# Treatment of central diabetes insipidus

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**INTRODUCTION** — The major symptoms of central diabetes insipidus (DI) are polyuria, nocturia, and polydipsia due to the concentrating defect. Treatment of this disorder is primarily aimed at decreasing the urine output, usually by increasing the activity of antidiuretic hormone (ADH, also called arginine vasopressin or AVP).

Replacement of previous and ongoing fluid losses is also important. Most patients with central DI have a normal or only mildly elevated plasma sodium concentration because concurrent stimulation of thirst minimizes the degree of net water loss. However, hypernatremia can occur if thirst is impaired or the patient has no access to water [1]. Correction of the hypernatremia requires repair of this free water deficit. (See "Treatment of hypernatremia".)

The treatment of central DI will be reviewed here. The causes of this disorder and the approach to the patient with polyuria are discussed separately. (See "Clinical manifestations and causes of central diabetes insipidus" and "Diagnosis of polyuria and diabetes insipidus".)

**CHOICE OF THERAPY** — There are three main options for the treatment of polyuria in patients with central DI:

- Desmopressin, which is an ADH analog and is the preferred drug in almost all patients.
- Other drugs, such as chlorpropamide, carbamazepine, thiazide diuretics, and nonsteroidal anti-inflammatory drugs.
- A low-solute (mostly low-sodium, low-protein) diet. In normal individuals, the urine output is primarily determined by fluid intake, a relationship that is mediated by changes in the release of antidiuretic hormone (ADH). When the urine osmolality is fixed, as in untreated DI, the urine output is determined by the intake and subsequent urinary excretion of solutes (mostly sodium salts and urea), which has been called the renal solute load. As an example, at a fixed urine osmolality of 100 mosmol/kg, the urine output will be 6 L/day if urinary solute excretion is 600 mosmol/day and 3 L if urinary solute excretion is 300 mosmol/day on a low-sodium, reduced-protein diet. A low-solute diet can be combined with a thiazide diuretic. (See 'Low-solute diet and thiazide diuretics' below.)

The choice of therapy varies with the severity of the polyuria. Patients with partial DI and mild to moderate polyuria and nocturia may be adequately controlled with a low-solute diet (if acceptable to the patient) and, if necessary, a thiazide diuretic. Although these modalities also reduce the urine output in patients with marked polyuria and nocturia, desmopressin therapy is usually required for symptom control. Desmopressin can also be used in patients with less severe DI who do not want to comply with a low-solute diet.

**THERAPEUTIC GOAL** — The only symptoms of DI are polyuria, nocturia, and thirst (unless the patient has a hypothalamic lesion causing hypodipsia). Thirst is essential so that the excess urinary water losses can be replaced. Patients without an intact thirst mechanism can develop severe hypernatremia. (See "Etiology and evaluation of hypernatremia", section on 'Hypothalamic lesions affecting thirst or osmoreceptor function'.)

The initial aim of therapy is to reduce nocturia, thereby providing adequate sleep, most often by the administration at bedtime of desmopressin, which is the **preferred therapy** for central DI. Once this is achieved, one aims for

**partial** control of the diuresis during the day since complete control can lead to retention of water and hyponatremia.

**Risk of hyponatremia** — Water retention leading to the development of hyponatremia is a potential risk in patients with central DI who are treated with desmopressin or other therapies that increase the response to or secretion of ADH (eg, chlorpropamide and carbamazepine). Once desmopressin is given, the patient has nonsuppressible ADH activity and may be unable to excrete ingested water normally, possibly leading to hyponatremia, as occurs in patients with the syndrome of inappropriate ADH secretion. (See "Pathophysiology and etiology of the syndrome of inappropriate antidiuretic hormone secretion (SIADH)", section on 'Pathogenesis of hyponatremia'.)

Although thirst will be suppressed by effective therapy, much of the fluid intake during the day is not driven by thirst (eg, coffee with breakfast, soda with lunch and dinner). In addition, previously untreated patients may have become accustomed to drinking large amounts of fluids and may continue to do so for a short period after the initiation of effective therapy to control polyuria, possibly resulting in the development of hyponatremia. Thus, we suggest measuring the serum sodium one to two days after the initiation of desmopressin therapy and, if the initial measurement is normal, repeating the measurement at four days.

Once a stable dose of desmopressin is achieved, annual or biannual monitoring of the serum sodium may be performed. If a patient treated with a stable dose of desmopressin begins experiencing increased urinary frequency or nocturia, and/or the serum sodium is elevated, a 24-hour urine should be collected to ascertain whether the patient is polyuric.

Preventing water retention is more difficult in infants and young children and more frequent monitoring of the serum sodium concentration is recommended. (See 'Monitoring of serum sodium' below.)

**Dosing to prevent hyponatremia** — Given the risk of hyponatremia, patients treated with desmopressin should be educated about the symptoms that may be induced by hyponatremia. These include nausea, vomiting, headache, lethargy, and, if severe, seizures and coma. Patients should be instructed to call the clinician at the first sign of such manifestations. (See "Manifestations of hyponatremia and hypernatremia", section on 'Hyponatremia'.)

Desmopressin dosing is an empiric process. Hyponatremia can usually be avoided by giving the **minimum** desmopressin dose that is required to control the polyuria. The initial aim of therapy is to reduce nocturia, thereby permitting adequate sleep. Thus, the first dose (0.1 or 0.2 mg tablet or 5 to 10 mcg of the nasal spray) is typically given at bedtime. The size of and necessity for a daytime dose is determined by the effectiveness of the evening dose. If, for example, polyuria does not recur until noon, then one-half the evening dose may be sufficient at that time.

**Course of DI and duration of therapy** — The duration of central DI varies with the cause. As examples, DI is permanent in idiopathic disease, most often transient following neurosurgery (usually transsphenoidal) or trauma, and may be reversible with appropriate therapy in patients with infiltrative diseases. The supportive data are presented elsewhere. (See "Clinical manifestations and causes of central diabetes insipidus".)

Desmopressin therapy should be continued for as long as the patient has symptomatic central DI. As mentioned above, the goal of therapy is control of nocturia and partial control of polyuria during the day since more aggressive therapy can promote the development of hyponatremia. The DI induced by neurosurgery or trauma is often transient. Thus, such patients should be questioned carefully at each visit about the degree of polyuria. If the polyuria is said to be less pronounced or to have ceased, the desmopressin dose can be gradually tapered and eventually withdrawn if polyuria does not recur.

**DESMOPRESSIN** — Since the primary problem in central DI is deficient secretion of ADH, control of the polyuria can be achieved by hormone replacement. In the past, this was achieved by intramuscular injections of vasopressin (Pitressin) tannate in oil, which is no longer available. This preparation had two problems: the requirement for intramuscular administration; and the occasional development of anti-vasopressin antibodies with a secondary increase in urine output that appears to be ADH resistant [2].

Intramuscular vasopressin has been replaced by desmopressin (dDAVP), a two-amino acid substitute of ADH that has potent antidiuretic but no vasopressor activity [3].

**Preparations** — Desmopressin comes in liquid form that is usually administered intranasally, in an oral tablet form, and in a parenteral formulation (table 1). The intranasal preparation can be blown into the nose by the patient with a curved, dose-calibrated small plastic tube or delivered with a nasal spray. An initial dose of 5 mcg at bedtime can be titrated upward in 5 mcg increments depending upon the response of the nocturia and then additional daytime doses added. The daily maintenance dose is about 5 to 20 mcg once or twice a day.

The desmopressin metered spray bottle is currently used more commonly than the rhinal tube because of greater convenience of administration. Although flexibility is more limited with the metered spray bottle because the minimum dose is 10 mcg, this does not represent a problem for most patients. The usual daily maintenance dose is 10 to 20 mcg intranasally once or twice a day. Using a urine osmolality of 400 mosmol/kg or greater to judge effect, the mean duration of action after 10 and 20 g intranasal doses was seven to nine hours, respectively [4].

An oral tablet preparation of desmopressin is also available [5]. The absorption of desmopressin in normal persons is decreased by 40 to 50 percent when taken with meals [6]. This usually has little effect on the antidiuretic action but administering the drug in the fasting state may be tried if there is a poor response to the usual doses taken with meals.

The oral form has about one-tenth to one-twentieth the potency of the nasal form because only about five percent is absorbed from the gut. Thus, a 0.1 mg tablet is the equivalent of 2.5 to 5 mcg of the nasal spray. However, because the oral dose cannot be precisely predicted from a previous nasal dose, transfer of patients from nasal insufflation to oral therapy usually requires some dose retitration.

The initial dose of the tablet form is 0.05 mg (one-half a 0.1 mg tablet) at bedtime with titration as with the liquid form. The usual daily maintenance dose ranges from 0.1 mg to 0.8 mg in divided doses but may be as high as 1.2 mg/day.

There are few long-term data on the use of the tablet form of desmopressin. In one study, eight children with central DI were treated and followed for up to 3.5 years [7]. There was no attenuation of the antidiuretic effect, and no side effects or antibody formation were noted. In another report, ten adults had satisfactory maintenance of the antidiuretic effect over one year with doses of 0.3 to 0.6 mg/day given in two to three doses per day; doses larger than 0.2 mg had no greater effect, eg, 0.4 versus 0.2 mg, but probably lasted longer [8].

Desmopressin has also been developed as a sublingual lyophilisate (melt) formulation containing 60, 120, and 240 g. This formulation improves the bioavailability of desmopressin by approximately 60 percent compared with the tablet.

Although patients generally prefer the oral preparation because of ease of administration, not all patients have an adequate response. As a result, we recommend starting with the intranasal preparation; this ensures that the patient understands what constitutes a good antidiuretic response prior to performing a trial of oral therapy.

If desmopressin cannot be administered intranasally or orally, it can be given subcutaneously. A usual antidiuretic dose is 1 mcg administered subcutaneously every 12 hours. Some patients do not respond well to subcutaneous desmopressin due to inadequate absorption. Such patients can be treated with 2 mcg of desmopressin acetate given intravenously over two minutes; the duration of action, as judged by increased urine osmolality, will be 12 hours or more [9,10].

Desmopressin is **safe** during pregnancy for both the mother and the fetus [11].

**OTHER DRUGS** — For the vast majority of patients with central DI, desmopressin is readily available, safe, and effective. Other drugs that can be used are thiazide diuretics, which act independent of ADH, and, in patients with partial central DI (ie, there is some circulating vasopressin), drugs that increase ADH release or enhance ADH effect on the kidney such as chlorpropamide, carbamazepine, clofibrate, and nonsteroidal anti-inflammatory drugs.

These drugs are associated with more side effects than desmopressin and are generally less effective, lowering the urine output by 25 to 60 percent, although a greater effect may be seen with thiazide diuretics.

Thiazide diuretics and nonsteroidal anti-inflammatory drugs also constitute the only effective therapy for nephrogenic DI, which is characterized by ADH resistance. (See "Treatment of nephrogenic diabetes insipidus".)

**Chlorpropamide** — Chlorpropamide, an oral hypoglycemic agent, is the most commonly used antidiuretic drug after desmopressin [12,13]; it appears to act by enhancing the renal response to ADH or to desmopressin. Studies in animals suggest that this response may be mediated by enhanced sodium chloride reabsorption in the thick ascending limb (thereby increasing the degree of medullary hypertonicity) and/or by increased collecting tubule permeability to water; how these changes occur is unclear [14,15]. The usual dose is 125 to 250 mg, once or twice a day; higher doses may produce a somewhat greater response but also increase the risk of hypoglycemia [13]. Chlorpropamide can lower the urine output by as much as 50 percent [12].

**Carbamazepine or clofibrate** — Carbamazepine (used to treat seizures and tic douloureux) in a dose of 100 to 300 mg twice daily and clofibrate (used in the treatment of hyperlipidemia) in a dose of 500 mg every six hours can ameliorate the polyuria in partial central DI [13,16,17]. Carbamazepine appears to enhance the response to ADH [18], whereas clofibrate may increase ADH release [17]. Carbamazepine can lower the urine output by as much as 50 to 60 percent [16] and clofibrate by a mean of 50 percent but is not as predictably effective as carbamazepine [17].

**Thiazide diuretics** — The induction of mild volume depletion with a low-sodium diet plus a thiazide diuretic (such as hydrochlorothiazide, 25 mg once or twice daily or its equivalent) is a first-line therapy in nephrogenic DI and is also effective in central DI [19,20]. As little as a 1 to 1.5 kg weight loss can reduce the urine output by more than 50 percent, from 10 L/day to below 3.5 L/day in one study of patients with nephrogenic DI [21]. (See "Treatment of nephrogenic diabetes insipidus", section on 'Diuretics'.)

The effect of thiazide diuretics is presumably mediated by a hypovolemia-induced increase in proximal sodium and water reabsorption, thereby diminishing water delivery to the ADH-sensitive sites in the collecting tubules and reducing the urine output. The thiazide effect is additive to that of the other modalities. Thiazides also tend to modestly raise the plasma glucose concentration, thereby decreasing the likelihood of hypoglycemia in patients who are also treated with chlorpropamide [12]. (See 'Chlorpropamide' above.)

**NSAIDs** — Nonsteroidal anti-inflammatory drugs (NSAIDs) increase urinary concentrating ability by inhibiting the renal synthesis of prostaglandins, which are ADH antagonists [22]. In normal subjects, pretreatment with an NSAID increases the antidiuretic effect of a submaximal dose of ADH, amplifying the increase in urine osmolality by more than 200 mosmol/kg [23]. The net effect in patients with DI may be a 25 to 50 percent reduction in urine output [24-26], a response that is partially additive to that of a thiazide diuretic [25].

Not all NSAIDs are equally effective in a given patient. As an example, some patients have a good response to indomethacin but derive little if any benefit from ibuprofen [24].

**CHILDREN** — In addition to removing the underlying causes, if possible, children with DI are treated with a low-solute diet to reduce urinary solute excretion and therefore the urine output, and pharmacologic therapy with desmopressin and/or a thiazide diuretic. Chlorpropamide, carbamazepine and clofibrate should **not** be used in children since limited data suggest that they are less effective than desmopressin and have significant adverse effects [27]. (See "Clinical manifestations and causes of central diabetes insipidus".)

The management of central DI varies with the age of the child.

**Older children** — Older children with an intact thirst mechanism are able to regulate their fluid balance, and independently access free water and monitor their urine output. As a result they can be treated in a manner similar to adults with oral or intranasal desmopressin.

The dosing of both oral and intranasal desmopressin in children older than 12 years of age is the same as in adults.

(See 'Desmopressin' above.)

- The initial oral dose is 0.05 mg at bedtime and is titrated to a desired response to an upper daily limit of 1.2 mg (divided two to three times a day).
- The initial intranasal dose begins at 5 mcg at bedtime and is titrated to a desired response to an upper daily dose of 40 mcg (divided two times a day).

In children younger than 12 years of age, the same initial desmopressin dose is used, but the upper daily limit of the oral medication is 0.8 mg (divided two to three times a day), and the upper daily limit of the intranasal preparation is 30 mcg (divided two times a day).

Thiazide diuretic therapy and a low-sodium diet are used to induce mild volume depletion, which will reduce the urine output. The dose of the thiazide is weight based. Adolescents can be treated with same dose used in adults (hydrochlorothiazide, 25 mg once or twice daily or its equivalent). (See 'Thiazide diuretics' above.)

**Infants and small children** — Treatment of infants and small children with central DI is challenging for the following reasons:

- Oral or intranasal administration of desmopressin is difficult to administer accurately in infants and small children; thus, when used, desmopressin is often given subcutaneously. (See 'Subcutaneous desmopressin therapy' below.)
- Infants and small children are unable to both access fluids and articulate thirst to care providers.
- It is often challenging to ascertain the volume of urine output in children who are not toilet trained.

Infants receive all or most of their nutrition in liquid form. As a result, they are at risk for hyponatremia when treated with desmopressin therapy because of their high obligatory oral fluid requirement (150 mL/kg per day). Thus, frequent measurement of the serum sodium concentration is essential at the initiation of therapy and one to two days after any change in desmopressin dose.

Two approaches are used to treat infants and small children: a low-solute diet plus thiazide diuretics, which is generally preferred; and subcutaneous desmopressin [19]. With both of these approaches, families need to be taught to monitor urine output (frequency and number of wet diapers) and identify signs of hyponatremia or hypernatremia, which are often nonspecific and include irritability and lethargy. When oral intake is reduced, as occurs with intercurrent illness, and/or fluid losses are increased, as occurs with vomiting and diarrhea, vigilance should be increased to detect signs of hypovolemia (ie, dry mucous membranes, decreased urine output, sunken fontanelle, and decreased weight). (See "Clinical assessment and diagnosis of hypovolemia (dehydration) in children", section on 'Clinical assessment'.)

**Low-solute diet and thiazide diuretics** — A low-solute diet (low salt and low protein [which is metabolized to urea]) and a thiazide diuretic can be used to reduce the urine output and therefore thirst in infants and toddlers with central DI who are not treated with desmopressin. When the urine osmolality is fixed, as in central DI without desmopressin therapy, the urine output is determined by the intake and subsequent excretion of solutes such as sodium salts and urea, which has been called the renal solute load. (See 'Choice of therapy' above.)

For infants who are dependent upon a milk diet, human milk is preferred because of its proven nutritional and immunologic benefits and a lower solute load compared with Similac PM 60/40 (low-solute cow milk-based formula), regular cow milk-based formula, soy-based formula, and cow's milk (75, 92, 110, 126, and 235 mosmol/L, respectively). (See "Infant benefits of breastfeeding".)

The efficacy of a low-solute diet can be illustrated by the following example. Suppose an infant with a daily intake of 750 mL of human milk has a maximum urine osmolality of 100 mosmol/kg. This quantity of human milk provides 56 milliosmoles of solute per day (0.75 L x 75 milliosmoles/L) so that the daily urine volume would be 0.56 L (56 milliosmoles per day/100 milliosmoles/L). Changing to a regular cow milk-based formula would increase the renal

solute load to 83 mosmol/day (0.75 L x 110 milliosmoles/L) and the daily urine volume would increase by 0.28 L to 0.84 L (ie, from 560 to 840 mL/day).

Thiazide therapy is typically given with the low-solute diet to induce mild volume depletion, which will further reduce the urine volume. Oral hydrochlorothiazide is commonly used in infants up to six months of age at a dose of 2 to 3 mg/kg per day divided in two doses, maximum dose: 37.5 mg/day. The dose in older infants and small children is 2 mg/kg per day (divided in two doses).

**Subcutaneous desmopressin therapy** — Infants and small children treated with desmopressin therapy are at considerable risk for water intoxication and hyponatremia as they may not be able to eliminate the daily water load. This risk may be increased because accurate and consistent dosing of oral and intranasal desmopressin is difficult due to variable absorption and the challenge of administering these preparations to infants and small children.

As a result, if desmopressin is to be used, several experts prefer subcutaneous desmopressin, which is more reliably administered to infants and small children. The starting dose is 0.01 mcg/day, which is titrated to a desired response (eg, reduction in urine output, while maintaining a normal serum sodium). The reported range of dosing is 0.02 to 0.08 mcg/day [19,28].

**Monitoring of serum sodium** — Infants and small children differ from older children and adults since all or almost all of their calories are consumed as liquids, not as solids. As a result, monitoring of the serum sodium concentration and body weight is important to detect hypernatremia due to water loss with a low-solute diet and thiazide diuretic and to detect hyponatremia due to water retention resulting from desmopressin therapy.

We suggest the following approach in infants and small children treated with a **low-solute diet and a thiazide diuretic**:

- The serum sodium should initially be measured at least daily.
- If the serum sodium is normal at one to two days, we suggest repeat measurement at three to four days and then at every patient visit. If the serum sodium is elevated, fluid intake should be increased and the serum sodium measured serially until it is stable in the normal range.
- The serum sodium should be measured immediately whenever there is an alteration in clinical status, particularly when an intercurrent illness impairs fluid intake and/or increases fluid losses, both of which will tend to raise the serum sodium.
- Infants should be weighed frequently since weight loss or less than expected weight gain could be indicative of water loss and hypernatremia in between usual measurements of the serum sodium concentration. Normal healthy infants lose up to 10 percent of their birth weight during the first week of life, a loss that is regained by two weeks of age. Thereafter, a healthy infant should gain weight at a rate of approximately 30 g/day in the first three months, 20 g/day from three to six months, 15 g/day from six to nine months, 12 g/day from nine to twelve months, and 8 g/day from one to three years. (See "Normal growth patterns in infants and prepubertal children", section on 'Weight gain'.)

We suggest the following approach in infants and small children treated with desmopressin:

- The serum sodium should be measured at least daily after the initial dose of desmopressin as well as after any dose adjustment [19,28].
- If the serum sodium is normal at one to two days, we suggest repeat measurement at three to four days since some young children have a later onset of hyponatremia.
- If any serum sodium measurement is below normal, the desmopressin dose should be reduced and the serum sodium measured one to two days later.
- In children on a stable dose of desmopressin, the serum sodium should be measured every one to two years.

- Infants should be weighed frequently since more than expected gains, as defined in the preceding paragraph, could reflect water retention and hyponatremia.

Hyponatremia is less likely to occur in older children and adults treated with desmopressin since, as noted above, the goal of therapy is only partial control of the polyuria during the day, which minimizes the risk of water retention. (See 'Dosing to prevent hyponatremia' above.)

**PROBLEM WITH INTRAVENOUS FLUID REPLACEMENT** — When thirst is intact and there is free access to water, most patients with central DI can replace their water losses orally. Patients who are unable to drink water must be treated with intravenous dextrose and water (because intravenous sterile water without dextrose causes hemolysis).

There is a potential complication if this is performed before the polyuria is corrected by the administration of desmopressin. In adults, the intravenous administration of dextrose and water at more than 1000 mL/hour delivers glucose at a rate that exceeds endogenous metabolic capacity for glucose even in patients without diabetes mellitus, possibly leading to severe and symptomatic hyperglycemia [29]. Thus, intravenous rates of fluid replacement with dextrose in water should be limited to a maximum of 500 to 750 mL/hour and serum glucose levels should be monitored. Avoiding excess dextrose administration can be more readily achieved by administering desmopressin to reduce the urine flow rate.

This sequence can also occur when patients with central DI and impaired consciousness present with polyuria and hypernatremia of unknown cause. One way to avoid this is to ensure that patients with central DI have a Medic Alert bracelet so that treating clinicians will be aware of the need to administer desmopressin in such instances.

The development of hyperglycemia for any reason may have an additional effect that can be confusing clinically. Marked glucosuria can lead to an osmotic diuresis that is **ADH resistant**. In this setting, the urine osmolality is typically similar to the plasma osmolality and polyuria is driven by the solute load. The administration of insulin to correct the hyperglycemia will restore responsiveness to ADH.

**INFORMATION FOR PATIENTS** — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5$^{th}$ to 6$^{th}$ grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10$^{th}$ to 12$^{th}$ grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient information: Diabetes insipidus (The Basics)")

**SUMMARY AND RECOMMENDATIONS**

- The major symptoms of central diabetes insipidus (DI) are polyuria, nocturia, and polydipsia. Most patients have a normal or only mildly elevated plasma sodium concentration because concurrent stimulation of thirst minimizes the degree of net water loss. Treatment of this disorder is aimed at decreasing the urine output. (See 'Therapeutic goal' above.)

- There are three major therapeutic options: a low-solute (sodium and protein) diet; desmopressin (dDAVP), an ADH analog; and other drugs, including thiazide diuretics. The choice of therapy varies with the severity of the polyuria. Patients with partial DI and mild to moderate polyuria and nocturia may be adequately controlled with a low-solute diet (if acceptable to the patient) and, if necessary, a thiazide diuretic. Although these modalities also reduce the urine output in patients with marked polyuria and nocturia, desmopressin therapy is usually

required for symptom control. Desmopressin can also be used in patients with less severe DI who do not want to comply with a low-solute diet. (See 'Choice of therapy' above.)

- The initial aim of therapy with desmopressin is to reduce nocturia, thereby permitting adequate sleep; after this is achieved, one aims for control of the diuresis during the day. The size of and necessity for a daytime dose is determined by the effectiveness of the evening dose. (See 'Desmopressin' above.)

- Desmopressin can be administered intranasally, orally, subcutaneously, or intravenously. The intranasal preparation should be used initially as not all patients respond to oral therapy. (See 'Preparations' above.)

    - For the intranasal preparation, an initial dose of 5 mcg at bedtime can be titrated upward in 5 mcg increments depending upon the response of the nocturia. The usual daily maintenance dose is 5 to 20 mcg once or twice a day.

    - For the oral preparation, the initial dose is 0.05 mg (one-half a 0.1 mg tablet) at bedtime with subsequent titration as with the intranasal preparation. The usual daily maintenance dose ranges from 0.1 mg to 0.8 mg in divided doses but may be as high as 1.2 mg/day.

    - For the subcutaneous preparation, the usual dose is 1 mcg every 12 hours.

    - For intravenous administration (in patients who do not have an adequate response to the subcutaneous preparation), 2 mcg of desmopressin acetate may be given over two minutes; the duration of action is 12 hours or more.

- Desmopressin can lead to water retention and hyponatremia if the urine is concentrated for most of the day. This can usually be avoided by giving the minimum required dose to control the polyuria and not administering another dose until the patient has had a period of brisk diuresis, indicating that the effect of the previous dose of desmopressin had waned. The serum sodium concentration should be checked at 24 hours after the initiation of desmopressin therapy and patients educated about the symptoms that may be induced by hyponatremia. These include nausea, vomiting, headache, lethargy, and, if severe, seizures and coma. Patients should be instructed to call the clinician if such manifestations occur. (See 'Risk of hyponatremia' above and "Manifestations of hyponatremia and hypernatremia", section on 'Hyponatremia'.)

- Desmopressin therapy should be continued for as long as the patient has central DI. The duration of central DI varies: DI is permanent in idiopathic disease, improves in some elderly patients with familial disease, may be transient following neurosurgery (usually transsphenoidal), and may be reversible with appropriate therapy in patients with infiltrative diseases. (See 'Course of DI and duration of therapy' above and "Clinical manifestations and causes of central diabetes insipidus".)

- Other drugs that may decrease diuresis include chlorpropamide, carbamazepine and clofibrate, nonsteroidal anti-inflammatory drug (NSAID) and thiazide diuretics. (See 'Other drugs' above.)

- The treatment of children with central DI varies with the age of the child. (See 'Children' above.)

    - Older children (more than 12 years of age) can be treated in a similar manner as adults with oral or intranasal desmopressin. (See 'Older children' above.)

    - Children younger than 12 years of age may be given the same initial desmopressin dose, but the upper daily limit of the oral medication is 0.8 mg (divided two to three times a day), and the upper daily limit of the intranasal preparation is 30 mcg (divided two times a day). (See 'Older children' above.)

      Thiazide diuretic therapy and a low-sodium diet are used to induce mild volume depletion, which will reduce the urine output. The dose of the thiazide is weight based. Adolescents can be treated with same dose used in adults (hydrochlorothiazide, 25 mg once or twice daily or its equivalent). (See 'Older children' above.)

- Infants and small children should be treated with a low-solute diet (low salt and low protein) plus a thiazide diuretic. This will reduce the urine output and therefore thirst in infants and toddlers with central DI. For infants who are dependent upon a milk diet, human milk is preferred, if possible, because of its proven nutritional and immunologic benefits and lower solute load compared with formulae or cow's milk. (See 'Infants and small children' above.)

  Thiazide therapy is typically given with the low-solute diet to induce mild volume depletion. Oral hydrochlorothiazide is commonly used in infants up to six months of age at a dose of 2 to 3 mg/kg per day divided in two doses, maximum dose: 37.5 mg/day. The dose in older infants and small children is 2 mg/kg per day (divided in two doses). (See 'Low-solute diet and thiazide diuretics' above.)

  If desmopressin is required in infants and small children, subcutaneous desmopressin is the preferred preparation since it is more reliably administered and its effect is more predictable than oral and intranasal desmopressin. The starting dose is 0.01 mcg/day, which is titrated to a desired response (eg, reduction in urine output, while maintaining a normal serum sodium). The reported range of dosing is 0.02 to 0.08 mcg/day. (See 'Subcutaneous desmopressin therapy' above.)

  Infants and small children differ from older children and adults since all or almost all of their calories are consumed as liquids, not as solids. As a result, monitoring of the serum sodium concentration and body weight is important to detect hypernatremia due to water loss with a low-solute diet and thiazide diuretic and to detect hyponatremia due to water retention resulting from desmopressin therapy. (See 'Monitoring of serum sodium' above.)



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## GRAPHICS

### Dose comparison of different formulations of desmopressin

| | Melt | Tablets | Spray | Solution for injection |
|---|---|---|---|---|
| **Dose comparison** | 60 mcg | 100 mcg | 2.5 mcg | N/A |
| | 120 mcg | 200 mcg | 5 mcg | Less than 0.5 mcg |
| | 240 mcg | 400 mcg | 10 mcg | Less than 1 mcg |

NOTE: The indication of desmopressin is varying between countries and regions, not all desmopressin formulations are approved for the treatment of neurohypophyseal diabetes insipidus in all countries. Based on unpublished BA studies (CS004, RG84063-102, 45A02/48).



Graphic 90924 Version 1.0

## Disclosures

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