Polyuria (PU) and polydipsia (PD) are common presenting complaints in small animal practice, and although the owner may only observe or report PU or PD, they always occur together. It is important to have a logical and practical diagnostic approach to PU/PD because there are a multitude of congenital and acquired causes. These causes are divided into two broad categories, primary polydipsia with resultant polyuria and primary polyuria with compensatory polydipsia. It is not possible clinically to distinguish between primary polydipsia and primary polyuria, and with some conditions both are contributing.

Primary polydipsia can be a physiologic response (increased environmental temperature, dry food diet), the result of a behavioral disorder (historically referred to as psychogenic water drinking), or associated with other medical conditions (hyperthyroidism, fever, pain, gastrointestinal disease, hepatoencephalopathy). Behavioral polydipsia is an uncommon cause of PU/PD in the dog (rare in the cat) and is a diagnosis of exclusion.

The production of concentrated urine is dependent on three mechanisms: the ability to make and secrete anti-diuretic hormone (ADH), functional kidneys that are able to respond to ADH, and the presence of an osmotic gradient in the renal medulla. Primary polyuria is the result of dysfunction or failure of one of these mechanisms and is divided into central diabetes insipidus (rare disorder caused by partial or complete deficiency of ADH), primary nephrogenic diabetes insipidus (very rare congenital disorder caused by an inability of the kidney to respond to ADH), and secondary nephrogenic diabetes insipidus (most common cause of PU/PD that encompasses many conditions). We rarely use the term secondary or acquired nephrogenic diabetes to describe the clinical condition but rather use the name of the primary disease process or condition that is causing PU/PD. The acquired inability to respond to ADH is either related to loss of the osmotic gradient in the renal medulla or a process or substance that interferes with the action of ADH in the kidney.

The evaluation of a patient with the primary complaint of PU/PD should begin with a critical assessment of the signalment and history and a thorough physical examination. Although water quantification may provide useful information, it is important to recognize that pet owners may observe an increase in water intake before the volume of water consumed is in a range that is considered excessive (80 – 100 ml/kg/day).

**Signalment**
The three most common causes of PU/PD occur in middle-aged to older dogs (chronic kidney disease, hyperadrenocorticism, diabetes mellitus). Three common diseases of older cats (chronic kidney disease, hyperthyroidism, diabetes mellitus) are the most common causes of PU/PD in this species. Behavioral primary polydipsia more commonly occurs in young, medium to large-breed, working dogs with high anxiety and/or insufficient exercise/activity. Pyometra should be considered in any intact female dog.

**History**
Confirm the presence of polyuria rather than pollakiuria or dysuria (urine specific gravity will provide further evidence/support) and determine if an increase in water intake has been observed. Determine if the animal has the need to urinate at night, has inappropriate voiding, and/or a recent onset or worsening
of urinary incontinence. Determine if there are other clinical signs that help to identify the primary disease process. Rule out iatrogenic causes and drug administration.

**Physical examination**
Supportive evidence for a number of the more common causes of PU/PD can be obtained with a complete and thorough physical examination. Weight loss and decreased lean muscle mass - chronic kidney disease, diabetes mellitus (presence of cataracts in dogs provides additional support), hyperthyroidism (thyroid nodule/slip provides additional support); weight gain, potbellied appearance, hepatomegaly, symmetrical alopecia - hyperadrenocorticism; vulvar changes and vaginal discharge - pyometra in intact female dogs; perianal mass - apocrine gland anal sac adenocarcinoma (AGASACA); peripheral lymphadenopathy - lymphoma.

The initial diagnostic testing should be easy to perform and interpret, provide the most information, and be safe for the patient. Typically, this is going to consist of a complete blood count, biochemistry profile, urinalysis, and total T₄ concentration (cats). This combination of tests will rule out (or support) the most common causes of PU/PD in dogs and cats.

**Complete blood count**
Unremarkable / not very helpful in most cases. Exceptions include findings consistent with leukemia or polycythemia.

**Biochemistry profile**
Renal disease (increased BUN, creatinine, SDMA); diabetes mellitus (hyperglycemia); lymphoma, AGASACA, hyperparathyroidism (hypercalcemia); hypoadrenocorticism (hyponatremia, hyperkalemia, increased BUN and creatinine); hyperadrenocorticism (increased ALP +/- increased ALT, hypercholesterolemia); liver disease / portosystemic shunt (decreased BUN, albumin, glucose, and/or cholesterol).

**Urinalysis**
Documentation of isosthenuria (USG 1.008 – 1.012), hyposthenuria (USG < 1.008), or glucosuria supports the existence of polyuria. If the urine is concentrated (USG > 1.025 – 1.035) without the presence of glucose, it is likely that the observed urinary tract signs are related to lower urinary tract disease rather than polyuria. It can be helpful to have the owner collect urine samples randomly (especially an early morning sample if the dog does not have access to water overnight) over multiple days. Documentation of a USG > 1.025 (without glucose) on any urine sample confirms concentrating ability. Presence of glucosuria supports diabetes mellitus (if concurrent hyperglycemia) or renal tubular disorders.

<table>
<thead>
<tr>
<th>Common Causes of PU/PD</th>
<th>Method of Confirmation</th>
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<tbody>
<tr>
<td>Kidney disease; Pyelonephritis</td>
<td>Biochemistry profile, SDMA</td>
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<tr>
<td></td>
<td>Urinalysis</td>
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<td></td>
<td>Urine culture</td>
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<td>Abdominal ultrasound</td>
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<td>GFR measurement</td>
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### Additional Testing

Should be performed as needed and targeted based on the examination findings and results of the CBC, biochemistry profile, and urinalysis.

- Body cavity imaging (radiographs and ultrasound)
- Testing for hyperadrenocorticism
- Testing for hypoadrenocorticism
- Assessment of liver function
- Assessment of glomerular filtration rate - iohexol clearance test

The vast majority of dogs and cats presented for PU/PD will have one of the above conditions identified during the initial evaluation or follow-up testing. If it is not possible to determine the cause of PU/PD and dilute urine has been confirmed, it is reasonable to suspect that the animal may have primary polydipsia or central diabetes insipidus. One can use serum osmolality to help differentiate central diabetes insipidus from primary polydipsia. The serum osmolality should be high-normal or increased with central diabetes insipidus because the animal is drinking excessively in an attempt to replace a free water deficit due to excessive urination. With primary polydipsia, the serum osmolality would be expected to be low-normal or decreased because excessive water intake leads to dilution and increased urine production. It is at this
stage (after a complete and thorough evaluation) that a DDAVP (synthetic ADH) trial is acceptable. It is recommended that tablets rather than nasal drops in the conjunctival sac be used. The recommended initial dose of DDAVP is 0.05 mg for dogs weighing < 5 kg and cats, 0.1 mg for dogs weighing 5 – 20 kg, and 0.2 mg for dogs weighing > 20 kg given every 12 hours. If an inadequate response is observed, the dosing frequency should be increased to every 8 hours. If a treatment response is observed, the DDAVP dose or frequency or both can be decreased to the minimum dose necessary to control the PU/PD.

**References**

References available upon request.

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**It Has to Be Cushing’s: Approach to Confirming A Diagnosis of Hyperadrenocorticism (HAC)**

**Screening Tests** (Figure 1)

**Basal or Resting Cortisol Concentration**
- No diagnostic value for HAC

**Urine cortisol to creatinine ratio (UCCR)**
- Most commonly used to rule out HAC when there is a low index of suspicion
- False-positive results are common because stress/non-adrenal illness can cause an increase in the UCCR
- Recommend performing a low-dose dexamethasone suppression test or ACTH stimulation test after obtaining a positive UCCR because of the lack of specificity (high risk of false positive results)
- Protocol:
  - Client/owner collects a urine sample at home. Urine should not be collected in the hospital or within 48-72 hours of a clinic/hospital visit because the stress of a clinic/hospital visit has been shown to increase the UCCR and increases the possibility of a false-positive result.
    - Typically recommend first urination in the morning
    - Using pooled samples (3 consecutive days) may provide a more representative result
- Interpretation:
  - Normal ratio (below the laboratory cut-off)—HAC is very unlikely
  - Abnormal ratio (above the laboratory cut-off)—recommend performing another screening test (low-dose dexamethasone suppression test or ACTH stimulation test) to confirm HAC prior to initiating therapy
**Low-dose Dexamethasone Suppression Test (LDDS)**

- Highly sensitive test
- Increased risk of false-positive result with non-adrenal illness than ACTH stimulation test (not a significant concern if screening an appropriate population)
- Can also serve as a differentiating test if positive and criteria for pituitary dependent HAC is met

**Protocol:**

- Collect baseline blood sample
- Administer 0.01-0.015 mg/kg of dexamethasone or dexamethasone SP intravenously (preferred) or intramuscularly
- Collect blood samples at 4 and 8 hours after the administration of dexamethasone

**Interpretation:**

- Normal dog- complete suppression at 4 and 8 hours
- Consistent with HAC- lack of suppression at 4 and/or 8 hours
  - Lack of suppression does NOT confirm the presence of a functional adrenal tumor (FAT).
- Consistent with pituitary dependent hyperadrenocorticism (PDH)
  - Suppression at 4 hours with an escape at 8 hours
  - Suppression at 4 and/or 8 hours to less than 50% of the baseline cortisol concentration
  - Lack of suppression at 4 hours with suppression at 8 hours (inverse pattern)

**ACTH Stimulation Test**

- Less sensitive test than LDDS test
- Less risk of false-positive result than LDDS test
- Only test that can diagnose iatrogenic HAC

**Protocol:**

- Obtain baseline blood sample
- Administer synthetic ACTH (cosyntropin or tetracosactrin) intravenously at a dose of 5 μg/kg (maximum dose 250 μg/dog)
- Obtain blood sample 1 hour after administering ACTH (post-ACTH). Some clinicians also collect a 2-hour post-ACTH sample in order not to miss (get a false-negative result) the small percentage of dogs that have peak cortisol secretion after 2 hours rather than 1 hour.

**Interpretation:**

- Normal dog- post ACTH cortisol concentration below the laboratory cut-off
- Consistent with HAC- post ACTH cortisol concentration above the laboratory cut-off
Figure 1. The author’s approach to screening for HAC. The decision to perform additional screening tests following a negative LDDS test is based on the degree of clinical suspicion. In situations of high clinical suspicion, it is important to remember that no screening test is perfect. It may be necessary to perform multiple screening tests or repeat testing at a later date in order to confirm the diagnosis in early or more challenging cases.

Differentiating Tests (Figure 2)

High-dose Dexamethasone Suppression Test

- Protocol (same as LDDS test but with higher dose of dexamethasone):
  - Collect baseline blood sample
  - Administer 0.1 mg/kg of dexamethasone or dexamethasone SP intravenously (preferred) or intramuscularly
  - Collect blood samples at 4 and 8 hours after the administration of dexamethasone

- Results can support the presence of PDH
- Results CANNOT confirm the presence of FAT
- Interpretation:
• Consistent with PDH
  ▪ Complete suppression at 4 and/or 8 hours
  ▪ Cortisol concentrations less than 50% of baseline concentration at 4 and/or 8 hours
• Lack of suppression does not confirm the presence of a FAT.

Endogenous ACTH Concentration

• Single blood sample
• Immediately centrifuge and separate plasma from cells and freeze until shipping. Ship overnight on ice. This will minimize the amount of degradation, which is a concern with inappropriate sample handling.
• Possible to confirm PDH or FAT
• Interpretation:
  o Consistent with PDH- ACTH concentration is normal or increased
  o Consistent with presence of a FAT- ACTH is low or undetectable

Ultrasonography

• Evaluate size and appearance of adrenal glands
• Can confirm presence of an adrenal tumor
• Aid in the detection of concurrent illness

Occult Hyperadrenocorticism

• Historically known as “atypical hyperadrenocorticism”
• Clinical signs, physical examination findings, and clinicopathologic findings support a diagnosis of HAC, but the UCCR, LDSS test, and ACTH stimulation test fail to support
• It has NOT been proven that sex hormones are responsible for this syndrome.
• Reasons to suspect Occult HAC
  o Clinical signs consistent with HAC
  o Screening tests do not support
• Presence of an adrenal tumor supports the diagnosis
  o Lack of tumor does not rule out diagnosis
• If clinical signs are mild, retest for classical HAC when signs worsen
• If clinical signs are moderate/severe, perform an abdominal ultrasound
  o Normal adrenal glands- reconsider diagnosis
  o Bilateral adrenomegaly- consider confirming PDH with cross-sectional imaging
• May be mild or early HAC
• May be food-dependent HAC (considered rare)
• Specificity of sex hormone panel is low- interpret with caution
Figure 2. The author’s approach to differentiating PDH from FAT. The author believes it is important to confirm FAT with ultrasound and endogenous ACTH prior to surgery because asymmetric adrenal gland enlargement and nodular hyperplasia is not uncommon with PDH.

References