# Chapter 16: Disorders of Serum Sodium Concentration in the Elderly Patient

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## HYPONATREMIA

Disorders of serum sodium concentration are the most common electrolyte abnormalities seen in the geriatric population.[1] Furthermore, the development of serum sodium abnormalities is associated with increased morbidity and mortality in affected patients.[2] Often, however, the severity of the primary process contributing to the development of the abnormal serum sodium is responsible for the unsatisfactory outcome. The most common disorder of serum sodium concentration in the geriatric population is hyponatremia. Factors contributing to the development of hyponatremia in the elderly include age-associated decreases in GFR and free water clearance, as well as sodium losses from decreased activity of the renin-angiotensin-aldosterone system and increased activity of natriuretic hormones. The latter, however, may reflect the early development of fluid retention as may occur with excessive sodium intake from processed foods or subclinical cardiac disease. In addition, studies have suggested increased vasopressin activity in some elderly patients.

Patients in outpatient settings exhibit hyponatremia in about 5% of those tested, with occurrence rates increasing to as high as 20% in hospitalized geriatric patients and 30% in patients seen in intensive care units.[3] The most common cause of hyponatremia in this population involves abnormalities of secretion of the pituitary hormone arginine vasopressin (AVP), also called antidiuretic hormone (ADH).

### Clinical Diagnosis

Successful evaluation of serum sodium abnormalities in the elderly depends on obtaining a careful history especially noting reports of weight loss that can be associated with neoplastic disease, changes in the level of daily activities that can be associated with endocrine abnormalities, and medication history that can produce information implicating drugs that facilitate sodium excretion or stimulate AVP secretion. In addition, a thorough physical examination, including orthostatic BP changes, is essential for the accurate determination of the patient's body fluid status. This determination may be especially difficult in elderly patients who may have chronic changes in skin turgor that are more associated with aging than they are with the state of hydration.

### Laboratory Diagnosis and Therapy

When the history and physical are completed, assessment of laboratory data are essential (Figure 1).

First, a plasma osmolality must be obtained to ensure that one is dealing with hypo-osmolar hyponatremia. Normo-osmolar hyponatremia as can occur with certain compounds such as mannitol, which can also cause hyperosmolality in normonatremic patients, and hyperosmolar hyponatremia caused by hyperglycemia must be ruled out. Furthermore, other serum studies are important to decide whether levels of substances such as blood urea nitrogen and uric acid are elevated and thereby consistent with volume depletion or whether these levels seem to be diluted as would be seen with water excess occurring in the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Finally, urine sodium concentration and urine osmolality must be measured to ascertain the endocrine and renal responses to the hypo-osmolar state.

In dehydrated patients, levels of urine sodium can be considered low (*i.e.*, sodium conservation) when the spot urine sodium concentration is $<20$ mEq/L; in older patients, where sodium conservation may be limited,[4] levels up to 30 mEq/L may also

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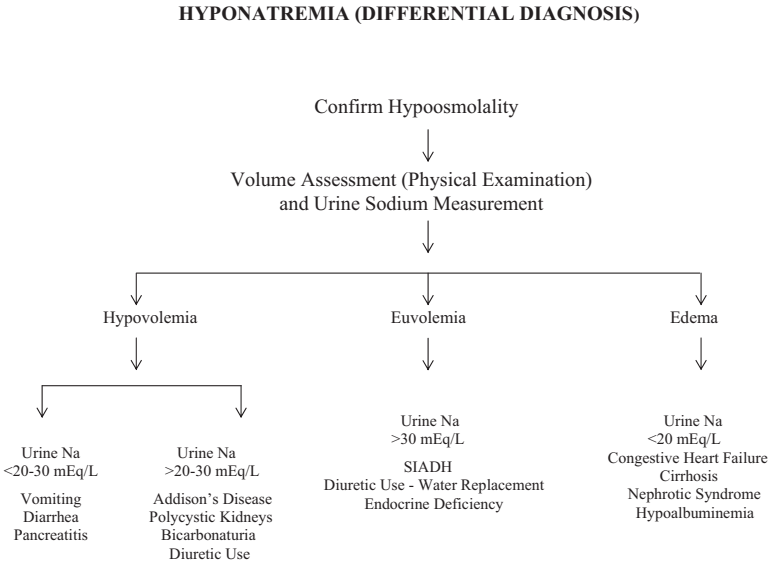


**Figure 1.** Hyponatremia (differential diagnosis).

be considered indicative of some degree of conservation of sodium. These urine sodium levels will often be associated with urine osmolality values at least 1.5 times that of the plasma, suggesting attempts at water conservation in response to fluid deficits. Such patients generally respond to the replacement of intravascular volume with normal saline. Patients who appear dehydrated but who have elevated urine sodium levels (>30 mEq/L) often have urine osmolalities closer to that of the plasma levels and should be considered to have renal salt wasting in the face of intravascular volume contraction. They should also be treated with normal saline while attempts to diagnose the underlying abnormality are made. Various formulas such as the Adrogué-Madias formula (Figure 2) have been used in an attempt to predict the increase in serum sodium that can occur when various concentrations of sodium replacement therapy are employed.[5] If more or less than 1 L of replacement fluid is used, the change in serum sodium will vary directly in proportion to the amount of fluid administered.

When patients appear to be fluid overloaded or edematous, they may have one of several edema-forming states, including congestive heart failure, nephrotic syndrome, and cirrhosis. The poor renal perfusion associated with any of these states is generally associated with urine sodium concentrations in the lower ranges (<20 to 30 mEq/L) and a tendency to urine osmolalities closer to that seen in the plasma. These disorders are generally treated by addressing the primary underlying abnormality and using diuretic regimens.

**ADROGUÉ-MADIAS FORMULA**

$$\text{Change in serum sodium concentration with 1L of infusate} = \frac{\text{Infusate sodium concentration} - \text{Patient serum concentration}}{\text{Total body water} + 1\text{L}}$$

**Figure 2.** The Adrogué-Madias Formula for the prediction of the change in serum sodium that can occur following intravenous sodium replacement therapy.

In elderly hyponatremic patients who appear euvolemic and have elevated urine sodium concentrations (>20 or 30 mEq/L) and elevated urine osmolalities suggesting inappropriate water retention, a diagnosis of SIADH is often made.[6] Here it is important to rule out endocrine abnormalities such as hypoadrenalism and hypothyroidism. In addition, a careful search for drugs that stimulate AVP or facilitate the effects of AVP in the kidney should be undertaken. If these considerations are eliminated from diagnostic possibilities, the patient should be evaluated for other causes of SIADH. Table 1 lists some of the commonly associated central nervous system disorders, tumors, and drugs associated with inappropriate AVP secretion. Certain drug therapies such as SSRIs may pose a special risk for the development of hyponatremia in the elderly, especially those who are older and smaller in body size.[7]

**Table 1.** Common causes of SIADH

| |
|---|
| Central nervous system disease |
| Trauma |
| Stroke |
| Infection |
| Tumor |
| Intracranial bleeding |
| Neoplasms |
| Lung |
| Pancreas |
| Prostate |
| Throat |
| Lymphoma |
| Drugs |
| SSRIs |
| Carbamazepine |
| Opiates |
| Cyclophosphamide |
| Mirtazapine |

If primary causes of the syndrome SIADH cannot be immediately eliminated, patients should be treated with therapies that can reverse the hyponatremia.[8] In patients with a history with confounding factors such as the possible prior use of diuretic agents, a trial of normal saline administration may be used. In patients with severe hyponatremia, *i.e.,* serum sodium concentrations <110 mEq/L, it may be appropriate to use multiple 100-ml intravenous aliquots of hypertonic (3%) saline to improve the serum sodium levels to avoid more serious complications of hyponatremia such as seizures or profound coma. In patients with serum sodium concentrations in the 111- to 120-mEq/L range, therapies may include lesser amounts of hypertonic saline, and greater reliance on fluid restriction and agents that interfere with AVP effect, such as demeclocycline and the new AVP receptor antagonists. With lesser degrees of hyponatremia, *i.e.,* serum sodium 121 to 129 mEq/L, fluid restriction, demeclocycline, and AVP receptor antagonists can be used.

Other approaches to hyponatremia include saline infusions and furosemide being used to replace existing hypotonic intravascular fluid with fluid of a higher sodium concentration. In hyponatremic patients with central nervous system disease, cerebral salt wasting should be ruled out. This disorder is associated with natriuretic peptide responses as well as AVP effect, sodium loss, and signs of volume deficit and should be treated with volume replacement. These hyponatremic patients often exhibit unusually high urine sodium concentrations.

### New Therapies

Over the last several years, a new class of drugs has been studied that specifically block the effect of AVP on the collecting tubule. One such drug that has been approved by the FDA for clinical use, conivaptan, belongs to the group of drugs called vasopressin receptor antagonists (vaptans), because they block the binding of AVP to the AVP V2 receptor on the renal tubule.[9] Conivaptan has been approved for use in hospitalized patients in an intravenous preparation, and it has been approved for therapy of both euvolemic hyponatremia (*e.g.,* SIADH) and hypervolemic hyponatremia (*e.g.,* heart failure). Conivaptan is rapidly acting and can be given as an intravenous bolus, which can be followed by 1 d to as many as 4 d of intravenous infusion. Frequent monitoring of the results of intravenous therapy should be done during the phase of active correction, with serum sodium measurements every 4 to 6 h during the first day, perhaps two to three times a day during the second day, and less frequently during the subsequent 2 d. With lesser degrees of hyponatremia, it is still unclear what the specific indications for therapy are, and what the benefits of changes in the level of hyponatremia may be, but it has been suggested that central nervous system function and gait stability may be adversely affected by even mild to moderate degrees of chronic hyponatremia.

### Rate of Correction

Acute hyponatremia should be treated more aggressively, whereas chronic hyponatremia should be addressed in a more conservative manner. Current recommendations are that serum sodium should not increase >12 mEq/L over a 24-h period and no more than 18 mEq/L over a 48-h period.

### Complex Clinical Syndromes

Finally, complicated situations have been described in which patients are hyponatremic and seem to have excess AVP activity as well as sodium depletion syndromes.[10] On attempts at correction with saline, including hypertonic saline, patients may exhibit a response in which volume correction shuts off AVP secretion and causes a profound water diuresis with rapid increases in the serum sodium concentration and a tendency toward too rapid correction. When this occurs, reversal therapy may be required with the administration of free water and/or AVP (usually as the AVP agonist desmopressin). In addition, patients on drugs that stimulate AVP secretion may have the effects of these drugs wear off during the period that therapies are undertaken, also resulting in unexpectedly rapid correction.

### Conclusion

Disorders of serum sodium, especially hyponatremia, are common in the geriatric population and often are related to excess vasopressin secretion. A trial of saline administration may be considered before standard approaches to therapy that now include vasopressin blocking drugs. Complex clinical syndromes often occur and may be related in part to drugs associated with inappropriate vasopressin secretion.

## HYPERNATREMIA

Hypernatremia is a common occurrence in elderly patients.[2] The issues relating to the development of an increased serum sodium can involve deficient free water intake, abnormal regulation of AVP secretion, decreased renal responsiveness to AVP secretion, and finally free water losses that are associated with inadequate replacement.

### Clinical Diagnosis

The evaluation of elderly patients with hypernatremia starts with a careful history. Details in the history that are important involve decreases in weight, decreases in intake either because of lack of interest or availability, and history from caretakers about types of fluids and types of nutritional additives used and/or laxative use. Physical examination would involve the assessment of volume status, with particular attention to the degree of BP decrease in cases where severe hypernatremia is associated with significant hypotension.

### Laboratory Diagnosis and Therapy

Hypernatremia can be defined as a serum sodium concentration greater than the normal level, which is usually considered up to 145 mEq/L. In general, patients with hypernatremic states can be segregated by their measured urine osmolality.

The ratio of urine osmolality to plasma osmolality is useful in defining AVP responses. Also, as in the hyponatremic patient, assessment of spot urine sodium concentration will be helpful to discern the type of hypernatremic state that has developed (Figure 3).

Variable but low urine osmolalities and variable urine sodium concentrations can be seen with central diabetes insipidus depending on the extent of the lesion, sodium intake, and intravascular volume status. Central diabetes insipidus may be associated with varying degrees of AVP deficiency, which can be the result of a variety of intracerebral lesions (Table 2).

Water deprivation tests with clinical follow-up and AVP administration can be used to help diagnose central *versus* nephrogenic diabetes insipidus. Measurement of plasma AVP levels can also be useful to differentiate central from nephrogenic diabetes insipidus.[1] Patients with more isotonic urine and urine sodium concentrations that tend to be elevated, >20 to 30 mEq/L, can have disorders associated with osmotic diuresis, diuretic therapy, and other instances of renal dysfunction where endocrine and renal responses cannot offset fluid and sodium losses, which are mandated by osmolar excretion or renal disease. Urine osmolalities that are clearly higher than measured plasma osmolality and urine sodium levels <20 to 30 mEq/L generally are associated with endocrine and renal responses to extreme fluid losses. This can be seen with decreased thirst or water availability or gastrointestinal losses such as vomiting and diarrhea and lack of water replacement particularly in warm environments as may be seen in a nursing home situation. Hypernatremia in the elderly is commonly associated with fluid loss, limitation in urinary concentrating ability, intravascular volume depletion, and inadequate replacement caused by decreased thirst, limited mentation, limited fluid availability, and/or inadequate fluid prescription.

Central nervous system disorders associated with lack of AVP secretion are treated with intravenous or oral dilute fluid and, as needed, AVP replacement therapy. Patients with nephrogenic disorders should be initially approached therapeutically by avoiding, if present, the agent or agents associated with resistance to the effects of AVP. Additional therapy for nephrogenic diabetes insipidus can include decreases in the intravascular volume with a mildly restricted sodium diet and thiazide diuretics.

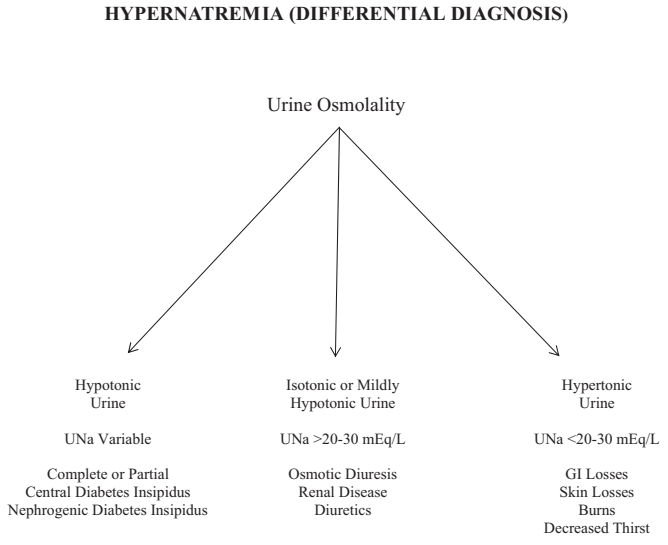


**Figure 3.** Hypernatremia (differential diagnosis).

**Table 2.** Cerebral lesions that can affect hypothalamic function

| |
|---|
| Trauma |
| Infection |
| Tumors |
| Hystiocytosis |
| Vascular abnormalities |

## Rate of Correction

In general, water deficits are calculated using a standard formula (Figure 4), and physicians are generally advised to correct half of the deficit over the first 24 h.

Patients in shock must be treated aggressively with rapid volume replacement with normal saline. Once the patient shows a normal BP, hypotonic replacement can be performed at a more moderate rate. This replacement may consist of hypotonic saline, dextrose, and water with careful monitoring of serum glucose or oral water administration. Rare cerebral lesions that damage or eliminate osmoreception can result in unusual clinical syndromes in which volume expansion results in significant water diuresis and hypernatremia.[11] As with hyponatremic states, water deficits are more rapidly replaced in more acute conditions and more slowly replaced when the patients are relatively asymptomatic and the condition has existed for some time. Too rapid dilute replacement therapy can be associated with the development of cerebral edema.[12] Central nervous system function should be monitored carefully.

## Conclusion

Physiologic changes associated with aging and lack of mobility may facilitate the development of hypernatremia in elderly patients. Careful history and laboratory evaluation are essential to determine the correct diagnosis and can include measurement of plasma vasopressin levels. Calculation of water deficits will assist in developing a sound therapeutic plan and avoid improper rates of correction.

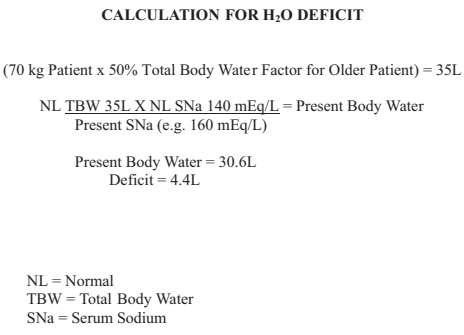


**Figure 4.** The calculation for $H_2O$ deficit in an elderly hypernatremic patient is outlined.

## TAKE HOME POINTS

- Differential diagnosis of hyponatremia should be performed with confirmation of hypoosmolality by means of measurement of plasma osmolality
- After volume assessment is attempted, spot urine sodium levels should then be evaluated to separate salt conserving and salt losing states
- Urine osmolality will further aid in assessing whether appropriate responses to the plasma dilution are occurring
- Therapy should proceed in a manner formulated to avoid too rapid or overcorrection
- Hypernatremia may be preventable in controlled situations such as a nursing home by avoiding warm environments and excess protein in the diet, and provision of adequate hydration
- Normal saline may be required as initial therapy for hypotensive, hypovolemic, hypernatremia
- Standard measurements including plasma osmolality, urine osmolality, and spot urine sodium concentration will help in the differential diagnosis
- Too rapid correction or overcorrection should be avoided

## DISCLOSURES

None.

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## REVIEW QUESTIONS: DISORDERS OF SERUM SODIUM CONCENTRATION IN THE ELDERLY PATIENT

1. Hyponatremia is common in elderly patients. Which of the factors listed is not a common cause for its development?
   a. Central nervous system disease
   b. Neoplasm
   c. Living in warm climates
   d. Antidepressant drug therapy
   e. Endocrine disorders

2. Diagnostic evaluation of hyponatremic patients include measurement of:
   a. Serum osmolality
   b. Urine sodium level
   c. Urine osmolality
   d. Serum BUN and uric acid level
   e. All of the above

3. SIADH can result from the use of SSRIs. What would be appropriate therapy in such a patient?
   a. Discontinue the drug
   b. Water restriction
   c. Use a diuretic which works on the Loop of Henle
   d. Use a vasopressin blocking drug
   e. All of the above

4. A patient has a serum sodium level of 116 mEq/L. Hypertonic saline infusion is started. In 6 h, the serum sodium level is 126 mEq/L. Which treatment would be least appropriate?
   a. Change to normal saline infusion
   b. Stop the hypertonic saline infusion
   c. Administer a quantity of free water and consider vasopressin therapy
   d. Increase the frequency of serum sodium measurements
   e. Closely observe the patient for CNS changes

5. Which factor would not contribute to the development of hypernatremia in elderly patients?
   a. Sodium intake
   b. Immobility
   c. Careful control of environmental temperature
   d. Drug therapy
   e. Decreased alertness

6. What fluid or fluids would be first choice for a patient with hypernatremia and hypotension?
   a. 1/2 normal saline
   b. Dextrose and water alternating with normal saline
   c. Normal saline
   d. Dextrose and water alternating with 1/2 normal saline
   e. Dextrose and water

7. A patient with hypernatremia has an elevated plasma vasopressin level, hypertonic urine, and urine sodium level $<20$ mEq/L. The most likely diagnosis would be:
   a. Fluid losses via the skin or GI tract
   b. Complete central diabetes insipidus
   c. Osmotic diuresis with increased dietary protein
   d. Excess diuretic use
   e. Abrupt discontinuation of SSRI use