Hyponatremia in the Psychiatric Patient:

Patients receiving psychiatric care frequently develop medical problems, with electrolyte abnormalities being especially common. Hyponatremia is frequently encountered, and if prompt diagnosis and treatment are not provided, irreversible neurological deficits and even death can result. It is therefore necessary for the psychiatrist, as well as internists and family practitioners caring for psychiatric patients, to be familiar with the presentation, diagnosis, and management of hyponatremia. This article provides a comprehensive overview of the pathogenesis, predisposing factors, diagnostic evaluation, and management of hyponatremia. It includes special emphasis on the syndrome of inappropriate antidiuretic hormone (SIADH), a disorder associated

---

Dr. Buff is chief, Division of Geriatrics, and assistant program director, Internal Medicine Residency Training Program, St. John’s Episcopal Hospital, Far Rockaway, and assistant professor of medicine, State University of New York Health Science Center at Brooklyn, New York. Dr. Markowitz is chief, Division of Endocrinology, and chairman, Department of Medicine, St. John’s Episcopal Hospital, Far Rockaway, and clinical associate professor of medicine, State University of New York Health Science Center at Brooklyn, New York.

Address reprint requests to Daniel D. Buff, MD, Department of Medicine, St. John’s Episcopal Hospital, 327 Beach 19th Street, Far Rockaway, NY 11691.

The authors have no industry relationships to disclose.
A Review of Diagnostic and Management Strategies

with psychotropic medications to which psychiatric patients may be particularly susceptible.

INCIDENCE IN PSYCHIATRIC PATIENTS

Before examining the incidence of SIADH in patients receiving psychotropic medications, three points should be noted. First, hyponatremia in general, and idiopathic SIADH in particular, are not uncommon entities in many patient populations. For example, in two studies of patients admitted to acute care hospital wards, 5% to 7% had significant hyponatremia, with SIADH accounting for many of the cases.1,2

Second, patients requiring psychiatric care frequently have comorbidities that can cause hyponatremia and SIADH. Miller et al.3 demonstrated that in elderly nursing home patients — a group known to have a high rate of psychotropic use — more than half had at least one episode of hyponatremia during a 12-month period. Although some of these cases were due to idiopathic or psychotropic-related SIADH, most were linked to the high incidence of comorbidities, such as cardiac and neurological disorders, that predisposed these patients to hyponatremia.3

Third, there is increasing evidence that the normal aging process may in and of itself predispose the elderly to SIADH. With increasing age, there are changes in antidiuretic hormone (ADH) secretion, renal and neurological function, and atrial natriuretic factor levels that impair the ability of the elderly to regulate fluid and electrolyte levels.4,5 In an early study of blood pressure in the elderly, 7% of a healthy, community-dwelling population were found to have hyponatremia.6 Anpalahan 7 found 13% of elderly patients in a rehabilitation hospital had SIADH; approximately half of the cases were idiopathic. Similarly Miller et al.4 reported that in an ambulatory geriatric clinic, 7% of patients had SIADH; idiopathic cases accounted for 26% of the cases.

These data indicate that hyponatremia and SIADH are not uncommon, and that the elderly, who may have confounding comorbidities and represent a majority of the patients receiving psychotropic medications,8 are predisposed to SIADH. Given these facts, it is not unexpected that SIADH would be linked to psychiatric medication use. However, whether psychotropic medications cause hyponatremia and SIADH, or are merely innocent bystanders is uncertain.

From a physiological standpoint, psychotropic medications have been postulated to cause SIADH by increasing ADH secretion from the posterior pituitary and potentiating ADH effect on the kidney.9 Psychotropics can alter dopamine, serotonin, and cholinergic activity, all of which can affect ADH secretion.10,11 Carbamazepine in particular has been associated with increased ADH levels, as well as altered renal physiology.12-14

Psychiatric patients also may experience hyponatremia due to disorders other than SIADH. For example, the anticholinergic effects of psychotropic medications can induce dry mouth and chronic thirst, possibly promoting excess water intake.15

In addition to these pharmacologic data, clinical data also support the relationship between psychiatric medications and SIADH. Madhusoodanan et al.16 reviewed the literature and found 172 case reports linking psychotropic medications to hyponatremia.16 Liu et al.17 found 736 cases of hyponatremia and SIADH associated with selective serotonin reuptake inhibitor (SSRI) use, most from an unpublished database.

While single case reports and small case series can be misleading, several do describe the recurrence of hyponatremia with medication rechallenge.16-18 Additionally, some large studies have reported an association between psychotropic medications and hyponatremia.19-22 For example, in a study of 32 elderly patients treated with an SSRI, 25% developed hyponatremia, of which half were due to SIADH.23

It would appear, then, that patients requiring psychiatric care are predisposed to hyponatremia, either due to age alone or associated comorbidities. Additionally, convincing data indicate psychotropic medications can induce hyponatremia and SIADH. Combined, these factors point to a significant risk of hyponatremia in patients taking psychiatric medications.
NORMAL WATER AND SODIUM BALANCE

The distribution of water between the intracellular and extracellular spaces is determined by osmotic forces. Water will flow freely across most membranes in order to maintain an osmotic balance. As sodium is the predominant extracellular solute, it is the major determinant of serum osmolality.9

Under usual circumstances, serum osmolality is tightly maintained at 275 to 290 mOsm/kg by a balance between free water intake and loss. When this balance is lost and excretion outpaces intake, the effective plasma volume decreases and serum osmolality rises. Hyponatremia, hypotension, and hyperosmolality stimulate the thirst mechanism via the hypothalamus in order to increase free water intake. Also stimulated is the release of ADH from the posterior pituitary, which increases reabsorption of water from the kidney and thereby decreases free water loss in the urine.9,24-25

ETIOLOGY OF HYponATREMIA

Hyponatremia has been variably defined as a serum sodium level less than 130 to 137 mEq/L, with a level less than 130 most consistent.9,25-27 While reviewing the different causes of hyponatremia can be a daunting task, classifying etiologies by the associated serum osmolality can be helpful.

Hyponatremia rarely occurs in the setting of increased osmolality, when nonelectrolyte solutes accumulate in the extracellular space causing water to flow in from the intracellular compartment. These solutes cause the serum osmolality to increase but the serum sodium concentration to decrease.5

The most common cause of hyponatremia is the elevated glucose levels in diabetes mellitus. Clinical data have shown that for every increase of 100 mg/dL of serum glucose level above normal, there is a concomitant decrease of 1.7 mEq/L in serum sodium level. Hypertonic mannitol as used in the treatment of intracerebral herniation is a less common cause of hyperosmolar hyponatremia.27

Hyponatremia associated with normal serum osmolality is a laboratory artifact of earlier generation equipment that measured serum sodium level by flame photometry. This form of hyponatremia, termed pseudohyponatremia, occurs when flame photometry equipment is used to measure serum sodium level in the setting of severe hypertriglyceridemia or paraproteinemia. Fortunately, pseudohyponatremia is becoming a phenomenon of the past, as newer generation laboratory equipment can directly measure serum sodium level with ion-specific electrodes.28-30

The third and by far most clinically important form of hyponatremia is hyposmolar hyponatremia. This form occurs when either there is an excessive intake of free water or when there is impaired free water excretion.27 Because the kidneys are so efficient in controlling the extracellular fluid volume, hyponatremia due to excess water intake is uncommon. For example, a 70-kg patient would have to drink more than 14 L of free water a day in order to overwhelm renal capacity to respond.21 Although a formidable task, psychiatric patients can exceed this water intake when given free access to water. This results in psychogenic polydipsia, a disorder that represents the most common cause of hypo-osmolar hyponatremia due to increased water intake.9,26-27

Much more frequently encountered as a cause of hypo-osmolar hyponatremia are disorders due to impaired renal excretion of free water. This group of disorders constitutes the real diagnostic challenge of hyponatremia and will be discussed in greater depth in the following section.

HYPO-OSMOLAR HYponATREMIA WITH IMPAIRED RENAL WATER EXCRETION

Just as all forms of hyponatremia can be placed into three groups based on serum osmolality, the hypo-osmolar hyponatremia due to impaired renal excretion of free water also can be placed in three groups, in this case based on extracellular fluid volume. This volume is accurately assessed by a simple physical examination that focuses on nucius membrane moisture status, skin turgor, and the presence of dependent edema.9

The first group includes patients with hypo-osmolar hyponatremia and decreased extracellular volume who have lost both sodium and water, but the sodium losses exceed the water losses. Such conditions include diuretic excess; salt wasting nephropathy; primary adrenocortical deficiency; large volume diarrhea, vomiting, and perspiration; and fluid sequestration syndromes.9,28,29,27

The second group encompasses hypo-osmolar hyponatremia associated with an increased extracellular volume status. These constitute the so-called sodium avid conditions, such as congestive heart failure, cirrhosis, nephrotic syndrome, hypoalbuminemia, renal failure, and preg-
nancy. Although these disorders are associated with excess total body sodium, the total body water excess is even more impressive, resulting in a decreased serum concentration of sodium.

The final group comprises hypoosmolar hyponatremia associated with a normal extracellular volume status. More accurately, these disorders have a mild increase in extracellular volume, but not enough to result in physical signs of fluid overload. Causes of euvolemic hypoosmolar hyponatremia include hypothryroidism, secondary adrenocortical deficiency, thiazide use, and SIADH.

Also in this third group is a condition termed reset osmostat syndrome. In this syndrome, the osmotic threshold of the hypothalamus is reset downward so that a serum sodium in the range of 125 to 130 mEq/L is maintained. Generally a relatively benign condition, reset osmostat is most often seen in the setting of acute illness, although apparently healthy patients also may present with this. Because SIADH is the primary focus of psychotropic-related hyponatremia, it will be discussed in more detail below.

SYNDROME OF INAPPROPRIATE ANTIURETIC HORMONE

Of the forms of euvolemic hypoosmolar hyponatremia, SIADH has received the most attention and is associated with a long list of conditions. Most often, SIADH results from neoplasms, central nervous system disorders, pulmonary disorders, and medications. Many cases are considered idiopathic, as no clear etiology has been identified. Idiopathic SIADH may comprise as much as 50% to 60% of patients with SIADH, particularly when this disorder occurs in the elderly.

Syndrome of inappropriate antidiuretic hormone associated with cancer results from unregulated ectopic production of antidiuretic hormone by the tumor cells. Cancers most often associated with SIADH are those of the lung, gastrointestinal tract, and genitourinary tract.

Other forms of SIADH alter the normal osmoregulation of ADH release, although the mechanism of this alteration has not been clarified. Pulmonary infections, such as bacterial, viral, and fungal pneumonia and tuberculosis can result in SIADH, as can cystic fibrosis, asthma, pneumothorax, and positive-pressure ventilation. Syndrome of inappropriate antidiuretic hormone associated with central nervous system disorders usually involves strokes, both ischemic and hemorrhagic. Other associated CNS conditions include multiple sclerosis, amyotrophic lateral sclerosis, Guillain-Barré syndrome, meningitis, and encephalitis. Psychosis also can result in SIADH.

A variety of medications have been associated with SIADH. Elevated ADH levels can result from administration of exogenous vasopressin, DDAVP (desmopressin acetate), or oxytocin. Reliable data for an association with vincristine, cyclophosphamide, and chlorproamide are available. Psychotropic medications have been associated extensively with SIADH, including carbamazepine, phenothiazines, tricyclic antidepressants, monoamine oxidase inhibitors, mood stabilizers, and SSRIs. Details regarding these associations with psychotropic medications are provided in the other articles in this issue.

LABORATORY DIAGNOSIS OF HYPOONATREMIA

The laboratory diagnosis of hyponatremia can be simplified into five steps based on the discussion above regarding etiology. These steps are summarized in the Sidebar on page 324.

Step 1

The presence of hyponatremia is confirmed on a laboratory result by repeating the serum sodium test. Once confirmed, a careful history and physical examination is required. The purpose of the history and physical examination is to assess for symptoms and signs of hyponatremia, and to search for possible causes.

Step 2

Serum osmolality is either calculated or measured directly. Measurement usually takes considerable time, while the calculation can be made from basic laboratory data. The formula for calculation of serum osmolality is serum osmolality = (2 x serum sodium) + (serum glucose/18) + (BUN/2.8).

The normal range is 275 to 290 mOsm/kg.

Increased serum osmolality associated with hyponatremia indicates the presence of a nonelectrolyte solute, specifically hyperglycemia or mannitol. Normal serum osmolality indicates pseudohyponatremia, mandating the measurement of serum triglycerides and proteins. If a decreased serum osmolality is documented, proceed to Step 3, the measurement of urine osmolality.

Step 3

Measuring urine osmolality in the setting of hyponatremia allows one to determine whether the problem represents excessive water intake or impaired renal water excretion. When serum osmolality drops, the normal response is suppression of ADH release and production of a maximally dilute urine. This is exactly what occurs in psychogenic polydipsia, and the resulting urine osmolality is very low, usually less than 100 mOsm/kg. On the other hand, when the problem is impaired renal water handling, the normal response to hypo-osmolality is absent, and the urine osmolality is inappropriately equal to or higher than 100 mOsm/kg. This result indicates progression to Step 4.

Step 4

This step involves placing the patient into one of the three categories based on
The Stepwise Diagnostic Evaluation of Hyponatremia

Step 1
Confirm presence of hyponatremia and perform detailed history and physical

Step 2
Measure or calculate serum osmolality (normal 275 to 290 mEq/L)
- If high, suspect solute excess such as hyperglycemia
- If normal, suspect pseudohyponatremia and measure triglycerides and serum proteins
- If low, proceed to next step

Step 3
Measure urine osmolality
- If <100 mOsm/kg, suspect psychogenic polydipsia
- If ≥100 mOsm/kg, proceed to next step

Step 4
Assess extracellular fluid status*
- If low, suspect overdiuresis, salt wasting, third spacing, or fluid loss
- If high, suspect congestive heart failure, cirrhosis, or renal failure
- If normal, proceed to next step

Step 5
Perform the following:
- Obtain history to assess for thiazide use
- Perform thyroid function tests to assess for hypothyroidism
- Measure serum cortisol level to assess for adrenal insufficiency
- If the above are negative, suspect syndrome of inappropriate antidiuretic hormone (SIADH)

*Measuring urine sodium can clarify the diagnosis within each of the three volume status groups in Step 4; see text for details

volume status. This is best done via the physical examination, with confirmatory laboratory data. Increased volume status indicates congestive heart failure, cirrhosis, or renal failure. Decreased volume status indicates overdiuresis, salt wasting, third spacing, and fluid losses. Normal volume status indicates thiazide diuretic effect, hypothyroidism, adrenal insufficiency, and SIADH.

Measurement of the urine sodium as part of Step 4 can make the diagnosis more clear within each of the three volume-based groupings. Within the hypervolemic group, most diagnoses carry a low urine sodium level (less than 10 mEq/L), with the exception of renal failure; both acute and chronic renal failure usually is associated with a urine sodium level greater than 20 mEq/L. Of course, measurements of blood urea nitrogen and serum creatinine levels should clarify this diagnosis.

Within the hypovolemic group, most diagnoses also carry a urine sodium level less than 10 mEq/L, with the exception of those conditions that involve renal sodium losses (overdiuresis, salt-wasting nephropathy, and hypoaldosteronism). Urine sodium levels are not as helpful in the euvolemic group, as values for most diagnoses range 20 to 30 mEq/L or higher. Once it has been determined the patient has euvolemic hypo-osmolar hyponatremia, proceed to Step 5.

Step 5
The correct diagnosis is elucidated by a history of a thiazide diuretic use, measurement of thyroid function tests, and measurement of cortisol levels. Exclusion of problems in these three areas leaves SIADH, which essentially is a diagnosis of exclusion within the euvolemic category.

CLINICAL PRESENTATION

Whether hyponatremia leads to symptoms is dependent on the degree of hyponatremia and the rate at which it develops. Generally, patients do not develop signs or symptoms unless the serum sodium level falls below 125 mEq/L. However, even lower serum sodium levels may be well tolerated if the hyponatremia develops slowly over days or weeks, thereby allowing adaptive mechanisms to take effect. Alternatively, relatively mild hyponatremia can be quite symptomatic if it develops rapidly over the course of a few hours.2,27,31

Symptoms of hyponatremia are primarily related to the central nervous system. As serum osmolality and sodium level drop, water enters the brain, resulting in cerebral edema. If this process is gradual, adaptive mechanisms can emerge that result in solute efflux from the brain. Water will then follow the solute and brain swelling declines.27 If, however, the process is rapid or overwhelms the adaptive process, cerebral edema progresses and intracranial hypertension develops. This leads to the symptoms seen with hyponatremia.31

Initially, symptoms include anorexia, headache, nausea, malaise, and apathy. Without treatment or adaptation, symptoms will worsen, leading to lethargy, disorientation, and muscle cramps. More serious and at times irreversible symptoms such as seizures, focal neurological deficits, pathological reflexes, and Cheyne-Stokes respiration can then develop. Finally, coma, brain-stem herniation, and death can result.2,27,31

Hyponatremia in the psychiatric patient presents unique diagnostic difficulties because it can be difficult to distinguish whether symptoms are due to hyponatremia, the underlying psychiatric condition, or the psychotropic medications. Additionally, many psychiatric patients are unable or unwilling to accurately describe their symptoms, or to complain that they do not feel well. Clearly, in the psychiatric patient, accurate diagnosis of hyponatremia
requires a high index of suspicion and careful monitoring.

**TREATMENT**

Just as the presence of symptoms is dependent on the degree of hyponatremia and the rapidity at which it develops, so too do these factors guide management. In patients with no symptoms and relatively mild hyponatremia, the goal of management is to diagnose the cause of hyponatremia and provide disease-appropriate treatment. The remainder of this discussion will focus on the treatment of symptomatic SIADH.

In patients who are mildly symptomatic from SIADH, fluid restriction is the mainstay of treatment. This allows the kidneys to slowly excrete free water excess, and the serum sodium level gradually returns to normal. If intravenous therapy is deemed necessary, normal saline infusions, usually coupled with a loop diuretic, such as furosemide, are provided. The diuretic allows for excretion of sodium equal to the amount infused but in a larger volume, resulting in net free water loss.7-36

Patients with severe symptoms and those with significantly reduced serum sodium levels (less than 120 to 125 mEq/L) are candidates for hypertonic 3% saline infusions. Again, loop diuretics are usually administered to promote free water clearance and prevent fluid overload. Attention also must be paid to correcting associated electrolyte abnormalities, such as hypokalemia and hypomagnesemia.

Ideally, patients receiving 3% saline should undergo intense monitoring, usually in the intensive care unit setting. In part, this is because frequent monitoring of the sodium response to therapy is required in order to prevent the development of the most feared complication of overtreatment, central pontine myelinolysis.5-18,25,36

As mentioned above, with the development of serum hypo-osmolality, fluid flows into the brain tissue to equalize the osmotic gradient. The normal brain adaptation to this is a loss of brain solute to reverse the flow of fluid out of the brain.

If the hyponatremia is overcorrected or corrected too rapidly, a further osmotic gradient favoring continued outflow of fluid from the brain is created. If this outflow is not matched by appropriate sodium replacement, a fatal cerebral edema may result.7-36

The usual clinical manifestation of central pontine myelinolysis is as follows: the severely symptomatic patient will initially improve as the serum sodium level is corrected. However, one to several days later, the patient will again deteriorate despite continued improvement in the serum sodium level. Symptoms of central pontine myelinolysis include quadriplegia, seizures, pseudobulbar palsy, coma, and death.

Treatment for central pontine myelinolysis is supportive, but the prognosis is poor. Patients at particular risk include alcoholics and others with liver disease, and patients with malnutrition, hypokalemia, and burns.7-36 Patients with psychiatric illnesses may be at increased risk for central pontine myelinolysis, as substance abuse, malnutrition, and electrolyte disturbances are common in this patient population.

In order to limit the risk for central pontine myelinolysis, recommendations have been made regarding the rate at which the serum sodium level is corrected. Current recommendations are to increase the serum sodium level no more than 1 to 2 mEq/L per hour and no more than 8 to 12 total mEq/L per 24 hours. Intravenous saline can be stopped when the serum sodium level reaches 120 to 125 mEq/L, with further increases in sodium level effected through fluid restriction.2,5-31,36

Although the recommendations appear to represent only modest increases, it is important to remember that even small increases in serum sodium level on the order of 3 to 8 mEq/L can decrease the risk of cerebral edema and hyponatremic seizures.7-38 The only justification for exceeding the recommended correction rates is persistent severe symptoms, such as coma and seizures, that have not responded to conventional treatment. In these cases, modest increases in the rate of correction can be considered, as the risk of irreversible neurological deficits from continuing hyponatremia outweighs the risk of central pontine myelinolysis.7-36

Long-term treatment of SIADH is dependent on the underlying etiology. Reversible pulmonary processes, central nervous system lesions, and neoplasms should be treated, and offending medications should be held. After stopping offending medications, it may take several weeks for ADH levels and the serum sodium level to return to normal.16,17 If SIADH is considered idiopathic or the response to treatment is inadequate, chronic treatment will be required to prevent recurrent hyponatremia.

In addition to continuing water restric-
tion to less than 1 liter of free water per day,39 long-term treatment of SIADH has been accomplished with a variety of medications. Increased sodium intake in the form of salt tablets, combined with loop diuretics to promote free water excretion, has proven efficacious.27

Demeclocycline in a dosage of 600 to 1,200 mg/day in 3 to 4 divided doses also has been used with some success. This member of the tetracycline antibiotic group can antagonize the effects of ADH at the level of the kidney, thereby creating a nephrogenic diabetes insipidus that counteracts the inappropriate ADH.40

Demeclocycline requires 7 to 14 days before its effects are seen, and its use mandates the monitoring of renal function to detect nephrotoxicity, liver function to detect liver toxicity, and serum sodium level to prevent overcorrection. Demeclocycline also can cause phototoxicity.41

Another long-term adjunct to fluid restriction in chronic SIADH is fludrocortisone, 0.05 to 0.2 mg twice daily. Results with this hormone also require 7 to 14 days, and it exerts its effects by promoting sodium retention. However, fludrocortisone induces potassium excretion, which may need to be supplemented and may induce hypertension.27,41

Phenytoin, which can inhibit ADH release, and lithium, which can inhibit ADH effects, also have been used for chronic SIADH. There is less experience with these than with other treatments.16

A new form of treatment currently under investigation is that of ADH receptor antagonism. There are two forms of ADH receptors, with the V2 receptor located primarily in the kidney and responsible for the renal effects of ADH.42 Antagonists to the V2 receptor have been developed and have been used successfully to treat different forms of hyponatremia with elevated ADH levels such as congestive heart failure, cirrhosis, and SIADH.43,44 In time, V2 receptor antagonists may become a mainstay in the therapy of many forms of hypo-osmolar hyponatremia. Acute and long-term treatment options are summarized in the Table.

PREVENTION

The primary means of preventing hyponatremia in patients with psychiatric disorders is to have a high index of suspicion and to periodically monitor serum electrolytes while treating with psychotropic medications. Additionally, there may be certain patient groups that are particularly high risk for hyponatremia and in whom more intensive monitoring is indicated.

As mentioned previously, because of changes related to the aging process and an increased incidence of comorbidities, elderly patients appear to be at increased risk for the ADH-promoting effects of psychotropic medications. Although not a consistent finding in studies of carbamazepine-induced hyponatremia,45 advanced age does appear to be a risk factor in studies of SSRI-related SIADH.16,17

Although 60% to 70% of patients with hyponatremia due to antidepressants are women,16,17 it is unclear if female gender alone is an independent risk factor. In general, women experience more adverse drug reactions than men, and because women constitute the majority of patients with depression,8 women are more likely to receive antidepressants.

Additionally, observed differences in the manner in which men and women use health care resources may result in sex-related biases in the recognition and reporting of adverse drug reactions.17 Female gender is also important because elderly women taking thiazides may be at increased risk for central pontine myelinolysis, and younger women may be at increased risk for postoperative hyponatremic encephalopathy.31

The total daily dosage of psychotropics has not been found to be a risk factor for hyponatremia, but most cases are diagnosed 10 to 14 days after an offending drug is started or the dose increased.16,17 While a prior history of hyponatremia due to medications has not been proven to be a risk factor, it would appear prudent to consider such patients at increased risk, even if a different class of medication is being administered.15,16

CONCLUSION

Hyponatremia that develops during psychotropic treatment is not an uncom-
mon disorder and has a variety of causes. Monitoring for its presence is prudent, as significant hypotension can lead to irreversible neurological deficits and death. Psychiatric patients pose a particular challenge. These patients appear to be predisposed to hypotension, psychotropic medications promote increased ADH levels, and their psychiatric disorders may delay diagnosis of the electrolyte abnormality. As the primary providers of psychotropic medications, psychiatrists should be aware of the diagnostic and management issues detailed in this article.

REFERENCES
42. Arieff A. Treatment of hypotensive encephalopathy with antagonists to antidiuretic hormone. J Lab Clin Med. 2001;138:8-10.