Illustration by Felecia Paras

Diabetes Insipidus

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ABSTRACT: Diabetes insipidus is a metabolic disorder caused by a deficiency in the production of or response to arginine vasopressin (AVP). The lack of, or inability to appropriately respond to, AVP results in a lack of tubular reabsorption of water and in urine of low specific gravity. Two main categories of diabetes insipidus are recognized in veterinary medicine: central and nephrogenic.

Diabetes insipidus is a metabolic disorder caused by decreased production of or inadequate response to arginine vasopressin (AVP).[1] A deficiency of AVP, or an inability of the distal tubule or collecting ducts to respond to AVP appropriately, results in a lack of tubular reabsorption of water and urine of low specific gravity.[2]

The main categories of diabetes insipidus recognized in veterinary medicine are central diabetes insipidus (CDI) and nephrogenic diabetes insipidus (NDI). *CDI* is defined as decreased secretion or production of AVP, whereas *NDI* is defined by an inability of the kidneys to respond appropriately to AVP. Dogs and cats with diabetes insipidus usually present with polyuria and polydipsia (PU/PD). However, these clinical signs are also present in animals with several more common diseases. In dogs, the most common causes of PU/PD include renal failure, hyperadrenocorticism, diabetes mellitus, and pyometra; in cats, they include renal failure, diabetes mellitus, and hyperthyroidism.[3] Primary or psychogenic polydipsia is another diagnostic differential to consider in a patient with suspected diabetes insipidus. This disease is characterized as compulsive consumption of more water than the kidneys can normally excrete. Primary polydipsia caused by a dysfunction of the thirst center has not been reported in dogs or cats. Psychogenic polydipsia has been reported in dogs, with no specific breed or gender predisposition; it has not been documented in cats.[4] When considering diabetes insipidus as a diagnostic differential in a patient that has PU/PD, it is important to first rule out the more common causes (see the box on page 44).

[a]Dr. Ross discloses that she has received financial support from Biopal, Inc., Worcester, MA.

PHYSIOLOGY OF WATER BALANCE

To understand how diabetes insipidus causes PU/PD, it is important to first understand the key components of normal water balance: water intake, sensation of thirst, and regulation of water excretion by the kidneys. The normal water intake in dogs and cats varies from 20 to 70 ml/kg/day, and the normal urine output varies between 20 and 45 ml/kg/day.[2] Animals are considered polydipsic if water consumption is greater than 100 ml/kg/day and polyuric if urine production is greater than 50 ml/kg/day.[4] Water intake and loss vary from day to day, leading to changes in plasma osmolality; however, they are normally balanced so that this change is minimal. In a healthy animal, the secretion of AVP and the thirst response work to normalize the plasma osmolality and restore the circulating volume to normal.

Common Causes of Polyuria and Polydipsia

Dogs
- Renal failure
- Hyperadrenocorticism
- Diabetes mellitus
- Glucocorticoid therapy
- Pyometra
- Hypercalcemia
- Hypoadrenocorticism
- Hepatic insufficiency

Cats
- Renal failure
- Diabetes mellitus
- Hyperthyroidism
- Postobstructive diuresis

The thirst mechanism of animals with diabetes insipidus is typically intact. Osmoreceptors within the hypothalamus sense minute changes in plasma osmolality and the effective circulating volume. An increase in osmolality of as little as 1% affects the intake of water by increasing the sensation of thirst, leading to ingestion of water; it also increases the secretion of AVP, leading to water conservation by the kidneys. The stimulus for the sensation of thirst is thought to be very similar or equivalent to that for AVP release. It is unclear whether this stimulus is caused by the osmoreceptors that sense an increase in the plasma osmolality or those that sense volume depletion.[5]

Role of Arginine Vasopressin

AVP, also called *antidiuretic hormone,* is a key component in regulating water intake and excretion. AVP is a polypeptide that is synthesized in the supraoptic and paraventricular nuclei within the hypothalamus and is stored in the posterior lobe of the pituitary gland[5] (Figure 1). When secreted in response to changes in fluid homeostasis, AVP helps control renal water reabsorption, the amount of urine produced, urine concentration, and, therefore, water balance. The main stimulus for AVP secretion is an increase in serum osmolality or a decrease in the effective circulating volume.[6] The normal serum osmolality is 280 to 310 mOsm/kg, and increases of 1% or more stimulate AVP secretion.[6]

The two main receptors for AVP within the kidneys are V_1 and V_2. The V_2 receptor mediates the antidiuretic response to AVP. When AVP binds to V_2 receptors, it causes a cascade of events, including the G protein–coupled up-regulation of adenylyl cyclase, which leads to further production of cyclic adenosine monophosphate (cAMP) and activation of cAMP-dependent kinases. These in turn promote the shuttling and insertion of an aquaporin (AQP) water channel within the apical membrane of the collecting duct, resulting in increased water reabsorption from the tubular lumen.[6–8] The binding of AVP to V_2 receptors also induces the release of factor VIII and von Willebrand's factor from endothelial cells.[6,9] In contrast, the binding of AVP to renal V_1 receptors is responsible for vasoconstriction and increased prostaglandin release[6] (Figure 2).

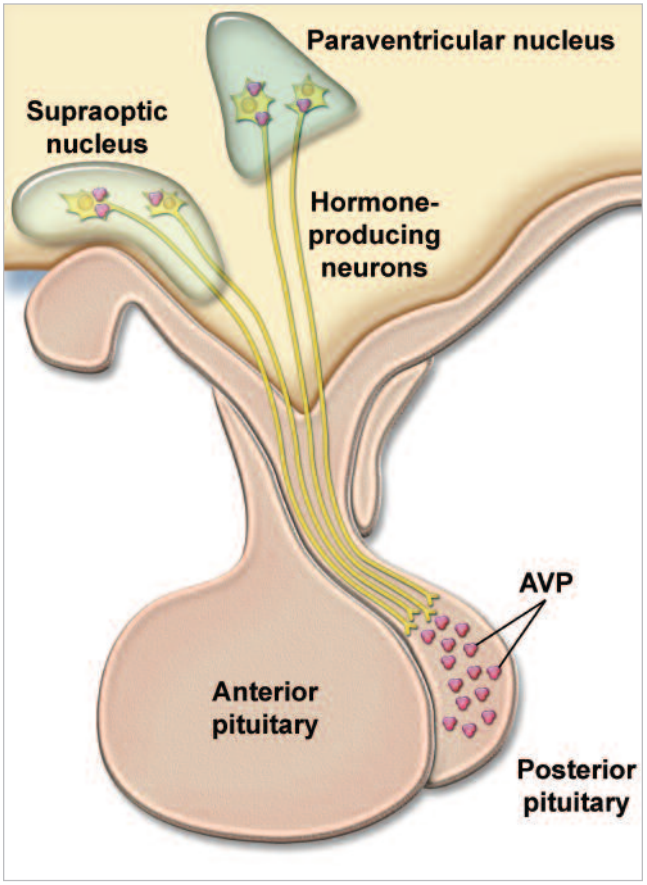


Illustration by Felecia Paras

Figure 1. Diagram of the pituitary illustrating AVP release from the supraoptic and paraventricular nuclei and storage in the posterior pituitary.

Role of Aquaporins

Aquaporins are a family of integral membrane proteins that function as water-discriminating channels.[10] Twelve mammalian aquaporins have been identified, and seven different renal aquaporins have been corre-

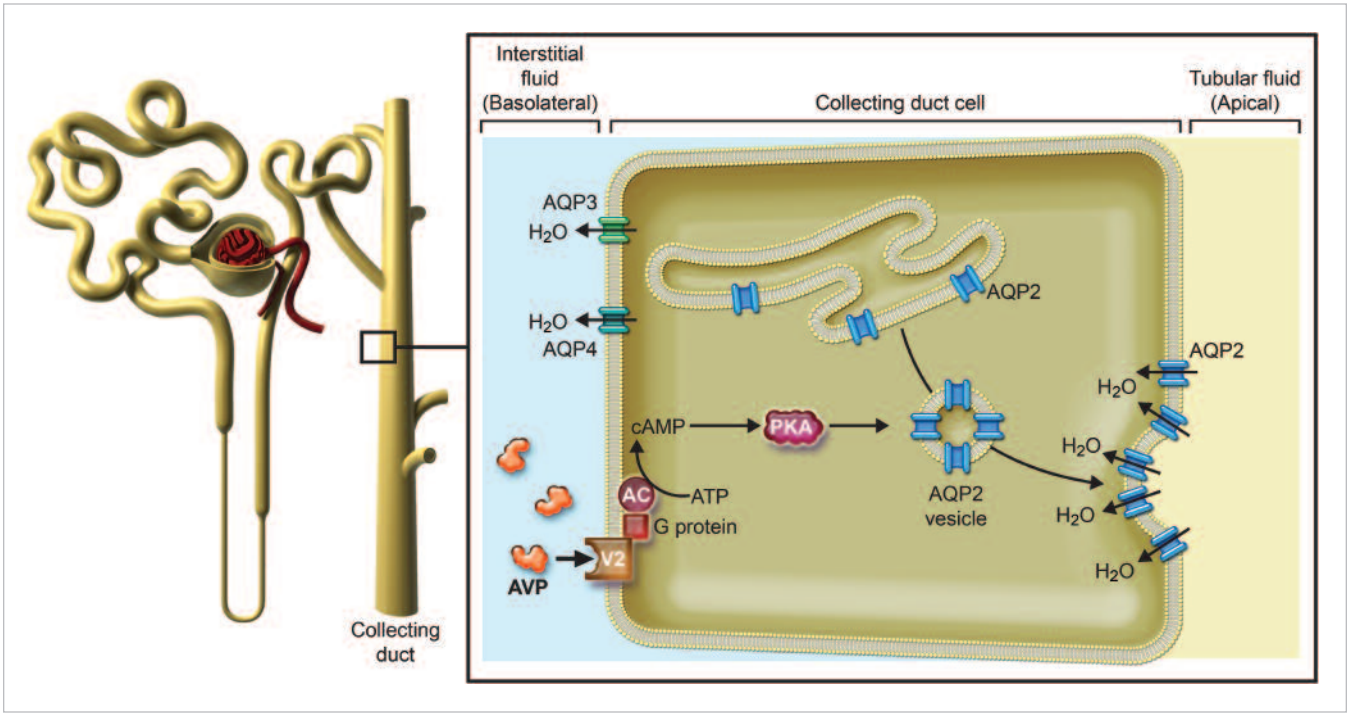


Illustration by Felecia Paras

Figure 2. Depiction of the binding of AVP to the V_2 receptor, which initiates a cascade of events: activation of G protein, increased production of cAMP, activation of protein kinase A (PKA), and insertion of AQP2 in the apical membrane surface of the collecting duct as well as reabsorption of water. *AC* = adenylate cyclase

lated with segmental permeability of the nephron.[8,10] Of the seven identified renal aquaporins, AQP2 appears to be the most important with regard to water homeostasis. AQP3 and AQP4 are located on the basolateral membrane of the kidney collecting ducts and act to facilitate water transport from the cell to the interstitium. AQP2 is a vasopressin-regulated water channel located on the apical membrane and within intracellular vesicles of the collecting duct principal cells.[8,10] When AVP binds to V_2 receptors, it promotes the insertion of AQP2-containing vesicles into the normally watertight luminal membrane, thereby increasing the permeability of the membrane to water.[8,10,11] When there is no longer a stimulus for AVP secretion, the AQP2 channel is removed from the luminal membrane by endocytosis.[6,7]

AQP2 is found in the urine in both soluble and membrane-bound forms.[10] The urinary excretion of AQP2 reflects physiologic regulation of the AQP2 water channels by vasopressin.[11]

PATHOPHYSIOLOGY

Central Diabetes Insipidus

CDI is a polyuric syndrome created by the insufficient secretion of AVP from the neurohypophysis.[1] The deficiency of AVP can be absolute or partial. An absolute deficiency causes persistent hyposthenuria (urine specific gravity [USG] ≤1.006) with severe diuresis. Partial CDI is defined as an incomplete deficiency of AVP and may result in a slightly higher USG, ranging from 1.008 to 1.020. No age, breed, or sex predilection is associated with the development of CDI. CDI can result from any condition that damages the neurohypophyseal system. Causes of CDI include head trauma, which can lead to either transient or permanent CDI; neoplasia; and hypothalamic–pituitary malformations (cysts). Primary intracranial tumors that can lead to CDI include craniopharyngioma and pituitary adenocarcinoma.[2,12] Advanced imaging techniques such as magnetic resonance imaging (MRI) or computed tomography (CT) would be warranted in the workup of CDI secondary to a suspected intracranial lesion. Metastatic neoplasms that have been implicated as underlying causes of CDI include mammary carcinoma, lymphoma, malignant melanoma, and pancreatic carcinoma.[2] However, in most cases, the cause of CDI cannot be identified (idiopathic CDI).

Table 1. Causes of Acquired NDI[8]

Cause	Proposed Effect on AQP2
Hypokalemia[a]	Down-regulation
Lithium[b]	Down-regulation
Hypercalcemia/ hypercalciuria[a]	Down-regulation or interference with shuttling mechanism
Ureteral obstruction	Down-regulation
Kidney failure	Decreased V_2 receptor transcripts with secondary down-regulation
Paraneoplastic syndrome[c]	Interference with production, function, or both

[a]Causes vasopressin resistance.
[b]Drug most commonly associated with NDI in humans.
[c]Cohen M, Post G. Nephrogenic diabetes insipidus in a dog with intestinal leiomyosarcoma. *JAVMA* 1999;215(12):1818-1820.

Nephrogenic Diabetes Insipidus

NDI is defined as an inability of the kidneys to concentrate urine despite adequate concentrations of vasopressin.[8] NDI may develop secondary to a congenital genetic defect or to an acquired disease process.

Congenital NDI is a rare disorder in humans and even rarer in veterinary medicine. The two modes of transmission in humans are X-linked and autosomal recessive. X-linked NDI accounts for 90% to 95% of affected patients. The defect lies within a mutation of the V_2 receptor gene located on the X chromosome, and more than 130 different V_2 receptor mutations have been described.[8] Mutation of the V_2 receptor results in one of three outcomes: (1) decreased binding of AVP to the receptor; (2) impaired intracellular coupling of the V_2 receptor–AVP G protein to the adenylyl cyclase system; or (3) diminished synthesis or accelerated degradation of the V_2 receptor.[13] Autosomal recessive NDI accounts for the remaining 5% to 10% of human congenital NDI cases.[10] In this type of NDI, the mutation occurs in the AQP2 water channel gene, and one of three defects can be observed: (1) the AQP2 channel is not produced; (2) the shuttling of AQP2 from the endoplasmic reticulum or the Golgi apparatus to the luminal membrane is impaired; or (3) the AQP2 channel is nonfunctional.[8,13]

When considering the differential diagnosis of an animal with PU/PD, it is important to remember that congenital NDI is extremely rare in veterinary medicine, and most cases of NDI are considered to be acquired. The few reported cases of congenital NDI have involved either puppies or adult dogs younger than 2 years. Breitschwerdt and Hribernik[14] reported a case of congenital NDI in an 18-month-old intact female Boston terrier that was known to have had PU/PD since 6 months of age. Another case of congenital NDI was diagnosed in a 2-year-old Shiba inu after successful treatment for demodicosis.[15] The dog was consuming between 6,500 and 7,500 ml/day (approximately 800 to 950 ml/kg/day) of water. Congenital NDI has not been reported in cats.[5,16]

The acquired form of NDI is a secondary manifestation of a primary disease process. Acquired NDI is characterized by a reduction in the AQP2 water channels in the cells of renal collecting ducts or interference with AQP2 transport to the apical membrane of the collecting duct.[8] There are many causes of acquired NDI (Table 1). Because acquired NDI is not a primary disease process, the signalment for dogs and cats presenting with this form of diabetes insipidus varies.

DIAGNOSIS

The initial diagnostic workup of a dog or cat with diabetes insipidus should begin by verifying that PU/PD is present and completing a thorough history and physical examination. Making the specific diagnosis relies on eliminating the more common causes of PU/PD. As part of the workup for an animal with PU/PD, a minimum database (complete blood count, biochemistry profile, urinalysis with culture and sensitivity testing) should be obtained. Laboratory test results are usually within normal limits for dogs and cats with CDI, congenital NDI, and psychogenic water consumption, except for the USG, which is usually less than 1.006.[12] In some cases of partial AVP deficiency, the USG varies between 1.008 and 1.020.[5] If, however, the animal has experienced water restriction, the following may occur: erythrocytosis, hyperproteinemia, hypernatremia, and azotemia.[1] A diagnosis of CDI should be considered in any animal that has a history of head trauma and develops PU/PD, hypernatremia, and hyposthenuria. Intracranial neoplasia should be considered in the workup of patients, especially elderly animals, that present with neurologic signs and a history of PU/PD. These clinical signs should prompt the clinician to consider further imaging using modalities such as CT or MRI. If the initial laboratory results are within normal limits, additional diagnostics, such as abdominal radiography, ultrasonography, tests for hyperadrenocorticism, and, in cats, measurement of serum thyroid levels, should be considered to rule out common causes of PU/PD.

Steps of the Modified Water Deprivation Test

Necessary equipment

- Accurate scale
- Refractometer (used to measure USG and to estimate urine osmolality and total solids)
- Urinalysis strips or in-house chemistry equipment to evaluate for azotemia
- Centrifuge with hematocrit tubes to evaluate packed cell volume

Phase 1

- Have the owner determine the patient's unrestricted water intake for 24 hours.
- Decrease the patient's water consumption slowly (approximately 10%/day) over 3 to 5 days leading up to the day of the test. Owners should be made aware of the dangers of water restriction and the clinical signs associated with severe hypertonic dehydration (irritability, weakness, and ataxia, which can progress to stupor and coma in extreme cases).

Phase 2

- Start test:
  - —Stop all access to food and water.
  - —Empty the bladder.
  - —Obtain body weight.
  - —Measure USG.
  - —Measure serum and urine osmolality and blood urea nitrogen.
  - —Assess hydration.
- Empty the bladder every 1 to 2 hours.
  - —Measure USG and/or urine osmolality. The urine osmolality can also be estimated by multiplying the last two numbers of the urine specific gravity by 36.
  - —Assess body weight and hydration: skin turgidity, hematocrit and total solids, and blood urea nitrogen.
- Monitor closely for one of the following end points:
  - —USG >1.030 (dog) or >1.035 (cat)
  - —Loss of 5% of body weight
  - —Clinical dehydration
  - —Development of azotemia
  - —Serum osmolality >320 mOsm/kg

If the patient fails to adequately concentrate its urine (>1.030 [dog] or >1.035 [cat]) during the test after losing ~5% or more of its body weight, proceed with administration of exogenous AVP.

Phase 3

- Administer exogenous AVP (four drops of the intranasal preparation placed within the conjunctival sac; see text for alternative doses).
  - —Empty the bladder every 2 hours for 8 to 12 hours.
  - —Measure the USG and/or the urine osmolality or estimate the urine osmolality as described in phase 2 each time the bladder is emptied.
  - —Offer the patient small amounts of water approximately 2 hours after AVP administration.
  - —CDI is diagnosed when the USG or urine osmolality increases by 50% or more.

Serum Osmolality Testing

If the above tests are normal, a repeatable USG of less than 1.006 has been documented, and the more common causes of PU/PD have been ruled out, three diagnostic differentials remain: CDI, congenital NDI, and psychogenic water consumption. Given that congenital NDI is very rare and that all other causes of PU/PD have been ruled out, a simple measurement of serum osmolality may aid in differentiating CDI from psychogenic water consumption. The serum osmolality in a patient with CDI should be in the high-normal range or above normal (280 to 320 mOsm/kg).[5] A patient with psychogenic polydipsia would have a low-normal to below-normal serum osmolality (≤275 mOsm/kg) caused by ingestion of water in excess of the kidneys' ability to excrete it appropriately.[1,5]

If the results of the serum osmolality test are equivocal, the tests used to differentiate CDI, NDI, and psychogenic water consumption include response to AVP administration and the modified water deprivation test (MWDT; see the box above).

Exogenous Arginine Vasopressin Administration

Administration of exogenous AVP can help differentiate CDI from NDI and is not associated with the potential dehydration complications of the MWDT. We recommend the use of synthetic AVP (desmopressin [1-desamino-8-D-arginine vasopressin]; DDAVP). The dose of DDAVP is empirical and has been reported to be 0.1 mg PO tid for 7 days for a 44-lb (20-kg) dog and 0.2 mg PO tid for 7 days for a 88-lb (40-kg) dog. One to four drops of DDAVP nasal spray can be placed in the conjunctival sac every 12 hours for 5 to 7 days.[17] An increase in USG of at least 50% compared with pretreatment USG by day 5 to 7 or a specific gravity greater than 1.030 supports the diagnosis of CDI.[5] There should be only a minimal increase in USG in dogs and

cats with congenital NDI.[5] Owners should also notice a decrease in water intake and urine production by the end of the trial period if the PU/PD is caused by CDI. A drawback to this approach is that exogenous AVP may also result in concentrated urine in patients with other disorders, such as psychogenic polydipsia and hyperadrenocorticism.

Modified Water Deprivation Test

The MWDT is not commonly conducted because it is time consuming (6 to 12 hours), is uncomfortable for the animal, and requires emptying of the bladder, which can be difficult in properly housetrained pets and female animals. More important, it can be dangerous without proper monitoring because it can result in severe dehydration, azotemia, electrolyte shifts, and even death. However, it is important to understand how the test is conducted and the proper interpretation of the results.

The MWDT is designed to determine whether endogenous AVP is appropriately released in response to dehydration and whether the kidneys can appropriately respond to AVP. The steps of the test are outlined in the box on page 48. The initial phase is designed to minimize the effects of renal medullary washout before total water restriction and thereby improve the overall accuracy of the test. The second phase is the most dangerous part of the test and requires fairly intensive monitoring. During this phase, the patient is denied all access to food and water. The bladder is emptied, and the patient is monitored every 1 to 2 hours. Monitoring involves measurement of body weight, USG, packed cell volume, and blood urea nitrogen and clinical assessment of hydration. The end point of the second phase is achieved when normal urine concentrating ability is demonstrated (USG >1.030 in dogs and >1.035 in cats), there has been a 5% loss in body weight, or clinical dehydration or azotemia occurs. Failure to release or respond to endogenous AVP is demonstrated by the inability to concentrate urine despite dehydration (loss of 5% body weight).[5] If urine concentration is demonstrated during the MWDT, a diagnosis of psychogenic polydipsia can be presumed.

If urine concentration is not demonstrated during the second phase of the MWDT, DDAVP is administered to determine if the kidneys can respond appropriately. This is the third phase of the MWDT. The dose is approximately four drops of the intranasal preparation placed in the conjunctival sac. As an alternative, 10 to 20 µg of synthetic DDAVP can be given intravenously or subcutaneously. DDAVP has its maximal effect between 2 and 8 hours after administration, regardless of the route given; however, a response is typically seen within 2 to 3 hours of administration.[5,12] After administration, urine samples should be obtained every 1 to 2 hours for 8 to 12 hours, again assessing the USG and osmolality. Small amounts of water are offered once a response is seen. An increase in the urine osmolality of 50% (from baseline) or more is diagnostic for CDI[12] (Figure 3). Patients with partial CDI will have a rise of at least 15% in urine osmolality after DDAVP administration, and those with congenital NDI will have little to no increase (typically <5%).[12]

The most pronounced complication of the MWDT is severe dehydration. Animals can become severely hypernatremic and begin to show signs of central nervous system dysfunction, including irritability, weakness, and ataxia. As the hypernatremia becomes more severe, the animal can become stuporous, which can progress to coma or seizures. To avoid these complications, all other diagnostics for causes of PU/PD should be completed before the MWDT is deemed necessary. Close monitoring during the test is essential.[5]

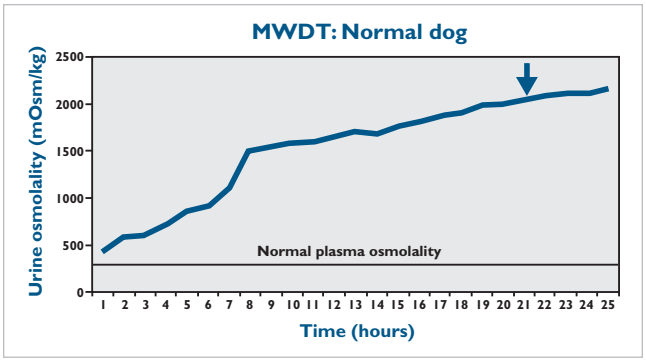
Plasma Arginine Vasopressin Measurement

Another diagnostic tool that can be used in the workup of diabetes insipidus is the measurement of plasma AVP concentration. There are few reports in the veterinary literature that document the lack of appropriate synthesis or release of AVP. In 1989, Post and colleagues[18] demonstrated a low AVP concentration (<1.35 pg/ml) in two Afghan hound puppies after a 5% loss of body weight during the MWDT. The plasma AVP concentration should be measured after a 5% body weight loss (indicating dehydration) has been achieved during the MWDT and before exogenous AVP administration. A low AVP concentration in a dehydrated patient indicates either a lack of AVP production or inappropriate secretion from the hypothalamus. The biggest obstacle to conducting this diagnostic is finding a laboratory to run the assay. Usually, the assay is conducted at a human facility without complication because the amino acid sequence for vasopressin is the same in most species, except for swine.[5]

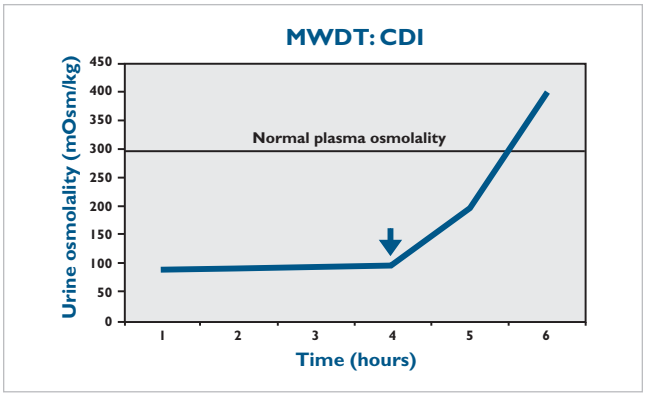
Urinary Aquaporin-2 Excretion

On the horizon for diagnosing polyuric syndromes is the implementation of measuring urinary AQP2 excretion. Urinary AQP2 excretion in humans and rats has been shown to correlate with changes in vasopressin excre-

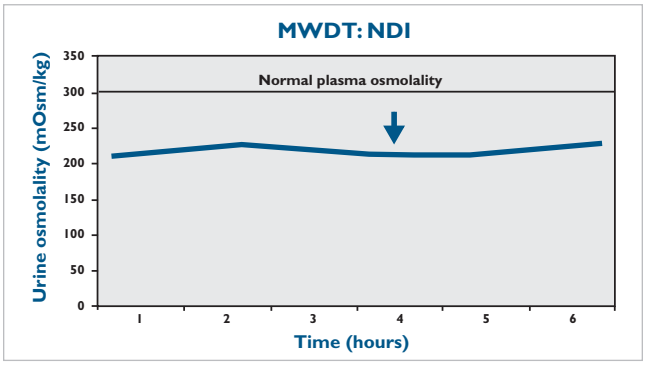
Figure 3. Urine osmolality changes in dogs during the MWDT. In each case, AVP was administered after a loss of 5% body weight due to dehydration.



In a healthy dog, water deprivation causes an increase in urine osmolality, and the administration of AVP (*arrow*) causes less than a 10% change in urine osmolality. A dog with polyuric polydipsia would have a similar graph; however, the time to dehydration would depend on the degree of medullary washout.



In a dog with CDI, AVP administration (*arrow*) causes a greater than 50% increase in urine osmolality. Note the short time to 5% weight loss and AVP administration.



In a dog with NDI, AVP administration (*arrow*) results in no increase in urine osmolality. Again, note the short time to AVP administration.

tion[19] and has the potential to be used as a marker for collecting duct responsiveness to AQP2. In dogs, the urinary AQP2 excretion was found to closely correlate to changes in vasopressin, demonstrated by water loading, hypertonic saline infusion, and IV administration of DDAVP.[19]

In the development of a radioimmunoassay for the detection of urinary AQP2 in dogs, van Vonderen and colleagues[10,19] showed that AQP2 excretion decreased from basal levels by 26% 2 hours after water loading. They also found that urinary AQP2 excretion increases during endogenous and exogenous AVP release (demonstrated by hypertonic saline infusion and exogenous administration of DDAVP). They concluded that more studies are needed to determine whether measurement of urinary AQP2 would be a better diagnostic tool than the MWDT for differentiating polyuric syndromes such as CDI, NDI, and primary polydipsia in animals.

TREATMENT

Congenital Diabetes Insipidus

Therapy for CDI is not mandatory as long as the animal has unlimited access to water and is housed in an environment in which the polyuria can be managed. If the owner decides to pursue medical management of CDI, the drug of choice is DDAVP. DDAVP has three times the antidiuretic action of AVP, with minimal to no vasopressor or oxytocin activity.[5] Intranasal, oral, intravenous, and subcutaneous formulations are available. In animals, the intranasal preparation is most commonly administered into the conjunctival sac. One drop contains 1.5 to 4.0 µg of DDAVP.[12] The recommended dose is one to four drops every 12 to 24 hours.[17] The oral formulation comes in 0.1-mg and 0.2-mg tablets. One suggested dose is 0.1 mg PO tid for dogs weighing less than 44 lb (20 kg) and 0.2 mg PO tid for dogs weighing more than 44 lb.[17] The maximal effect of the drug is reached 2 to 8 hours after administration, and the duration of effect varies from 8 to 24 hours, regardless of the route of administration.[5] The intranasal formulation can be given parenterally; however, it is not a sterile solution and should be filtered before subcutaneous or intravenous injection.

In general, DDAVP is a safe drug. Complications are uncommon, with the most prevalent being hyponatremia and failure to reduce water intake secondary to damage of the inhibitory component of the thirst mechanism.[13] If the animal develops hyponatremia, DDAVP should be given only when polyuria returns. Administration into the conjunctival sac may cause irritation in some dogs.

Alternative therapies include sulfonylurea drugs and diuretics. Chlorpropamide is a sulfonylurea that stimulates the secretion of AVP and is thought to sensitize the renal tubules to AVP, perhaps by increasing cAMP within the renal tubular cells. The recommended dose for dogs and cats with partial CDI is 10 to 40 mg/kg/day.[20] Adverse effects include hypoglycemia, nausea, and skin eruptions. Thiazide diuretics act by interfering with the transport of sodium ions across the renal tubular epithelium, with the principal effect occurring at the cortical collecting duct. Thiazides are thought to have a paradoxic effect in patients with diabetes insipidus by increasing proximal tubular sodium and water resorption, therefore causing a decrease in water delivery by inhibiting sodium reabsorption in the ascending loop of Henle.[5] The recommended dose is 2.5 to 5.0 mg/kg PO bid.[20]

Nephrogenic Diabetes Insipidus

Therapy for congenital NDI in humans includes the use of thiazide diuretics in combination with amiloride, which is an antikaliuretic.[13] It has been reported that humans with congenital NDI have increased prostaglandins, most notably prostaglandin E_2 (PGE_2), which suppress cAMP formation within the collecting duct and interfere with the action of vasopressin. The increase in prostaglandins impairs the effect of any antidiuretic, as well as the vascular action of AVP.[13] Therefore, prostaglandin inhibitors, such as indomethacin, are used in human patients to reduce polyuria via the inhibition of PGE_2 synthesis.[13] Novel therapies not yet available to veterinarians include gene therapy to rescue mutant V_2 receptors and chemical chaperones to guide mutant AQP2 proteins from the endoplasmic reticulum to the apical membrane.[8]

The response to treatment for dogs with congenital NDI is difficult to assess given the limited number of cases reported. The case reported by Breitschwerdt and Hribernik[14] showed a moderate response to treatment, indicated by decreases in water consumption and urine production. However, Takemura[15] reported a much better response to treatment in a 2-year-old intact male Shiba inu with diagnosed congenital NDI. The dog was given ample access to water and was started on a low dose of hydrochlorothiazide (2 mg/kg bid) in addition to a low-sodium diet. The dog's water consumption was reported to decrease from 6,500 ml/day to 1,400 ml/day.

Acquired NDI is secondary to some underlying cause. Appropriate therapy should therefore be directed at treating the specific disease process that is causing the abnormal response to AVP.

PROGNOSIS

The prognosis for CDI is good with appropriate therapy, and most animals become asymptomatic. CDI caused by trauma typically resolves within 2 weeks of the inciting incident. If CDI is caused by a hypothalamic or pituitary tumor, the prognosis is poor to guarded. Neurologic signs usually develop within 6 months of diagnosis; however, limited success has been achieved with the use of chemotherapy and radiation therapy. The prognosis for animals with congenital NDI is typically guarded to poor because of limited therapeutic options and a generally poor response to therapy. However, there have been a few reported cases of successful treatment.[14] The prognosis for animals with acquired NDI varies, depending on the underlying cause.

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ARTICLE #3 CE TEST

This article qualifies for 2 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. ***Subscribers may purchase individual CE tests or sign up for our annual CE program.*** *Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program. CE subscribers can take CE tests online and get real-time scores at* ***CompendiumVet.com****.*

1. The normal water intake for dogs and cats is
a. 10 to 20 ml/kg/day.
b. 20 to 70 ml/kg/day.
c. 100 to 200 ml/kg/day.
d. >200 ml/kg/day.

2. AVP is synthesized in the
a. kidneys.
b. hypothalamus.
c. posterior lobe of the pituitary.
d. anterior lobe of the pituitary.

3. Which of the following statements regarding AVP is correct?
a. The binding of AVP to the V_2 receptor increases vascular resistance.
b. The binding of AVP to the V_1 receptor induces the release of factor VIII and von Willebrand's factor.
c. The binding of AVP to the V_2 receptor is a G protein–coupled up-regulation of adenylyl cyclase that initiates a cascade of events involving AQP2.
d. A decrease in serum osmolality or an increase in circulating volume leads to secretion of AVP from the neurohypophysis.

4. Which of the following statements regarding NDI is correct?
a. NDI is a polyuric syndrome associated with decreased amounts of AVP.
b. Congenital NDI has never been reported in a cat.
c. The most common intracranial tumors associated with NDI include craniopharyngioma and pituitary adenocarcinoma.
d. Affected animals demonstrate an increase in urine osmolality when an MWDT is conducted.

5. Which of the following statements regarding the use of AVP in the diagnosis of diabetes insipidus is correct?
a. Supplementation with exogenous AVP is used to determine whether the anterior pituitary can appropriately respond.
b. The urine osmolality in a patient with NDI increases by 50% or more after the administration of AVP.
c. A dog with psychogenic polydipsia will demonstrate an increase in urine osmolality by 50% or more after the administration of AVP.
d. The urine osmolality in a dog with absolute CDI will increase by at least 50% after the administration of AVP.

6. Which of the following statements regarding the diagnosis of diabetes insipidus is correct?
a. A normal dog will dehydrate (i.e., lose 5% of its body weight) in the same amount of time as a patient with diabetes insipidus.
b. The MWDT is commonly used to rule out the more common causes of PU/PD.
c. The serum osmolality in a patient with CDI should be in the high-normal range or >320 mOsm/kg .
d. The end point for the MWDT is 8 hours.

7. Which of the following statements regarding the treatment of CDI is correct?
a. Medical therapy for CDI is required; otherwise, the animal will die of dehydration.
b. DDAVP, the synthetic analogue used to treat CDI, has 10 times the antidiuretic action of AVP.
c. One advantage of treating with DDAVP is that it has no vasopressor or oxytocin activity.
d. DDAVP has its maximal effect 12 to 24 hours after administration.

8. Which of the following statements is false?
a. The MWDT is a safe and quick way to diagnose polyuric syndromes in animals.
b. The MWDT determines whether endogenous AVP is appropriately released in response to dehydration and whether the kidneys can appropriately respond to AVP.
c. Demonstration of adequate urine concentrating ability during the MWDT is diagnostic for psychogenic polydipsia.
d. The most common complication of the MWDT is severe dehydration.

9. Acquired NDI in animals has been reported with which of the following?
a. ureteral obstruction
b. kidney failure
c. intestinal leiomyosarcoma
d. all of the above

10. Which of the following statements regarding water intake and urine production in dogs is incorrect?
a. Polydipsia is defined as water consumption >45 ml/kg/day.
b. Normal urine output is between 20 and 45 ml/kg/day.
c. Polyuria is defined as urine production >50 ml/kg/day.
d. Normal water intake is from 20 to 70 ml/kg/day.