



4-2018

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Elizabeth More Lennon  
elennon1@utk.edu

Shelly L. Vaden  
*North Carolina State University*, slvaden@ncsu.edu

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### Recommended Citation

Lennon EM, Hummel JB, Vaden SL. Urine sodium concentrations are predictive of hypoadrenocorticism in hyponatraemic dogs: a retrospective pilot study. *J Small Anim Pract*. 2018 Apr;59(4):228-231. doi: 10.1111/jsap.12792. Epub 2017 Dec 20. PubMed PMID: 29266322.

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**Urine Sodium Concentrations are Predictive of Hypoadrenocorticism in Hyponatremic Dogs: A Retrospective Pilot Study**

E.M. Lennon<sup>1</sup>, DVM PhD DACVIM, J.B. Hummel<sup>2</sup>, DVM DACVIM, S.L. Vaden<sup>3</sup>, DVM PhD DACVIM

<sup>1</sup>University of Tennessee College of Veterinary Medicine, 2407 River Dr, Knoxville TN 37996;  
elennon1@utk.edu

<sup>2</sup>IDEXX Diagnostics, Cary, NC; James-Hummel@idexx.com

<sup>3</sup>North Carolina State University College of Veterinary Medicine, 1060 William Moore Dr,  
Raleigh NC 27607; slvaden@ncsu.edu, (919)513-6235

Short title: Urine Sodium Concentrations Predict Hypoadrenocorticism

Corresponding author: Shelly Vaden, North Carolina State University College of Veterinary  
Medicine, 1060 William Moore Drive, Raleigh NC 27606; slvaden@ncsu.edu

Abbreviations:

HypoNa      Hyponatremic

This study was presented in abstract form at the 28th annual Forum of the American College of  
Veterinary Internal Medicine, Anaheim CA.

2 **Summary**

3 *Objectives:* To determine if a urine sodium concentration could be used to rule out  
4 hyponatremia in hyponatremic dogs.

5 *Methods:* Review of medical records of hyponatremic dogs (serum sodium < 135 mmol/L)  
6 that had recorded urine sodium concentrations. Twenty hyponatremic dogs were included;  
7 11 diagnosed with classical hyponatremia and nine with non-adrenal causes of  
8 hyponatremia. A Wilcoxon sum rank test was used to compare results between groups.

9 *Results:* No dog with hyponatremia had a urine sodium concentration < 30mmol/L.  
10 Urine sodium concentration in dogs with hyponatremia was significantly higher  
11 (median 103 mmol/L, range: 41-225), than in dogs with non-adrenal illness (median: 10  
12 mmol/L, range: 2-86) ( $p < 0.0005$ ). Serum sodium concentrations were not significantly  
13 different between dogs with hyponatremia and dogs with non-adrenal illness.

14 *Clinical Significance:* These results suggest that urine sodium concentrations can be used to  
15 prioritise a differential diagnosis of hyponatremia in hyponatremic dogs. A urine  
16 sodium concentration < 30 mmol/L in a hyponatremic dog makes classical  
17 hyponatremia an unlikely cause of the hyponatremia. Nevertheless, because of the  
18 small sample size our results should be interpreted with caution and a larger follow-up study  
19 would be valuable.

20 **Keywords**

21 hyponatremia, aldosterone, hyponatremia, urine sodium

22

23

24

25 **Introduction**

26           Classical primary hypoadrenocorticism is a syndrome that is often challenging to  
27 diagnose due to its vague clinical signs and lack of pathognomonic clinicopathologic data.  
28 Many dogs with hypoadrenocorticism are critically ill and require expensive care and  
29 hospitalisation before a definitive diagnosis is made. Serum cortisol is usually measured by  
30 reference laboratories, typically with a waiting period from the time a sample is collected.  
31 Therefore, a test available in an emergency setting that could be used to help to prioritise  
32 the differential diagnosis of hypoadrenocorticism in a critically ill patient would have value in  
33 providing a tentative prognosis prior to expensive care and hospitalisation.

34           In classical hypoadrenocorticism, aldosterone deficiency results in renal sodium  
35 wasting and potassium retention, resulting in hyponatraemia and hyperkalaemia (Willard et  
36 al., 1982, Melian and Peterson, 1996, Rakich and Lorenz, 1984, Haviland et al., 2016, Adler  
37 et al., 2007). Dogs with classical hypoadrenocorticism become total-body volume- and  
38 sodium-depleted, which can result in severe neurologic and cardiovascular complications  
39 (Melian and Peterson, 1996, MacMillan, 2003, Brady et al., 1999).

40           In a hypovolaemic hyponatraemic state, the renal tubules should actively resorb  
41 sodium, resulting in minimal loss of sodium into the urine (Tyler et al., 1987, Kamel et al.,  
42 1989, Spasovski et al., 2014, Ball and Iqbal, 2016, Fenske et al., 2010). However, in the  
43 case of renal sodium wasting, which occurs with aldosterone deficiency or renal tubular  
44 injury, high urine sodium concentrations (greater than 30-40 mmol/L) can result despite  
45 hypovolaemia or hyponatraemia (Milionis et al., 2002, Waldrop, 2008, Buffington and  
46 Abreo, 2016). In human medicine, urine sodium concentrations are an important part of  
47 the diagnostic algorithm for hyponatraemia (Spasovski et al., 2014, Ball and Iqbal, 2016,  
48 Fenske et al., 2010). The diagnostic utility of urine sodium concentrations are not well

49 documented in veterinary patients, although extrapolation from humans has been  
50 suggested (Waldrop, 2008). Based on findings in humans, expected urine sodium  
51 concentrations in hyponatraemic dogs with classical primary hypoadrenocorticism should be  
52 > 30 mmol/L, while dogs with hyponatraemia due to most other common causes  
53 (hypovolaemia, vomiting and diarrhoea, sepsis, and effusions) should have renal  
54 conservation of sodium, resulting in small amounts of sodium in the urine ( < 30 mmol/L).  
55 Therefore, measurement of a urine sodium concentration may be a useful diagnostic tool to  
56 prioritise the likelihood of hypoadrenocorticism in cases with consistent history, physical  
57 examination, and serum chemistry findings.

58         Although many clinicians are familiar with measurement of fractional excretion of  
59 electrolytes, where the electrolyte is normalised to creatinine, the absolute measurement of  
60 electrolyte concentrations can provide useful information even in the absence of  
61 normalisation to creatinine. Urine sodium excretion has been described in normal dogs, but  
62 expected ranges have not been established for dogs with hyponatraemia (DiBartola et al.,  
63 1980, Hartenbower et al., 1974). In the case of total body hyponatraemia and normal renal  
64 tubular function, sodium is highly conserved; almost all sodium is resorbed from the renal  
65 tubule, resulting in very small amounts of sodium in the urine, regardless of the degree of  
66 urine concentration as measured by the urine specific gravity or the urine creatinine  
67 concentration (Ball and Iqbal, 2016, Spasovski et al., 2014).

68         In humans, there are limited causes of hyponatraemia with absolute urine sodium  
69 concentration > 30-40 mmol/L. These situations include the syndrome of inappropriate ADH  
70 secretion (SIADH), classical primary hypoadrenocorticism, osmotic diuresis, hypothyroidism,  
71 diuretic usage, renal tubular damage and some causes of vomiting with hypochloraemic  
72 alkalosis (Milionis et al., 2002, Ball and Iqbal, 2016, Spasovski et al., 2014, Verbalis et al.,  
73 2013). Of these aetiologies, those that occur with relative frequency in the dog are

74 hypoadrenocorticism, diuretic usage, hypothyroidism, vomiting with hypochloraemic  
75 alkalosis and renal tubulopathy.

76 Therefore, in patients in which hypoadrenocorticism is suspected based on physical  
77 examination, complete blood count, serum chemistry, (especially when hyponatraemia is  
78 present), and urinalysis, a test to prioritise the likelihood of hypoadrenocorticism before  
79 obtaining the results of an adrenocorticotrophic hormone (ACTH) stimulation test would be  
80 valuable.

81 The purpose of this study was to determine if urine sodium concentrations could be  
82 used to exclude hypoadrenocorticism as a cause of hyponatraemia in dogs. We  
83 hypothesised that a high urine sodium (expected > 30-40 mmol/L based on studies in  
84 humans) could exclude classical hypoadrenocorticism as the cause of hyponatraemia in  
85 dogs. This may help owners with financial limitations make informed decisions about  
86 pursuing treatment for their pet and may help clinicians prioritise differential diagnoses,  
87 which may result in an earlier initiation of treatment such as glucocorticoids and  
88 mineralocorticoids and limited diagnostic testing.

89

## 90 **Materials and Methods**

### 91 *Case identification*

92 A retrospective search for hyponatraemic dogs that had urine sodium concentrations  
93 measured contemporaneously was performed by searching a computerised clinical  
94 pathology database for urine sodium results from 2003 - 2008, and a paper file of urine  
95 sodium results before 2003. Dogs with a serum sodium concentration less than 135 mmol/L  
96 (reference range 140-166 mmol/L) in a serum chemistry panel at the time of hospital  
97 admission were included in the study.

98 Medical records were reviewed, and all medications administered as well as final  
99 diagnosis were recorded. Final diagnosis was made by the attending clinician at the time the  
100 case was treated in the hospital, and available medical records were reviewed to ensure  
101 agreement. Exclusion criteria included a diagnosis of diabetes mellitus, administration of  
102 intravenous or subcutaneous fluids for greater than 12 hours before collection of urine, or  
103 any administration of diuretics, hypertonic saline, mitotane (Lysodren; Bristol Myers  
104 Squibb), trilostane (Vetoryl; Dechra), mineralocorticoids, aminoglycosides, contrast media,  
105 or chemotherapeutics before collection of urine. Twelve hours was chosen as the cutoff time  
106 prior to collection of urine in order to mimic a clinical situation, where urine from critically ill  
107 dogs is often not collected before initial stabilisation. Dogs were assigned to one of two  
108 groups depending on the final diagnosis documented in the medical record by the clinician  
109 managing the case. Dogs were diagnosed with hypoadrenocorticism if they had a pre- and  
110 post-ACTH cortisol < 2µg/dl without a history of corticosteroid administration.

#### 111 *Urine sodium measurement*

112 Urine sodium was measured using an indirect ion-selective electrode (indirect  
113 potentiometry). Instruments used to perform the measurements included Instrumentation  
114 Laboratory Genesis 21, Instrumentation Laboratory Monarch, and Roche Cobas system in a  
115 university veterinary clinical pathology laboratory. All instruments were validated for use on  
116 urine and at a low dynamic range of sodium concentration. Quality control was performed in  
117 accordance with manufacturer instructions.

#### 118 *Statistical analysis*

119 A Wilcoxon Sum Rank test was used to evaluate differences between groups and  
120 sensitivity and specificity were calculated according to standard methodology. Positive and  
121 negative predictive values were calculated using a prevalence of 13%, which is the average

122 of three previously published studies (Gold et al., 2016, Lennon et al., 2007, Kemppainen et  
123 al., 1983).

124

## 125 **Results**

126 Forty-one dogs had hyponatraemia and urine sodium concentrations available. Of  
127 those, 13 dogs were excluded because of intravenous or subcutaneous fluid administration  
128 before collection of urine, five were excluded because of furosemide administration, one was  
129 excluded because of mitotane administration, one was excluded because of administration  
130 of mineralocorticoids before urine collection, and one was excluded because of  
131 hyperglycaemia. In total, 20 dogs were included in the study.

132 Of the 20 dogs included in the study, 11 had a diagnosis of hypoadrenocorticism  
133 (presumed to be classical hypoadrenocorticism due to the presence of hyponatraemia and,  
134 in many cases, hyperkalaemia), and the remaining nine dogs had non-adrenal causes of  
135 hyponatraemia. Non-adrenal causes of hyponatraemia were effusions (n=4), pyelonephritis  
136 (n=1), distemper (n=1), sepsis (n=1), urethral obstruction (n=1), and uncharacterised  
137 intracranial disease (n=1).

138 There was no statistical difference in serum sodium concentration between the dogs  
139 with classical hypoadrenocorticism, (median 127, range 106-134) and the dogs with non-  
140 adrenal illness (median 131 mmol/L, range 121-133) (Figure 1). Median urine sodium  
141 concentration was significantly higher in dogs with hypoadrenocorticism (median 103  
142 mmol/L, range: 41-225 mmol/L) than dogs with non-adrenal causes of hyponatraemia  
143 (median 10 mmol/L (range: 2-86 mmol/L),  $p < 0.0005$ ) (Figure 2). Based on widely used  
144 cut-offs in human medicine as well as the results of this study, 30 mmol/L was chosen as a  
145 cut-off value (Spasovski et al., 2014). None of the dogs with hypoadrenocorticism had a  
146 urine sodium concentration  $< 30$  mmol/L. One dog with a non-adrenal cause of



147 hyponatraemia had a urine sodium concentration > 30 mmol/L. This dog had clear  
148 evidence of pyelonephritis documented in the medical record (pyuria and bacteriuria with  
149 granular casts and azotaemia).

150         Sensitivity of a urine sodium > 30 mmol/L to support of a diagnosis of  
151 hypoadrenocorticism was 100% (95% confidence interval: 71.51%-100%), and specificity  
152 was 88.89% (95% confidence interval: 51.75% to 99.72%). Assuming a prevalence of 13%  
153 based on the average of previously published rates,(Lennon et al., 2007, Bovens et al.,  
154 2014, Gold et al., 2016) positive predictive value was 61.38% (95% confidence interval:  
155 45.18% to 77.58%) and negative predictive value was 100% (Table 1).

156

## 157 **Discussion**

158         The results of this study suggest that urine sodium concentrations might be useful to  
159 help prioritise the likelihood of hypoadrenocorticism in hyponatraemic dogs. The finding of  
160 a single urine sodium concentration < 30 mmol/L in a hyponatraemic dog indicates that  
161 hypoadrenocorticism is unlikely, and other causes of hyponatraemia should be considered.  
162 However, a larger study would be necessary to determine if a urine sodium can be used to  
163 exclude hypoadrenocorticism as a differential diagnosis using a urine sodium concentration.  
164 A urine sodium concentration > 30 mmol/L in a hyponatraemic dog is supportive of, but not  
165 diagnostic for, hypoadrenocorticism as a cause of the hyponatraemia (*i.e.* classical  
166 hypoadrenocorticism).

167         In this study, all 11 dogs with hypoadrenocorticism had inappropriately high urine  
168 sodium concentrations (> 30 mmol/L) despite serum hyponatraemia, indicating a failure of  
169 efficient resorption of sodium in the renal tubule due to a lack of sufficient aldosterone.

170 One dog in the non-adrenal illness group had a urine sodium concentration > 30  
171 mmol/L. This dog had a diagnosis of pyelonephritis. Primary or secondary renal  
172 tubulopathies are also a common cause of elevated urine sodium (> 30 mmol/L) in human  
173 patients because of renal salt wasting (Spasovski et al., 2014). In human patients, other  
174 causes of hyponatraemia with a urine sodium concentration > 30 mmol/L include the  
175 syndrome of inappropriate ADH secretion (SIADH), osmotic diuresis, hypothyroidism,  
176 diuretic usage, renal tubular damage and some causes of vomiting with hypochloraemic  
177 alkalosis. Therefore, these differential diagnoses should be considered in the case of urine  
178 sodium > 30 mmol/L (Ball and Iqbal, 2016, Spasovski et al., 2014). In contrast, 8/9 of the  
179 dogs with non-adrenal illness had urine sodium concentrations < 30 mmol/L, as would be  
180 expected in the case of other causes of hyponatraemia, such as hypovolaemia, in which  
181 sodium is conserved (Spasovski et al., 2014).

182 Therefore, a urine sodium concentration < 30 mmol/L can be used to support the  
183 exclusion of classical hypoadrenocorticism as the cause of a dog's hyponatraemia.  
184 Specifically, a dog with hyponatraemia due to hypoadrenocorticism would be expected to  
185 have an inappropriately high urine sodium concentration. If urine sodium concentration is <  
186 30mmol/L, hyponatraemia is unlikely to be due to hypoadrenocorticism or other primary or  
187 secondary tubulopathies. Other differential diagnoses that should be considered include  
188 sepsis, other causes of hypovolaemia, effusions, and vomiting and diarrhoea.

189 The measurement of a urine sodium concentration could potentially be performed on  
190 in-house chemistry analysers since the technology to measure sodium in urine samples, ion-  
191 selective electrodes, are available in these machines. However, many available in-house  
192 analysers are not validated by the manufacturers for use on urine. If manufacturers offered  
193 this validation, this test would provide rapid, in-house results, enabling clinicians to  
194 prioritise a differential diagnosis of hypoadrenocorticism as a cause of hyponatraemia before  
195 receiving results of an ACTH stimulation test.

196           A limitation of this study is the small sample size and retrospective nature. A larger  
197 prospective clinical study which measured serum and urine sodium as well as aldosterone  
198 would be useful in order to evaluate the utility of this test to rule out a diagnosis of  
199 hypoadrenocorticism. Another limitation of this study was that serum aldosterone  
200 concentrations were not measured to confirm that the dogs had classical  
201 hypoadrenocorticism but hyponatraemia (serum sodium < 135 mmol/L) was used as a  
202 surrogate marker.

203           Urine sodium concentrations have not been investigated in atypical  
204 hypoadrenocorticism in dogs with normal serum sodium concentrations; if  
205 hypoadrenocorticism is highly suspected, an ACTH stimulation test should be performed. In  
206 this study, we have only evaluated urine sodium concentrations in hyponatraemic dogs, so  
207 the expected value in normonatraemic dogs with hypoadrenocorticism are unknown.

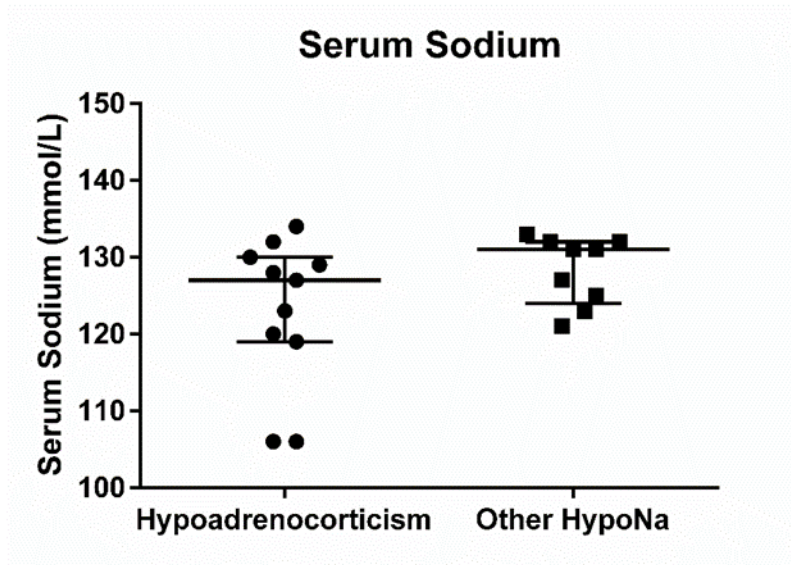
208           In conclusion, the authors propose that measuring urine sodium may be used to  
209 exclude hypoadrenocorticism with aldosterone deficiency as a cause of hyponatraemia, but  
210 a larger prospective study is necessary to further evaluate the utility of this test. A urine  
211 sodium concentration < 30 mmol/L in a hyponatraemic dog indicates that classical  
212 hypoadrenocorticism an unlikely cause of the hyponatraemia.

213

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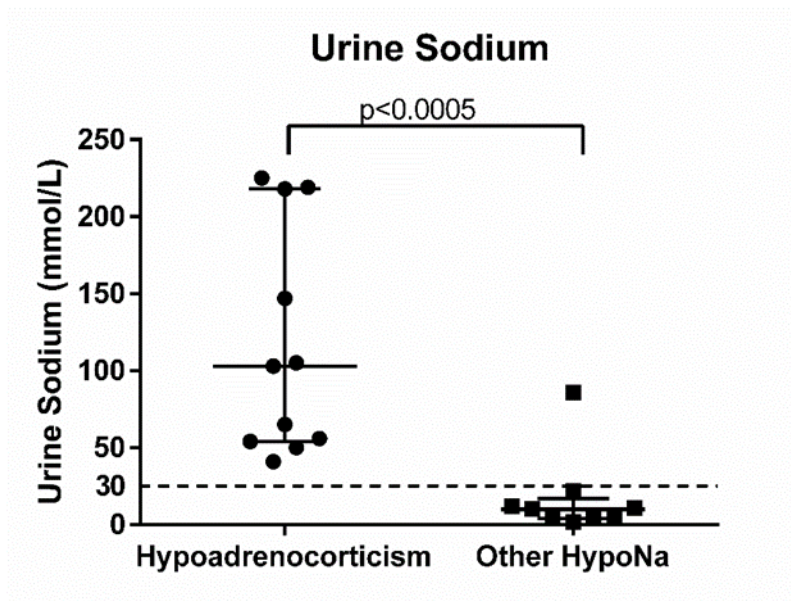
215 **Figure Legends**

216 Figure 1: Serum sodium concentrations are similar between dogs with hypoadrenocorticism  
 217 and dogs with non-adrenal causes of hyponatraemia (Other HypoNa).  $p=0.37$



218

219 Figure 2: Urine sodium concentrations are higher in dogs with hypoadrenocorticism than  
 220 non-adrenal illness (Other HypoNa). No dogs with hypoadrenocorticism had a urine sodium  
 221  $< 30$  mmol/L, indicated by the dashed line.  $p < 0.0005$ .



222

223 Table 1. Sensitivity and specificity of a urine sodium concentration for ruling out  
224 hypoadrenocorticism in hyponatremic dogs.

	Hypoadrenocorticism	Non-adrenal illness
Urine sodium > 30	11	1
Urine sodium < 30	0	8

225

226 Sensitivity: 100% (95% CI: 71.51%-100%); specificity: 88.89% (95% CI:  
227 51.75% to 99.72%). Positive predictive value: 61.38% (95% CI: 45.18% to  
228 77.58%); negative predictive value: 100%, assuming a prevalence of 13%.

229 No conflicts of interest have been declared.

230

- 231 ADLER, J. A., DROBATZ, K. J. & HESS, R. S. 2007. Abnormalities of serum electrolyte  
232 concentrations in dogs with hypoadrenocorticism. *J Vet Intern Med*, 21, 1168-73.
- 233 BALL, S. G. & IQBAL, Z. 2016. Diagnosis and treatment of hyponatraemia. *Best Pract Res*  
234 *Clin Endocrinol Metab*, 30, 161-73.
- 235 BOVENS, C., TENNANT, K., REEVE, J. & MURPHY, K. F. 2014. Basal serum cortisol  
236 concentration as a screening test for hypoadrenocorticism in dogs. *J Vet Intern Med*,  
237 28, 1541-5.
- 238 BRADY, C. A., VITE, C. H. & DROBATZ, K. J. 1999. Severe neurologic sequelae in a dog  
239 after treatment of hypoadrenal crisis. *J Am Vet Med Assoc*, 215, 222-5, 210.
- 240 BUFFINGTON, M. A. & ABREO, K. 2016. Hyponatraemia: A Review. *J Intensive Care Med*,  
241 31, 223-36.
- 242 DIBARTOLA, S., CHEW, D. & JACOBS, G. 1980. Quantitative urinalysis including 24-hour  
243 protein excretion in the dog. *Journal of the American Animal Hospital Association*, 16,  
244 537-546.
- 245 FENSKE, W., MAIER, S. K., BLECHSCHMIDT, A., ALLOLIO, B. & STORK, S. 2010. Utility and  
246 limitations of the traditional diagnostic approach to hyponatraemia: a diagnostic  
247 study. *Am J Med*, 123, 652-7.
- 248 GOLD, A. J., LANGLOIS, D. K. & REFSAL, K. R. 2016. Evaluation of Basal Serum or Plasma  
249 Cortisol Concentrations for the Diagnosis of Hypoadrenocorticism in Dogs. *J Vet*  
250 *Intern Med*, 30, 1798-1805.
- 251 HARTENBOWER, D. L., FRIEDLER, R. M., COBURN, J. W., MASSRY, S. G. & SELLERS, A.  
252 1974. Spontaneous variations in electrolyte excretion in the awake dog. *Proc Soc Exp*  
253 *Biol Med*, 145, 648-53.
- 254 HAVILAND, R. L., TOAFF-ROSENSTEIN, R. L., REEVES, M. P. & LITTMAN, M. P. 2016. Clinical  
255 features of hypoadrenocorticism in soft-coated wheaten terrier dogs: 82 cases  
256 (1979-2013). *Can Vet J*, 57, 387-94.
- 257 KAMEL, K. S., MAGNER, P. O., ETHIER, J. H. & HALPERIN, M. L. 1989. Urine electrolytes in  
258 the assessment of extracellular fluid volume contraction. *Am J Nephrol*, 9, 344-7.
- 259 KEMPPAINEN, R. J., THOMPSON, F. N. & LORENZ, M. D. 1983. Use of a low dose synthetic  
260 ACTH challenge test in normal and prednisone-treated dogs. *Res Vet Sci*, 35, 240-2.
- 261 LENNON, E. M., BOYLE, T. E., HUTCHINS, R. G., FRIEDENTHAL, A., CORREA, M. T.,  
262 BISSETT, S. A., MOSES, L. S., PAPICH, M. G. & BIRKENHEUER, A. J. 2007. Use of  
263 basal serum or plasma cortisol concentrations to rule out a diagnosis of  
264 hypoadrenocorticism in dogs: 123 cases (2000-2005). *J Am Vet Med Assoc*, 231,  
265 413-6.

- 266 MACMILLAN, K. L. 2003. Neurologic complications following treatment of canine  
267 hypoadrenocorticism. *Can Vet J*, 44, 490-2.
- 268 MELIAN, C. & PETERSON, M. E. 1996. Diagnosis and treatment of naturally occurring  
269 hypoadrenocorticism in 42 dogs. *J Small Anim Pract*, 37, 268-75.
- 270 MILIONIS, H. J., LIAMIS, G. L. & ELISAF, M. S. 2002. The hyponatraemic patient: a  
271 systematic approach to laboratory diagnosis. *Cmaj*, 166, 1056-62.
- 272 RAKICH, P. & LORENZ, M. 1984. Clinical signs and laboratory abnormalities in 23 dogs with  
273 spontaneous hypoadrenocorticism. *Journal of the American Animal Hospital  
274 Association*, 20, 647-649.
- 275 SPASOVSKI, G., VANHOLDER, R., ALLOLIO, B., ANNANE, D., BALL, S., BICHET, D.,  
276 DECAUX, G., FENSKE, W., HOORN, E. J., ICHAI, C., JOANNIDIS, M., SOUPART, A.,  
277 ZIETSE, R., HALLER, M., VAN DER VEER, S., VAN BIESEN, W. & NAGLER, E. 2014.  
278 Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Eur J  
279 Endocrinol*, 170, G1-47.
- 280 TYLER, R. D., QUALLS, C. W., JR., HEALD, R. D., COWELL, R. L. & CLINKENBEARD, K. D.  
281 1987. Renal concentrating ability in dehydrated hyponatraemic dogs. *J Am Vet Med  
282 Assoc*, 191, 1095-100.
- 283 VERBALIS, J. G., GOLDSMITH, S. R., GREENBERG, A., KORZELIUS, C., SCHRIER, R. W.,  
284 STERNS, R. H. & THOMPSON, C. J. 2013. Diagnosis, evaluation, and treatment of  
285 hyponatraemia: expert panel recommendations. *Am J Med*, 126, S1-42.
- 286 WALDROP, J. E. 2008. Urinary electrolytes, solutes, and osmolality. *Vet Clin North Am Small  
287 Anim Pract*, 38, 503-12, ix.
- 288 WILLARD, M. D., SCHALL, W. D., MCCAWE, D. E. & NACHREINER, R. F. 1982. Canine  
289 hypoadrenocorticism: report of 37 cases and review of 39 previously reported cases.  
290 *J Am Vet Med Assoc*, 180, 59-62.

291