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**DIAGNOSIS OF POLYURIA/POLYDIPSIA: CASE-BASED APPROACH**

Ellen N. Behrend, VMD, PhD, Diplomate ACVIM  
Auburn University  
Auburn, AL

**CASE 1**

**Signalment:** 12 year-old, castrated male mixed breed dog  
**History:** Polyuria/polydipsia past few weeks; having accidents in the house. Lives in Alabama. Mainly indoors. Up-to-date on vaccines and heartworm preventive. No travel history.  
**Physical examination:** Obese  
**Laboratory data:** Complete CBC, profile, urinalysis done. 
Abnormalities were: Calcium (mEq/L) 11.8 (9.0-11.2); urine specific gravity = 1.009 with 1-2 WBC/hpf and 2-3 RBC/hpf

**What is Polyuria/Polydipsia?**  
Polyuria has been defined as urine production > 45 ml/kg/24 hr in dogs and 40 ml/kg/24 hr in cats.¹ Polydipsia has been defined as water consumption > 100 ml/kg/24 hr in dogs and cats² but some difference may exist between species and another definition given is > 90 ml/kg/24 hr in dogs and > 45 ml/kg/24 hr in cats.¹ Values below these, however, may still be consistent with such a diagnosis. Other factors also need to be considered when deciding if polyuria/polydipsia are present. Animals that eat canned food drink less than those that eat dry food. Also, normal habits should be assessed. For example, even if water consumption is below 90-100 ml/kg/24 hr in a particular dog, if this is more than twice normal for that pet, a diagnosis of pu/pd may be warranted.

If any doubt exists as to whether polyuria/polydipsia (pu/pd) is present, its presence should be verified. To verify the diagnosis of pu/pd, water intake should be quantitated at home, as hospitalization can alter drinking habits. Urine specific gravity (USG) assessment may also be helpful. If USG is >1.015, it is unlikely that pu/pd is present. A USG showing maximal renal concentrating ability (>1.030 in dogs, >1.035 in cats) rules out the possibility of pu/pd.¹ If the USG is >1.030 and the owner believes the patient is polyuric, the history should be re-evaluated to make sure the problem is not dysuria, incontinence or a behavioral problem.³

**What are the Causes of Polyuria/Polydipsia?**  
To answer that question, understanding of the mechanisms regulating thirst and urine production is helpful. Anti-diuretic hormone (ADH) is released from the posterior pituitary, with the main function of causing water retention. Without ADH, dilute urine is excreted. When ADH is present, pores open in the membranes of the collecting ducts allowing passive movement of water from the hypotonic tubule lumen to the hypertonic medullary interstitium and concentrated urine is produced.⁴ Since reabsorption of water in this part of the nephron is passive, the osmotic force responsible, i.e. the concentrated renal medullary interstitium, is crucial.

The main stimulus to ADH release is increased extracellular fluid (ECF) osmolality. Below 280 mOsm/kg, serum ADH concentration is very low to non-detectable. Above this point, even a 1% increase in ECF osmolality stimulates ADH secretion. Maximal ADH secretion occurs at an ECF osmolality of 320 mOsm/kg. Anti-diuretic hormone is also released in response to a 10% decrease in circulating blood volume.⁴

Thirst is controlled similarly with major input from ECF osmolality and lesser input from blood volume changes. Hyperthermia, pain, emotion and certain drugs also increase thirst.

Production of concentrated urine has 3 requirements:
1. Adequate serum ADH concentration and the ability of the kidneys to respond to ADH. 2. Function of at least 33% of total nephron number, i.e. when >2/3 of the nephrons are lost, urine concentrating ability is lost. 3. A concentrated renal medullary interstitium.

Causes of pu/pd can be divided into those causing primary polydipsia vs. those causing primary polyuria (see Table).⁴ Primary polyuria is divided into the categories of osmotic diuresis, central diabetes insipidus (CDI), primary nephrogenic diabetes insipidus (NDI) and secondary NDI.⁴ CDI is caused by lack of ADH. In NDI, the kidneys’ ability to respond to ADH is compromised. In primary NDI, the problem is intrinsic to the kidneys. With secondary NDI, a non-renal problem interferes with the kidneys’ response to ADH.⁴

A complete history and physical examination should never be underestimated as an important tool for diagnosis of any disease. For pu/pd, the presence of post-obstructive diuresis or drug administration as a cause can be ruled out on the basis of history. Medications that can cause pu/pd include corticosteroids, phenobarbital, and diuretics. In dogs, use of progestins can lead to acromegaly. The owner should also be asked about any recent diet changes since the water content in food is an important water source and low protein diets can lead to low renal medullary tonicity.³ Questions specific to possible differential diagnoses should also be asked.

A CBC, biochemical profile and urinalysis alone can rule out a number of differential diagnoses. If the cause for pu/pd remains unknown after the minimum database has been performed, a urine culture should be submitted regardless of the urine sediment exam to determine if occult pyelonephritis is present. Pyelonephritis is not always accompanied by fever and perinephric pain, and in dilute urine, the sediment exam can be misleading. If the cause is then still not apparent, hyperadrenocorticism should be ruled out in dogs by use of an ACTH stimulation test or low-dose dexamethasone suppression test.⁴,⁵ Pu/pd may be the only clinical sign present.

**Case Summary:** Ionized calcium was measured and was normal. Urine culture was submitted and an E. coli grew (>100,000 cfu/ml). Dog placed on appropriate antibiotic for 4 weeks. Culture performed 1 week after starting antibiotics and 1 week after antibiotic therapy stopped. Both negative. Pu/pd resolved. Plan: Reculture urine 4 weeks later.

**Case 1 Table**

<table>
<thead>
<tr>
<th>Causes of polyuria/polydipsia</th>
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<tbody>
<tr>
<td><strong>Primary Polydipsia</strong></td>
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<tr>
<td>Psychogenic polydipsia</td>
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<tr>
<td>Liver disease</td>
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<tr>
<td>Neurological disease</td>
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<tr>
<td><strong>Primary Polyuria</strong></td>
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<tr>
<td>Osmotic diuresis</td>
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<tr>
<td>Chronic renal failure</td>
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<tr>
<td>Diabetes mellitus</td>
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<tr>
<td>Primary renal glycosuria</td>
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</tbody>
</table>
**Postobstructive diuresis**  
**Central diabetes insipidus**  
**Primary nephrogenic diabetes insipidus**  
**Secondary nephrogenic diabetes insipidus**

- Acromegaly  
- Drug administration  
- Liver disease  
- Hyperadrenocorticism  
- Hypercalcemia  
- Hyperthyroidism  
- Hypoadrenocorticism  
- Hypokalemia  
- Hyponatremia  
- Pyelonephritis  
- Pyometra  
- Very low protein diet  

CASE 2  
**Signalment:** 12-year-old, castrated male mixed breed dog  
**History:** Polyuria/polydipsia past few weeks. Mainly indoors. Up-to-date on vaccines and heartworm preventive.  
**Physical examination:** Normal.  
**Laboratory data:** Complete CBC, profile, urinalysis done.  
Abnormalities were: neutrophils 12.5 x 10^3/µL (3.0-11.5); lymphocytes 0.7 x 10^3/µL (1.0-4.8); ALT: 130 IU/L (10-120); ALP: 322 IU/L (11-210); urine specific gravity = 1.011 with inactive sediment; protein 1+. Urine culture negative.  

As with any other diagnostic work-up, look for the more likely and more common causes first before moving on to less likely diseases. In dogs, the 3 most common causes of pu/pd are renal failure, hyperadrenocorticism (HAC) and diabetes mellitus. In cats, the 3 most common causes are renal failure, diabetes mellitus and hyperthyroidism.  
Trying to diagnose psychogenic polydipsia, CDI or primary NDI should be the LAST step in a diagnostic work-up for polyuria/polydipsia. First, psychogenic polydipsia, CDI and primary NDI are uncommon. Second, results of the modified water deprivation test (MWDT), a test that can be performed to differentiate these three conditions, can be interpreted incorrectly if all secondary NDI causes have not been ruled out first. Secondary NDI can look like primary NDI or partial CDI with respect to results of the MWDT. Last, the MWDT is a time-consuming and potentially expensive test to perform.  
In this case, serum ALP activity is not very high and no other signs of hyperadrenocorticism (HAC) besides pu/pd is obviously present. However, Cushing’s needs to be tested for. Approximately 10% of dogs with HAC have a normal serum ALP activity. In addition, about 66% have proteinuria and/or hypertension. This dog may be proteinuric (1+ protein on urinalysis; a urine protein/creatinine (UPC) ratio is needed to quantify) and blood pressure should be measured. Even if the only abnormality identified (with measurement of liver enzyme activity, UPC, blood pressure, etc) were pu/pd, HAC should still be tested for. In cases such as these, the ACTH stimulation test is preferred.  
Assessment of hepatic function via measurement of bile acids is not indicated in this case given the (lack of) clinical signs and laboratory findings. However, if liver function is at all questionable or liver enzymes (ALT and/or ALP) are moderately to severely increased then bile acids should be measured before an MWDT is performed.  
**Case Summary:** An ACTH stimulation test was performed. Serum cortisol concentration pre-ACTH was 224 nmol/L (reference range 10-160 nmol/L; 8.1 µg/dL reference range 1-5 mcg/dl) and post-ACTH was 832 nmol/L (reference range 220-560 nmol/L; 30.1 µg/dL reference range 8-20 µg/dL). Systolic blood pressure was 190 mm Hg. UPC was 3.4. A diagnosis of HAC was made.  

CASE 3  
**Signalment:** 4 year-old, FS, Standard Poodle  
**History:** Recurrent vomiting/diarrhea past 1-2 mth. Treated with fluids and antibiotics and always got better but then relapsed. Past 2 days anorectic, vomiting ~8X/day.  
**Physical examination:** Thin, 5% dehydrated  
**Laboratory data:** Complete CBC, profile, urinalysis done.  
Abnormalities were: Hematocrit 35% (37-55); BUN: 50 mg/dl (7-28); Creatinine: 2.0 mg/dl (0.9-1.7); Albumin: 4.7 g/dl (2.7-4.5); Na: 128 mEq/L (145-158); K: 6.2 mEq/L (4.1-5.5); Cl: 95 mEq/L (106-127); Total CO2: 12 mEq/L (14-27); urine specific gravity = 1.015 with inactive sediment.  

The most likely differentials for this dog are hypoadrenocorticism and/or renal failure. Care should be taken in evaluating USG in azotemic patients in which a cause for pu/pd other than renal failure may also be present. A combination of inadequately concentrated urine and azotemia does not necessarily denote renal disease. Any cause of CDI or primary or secondary NDI can prevent the kidneys from concentrating urine in the face of prerenal causes of azotemia such as dehydration. If the cause for pu/pd is corrected, the azotemia will resolve if the kidneys are normal.  
**Case Summary:** An ACTH stimulation test was performed. Serum cortisol concentration pre-ACTH was <14 nmol/L (reference range 14-160 nmol/L; <0.5 µg/dL, reference range 1-5 mcg/dl) and post-ACTH was <14 nmol/L (reference range 220-560 nmol/L; <0.5 µg/dL, reference range 8-20 µg/dL). A diagnosis of hypoadrenocorticism was made and therapy initiated with DOCP and prednisone. At recheck one month after stabilization, serum Na, K, BUN and creatinine concentrations were normal and the USG was 1.032.  

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CASE 4

Signalment: 8 yr old FS yellow Labrador

History: For the past 2 weeks she has been lethargic and
has had a decreased appetite. Over the past month, she
has had some accidents in the house.

Physical examination: normal

Laboratory data: Complete CBC, profile, urinalysis done.
No abnormalities on bloodwork. Urine specific gravity =
1.004 with inactive sediment. Urine culture negative.
ACTH stimulation test normal.

Now is the time to do an MWDT. If the decision is made to
perform a MWDT, decrease the patient’s water consumption
slowly e.g. 120 ml/kg/day 72 hrs prior to the test, then 90
ml/kg/day 48 hrs prior and then 60-80 ml/kg/day for the last
24 hours.4  Prolonged pu/pd leads to renal medullary
washout, and this gradual decrease allows for
reconcentration of the renal medulla. The patient should be
watched carefully during this time for dehydration.

When the test begins, stop all access to water. At this
date the patient needs to be monitored carefully as
dehydration can occur quickly. Empty the bladder and obtain
an exact body weight. Measure USG and, if possible, a urine
and serum osmolality. A BUN should be measured and
hydration status assessed.4  Do not do an MWDT if azotemia,
dehydration, hypercalcemia or significant systemic disease is
present. During the test, empty the bladder every 60-120
minutes and measure USG and, if possible, urine osmolality.
Assess body weight and hydration hourly. Measurement of
serum osmolality periodically is ideal but not always
available.4

An endpoint to the test is reached when: USG is >1.030 in
dogs or 1.035 in cats; the patient is clinically dehydrated,
azotemic or appears ill; the serum osmolality is 320
mOsm/kg; or there is a loss of 5% of body weight.4  There is
no specific time limit to this test, and in patients with mild
pu/pd, an MWDT can take longer than 12 hours. If the
endpoint has not been reached when the clinic is closing, the
patient can be transferred to an overnight facility for
continuation of the MWDT, or the animal can be provided
with a maintenance water amount (2.75 ml/kg per hour that
the animal is unobserved). The next morning, the patient
should be weighed, the USG measured, the water withdrawn
and the test continued until an endpoint is reached.3

If the patient has concentrated adequately at the endpoint,
the diagnosis is psychogenic polydipsia. If there is
inadequate concentration, the bladder is emptied, water is
still withheld and aqueous ADH administered (0.55 U/kg IM
with a maximum of 5 U per dog or cat). The bladder is then
emptied every 30 minutes for 1-2 hours.4  Alternatively 10 to
20 µg of the sterile preparation of desmopressin acetate
(DDAVP, Rhone-Poulenc Rorer), a synthetic vasopressin
an analogue, can be given intravenously or 20 µg of DDAVP
(approximately 4 drops of the 100 µg/ml intranasal
preparation) can be administered into the conjunctival sac.6
Measurement of USG or urine osmolality should occur every
2 hours for 8 hours and then at 12 and 24 hours. The
maximal response to intravenous desmopressin usually
occurs 4 to 8 hours after administration, but it may take up to
24 hours.3  If adequate concentration occurs
(i.e. USG > 1.018 or urine osmolality increases at least fivefold),
the diagnosis is CDI. If urine still remains unconcentrated, the diagnosis is NDI.

CDI can be differentiated into partial, where ADH release is
subnormal but still present, and complete where no ADH
release occurs. In an MWDT, those with partial CDI show
some concentrating ability in response to absolute water
deprivation and then increase another 10-50% in response to
administration of exogenous ADH. Those with complete CDI
will not concentrate in response to dehydration but will when
given exogenous ADH.3,7

CDI can be congenital, idiopathic or due to trauma or
inflammation or a pituitary tumor. In a dog >6 years old, the
most common cause of CDI, either partial or complete, is a
pituitary tumor. Even if neurological signs are absent,
diagnostic imaging is warranted.7

An option to the MWDT when psychogenic polydipsia, CDI
and primary NDI remain as the only possible differential
diagnoses is to evaluate response to DDAVP therapy. In
some clinics this has become the test of choice as compared
to the MWDT for differentiating these three causes of pu/pd.

The patient’s 24-hour water intake for 2-3 days is
measured allowing free-choice water. A urine sample is
collected at a given time each day to check urine osmolality
and USG. After these initial days, the patient is treated with
DDAVP by administering the intranasal preparation
(1-4 drops placed in conjunctival sac) or the oral tablets
(0.1 mg) every 12 hours for 5-7 days.6  Water intake is
monitored and a urine sample obtained on the 5th to 7th day at
the same time of day as before treatment. A dramatic
reduction in water intake and/or increase in urine
concentration (i.e. >50%) provides strong evidence for CDI.
Moderate response is consistent with partial CDI.4  A mild
response is suggestive of psychogenic polydipsia. If no
response is seen, NDI is present.

Case Summary: An MWDT was performed and complete
CDI diagnosed. A CT scan of the brain was normal.
Therapy with DDAVP was initiated. After a few months, the
medication costs were decided to be too much. The dog
remained outside during the day when the owners were not
at home. Plenty of fresh water was available at all times.
She was brought inside at night and given a dose of DDAVP.

References available from author upon request.