UNDERSTANDING THE POLYURIC/POLYDIPSIC ANIMAL

Bradley Galgut, BVSc, DACVP
Director, Specialist Veterinary Clinical Pathologist
ASAP Laboratory

Polyuria (PU) and polydipsia (PD) are common presenting complaints in small animal practice. It is important to understand the physiology of water metabolism in order to understand why the animal is drinking and urinating excessively. A methodical, systematic approach to these cases should allow the clinician to determine the cause of the PU/PD and therefore manage/treat the animal appropriately.

Physiology of water metabolism

Water consumption and urine production are controlled by interactions between plasma osmolality, intravascular fluid volume, the thirst centre, the kidneys, the pituitary gland, and the hypothalamus. Imbalance or dysfunction in any of these can result in dyshomeostasis of water metabolism, PU, and usually compensatory PD. The exception is psychogenic polydipsia (primary polydipsia) where the polyuria is secondary and appropriate (at least initially).

In health, the osmolality of the plasma and therefore the ultrafiltrate passing through the glomeruli is about 300 mmol/kg. Approximately 75 % of the water that is filtered by the glomerulus is passively reabsorbed in the proximal tubule of the nephron via osmotic forces coupled to the reabsorption of sodium and glucose. The descending limb of the loop of Henle traverses down into the medulla through regions of increasing interstitial osmolality. Sodium, chloride and urea are the major solutes contributing to this interstitial osmolality. The descending limb is permeable to water allowing its passive movement out of the nephron into the interstitium, such that the tubular fluid at the bottom of the descending limb is highly concentrated (osmolality >1500 mmol/kg in dogs; >2400 mmol/kg in cats). The ascending limb is impermeable to water. As the tubular fluid moves up the ascending limb, solutes (primarily sodium and chloride) are actively removed (contributing to the high medullary interstitial osmolality) resulting in dilute tubular fluid at the top of the loop of Henle (~100 mmol/kg). The distal tubule/collecting ducts of the nephron descend back down through the medullary interstitium of increasing osmolality. This segment of the nephron is impermeable to water in its resting state, and it is here that antidiuretic hormone (ADH; vasopressin) plays a crucial role. ADH is synthesised in the hypothalamus and secreted from the posterior pituitary gland. It interacts with its receptors on the cells in the distal tubules and collecting ducts to increase water permeability. In the presence of ADH water leaves the tubular fluid osmotically, allowing the average dog or cat to concentrate its urine to well above 2000 mmol/kg.

The major stimuli for ADH release are 1) increasing plasma osmolality and 2) hypovolaemia, both of which are associated with dehydration. The action of ADH allows the body to conserve water to help lower plasma osmolality and increase plasma volume. If the body cannot produce ADH (central diabetes insipidus) or the distal renal tubular cells cannot respond to ADH (nephrogenic diabetes insipidus) the hypotonic filtrate from the top of the ascending limb passes unmodified through the distal tubule and collecting duct resulting in excretion of large volumes of dilute urine.

Central diabetes insipidus (CDI) may result from any condition that damages the neurohypophyseal system. In most cases it is idiopathic; however, CDI can occur as a consequence of trauma, neoplasia, inflammatory disease or pituitary malformation.

Nephrogenic diabetes insipidus (NDI) can be primary or acquired/secondary. Primary NDI is extremely rare; however, secondary/acquired NDI is very common. Secondary NDI refers to a group of renal and extra-renal diseases in which ADH is present but the renal tubules are not responsive to it. This group includes hypercalcaemia, canine pyometra (presumably due to the effect of bacterial toxins), hepatic insufficiency/failure, hypercortisolaemia, phenobarbitone therapy, and hypokalaemia.

Solute diuresis occurs when poorly-resorbable solutes (e.g. glucose, mannitol) are present in excess in the tubular fluid. This results in a reduced osmotic gradient between the tubular fluid and medullary interstitium and water resorption is therefore diminished. An abnormally increased volume of fluid reaches the distal tubules and can overwhelm the capacity to resorb water, even in the presence of maximal ADH secretion and functional ADH receptors.

A reduced osmotic gradient between the filtrate and the medullary interstitium can also occur if there is prolonged hyponatraemia, hypochloraemia and/or low urea. Low plasma concentrations of these substances results in reduced tubular fluid concentrations and consequently reduced resorption of these substances to maintain interstitial osmolality. This mechanism contributes to the polyuria seen in dogs with hypoadrenocorticism and hepatic insufficiency.

Key points:
The osmolality of plasma and therefore the glomerular ultrafiltrate is ~300mmol/kg.

For the kidneys to concentrate the filtrate:
1. ADH must be present
2. The epithelial cells of the distal nephron must be responsive to ADH
3. There must be a concentration gradient between the tubular fluid and the interstitium (osmolality of the interstitium > osmolality of the tubular fluid).

For the kidneys to dilute the filtrate:
1. Na^+ and Cl^- must be actively transported from the tubular fluid to the interstitium in the ascending limb of the loop of Henle (i.e. the ascending limb MUST be functional).
2. Very little/no water is removed from the tubular fluid in the distal nephron.

Isosthenuria is the term used when the urine osmolality approximates the plasma osmolality. In most domestic mammals isosthenuric urine typically has a urine specific gravity (USG) of 1.007-1.013. Isosthenuria implies that the kidneys have not concentrated nor diluted the urine.

Diagnostic approach to polyuria/polydipsia

To avoid unnecessary diagnostic testing, it is important to confirm from the outset that polyuria/polydipsia is present. A careful clinical history must be obtained to distinguish 'inappropriate' urination (pollakiuria, stranguria, haematuria etc) from polyuria. At the time the initial appointment is made, the owner should be encouraged to catch a urine sample from their pet at home (or multiple over a period of time) and bring it along to the consultation, as well as monitoring water consumption over several days. If the USG is >1.025 and there is no glucose on dipstick analysis, it is unlikely that the animal is polyuric and lower urinary tract disease (infection, urolithiasis, neoplasia etc) or incontinence should be suspected as the cause of inappropriate urination. Polyuric animals are also polydipsic and 24-hour water consumption >100 ml/kg (canine) is expected. In cats, references vary regarding the definition of polydipsia, with some quoting 24 hour water consumption >100 ml/kg and others quoting values of >45 ml/kg.

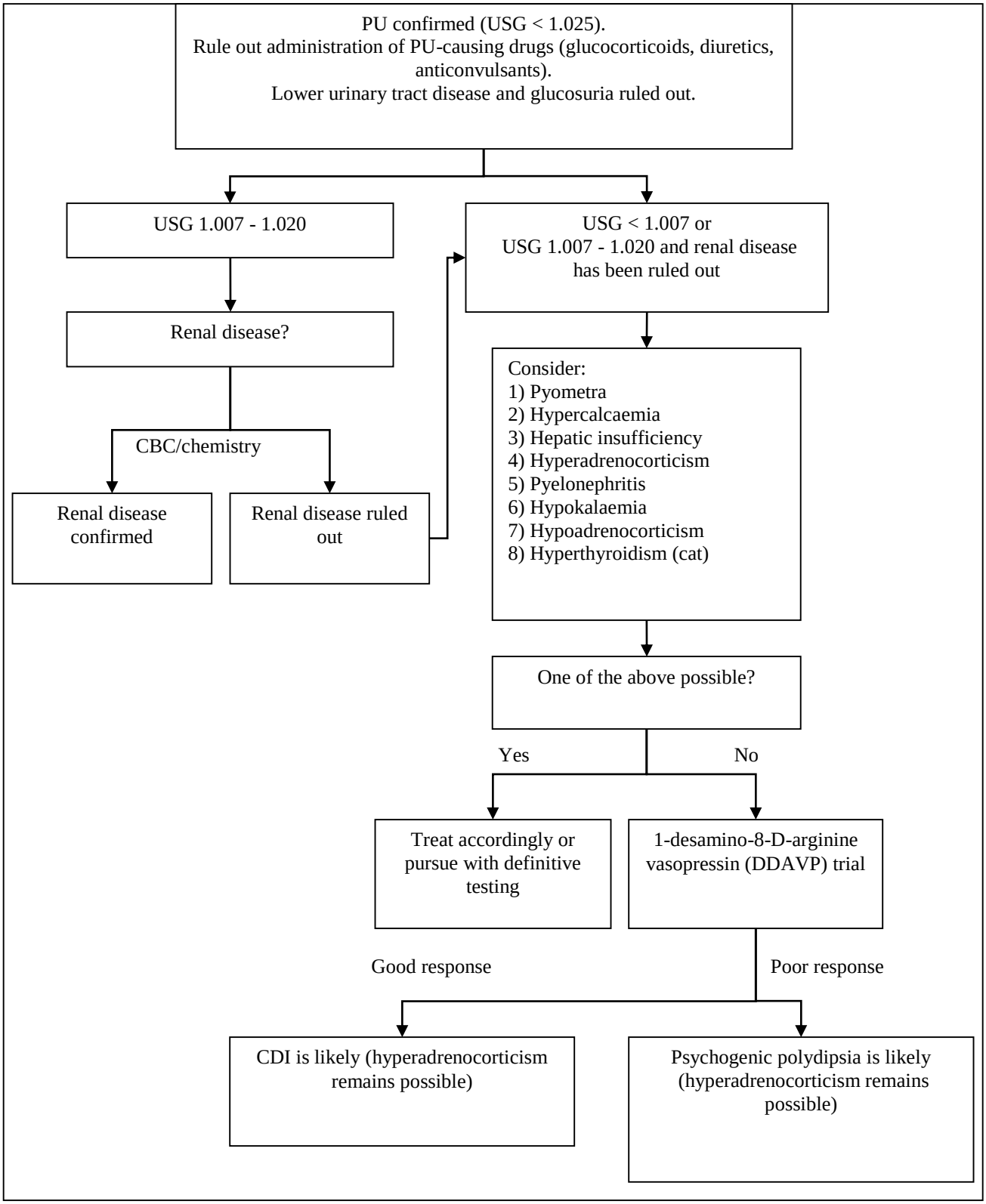
If the USG is >1.025 but glucosuria is present a diagnosis of diabetes mellitus should be suspected and confirmed by assessment of blood glucose +/- serum fructosamine. Rarely, dogs and cats can have glucosuria without hyperglycemia (renal glucosuria due to a renal tubular defect). This can be congenital in Basenji or Norwegian Elkhounds, or can be acquired due to toxic injury or infectious disease.

If the USG is <1.025 and glucosuria is absent, a thorough clinical examination and further diagnostic testing will be required. In many instances the signalment and initial clinical examination will provide clues as to the possible cause of the PU/PD, and further testing should be directed along these lines. For example, a pyrexic intact female dog with purulent vaginal discharge likely has pyometra and further testing should include abdominal imaging and CBC/chemistry. A dog with generalised lymphadenomegaly may have lymphoma, in which case hypercalcaemia should be considered. A dog with symmetrical alopecia, pot-belly, muscle weakness and hepatomegaly may have hyperadrenocorticism etc.

Recommended initial diagnostic tests include a CBC, a complete serum biochemistry profile, and urinalysis with bacterial culture (collected by cystocentesis). In older cats thyroxine should also be assessed. Depending on these initial results and clinical examination findings, further diagnostic testing (abdominal ultrasound, dynamic endocrine testing etc.) may be required, particularly if renal disease has been excluded as a cause.

The following algorithm can be followed to determine the cause of the PU:

Figure 1: Algorithm for polyuria/polydipsia



Historically the water deprivation test has been used to help differentiate animals with CDI, NDI and psychogenic polydipsia. However, the information that can be obtained from the water deprivation test may not be worth the risk as this test can be dangerous and even life-threatening if not performed under strict supervision. For example, dogs and cats with CDI or NDI can dehydrate and lose 3-5% of their body weight within as short a period as 3 hours when water is withheld. A 1-desamino-8-D-arginine vasopressin (DDAVP) trial is preferable. Trial therapy at home with oral DDAVP is recommended at a dose of 0.1 mg three times a day for 7 days for a 20 kg dog and 0.2 mg three times a day for a 40 kg dog. The dosage can be empirically adjusted for dogs and cats of different weights. Dogs and cats with CDI have a rapid response (usually in <7 days) and repeat urine sampling is expected to document concentrated urine. It is important that the trial be continued for at least 7 days to allow time for reestablishment of the medullary interstitial osmolality following the period of prolonged diuresis and medullary solute washout. Animals that do not respond to the DDAVP trial are more likely to have psychogenic polydipsia or NDI. Keep in mind that there is a small risk of water intoxication when this test is used.
Note that hyperadrenocorticoid dogs may or may not show a response to exogenous DDAVP administration, therefore it is important that this diagnosis be excluded by other means prior to the DDAVP trial.

Assessment of serum/plasma osmolality may also provide valuable information. For meaningful interpretation, dogs should be given unrestricted access to water in the lead up to sample collection. Dogs with central diabetes insipidus tend to have normal to high serum/plasma osmolality (>280 mmol/kg) since the primary stimulus for polydipsia is hypovolaemia and increased plasma osmolality due to losses of free water. Conversely, dogs with psychogenic polydipsia tend to have low-normal or low serum/plasma osmolality (<280 mmol/kg) since the excessive water intake results in hypervolaemia and reduced plasma osmolality.

References/suggested reading

1. Feldman EC. Polyuria and polydipsia. In: Ettinger SJ, Feldman EC. 7th ed. *Textbook of Veterinary Internal Medicine*. pp. 256-159. St. Louis, MO: Saunders, 2010.
2. Stockham SL, Scott MA. *Fundamentals of Veterinary Clinical Pathology*. 2nd ed. Ames, Iowa: Iowa State Press, 2008.
3. Feldman EC, Nelson RW. *Canine and feline endocrinology and reproduction*. 3rd ed. St. Louis, MO: Saunders, 2004.