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THE DIAGNOSTIC APPROACH TO POLYURIA IN THE DOG
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INTRODUCTION

Urine osmolality (Uosm: 161 - 2830) and urine specific gravity (Usg: 1.006 - >1.050) vary widely among healthy pet dogs.1 In some individual dogs Uosm fluctuates considerably during the day and Uosms close to plasma osmolality (Posm) may be reached. There is experimental evidence that water consumption increases with food intake and exercise.2 However, it is unlikely that the sometimes strong fluctuations in Uosm of pet dogs during the day can be explained solely as an effect of feeding. There may be individual differences in early satiation of thirst, as mediated through oropharyngeal receptors.1

Apparently in some pet dogs the low Uosms are associated with sufficiently high Uosms at other times of the day so that the owners do not perceive their dog to be polydipsic or polyuric. However, in other dogs the situation is more pronounced and the animals are presented to the veterinarian because of polyuria and polydipsia.3 Some of these animals may thus be recognised as having primary polydipsia. Therefore it is advisable to start the work-up of dogs with polyuria, in which most of the other differential diagnoses have been excluded (see below), by repeated measurements of Uosm and/or Usg during the day. Like in man, this approach may limit the number of further clinical studies.4

DIFFERENTIAL DIAGNOSIS

Apart from central diabetes insipidus there are in principal only two basic disorders which can account for increased water diuresis. These disorders are primary polydipsia and nephrogenic diabetes insipidus. Primary polydipsia is said to occur in hyperactive young dogs that are left alone during the day for many hours or have gone through significant changes in their environment. It has been observed that placing the animal in a completely different environment may stop the problem. The finding of the above mentioned spontaneous fluctuation of Uosm may be regarded as diagnostic of primary polydipsia.

In addition to these two basic and infrequently encountered differential diagnoses, a wide variety of conditions causes polyuria. In the young animal this may be congenital kidney disease, whereas at all ages acquired kidney disease may lead to polyuria. Especially in the middle-aged and elderly animals (endocrine) conditions such as hyperadrenocorticism, hyperthyroidism, pyometra, progestin-induced (luteal phase) growth-hormone excess, hyperparathyroidism and hypercalcemia of malignancy have to be considered.6,7 In several of these conditions impaired release of vasopressin and/or interference with its action may play a role in the polyuria.8,9,10

Hyperadrenocorticism (i.e., hypercortisolism or hyperaldosteronism) may induce impairment of the osmoregulation of vasopressin secretion. In addition, it may cause resistance to the effects of vasopressin at the level of the kidney.

Hypercortisolism or acromegaly is a syndrome of tissue overgrowth and insulin resistance due to excessive growth hormone (GH) production. In the dog, excessive GH production can be induced either by endogenous progesterone or by exogenous progestagens used for estrus prevention. Frequently the dogs are presented with polyuria. The polyuria is usually without glucosuria, but manifest diabetes mellitus can develop due to insulin resistance.

Pyometra is a complication of cystic endometrial hyperplasia (CEH), which develops during the luteal phase of the estrous cycle or is due to exogenous progestagens used for estrus prevention. Deposition of immune complexes in the glomerular capillary walls may cause a membranoproliferative glomerulonephritis. Loss of renal medullary hypertonicity, and as a consequence decreased concentrating
ability, has been described as a cause of the polyuria in dogs with pyometra. The polyuria may also be the result of decreased sensitivity of the renal V2 receptors. 

In virtually all dogs PU/PD is a prominent symptom of hyperthyroidism. The mechanism of the PU/PD in hyperthyroidism has not yet been elucidated completely. Probably, primary polydipsia plays an important role in the pathogenesis of PU/PD in hyperthyroidism.

Hypercalcemia may be caused by primary hyperparathyroidism or a malignancy. The latter, i.e., cancer associated hypercalcemia, is a paraneoplastic syndrome that results from the release of humoral factors (among which PTHrP) that induce hypercalcemia by stimulating osteoclastic bone resorption and increased renal calcium reabsorption. This humoral hypercalcemia of malignancy frequently occurs in dogs with apocrine adenocarcinomas of the anal sac or with malignant lymphoma. The impaired urinary concentrating ability may be due to increased renal medullary blood flow, decreased solute transport out of the loop of Henle, and/or interference with the action of vasopressin at the renal level.

The PU/PD in hepatic disease is usually associated with hepato-encephalopathy. The abnormal hepatic metabolism of amino acids may give rise to “false” neurotransmitters, which may lead to elevated ACTH secretion and consequently hypercortisolism.

Pyelonephritis may destroy the hypertonic renal medulla, resulting in dilute urine. Examination of urine sediment (after cystocentesis) may reveal white blood cells and bacteria. Radiographic contrast studies and/or ultrasonographic examination of the kidneys may be helpful in the diagnosis of pyelonephritis.

Dogs with the (rare) syndrome of vasopressin excess (syndrome of inappropriate antidiuresis, SIAD) may also exhibit polyuria.11

**DIAGNOSIS**

When history, physical examination and laboratory examinations do not lead to a diagnosis that might explain the polyuria, the next step can be a request to the owner to collect frequent urine samples (every 2 hours (and every 4 h during the night)) for a period of 24 h. In order to test for possible vasopressin resistance, this procedure may be repeated at the fourth day of administration of a vasopressin analogue (DDAVP, see below). When the Uosm pattern is not conclusive, a water deprivation test combined with vasopressin administration is most commonly used for differentiating the causes of polyuria.12 The test is difficult to perform correctly and unpleasant for the animal. In addition, it relies heavily on the emptying of the bladder, and is indirect because changes in urinary concentration are used as an index of vasopressin release.

In both nephrogenic diabetes insipidus and central diabetes insipidus Uosm will remain low during water deprivation. In complete diabetes insipidus Uosm will rise by 50% or more following administration of vasopressin, whereas in the partial forms of central diabetes insipidus the rise will be > 15%, and in nephrogenic diabetes insipidus there will be very little or no rise in Uosm. Because of the indirect character of the test, the results may not always be conclusive.

A more direct way to differentiate between the three basic causes of polyuria rests on the measurement of plasma vasopressin during osmotic stimulation by hypertonic saline infusion. The euhydrated animal is infused for 2 h via the jugular vein with 20% NaCl solution at a rate of 0.03 ml/kg body weight per minute. Samples for plasma vasopressin and Posm are obtained at 20 min intervals. The test requires very close observation of the animal and monitoring of Posm. This, and the fact that vasopressin is very sensitive to proteolytic breakdown, makes it advisable that the test is performed in institutions that have developed experience with the test.13 As in man this approach can improve the diagnostic accuracy. The advantage is not in the severe forms of central diabetes insipidus, as the standard indirect test will give a correct diagnosis. In all other categories of polyuria, i.e., in animals that concentrate their urine to various degrees during dehydration, the indirect test may be less reliable. However, as indicated above, with regard to the diagnosis of primary polydipsia also some reservation in the interpretation of the hypertonic stimulation is needed, because the condition may be associated with abnormalities in the vasopressin response to hypertonicity. It is not clear whether these changes in vasopressin release are the result or the cause of the polyuria.3
TREATMENT

The vasopressin analogue desmopressin, (DDAVP, 1-deamino, 9-D-arginine vasopressin), provides antidiuretic activity for about 8 hours. One drop (= 1.5 - 4 µg DDAVP) placed twice daily in the conjunctival sac sufficiently controls the polyuria in most dogs with central diabetes insipidus. With the administration of three drops a day the urine production usually returns to normal, but some owners (in part for financial reasons) prefer to apply the drug only twice daily. With the injectable preparation (4 µg once a day or every 12 h) of DDAVP the water consumption could be adequately controlled. The analogue can also be effective when administered as tablet; two or three times per day ½ tablet of 0.1 or 0.2 mg, depending on the size of the animal and the effect.

Nowadays vasopressin receptor antagonists that can be administered orally offer a very attractive alternative to water restriction for treatment of dogs with the syndrome of inappropriate secretion of antidiuretic hormone.14

REFERENCES


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