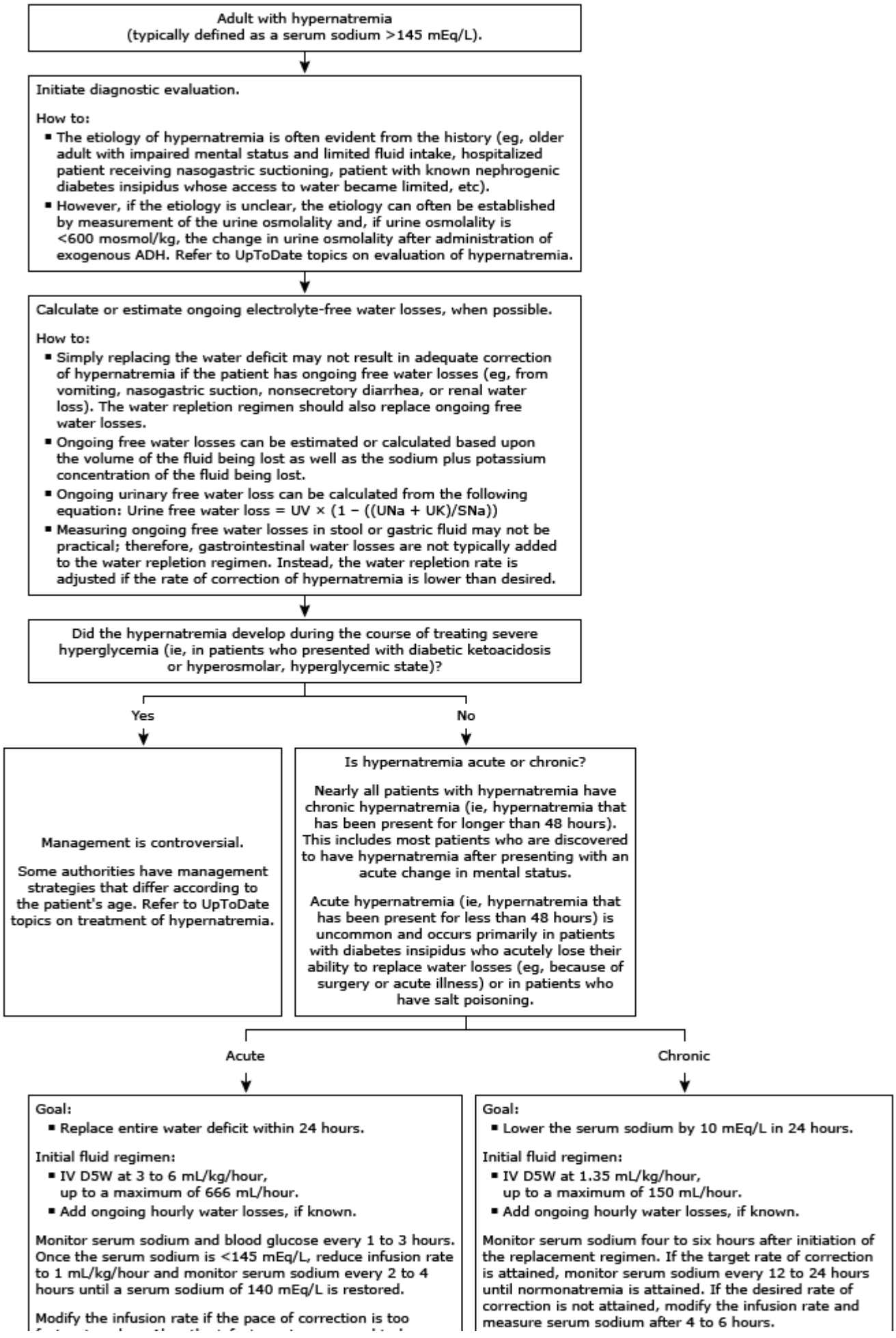
Relation between plasma ADH concentration and plasma osmolality in normal humans in whom the plasma osmolality was changed by varying the state of hydration. The osmotic threshold for thirst is a few mosmol/kg higher than that for ADH.

ADH: antidiuretic hormone.

Data from Robertson GL, Aycinena P, Zerbe RL. Neurogenic disorders of osmoregulation. Am J Med 1982; 72:339.

Graphic 65195 Version 5.0

Hypernatremia: General approach to the management in adults

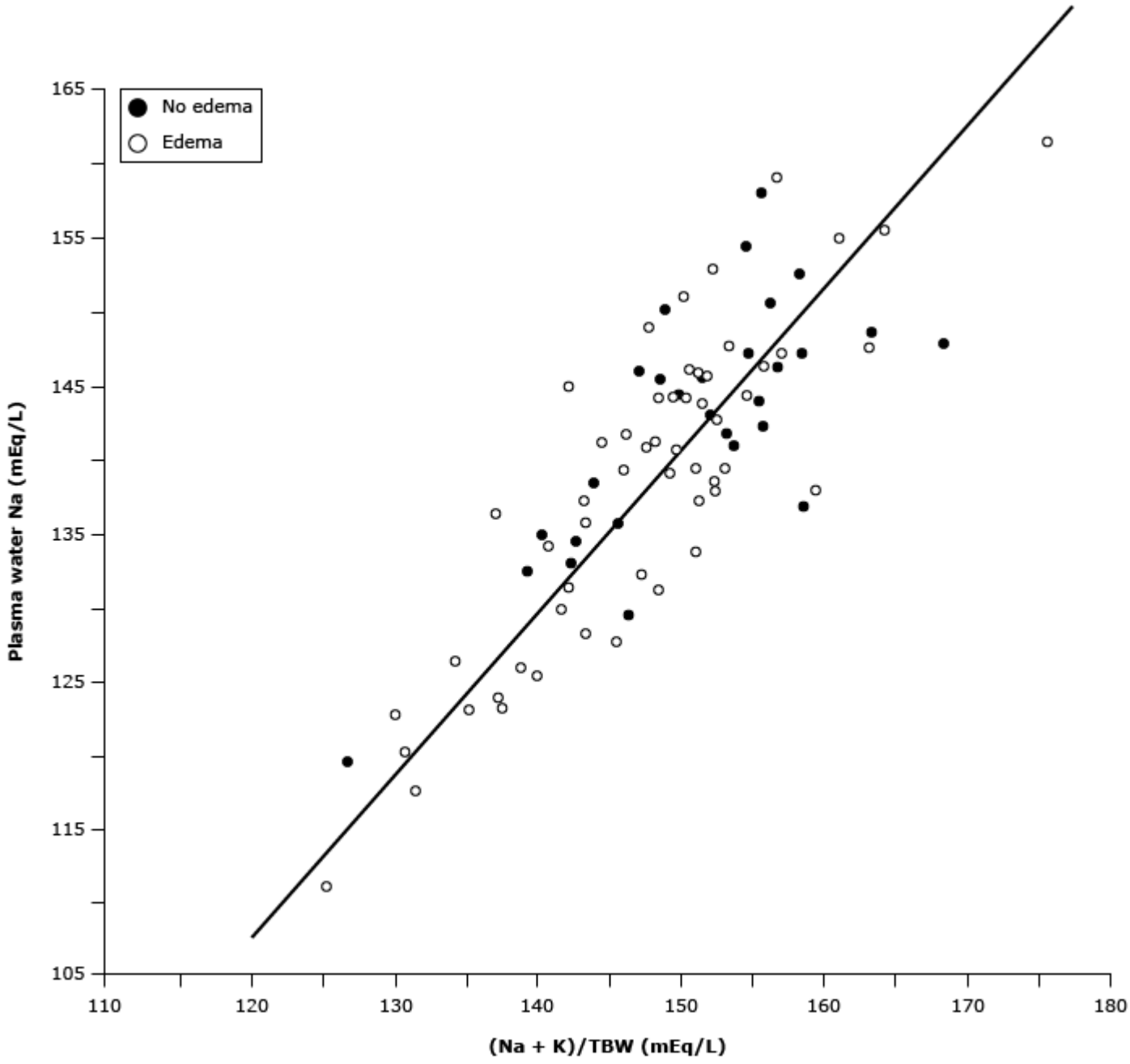

Adult with hypernatremia
(typically defined as a serum sodium >145 mEq/L).
Initiate diagnostic evaluation.
How to:
The etiology of hypernatremia is often evident from the history (eg, older adult with impaired mental status and limited fluid intake, hospitalized patient receiving nasogastric suctioning, patient with known nephrogenic diabetes insipidus whose access to water became limited, etc).
However, if the etiology is unclear, the etiology can often be established by measurement of the urine osmolality and, if urine osmolality is <600 mosmol/kg, the change in urine osmolality after administration of exogenous ADH. Refer to UpToDate topics on evaluation of hypernatremia.
Calculate or estimate ongoing electrolyte-free water losses, when possible.
How to:
Simply replacing the water deficit may not result in adequate correction of hypernatremia if the patient has ongoing free water losses (eg, from vomiting, nasogastric suction, nonsecretory diarrhea, or renal water loss). The water repletion regimen should also replace ongoing free water losses.
Ongoing free water losses can be estimated or calculated based upon the volume of the fluid being lost as well as the sodium plus potassium concentration of the fluid being lost.
Ongoing urinary free water loss can be calculated from the following equation: Urine free water loss = UV × (1 − ((UNa + UK)/SNa))
Measuring ongoing free water losses in stool or gastric fluid may not be practical; therefore, gastrointestinal water losses are not typically added to the water repletion regimen. Instead, the water repletion rate is adjusted if the rate of correction of hypernatremia is lower than desired.
Did the hypernatremia develop during the course of treating severe hyperglycemia (ie, in patients who presented with diabetic ketoacidosis or hyperosmolar, hyperglycemic state)?
Yes
No
Management is controversial.
Some authorities have management strategies that differ according to the patient's age. Refer to UpToDate topics on treatment of hypernatremia.
Is hypernatremia acute or chronic?
Nearly all patients with hypernatremia have chronic hypernatremia (ie, hypernatremia that has been present for longer than 48 hours). This includes most patients who are discovered to have hypernatremia after presenting with an acute change in mental status.
Acute hypernatremia (ie, hypernatremia that has been present for less than 48 hours) is uncommon and occurs primarily in patients with diabetes insipidus who acutely lose their ability to replace water losses (eg, because of surgery or acute illness) or in patients who have salt poisoning.
Acute
Chronic
Goal:
Replace entire water deficit within 24 hours.
Initial fluid regimen:
IV D5W at 3 to 6 mL/kg/hour, up to a maximum of 666 mL/hour.
Add ongoing hourly water losses, if known.
Monitor serum sodium and blood glucose every 1 to 3 hours. Once the serum sodium is <145 mEq/L, reduce infusion rate to 1 mL/kg/hour and monitor serum sodium every 2 to 4 hours until a serum sodium of 140 mEq/L is restored.
Modify the infusion rate if the pace of correction is too
Goal:
Lower the serum sodium by 10 mEq/L in 24 hours.
Initial fluid regimen:
IV D5W at 1.35 mL/kg/hour, up to a maximum of 150 mL/hour.
Add ongoing hourly water losses, if known.
Monitor serum sodium four to six hours after initiation of the replacement regimen. If the target rate of correction is attained, monitor serum sodium every 12 to 24 hours until normonatremia is attained. If the desired rate of correction is not attained, modify the infusion rate and measure serum sodium after 4 to 6 hours.

fast or too slow. Also, the infusion rate may need to be decreased if hyperglycemia develops. Electrolyte replacement (either sodium replacement in a patient with hypovolemia or potassium replacement in a patient with hypokalemia) can be given as a separate infusion or combined with the water replacement (eg, if the appropriate infusion rate of D5W is 100 mL/hour, then one-half isotonic saline can be given at 200 mL/hour).	Electrolyte replacement (either sodium replacement in a patient with hypovolemia or potassium replacement in a patient with hypokalemia) can be given as a separate infusion or combined with the water replacement (eg, if the appropriate infusion rate of D5W is 100 mL/hour, then one-half isotonic saline can be given at 200 mL/hour).

ADH: antidiuretic hormone; UV: urine volume; UNa: urine sodium concentration; UK: urine potassium concentration; SNa: serum sodium concentration; IV: intravenous; D5W: 5% dextrose in water.

Graphic 115660 Version 2.0

Determinants of the plasma sodium concentration



Among both normal subjects and patients with a variety of diseases, there is a very close correlation between the plasma water sodium concentration and the ratio of total body exchangeable solutes (primarily Na salts in the extracellular fluid + K salts in the cells) to the TBW. The exchangeable portion is used since approximately 30% of the body Na and a smaller fraction of the body K are bound in areas such as bone where they are "nonexchangeable" and therefore osmotically inactive.

Na: sodium; K: potassium; TBW: total body water.

Adapted from Edelman I, Leibman J, O'Meara MP, et al. J Clin Invest 1958; 37:1236, by copyright permission of the American Society for Clinical Investigation.

Graphic 71817 Version 4.0