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Diabetes Insipidus: An Overview and a Case Report

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ent that the nervous form of coccidiosis is not a well-understood syndrome. In spite of this fact, diagnosis of the syndrome and differentiation from other similar nervous conditions can be made if the following features are kept in mind:

1) Between seizures the animal appears normal with the exception of signs indicative of enteric coccidiosis;
2) Seizures may occur spontaneously but they can usually be induced by exciting the animal;
3) The seizures are epileptiform in type;
4) Animals exhibiting the nervous signs have a concurrent enteric infection;
5) Post-mortem findings are negative except for the lesions due to the enteric infection.

FOOTNOTES

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Diabetes Insipidus— An Overview and a Case Report

by R. L. Peiffer, Jr., D.V.M.

Antidiuretic hormone (ADH, vasopressin) is an octapeptide produced in the nuclei of the anterior hypothalamus. The major source of this hormone is the supraoptic nuclei with minor production taking place in the paraventricular and filiform nuclei. From these centers ADH is secreted down the supraopticohypophysial tract to the posterior pituitary where it is stored until released in response to the appropriate stimuli.

The hormone is released in response to increased solute concentration—primarily sodium and its salts—in the plasma or extracellular fluid. ADH is carried by the vascular system to the kidney where it renders the collecting duct epithelium more permeable to water, allowing osmotic equilibrium between the tubular fluids and the hyperosmotic interstitum. Dilution of plasma and/or extracellular fluids inhibits ADH release, completing the negative feedback system.

The thirst center is functionally and anatomically closely related to the antidiuretic mechanism. Osmotic stimulation of the supraoptic nuclei creates a sensation of thirst; dilution of plasma inhibits thirst.

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Thus by affecting oral fluid intake and urinary fluid loss the integrated activity of the thirst and antidiuretic mechanisms serves to regulate the plasma sodium concentration between 136 and 143 meg/liter in the normal animal (Fig. 1).[4] Plasma solute levels are of course intimately and dynamically related to the tonicity of other body fluid compartments.

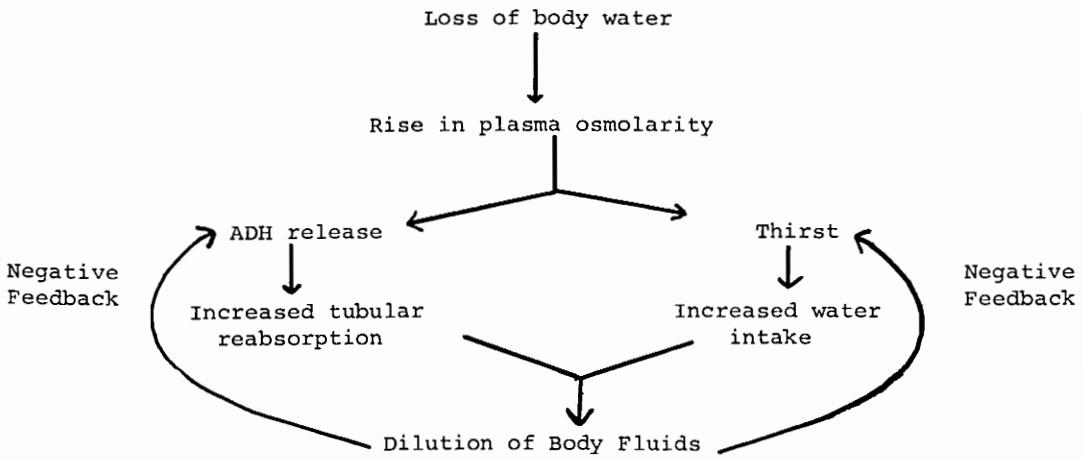
The vasopressor effect of ADH is of little physiological significance.[4]

Diabetes insipidus is an uncommon disorder resulting from any condition that affects the neurohypophysial system resulting in inadequate production or release of ADH. Generally it has been reported in middle-aged or older dogs with no sex or breed predisposition.[1,2] A familial tendency has been shown to exist in man but has not been reported in the dog.[1]

Almost half of the reported cases are idiopathic in nature, with no demonstrable lesions on post-mortem.[2] Primary and metastatic neoplasms seem to be the most common cause of confirmed diabetes insipidus in the dog.[1,2] Radiological diagnosis of pituitary neoplasia is not possible in the dog as in man; in the dog the pituitary is able to expand without causing pressure and subsequent decalcification of bone that is radiologically evident in man.[2] Other possible etiologies include head trauma and encephalitis. Even with lesions directly in the hypothalamus, diabetes insipidus is unlikely to occur. A small fraction of normal tissue is sufficient for normal function. Since the posterior and anterior pituitary have separate blood supplies, infarction of the latter need not be associated with malfunction of the former, and a space-occupying lesion is suspected when insufficiency of both occurs.[1,4]

The clinical manifestation of diabetes insipidus is one of a dramatic insatiable polydipsia which is secondary to a profuse polyuria due to the inability of the kidneys to retain body water. Normal drinking water intake is a variable value affected by such factors as ambient temperature, humidity, activity and diet; approximate values are 7–10 cc/lb./24 hours for the dog and 3–5 cc/lb./24 hours for the cat.[3] Normal urine production is likewise dependent upon diet and body size and weight as well as fluid intake. A normal range for the dog is 12–20 cc/lb./24 hours.[5] These rough approximations may increase by a factor of ten to twenty in clinical diabetes insipidus.[1,2,4]

Because of the large quantities of water consumed and urine formed, the abdomen may be "bloated" due to either a distended stomach or bladder. Gastric overdistension may cause vomition. Appetite may be normal, increased, or decreased. A dry skin and poor haircoat may be present. It must be emphasized that as long as the animal receives water *ad libitum*, hydration is maintained and health is not impaired despite lack of ADH. It is the cause of the ADH deficiency that may be reason for concern. Unconsciousness resulting from trauma or prolonged anesthesia and the associated inability to consume water,



or water deprivation, may be fatal.

The differential diagnosis includes the other conditions that are manifested by the polyuria-polydipsia syndrome. These include psychogenic water consumption, diabetes mellitus, chronic renal failure, pyometra, hyperadrenalcorticism, chronic liver disease, and renal diabetes insipidus. A diagnosis of the latter condition, reported in humans as an inability of the renal tubule to respond to ADH, has never been confirmed in the dog.[5]

An adequate history, thorough physical examination, and a few laboratory tests quickly lead the clinician down the path to an accurate diagnosis. The specific gravity of urine in diabetes insipidus is usually between 1.001 and 1.006; while the glomerular filtrate is not concentrated, solutes are normally reabsorbed. This observation must be made consistently in a serial test, ideally with the animal in a metabolism cage where 24 hour water intake and urine production can be monitored.

A slight to moderate elevation of serum sodium and total solute concentrations has been demonstrated statistically but is of no real diagnostic significance.[4]

A patient with persistent polyuria and urine of low concentration in the absence of any other outstanding clinical or laboratory findings indicates one of three conditions: (1) renal diabetes insipidus; (2) diabetes insipidus; and (3) psychogenic water consumption.

The use of urine and serum osmolality as a diagnostic tool has received attention in the literature. Both urine osmolality and specific gravity are measurements of the colligative properties of solutes in solvents. While the determination of osmolality by freezing point depression is a more precise method of evaluating the particle concentration, a refractometer is all that is essential for the veterinary clinician to diagnose diabetes insipidus.[2]

The animal's response to water deprivation is the simplest way to differentiate between a psychogenic water drinker and a case of diabetes insipidus. The bladder is emptied and the specific gravity is recorded. The animal is challenged to produce endogenous ADH by depriving it of all food and water for 8 to 24 hours and observing changes in urine volume and concentration. This must be done under close observation with frequent weighing of the animal to avoid severe dehydration. If a loss of 5 percent of body weight occurs or if patient health is jeopardized the test should be terminated.[5]

Dr. Bovee of Pennsylvania suggests that a gradual decrease in fluid intake over several days before conducting the water concentration test may produce more meaningful results in that if diabetes insipidus is not present, the kidney may not be able to respond maximally to ADH produced until medullary hypertonicity (depleted due to the long period of polyuria) is reestablished.

Continued polyuria with insignificant change in urine specific gravity (less than 1.010) indicates that the polyuria is primary and the polydipsia secondary. The pitressin concentration test must now be run to determine conclusively that the polyuria represents an ADH deficit. Increase in urine specific gravity indicates that the polydipsia was primary and the polyuria secondary. These findings are inconsistent with diabetes insipidus and would tend to steer the clinician toward a diagnosis of psychogenic polydipsia.

The pitressin concentration test is performed by injecting 1 unit of aqueous vasopressin per kg. of body weight (Pitressin^{R}, Parke Davis and Co., Detroit) subcutaneously up to a maximum dose of 20 units. The bladder is emptied 15 minutes after injecting the vasopressin so that residual dilute urine present in the bladder prior to the start of the test will not invalidate the results by mixing with urine formed after the hormone has started to take effect. One hour and 15 minutes after injecting vasopressin, collect urine for analysis and determine the specific gravity.[5] When elevation of the specific gravity of .004 magnitude occurs, the results substantiate a diagnosis of diabetes insipidus.[6] If the final urine specific gravity has shown no significant change, one may conclude that either 1) a diminished ability of the kidney to conserve fluid as a result of generalized chronic or acute renal disease is present or 2) renal diabetes in-

sipidus is present. Further renal function tests are indicated before eliminating the former and reaching the latter conclusion.

Treatment is symptomatic in the sense that determining the etiology is seldom possible. The potential for neoplasia as the cause is present. If this is the case, one should not expect remission of signs, and extension of the tumors may cause other abnormalities, such as the adiposogenital syndrome or adrenal malfunction. However, since information regarding etiology is scanty, the pet should not be condemned and treatment should be encouraged if the dog is valued at all by the owner.

Replacement therapy of ADH involves the use of vasopressin tannate in oil (Parke Davis and Co., Detroit). The drug is available in 1.0 ml ampules of 5 units/ml of ADH; .5 to 1.0 ml injected every 24 to 72 hours (approximately ¼ unit/kg.) is the optimum dosage. Paradoxically, thiazide duiretics, 2 mg./kg. tid, will also help to aleviate the symptoms, presumably by sustaining a condition of persistent mild salt depletion. These drugs used individually or in combination seldom bring about complete alleviation of the polyuria-polydipsia syndrome but do bring about dramatic improvement.[4] Dietary restrictions of protein and sodium may further reduce urine volume. It is interesting to note that animals falling into the renal diabetes insipidus category respond to thiazide and dietary treatment.[2,4] Of course water should be available *ad libitum*.

A Case Report:

On December 1, 1971, a 6 year old spayed female boxer, was admitted to the Iowa State University Small Animal Clinic with a history of polyuria-polydipsia over the past three months and consumption of up to 20 quarts of water a day. On physical examination the dog was bright, alert, in good flesh, and showed no outstanding abnormal findings. The initial laboratory results are listed in charts 1 and 2. One observes either a polycythemia of the red cell compartment or a state of dehydration

Chart 1 — Blood Work

	12–1–71	12–3–71
Hb	20	18.9
PCV	55.5	52
RBC	7.20	5.97
WBC	11,800	10,400
eosino.	1	1
seg.	94	87
lymph	5	9
mono	0	3
platelets	adequate	adequate
RBC morphology	normal	normal
blood parasites	negative	negative
BUN	13	11
Creatinine	1.1	...
Glucose	80	...
Total protein	7.8	...
Cholesteral	500	...
SGPT	146	90
Na	156.6	...
K	5.13	...
Ca	10.8	...
P	3.6	...
Fibrinogen	200	...
PSP excretion	...	60%, 20 min.

Chart 2 — Serial Urinalysis

	12–1–71	12–2–71 Initial	12–2–71 Water Deprivation 12 hours	12–2–71 Water Deprivation 18 hours	12–3–71	12–7–71 Initial	12–7–71 ADH Concentration Test 1 hour	12–7–71 ADH Concentration Test 3 hours
Color	lt. yellow	...	...	...	lt. yellow	...	...	...
s.g.	1.003	1.003	1.003	1.004	1.001	1.003	1.009	1.003
pH	7.0	...	...	...	6.5	...	...	...
albumin	neg.	...	...	...	neg.	...	...	...
acetone	neg.	...	...	...	neg.	...	...	...
sugar	neg.	...	...	...	neg.	...	...	...
blood	neg.	...	...	...	neg.	...	...	...
bilirubin	neg.	...	...	...	neg.	...	...	...
urobilinogen	0.1	...	...	...	0.1	...	...	...
sediment	neg.	...	...	...	neg.	...	...	...

with a hyperprotenemia. The white cell response is one of stress or glucocorticoid stimulation. The BUN and creatinine values indicated adequate glomerular filtration. Normal values here do not eliminate the possibility of chronic renal disease; in compensated end-stage kidney disease these values will not be outstanding. Cholesterol is increased. SGPT is acceptable for a middle-aged animal. Sodium is elevated while the other electrolytes fall within the normal range. The urinalysis shows a specific gravity of 1.003 which in a random sample tells us only that the tubules are functioning to produce dilute urine. In end-stage kidney disease one expects to see urine of a fixed specific gravity ($1.010 \pm .002$), essentially a glomerular filtrate not acted upon by non-functional tubules. The urobilinogen is a common finding in the dog due to this species' low renal threshold.

Polyuria and polydipsia were confirmed by observation. On the next day a water deprivation test was run and showed a specific gravity of 1.003 initially, 1.003 at the end of 12 hours, and 1.004 at the end of 18 hours. At this time the animal was depressed, had lost 4% of its initial body weight, and had vomited. At this point water deprivation was terminated.

The next day a phenolsulfophthalein (P.S.P.) dye excretion test was run. The patient excreted 60% of the dye in 20 minutes, indicating adequate renal perfusion and proximal tubular function.

A tentative diagnosis of diabetes insipidus was made. The dog was sent home with instruction to have access to an unlimited water supply.

On the seventh of December the patient was returned for a pitressin concentration test. Specific gravity was 1.003 initially, 1.009 at 1 hour, and 1.003 at 3 hours. The diagnosis was confirmed and after one week of thiazide and ADH replacement therapy the patient's water intake was ranging between 3 and 7 quarts a day.

Etiology was not determinable, but the prognosis must be guarded. Both the breed, age, and the possible suggestion of an early pituitary-adrenal axis stimulation make the clinician wary of the possibility of a tumor. The elevated cholesterol is unexplainable; classically such values are seen in hypothyroidism, hypoprotenemia, pancreatic endocrine or exocrine malfunction, or are dietary in nature.

The whole field of veterinary internal medicine is in its infancy. Hopefully the years ahead will be productive enough to remove the cloaks of obscurity that prevent more definitive elucidation of this and other problems.

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