Normal and Abnormal Water Balance: Polyuria and Polydipsia*

Katharine F. Lunn, BVMS, MS, PhD, MRCVS, DACVIM[a]

Colorado State University

Katherine M. James, DVM, PhD, DACVIM

Veterinary Information Network

ABSTRACT: Polyuria/polydipsia (PU/PD) is a common clinical problem in small animal practice. Most patients with PU/PD have primary polyuria, which may result from either a deficiency of antidiuretic hormone (ADH) or an inability of renal tubules to respond to ADH. Primary polydipsia is less common. This article discusses the interpretation of urine specific gravity, the definition of PU/PD, and a diagnostic approach to the problem. A list of the causes of PU/PD in dogs and cats is provided, and the authors emphasize the use of safe, simple, and interpretable diagnostic tests to rule out potentially harmful or life-threatening disorders. Alternatives to the water deprivation test are also presented.

Although a client may observe that a pet either drinks or urinates excessively, it is not possible for either of these conditions to persist in isolation; therefore, polyuria/polydipsia (PU/PD) is approached as a single medical problem. *Polyuria* has been classically defined as urine output in excess of 50 ml/kg/day.[1] *Polydipsia* is similarly defined as fluid intake exceeding 100 ml/kg/day.[1] In practice, these rigid definitions are often of limited value in determining whether PU/PD should be placed on the problem list for a given patient, for several reasons:

- **Water intake in dogs can be highly variable,** depending on environment, activity level, and diet, all of which are associated with different amounts of water intake to meet losses, particularly insensible losses. In studies[2] of a compara-

tively small and homogenous group of laboratory dogs, insensible losses (primarily due to evaporative respiratory water loss) varied almost 10-fold, depending on whether the individual dogs spent more of their time resting quietly or running and barking. Variation in water intake to compensate for variable losses in different dogs is further compounded by differences between individuals regarding how much water they prefer to drink.

- **Measurement of water intake can be difficult for many clients,** particularly in multipet households, and reliable measurement of urine output is almost impossible to achieve in a nonhospital setting.

- **Measurement of water intake or urine output in the hospital setting may not provide a true**

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*A companion article on hyponatremia and hypernatremia begins on page 589.

For frequently asked questions and answers regarding PU/PD, go to CompendiumVet.com.

reflection of the patient's normal behavior. Water intake may decrease or increase in the hospital setting, depending on the patient's potential urine-concentrating ability and response to the stress of hospitalization.

- **A patient may be clinically polyuric or polydipsic without exceeding the limits defined above.**

PU/PD may be included on the problem list if the owner reports increased water intake or urine output compared with what he or she perceives as normal for the pet and if the urine specific gravity (USG) is found to be persistently low. A related concern that clinicians may encounter, particularly with dogs, is detection of a low USG in a patient when the owner has *not* observed PU/PD. In some dogs, this may represent an appropriate physiologic response in an individual that chooses to drink more than the average dog. In other patients, it may be a manifestation of an underlying medical problem. Determination of the USG from the first urine sample voided in the morning, before the patient drinks,

extra water in the form of dilute urine. One example would be a dog that ingests a large amount of water while playing in a pool or other body of water. The production of hyposthenuric urine in this animal reflects a normal physiologic response: the diluting function of the kidneys maintains normal water balance in the presence of an increased water load. In contrast, if a dog is in a hot environment without access to water and pants for thermoregulation, resulting in respiratory water loss, then the appropriate response is the production of concentrated urine. Production of dilute urine under these circumstances would be a highly inappropriate response. Therefore, the clinician should always interpret a patient's USG in the context of the assessment of that patient's hydration status.

Another important concept in the interpretation of USG is consideration of the normal drinking behavior of the species in question. For example, a USG of 1.060 would be of concern in a puppy. Although this reflects good concentrating ability, it is not normal if compared

> *Measurement of water intake or urine output is not necessary to define the problem of polyuria/polydipsia.*

can be helpful in this situation. Most dogs that drink for enjoyment do not do so during the night; therefore, the first morning urine sample may be the most concentrated sample of the day. If the USG is sufficiently high, then PU/PD is not placed on the problem list. Conversely, if the first morning USG is consistently low, further diagnostic evaluation of PU/PD is warranted.

INTERPRETATION OF URINE SPECIFIC GRAVITY

The terms *normal* and *abnormal* are generally not useful in the interpretation of USG. Theoretically, a situation could arise in which a measured USG is greater than physiologically possible—for example, if a foreign substance is added to the urine sample after collection and contributed to specific gravity. In this case, a USG greater than 1.080 might be measured, and, for most patients, this would be considered abnormal. For the clinician assessing the results of urinalysis, it is much more helpful to consider whether the USG is *appropriate* or *inappropriate*. If a patient drinks water in excess of normal losses, it is appropriate for the kidneys to excrete the

with the expected USG in most puppies.[3] The production of highly concentrated urine indicates a significant antidiuretic response in this animal, and it would be expected that this would stimulate thirst, which most puppies would not resist. Thus the detection of this species-atypical USG should prompt the consideration of laboratory error, recent water restriction, or an abnormal thirst response.

The range of USG that would be considered typical for a dog is largely determined by clinical experience and opinion and is influenced by the wide variety of canine lifestyles. In general, dogs are similar to humans in that some individuals simply enjoy drinking. In addition, dogs as a species tend to have a strong thirst response and will readily drink available water. In our opinion, the typical range for canine USG is approximately 1.010 to 1.040. In contrast, the anticipated range of USG produced by a healthy cat is quite different. Clinical experience indicates that healthy cats on a dry diet usually have a USG of greater than 1.040, and cats on a canned diet may have USGs of 1.030 or greater. Apart from rare individual cats that enjoy drinking from

a water fountain or a running faucet, most cats do not drink in excess of their needs. Therefore, the typical range for feline USG is expected to be approximately 1.040 to 1.055 for cats fed dry food, with a somewhat decreased lower limit of this range for cats fed canned food exclusively.

Table 1 lists the terms that are widely used to classify USG. When interpreting USG, the following facts should be kept in mind:

- *Isosthenuria* refers to urine with an osmolality equal to that of glomerular filtrate or plasma. Isosthenuric urine is neither dilute nor concentrated.

- *Hyposthenuria* refers to urine with an osmolality less than that of plasma.

- *Hypersthenuria* refers to urine with an osmolality greater than that of plasma. By convention, the term is usually used for highly concentrated urine.

- The true ranges for isosthenuria, hyposthenuria, and hypersthenuria in an individual animal are defined by the osmolality of the individual's plasma. As this

conditions causing polyuria or polydipsia are present (e.g., psychogenic polydipsia). For example, a young animal with congenital renal disease that has CRF and primary NDI[4] can produce hyposthenuric urine due to a congenital renal inability to respond to antidiuretic hormone (ADH) if the renal failure is not severe. At the same time, clinicians should not disregard the role of renal disease in a patient with hyposthenuria because some diseases (e.g., pyelonephritis, leptospirosis, hypercalcemia) that inhibit concentrating ability will lead to renal failure if not diagnosed and treated. Clinicians should also recognize that patients with renal failure may retain concentrating ability, albeit less than that of healthy animals. A dehydrated dog with azotemic renal failure may, for example, produce urine with a specific gravity of 1.020. This value is minimally concentrated compared with glomerular filtrate, but the magnitude of concentration is inappropriate in a dehydrated patient.

While persistent isosthenuria is most suggestive of CRF, intermittent isosthenuria can occur with many causes of PU/PD. A random USG of greater than 1.030

> *Chronic renal failure is not ruled out by demonstrating hyposthenuria in a patient with polyuria/polydipsia.*

varies, so will the range of urine osmolalities that correspond to isosthenuria, hyposthenuria, and hypersthenuria. The values of USG used to describe these ranges correspond to the USG values that are typically observed in normal animals producing urine that is isosthenuric, hyposthenuric, or hypersthenuric with respect to plasma. This distinction becomes important in animals that are not normal (i.e., patients with an abnormally high or low plasma osmolality).

Marked hyposthenuria is most likely in patients with diabetes insipidus and psychogenic polydipsia; however, hyposthenuria can occur with examples of secondary nephrogenic diabetes insipidus (NDI), such as hyperadrenocorticism (HAC), hypercalcemia, and pyometra. The detection of hyposthenuria rules against stable chronic renal failure (CRF) as the sole cause of PU/PD. In CRF, the urine is usually isosthenuric or minimally concentrated. However, as discussed in the companion article (p. 589), patients with mild or moderate CRF retain the ability to dilute the urine, and, therefore, they are able to produce hyposthenuric urine, if additional

means that obligate PU/PD is unlikely to be present because the kidneys can produce concentrated urine. When interpreting USG, it is important to consider medical interventions that will interfere with the kidneys' ability to respond to disorders of fluid balance, such as fluid therapy, the use of diuretics, and the feeding of markedly protein-restricted diets.

CAUSES OF POLYURIA/POLYDIPSIA

As described in the companion article (p. 589), the ability of the kidneys to form concentrated urine depends on the presence of ADH, the ability of the renal tubules to respond to ADH, and maintenance of the high osmolarity of the renal medullary interstitial fluid. ADH binds to vasopressin (V2) receptors in the distal renal tubule, which activates intracellular second messenger systems, leading to the insertion of water channels (aquaporin-2) into the apical membrane of the epithelial cells.[5] This allows water to flow along the osmotic gradient between the distal convoluted tubule/collecting duct and the hypertonic renal medulla. An understanding of these normal processes allows classification of the cause

Table 1. Urine Specific Gravity and Osmolality Ranges

Clinical Term	Expected Range of Urine Specific Gravity	Corresponding Range of Urine Osmolality[a] (mOsm/kg)
Hyposthenuria	<1.008	<300
Isosthenuria	1.008–1.012	290–310 (dogs), 290–330 (cats)[b]
Minimally concentrated urine	1.013–1.030 (dogs), 1.013–1.040 (cats)	>310 (dogs), >330 (cats)[c]
Hypersthenuria	>1.035 (dogs), >1.045 (cats)	>1,500[c]

[a]Assumes the urine does not contain high molecular weight solutes.
[b]These values reflect the normal ranges of plasma osmolality for dogs and cats. DiBartola SP: Disorders of sodium and water, in DiBartola SP (ed): *Fluid Therapy in Small Animal Practice.* Philadelphia, WB Saunders, 2000, pp 45–72.
[c]It is more accurate to use the term *hypersthenuria* for any urine osmolality that exceeds plasma osmolality, but by convention, the term is usually applied to highly concentrated urine (i.e., osmolality >1,500 mOsm/kg).

of PU/PD according to the underlying pathophysiology.

The mechanisms leading to PU/PD can be divided into primary polydipsia with compensatory polyuria or primary polyuria with compensatory polydipsia. Disorders that lead to primary polyuria can be subdivided into those associated with reduced or absent ADH synthesis or release, failure of the renal tubule to respond to ADH, and reduction in the osmotic gradient between the filtrate in the distal convoluted tubule and the renal medullary interstitium. It is often impossible to distinguish clinically between primary polydipsia and primary polyuria; however, the evaluation of serum sodium ion (Na^+) concentration can sometimes be helpful. A patient with primary polydipsia may have a subnormal or low-normal Na^+ concentration, whereas patients with primary polyuria may have a high or high-normal Na^+ concentration. Serum sodium values cannot be used to make a definitive distinction because low or low-normal Na^+ concentration may also result from hypovolemia. However, abnormalities of Na^+ concentration can help prioritize subsequent diagnostic testing, and a high Na^+ concentration can serve as a warning that the patient should never be subjected to water restriction. In some patients, primary polyuria and primary polydipsia may coexist. For example, patients with liver failure may have primary polydipsia associated with hepatic encephalopathy but may also be polyuric due to low blood urea nitrogen (BUN) and loss of renal medullary hypertonicity.

Table 2 lists the known and reported causes of PU/PD in dogs and cats. The mechanism underlying the PU/PD is also listed if known. Although the list is long, many causes of PU/PD can be ruled in or out by obtaining a minimum database and conducting additional simple diagnostic tests. The most common causes of PU/PD in dogs are CRF, HAC, and diabetes mellitus. The most common causes in cats are CRF, hyperthyroidism, and diabetes mellitus. Central diabetes insipidus (CDI), primary NDI, and primary polydipsia can be investigated by the water deprivation test (WDT)[6]; however, they are all uncommon conditions.

Primary Polydipsia

Primary polydipsia may be a psychologic or behavior problem, often termed *psychogenic polydipsia.* There are few documented cases in the literature, but most clinicians associate this problem with active dogs that are not sufficiently exercised[6] or with pets in stressful environments.[1] Primary polydipsia may also be a manifestation of hepatic encephalopathy,[7] hyperthyroidism, or gastrointestinal disease.[8] A rare form of primary polydipsia in humans results from a lesion in the thirst center, but this has not been described in dogs and cats.[1]

Primary Polyuria

Reduced or absent ADH synthesis or secretion is termed *CDI* or *neurogenic diabetes insipidus.* The ADH deficiency may be partial or complete, resulting in partial or complete CDI. Causes include head trauma,[9–11] neoplasia,[12] and congenital defects.[13] Many cases are idiopathic.[12,14] Patients with complete CDI are profoundly polyuric and polydipsic, producing markedly hyposthenuric urine. Partial CDI results in less severe PU/PD, and USG can fall into the isosthenuric range in some patients.

Failure of the renal tubules to respond to ADH can result from primary (congenital) or secondary (acquired) NDI. Primary NDI is a rare disorder caused by a defect

Table 2. Causes, Classifications, and Underlying Mechanisms of Polyuria/Polydipsia

Cause	Classification	Mechanism(s)
Acromegaly	Primary polyuria (secondary NDI)	Osmotic diuresis due to diabetes mellitus[28]; interference with action of ADH?[29]
	Primary polyuria (CDI)	Partial CDI?[29]
CDI	Primary polyuria (CDI)	ADH deficiency (partial or complete)
Chronic partial ureteral obstruction	Primary polyuria (secondary NDI)	Down-regulation of aquaporin-2[5]
Chronic renal failure	Primary polyuria (secondary NDI)	Osmotic diuresis; impaired countercurrent mechanism
Diabetes mellitus	Primary polyuria (secondary NDI)	Osmotic diuresis
Diet, drugs, and toxins	Various	Several mechanisms
Fanconi syndrome and other tubulopathies	Primary polyuria (secondary NDI)	Osmotic diuresis
HAC	Primary polyuria (CDI)	Impaired release of ADH[1]
	Primary polyuria (secondary NDI)	Impaired tubule response to ADH[5]
	Primary polydipsia	Psychogenic polydipsia[27]
Hypercalcemia	Primary polyuria (secondary NDI)	Interferes with action of ADH on renal tubule[5]
Hyperthyroidism	Primary polyuria (secondary NDI)	Loss of medullary hypertonicity[1]
	Primary polydipsia?	Psychogenic?[1]
Hypoadrenocorticism	Primary polyuria (secondary NDI)	Loss of medullary hypertonicity
Hypokalemia	Primary polyuria (secondary NDI)	Down-regulation of aquaporin-2[5]; loss of medullary hypertonicity
Hyponatremia	Primary polyuria (secondary NDI)	Loss of medullary hypertonicity[30]
Leiomyosarcoma	Primary polyuria (secondary NDI)	Impaired tubule response to ADH[31,32]
Leptospirosis	Primary polyuria?	CRF, secondary NDI?
Liver failure	Primary polyuria (secondary NDI)	Loss of medullary hypertonicity[7]; impaired hormone metabolism[7]
	Primary polydipsia	Psychogenic polydipsia[7]
Pheochromocytoma	Primary polyuria (secondary NDI)	Excessive catecholamines[1]
Polycythemia	Primary polyuria (CDI)	Impaired release of ADH[33]
	Primary polyuria (secondary NDI)	Action of atrial natriuretic peptide[33]
Polyuric acute renal failure	Primary polyuria (secondary NDI)	Osmotic diuresis
Portosystemic shunt	Primary polyuria (secondary NDI)	Loss of medullary hypertonicity[34]; increased GFR[34]
	Primary polydipsia	Psychogenic polydipsia[18]
Postobstructive diuresis	Primary polyuria (secondary NDI)	Osmotic diuresis; down-regulation of aquaporin-2[5]
Primary hyperaldosteronism	Primary polyuria (CDI)	Impaired release of ADH[35]
	Primary polyuria (secondary NDI)	Impaired tubule response to ADH[35]
Primary NDI	Primary polyuria (primary NDI)	Congenital inability of nephron to respond to ADH[5]
Primary polydipsia	Primary polydipsia	Psychogenic polydipsia[6]; hepatic encephalopathy[7]; hyperthyroidism[1]; gastrointestinal disease[8]
Primary renal glycosuria	Primary polyuria (secondary NDI)	Osmotic diuresis
Pyelonephritis	Primary polyuria (secondary NDI)	Bacterial endotoxin reduces tubular sensitivity to ADH[5]; damaged countercurrent mechanism[1]
Pyometra	Primary polyuria (secondary NDI)	Bacterial endotoxin reduces tubular sensitivity to ADH[5]
Renal medullary solute washout	Primary polyuria (secondary NDI)	Decreased renal medullary tonicity with loss of osmotic gradient
Splenomegaly	Primary polydipsia?	Psychogenic polydipsia?[36]

ADH = antidiuretic hormone, *CDI* = central diabetes insipidus, *CRF* = chronic renal failure, *GFR* = glomerular filtration rate. *NDI* = nephrogenic diabetes insipidus

in the cellular mechanisms that allow the renal tubules to respond to ADH. Patients with primary NDI are unable to concentrate their urine despite adequate blood levels of ADH. Two forms of primary NDI have been described in humans, but there are very few case reports in dogs or cats.[1,4,5]

Secondary NDI encompasses most causes of PU/PD in dogs and cats. In addition, diseases that lead to loss of renal medullary hypertonicity or osmotic diuresis also essentially cause secondary NDI as the loss of the normal concentration gradient interferes with the effects of ADH. Secondary NDI leads to an impaired ability to concentrate urine in the presence of water deprivation and an impaired response to exogenous ADH. Because most causes of PU/PD lead to secondary NDI, the WDT is of little diagnostic value in these patients.

Renal Medullary Solute Washout

Loss of renal medullary solutes (particularly sodium and urea) leads to reduced medullary hypertonicity, which impairs the ability of the nephron to produce concentrated urine. This condition can be secondary to any cause of chronic PU/PD. Additional causes include diuretic therapy and fluid therapy. The presence of renal medullary solute washout can interfere with the results of a WDT or trial therapy for CDI (see Alternatives to the Water Deprivation Test, p. 619). Therefore, a period of gradual water deprivation to restore renal medullary hypertonicity is sometimes recommended before these tests are conducted.[1]

DIAGNOSTIC APPROACH TO POLYURIA/POLYDIPSIA
Signalment

The species, age, breed, and sex of the patient may guide the initial formulation of the differential diagnosis. For example, pyometra is usually a disease of intact females, and elderly cats with PU/PD are most likely to have CRF, diabetes mellitus, or hyperthyroidism.

History

The patient history may reveal changes that suggest specific causes of PU/PD. For example, a dog with HAC may be polyphagic and lethargic. A careful history of the patient's urinary habits should be obtained to distinguish between PU/PD and other abnormalities such as pollakiuria or behavior problems. Polyuric animals may have an increased frequency of urination but produce a large volume of urine with no signs of pain or straining. They may

show nocturia or may urinate inappropriately in the house. A previously continent pet may develop urinary incontinence. It is essential to obtain a complete medication and diet history in a patient exhibiting PU/PD. Medications associated with PU/PD include glucocorticoids, anticonvulsants, and diuretics. Markedly protein-restricted diets can impair renal concentrating ability by depleting renal medullary urea concentrations.

Physical Examination

A complete physical examination may yield findings suggestive of underlying causes of PU/PD. Examples include coat and skin changes, a potbellied appearance, and hepatomegaly in patients with HAC. Enlarged lymph nodes may suggest the presence of neoplasia, which can lead to hypercalcemia.

Urinalysis

Urinalysis should always be close to the top (if not at the top) of the diagnostic plan for the PU/PD patient. It should include pH, USG, sediment examination, and tests for the presence of hemoglobin, protein, glucose, ketones, and bilirubin. It can often be helpful to repeatedly measure USG when evaluating an animal with PU/PD to determine the patient's range of concentrating ability. This information may then be used to rank the diagnostic differentials for PU/PD. However, in many conditions that cause PU/PD, the USG may range between hyposthenuria, isosthenuria, and minimally concentrated, depending on the patient's hydration status and residual urine-concentrating ability.

Complete Blood Count and Serum Chemistry Profile

The complete blood count (CBC) and serum chemistry profile may reveal evidence of infection, inflammation, or disorders such as liver disease, endocrinopathies, hypercalcemia, and renal failure. Abnormalities on either test may allow many diagnostic differentials for PU/PD to be ruled in or out without further testing. However, subtle changes or values that are technically within the normal ranges may also provide diagnostic clues that suggest a direction for further investigation. Examples include low BUN, low-normal albumin, and low mean corpuscular volume in liver failure; high-normal BUN and creatinine, suggesting early or mild CRF; mild polycythemia and high platelets in HAC; and low-normal Na^+ concentration with high-normal serum potassium concentration in hypoadrenocorti-

cism. Clinicians should ensure that serum chemistry profiles are complete and include electrolytes because valuable diagnostic clues can be missed when only partial or abbreviated panels are evaluated. When chemistry or CBC values are borderline or unexpected, the tests should be repeated so that the findings can be verified. For example, a serum total calcium value that is slightly above the normal reference range should never be ignored. If a persistent elevation is noted, ionized calcium should be obtained.

Urine Culture

Urine culture is an essential early step in the evaluation of a patient with PU/PD. Bacterial or fungal pyelonephritis can cause secondary NDI, resulting in PU/PD that may be associated with hyposthenuria.[5,15] It is also important to recognize that many other causes of PU/PD, such as CRF, HAC, or diabetes mellitus, can predispose animals to urinary tract infection. If pyelonephritis is suspected but an initial urine culture has negative results, further tests are indicated, including

repeated urine cultures, abdominal ultrasonography, ultrasound-guided aspiration of the renal pelvis, and excretory urography, as well as possibly a trial course of antibiotics.

Thyroid Hormone Assay

A thyroid hormone assay is essential in any middle-aged or older cat with PU/PD. The total thyroxine (T_4) level should be obtained initially. If this value is normal and hyperthyroidism is still suspected, repeated total T_4 testing, free T_4 testing by equilibrium dialysis, or nuclear scintigraphy is indicated. Hyperthyroidism in dogs is uncommon and is usually associated with a palpable thyroid mass.[16] It is simply ruled out by serum total T_4 testing.

Adrenal Function Testing

The adrenocorticotropic hormone (ACTH) stimulation test is a useful first-line test of adrenal function in canine PU/PD. Although approximately 15% of pituitary-dependent and 40% of adrenal-dependent HAC cases have normal ACTH stimulation test results,[17] this test is very sensitive for the diagnosis of hypoadrenocorticism and is the only adrenal function test that identifies iatrogenic HAC.[1] Because of the limited sensitivity

of the ACTH stimulation test for the diagnosis of naturally occurring HAC, if there is clinical suspicion of this diagnosis from signalment, history, clinical signs, serum chemistry, urinalysis, or CBC results, a ACTH stimulation test with normal results should be followed by a low-dose dexamethasone suppression test.

Bile Acids

Acquired liver failure and congenital portosystemic shunts[7,18] can be associated with PU/PD. Many patients with these disorders have other appropriate historical or clinical findings or clues on a serum chemistry panel (a low BUN, albumin, or cholesterol level), but this is not true in all cases. Therefore, measurement of fasting and postprandial bile acids is indicated in the workup of PU/PD.

Leptospirosis Serology or Polymerase Chain Reaction Testing

Leptospirosis is relatively common in many regions of the United States. Early or mild infection can lead to PU/PD without azotemia.[19,20] The mechanism is not

Dogs with hyperadrenocorticism can have primary polydipsia, primary polyuria, or both.

known, but because the organisms preferentially localize in the kidneys, it may be a form of NDI or a manifestation of early CRF. Leptospirosis may be diagnosed by finding a single high (>1:800) microscopic agglutination test (MAT) titer, by demonstrating a fourfold rise in MAT titer, or by obtaining a positive polymerase chain reaction test result from urine.[20,21] Because delaying the diagnosis of leptospirosis could be harmful to the patient, and because leptospirosis is a zoonotic disease, early testing for leptospirosis is recommended in dogs with PU/PD in appropriate geographic locations.

Imaging Studies

Imaging studies are recommended when the history, physical examination, and diagnostic tests discussed above have not identified the cause of PU/PD. Thoracic and abdominal radiography and abdominal ultrasonography can be used to screen for neoplasia. Contrast studies or ultrasonography may be indicated in the pursuit of specific diagnostic differentials, such as excretory urography for pyelonephritis, ultrasonography to rule out stump pyometra, and adrenal ultrasonography for suspected HAC or pheochromocytoma. Brain imaging may be indicated if

CDI is suspected or diagnosed in an older dog.[12] Abdominal ultrasonography, portography, or rectal scintigraphy is indicated if a portosystemic shunt is suspected.

Assessment of Glomerular Filtration Rate

It is possible for a patient to have CRF without demonstrating azotemia. Loss of approximately 66% of functional renal mass results in loss of concentrating ability, but more than 75% of functional renal mass must be lost before azotemia develops. This is more likely to be a diagnostic problem in dogs because cats maintain enough concentrating ability, despite progressive loss of glomerular filtration rate (GFR), that PU/PD is not noted as a clinical problem. Once CRF progresses in a cat to the point of causing detectable PU/PD, the patient is generally also azotemic. These cases are, therefore, not a diagnostic challenge, and a GFR study is usually not indicated. In contrast, it is not unusual to evaluate a dog for PU/PD and detect only isosthenuria without significantly elevated BUN and creatinine concentrations. Thus a GFR measurement should be considered in a dog that repeatedly and consistently has isosthenuria or minimally concentrated urine for which no other explanation is found. GFR may be assessed by iohexol clearance, exogenous creatinine clearance, or nuclear scintigraphy.[22–24]

Water Deprivation Test

With careful patient selection, the WDT can be a useful tool, but in our opinion, its use is rarely justified. Therefore, the details of the test are not presented here, and interested readers should consult one of the many excellent available references.[1] The purpose of the WDT is to determine whether an animal can produce concentrated urine in response to water deprivation. This depends on the release of endogenous ADH and the ability of the kidneys to respond to ADH. If the patient does not produce concentrated urine, the final part of the WDT involves assessing the response to the administration of exogenous ADH. The WDT should be considered only when the differential diagnosis for PU/PD has been definitively narrowed down to CDI (partial or complete), primary NDI, and primary polydipsia. All causes of secondary NDI should be fully investigated before a WDT is considered. Although the WDT is simple in principle, in practice, there are several challenges involved in conducting this test correctly, and the results are often difficult to interpret. This test can also be dangerous to the patient if conducted incorrectly or if patient selection is inappropriate.

Available Forms of Desmopressin

Tablets—0.1 or 0.2 mg
Nasal solution—0.1 mg/ml (2.5-ml vial and 5-ml bottle); 1.5 mg/ml (2.5-ml bottle)
Parenteral injection—4 µg/ml (1-ml ampule and 10-ml multiple-dose vial)

ALTERNATIVES TO THE WATER DEPRIVATION TEST

In some patients, primary polydipsia can be diagnosed by obtaining several serial USGs and demonstrating the production of concentrated urine on at least some occasions.[25,26] This finding rules out primary polyuria as the cause of the PU/PD and confirms that the patient is capable of normal urine concentration. Because primary polydipsia can be a behavior problem, increased USG may also be noted when the patient's environment is changed (e.g., during hospitalization) and free access to water is provided.

As an alternative to the WDT, a desmopressin (1-desamino-8-D-arginine vasopressin; DDAVP, Aventis) response trial can be used to diagnose CDI.[27] Desmopressin is a synthetic analogue of ADH. The desmopressin response trial should be conducted only when causes of secondary NDI have been ruled out and when the patient can be closely observed. Before starting the trial, the pet owner should establish a baseline by measuring daily water intake for 2 to 3 days. The intranasal preparation of desmopressin is then given into the conjunctival sac (1 to 4 drops twice daily for 5 to 7 days) and the patient monitored for reduction in water intake or increase in USG. This is a logical approach because ultimately, if CDI is diagnosed, it is treated by desmopressin administration.[27] The available forms of desmopressin are listed in the box on this page. If the patient signalment, history, or serum Na+ concentration suggests primary polydipsia, a desmopressin response trial is not recommended due to the potential risk of inducing water intoxication. Results of the desmopressin response trial are interpreted as follows:

- Patients with CDI are expected to show a dramatic reduction in water intake, usually greater than 50%.
- Patients with HAC can show a variety of responses to desmopressin therapy, which can lead to mistakes in diagnosis. We and others[1,27] have noted that some dogs with HAC are able to concentrate their urine in response to water deprivation, suggesting that the polydipsia may be psychogenic; these patients may not produce concen-

trated urine during a desmopressin trial. Poor response to desmopressin in a patient with HAC may also be attributed to secondary NDI associated with glucocorticoid excess.[5] Other patients with HAC may show a partial response to desmopressin, suggesting the diagnosis of partial CDI.[6]

- Failure to concentrate the urine in response to a desmopressin trial occurs in both primary NDI and secondary NDI. The former is rare and only likely in very young animals. In a mature dog or cat, acquired causes of NDI are likely and must be investigated.

If the patient signalment and history are consistent with primary polydipsia, causes of secondary NDI have been fully investigated and ruled out, and serum Na^+ concentration is low or low normal, or the patient has not responded to a desmopressin trial, gradual water deprivation at home may be considered. The client should first be instructed to measure the patient's water consumption over 3 to 4 days and establish the normal daily intake. The water ration at home can then be decreased by 5% per day while food consumption and activity level are kept constant. The patient should be examined by the veterinarian daily, and body weight, USG, and BUN and Na^+ concentrations should be determined. The test should be discontinued if the patient shows any clinical signs of illness, loses 5% or more of body weight, or develops an elevated BUN or Na^+ concentration. If USG increases to 1.030 or greater, the diagnosis of primary polydipsia is confirmed. It must be stressed that this approach should be considered only when all other causes of PU/PD have been

ruled out, when the client is able to closely monitor the pet, and when the veterinarian is prepared to examine the animal daily. Due to the risks associated with water deprivation in a patient with obligate polyuria, this approach cannot be recommended unless it is preceded by a thorough evaluation for causes of primary polyuria, and it is only appropriate for clients who are motivated, well informed, and highly compliant.

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ARTICLE #2 CE TEST CE

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1. Which statement regarding PU/PD is true?
   a. Polyuria can persist in the absence of polydipsia.
   b. Polyuria is defined as urine output greater than 100 ml/kg/day.
   c. PU/PD can be placed on the problem list based on USG measurements and client observations.
   d. Polydipsia can be determined only through measurement of water intake in the hospital.

2. What is the correct definition of isosthenuria?
   a. USG of 1.010
   b. urine with an osmolality equal to that of plasma
   c. urine that is produced by a patient with CRF
   d. urine that is dilute

3. Which statement regarding USG is true?
a. It is best measured using a dipstick.
b. Water should always be withheld from a patient for 2 hours before obtaining urine for specific gravity measurement.
c. Dogs with primary polydipsia are capable of producing urine with a specific gravity of greater than 1.030.
d. High molecular weight particles have a more significant effect on osmolality than specific gravity.

4. CDI can be the result of
a. trauma.
b. congenital defects.
c. neoplasia.
d. all of the above

5. Which of the following are ruled out if the BUN and creatinine concentrations are within normal limits on a chemistry profile?
a. CRF
b. leptospirosis
c. pyelonephritis
d. none of the above

6. PU/PD associated with HAC is due to
a. primary polydipsia.
b. partial CDI.
c. secondary NDI.
d. all of the above

7. Which is not a cause of PU/PD?
a. polycythemia
b. bacterial cystitis
c. splenomegaly
d. portosystemic shunt

8. Which mechanism is proposed to explain PU/PD associated with hyperthyroidism?
a. psychogenic polydipsia
b. elevated cortisol levels
c. concurrent CRF
d. none of the above

9. Which condition is associated with down-regulation of aquaporin-2 water channels?
a. chronic partial ureteral obstruction
b. postobstructive diuresis
c. hypokalemia
d. all of the above

10. Which statement regarding the desmopressin response trial is true?
a. A desmopressin trial can be used to diagnose HAC.
b. The desmopressin response trial reliably distinguishes between primary and secondary NDI.
c. Desmopressin is only effective if given intravenously.
d. Patients with primary polydipsia are theoretically at risk for water intoxication during a desmopressin response trial.