Validation of a commercially available enzyme immunoassay for measurement of plasma antidiuretic hormone concentration in healthy dogs and assessment of plasma antidiuretic hormone concentration in dogs with congestive heart failure

Katherine F. Scollan, DVM; Barret J. Bulmer, DVM, MS; D. David Sisson, DVM

Objective—To validate the use of a human enzyme immunoassay (EIA) kit for measurement of plasma antidiuretic hormone (ADH) concentration in dogs and evaluate plasma ADH concentrations in dogs with congestive heart failure (CHF) attributable to acquired cardiac disease, compared with findings in healthy dogs.

Animals—6 healthy dogs and 12 dogs with CHF as a result of chronic degenerative valve disease or dilated cardiomyopathy.

Procedures—Plasma samples from the 6 healthy dogs were pooled and used to validate the EIA kit for measurement of plasma ADH concentration in dogs by assessing intra-assay precision, dilutional linearity, and spiking recovery. Following validation, plasma ADH concentrations were measured in the 6 healthy dogs and in the 12 dogs with CHF for comparison.

Results—The EIA kit measured ADH concentrations in canine plasma samples with acceptable intra-assay precision, dilutional linearity, and spiking recovery. The intra-assay coefficient of variation was 11%. By use of this assay, the median plasma concentration of ADH in dogs with CHF was 6.15 pg/mL (SD, 3.2 pg/mL; range, 4.18 to 15.47 pg/mL), which was significantly higher than the median concentration in healthy dogs (3.67 pg/mL [SD, 0.93 pg/mL; range, 3.49 to 5.45 pg/mL]).

Conclusions and Clinical Relevance—Plasma ADH concentrations in dogs can be measured with the tested EIA kit. Plasma ADH concentrations were higher in dogs with CHF induced by acquired cardiac disease than in healthy dogs. This observation provides a basis for future studies evaluating circulating ADH concentrations in dogs with developing heart failure. (Am J Vet Res 2013;74:1206–1211)

Chronic degenerative valve disease and DCM are the 2 most common acquired cardiac diseases of dogs. Both are progressive disorders that eventually result in overt CHF, causing considerable morbidity and death in affected dogs. Antidiuretic hormone, also referred to as arginine vasopressin or vasopressin, is a nonapeptide hormone synthesized within the hypothalamus; it contributes to the regulation of plasma osmolality and blood pressure. In addition to other well-characterized neurohormonal alterations in dogs with heart failure, excessive circulating concentrations of ADH may have a role in the relentless progression of cardiac decompensation over time. Such changes are well characterized in humans with CHF. Two important biological actions of ADH of particular relevance in patients with heart disease include vasoconstriction and expansion of plasma volume via the retention of solute-free water. In this context, ADH excess promotes the development of congestion and CHF.

**Abbreviations**

<table>
<thead>
<tr>
<th>ADH</th>
<th>Antidiuretic hormone</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDVD</td>
<td>Chronic degenerative valve disease</td>
</tr>
<tr>
<td>CHF</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>DCM</td>
<td>Dilated cardiomyopathy</td>
</tr>
<tr>
<td>EIA</td>
<td>Enzyme immunoassay</td>
</tr>
<tr>
<td>La:Ao</td>
<td>Left atrial-to-aortic root diameter</td>
</tr>
<tr>
<td>LVIDd</td>
<td>Diastolic left ventricular internal diameter</td>
</tr>
<tr>
<td>LVIDs</td>
<td>Systolic left ventricular internal diameter</td>
</tr>
<tr>
<td>RAAS</td>
<td>Renin-angiotensin-aldosterone system</td>
</tr>
</tbody>
</table>

Received December 12, 2012. Accepted April 18, 2013.

From the Department of Clinical Sciences, College of Veterinary Medicine, Oregon State University, Corvallis, OR 97331. Dr. Bulmer’s present address is Tufts Veterinary Emergency Treatment and Specialties, 523 South St, Walpole, MA 02081.

Supported by gifts from Dr. Dana Buoscio to the Cardiology Research Fund, College of Veterinary Medicine, Oregon State University.


Address correspondence to Dr. Scollan (kate.scollan@oregonstate.edu).
of hyponatremia, particularly when high doses of loop diuretics are used to relieve clinical signs of congestion.

Circulating concentrations of ADH in dogs with heart failure have not been studied extensively, in part because of the difficulty of measuring ADH plasma concentrations. In the past, ADH concentration has been measured mainly by radioimmunoassay, which is expensive to perform and has the disadvantages inherent to the preparation and handling of radioactive reagents. For humans, the development of an EIA kit has allowed faster and less hazardous measurement of plasma ADH concentration, albeit with limits of detection that are modestly less sensitive than those of the radioimmunoassay. Given the homologous structure of human and canine ADH, we hypothesized that a human EIA kit could be used to measure ADH in plasma samples obtained from dogs. To this end, the objective of the study reported here was to validate the use of a human EIA kit for measurement of plasma ADH concentration in dogs. Assuming this objective could be met, the intent was to evaluate plasma ADH concentrations in dogs with CHF attributable to acquired cardiac disease and compare those data with findings in healthy dogs. We hypothesized that plasma ADH concentrations would be higher in dogs with CHF induced by acquired cardiac disease than in healthy dogs.

Materials and Methods

Animals—Six healthy dogs without evidence of cardiac disease owned by students and employees at the veterinary teaching hospital at Oregon State University were used in the study. Plasma samples obtained from these dogs were used to validate the use of a human EIA kit for measurement of plasma ADH concentration in dogs and were analyzed for comparison with data from dogs with CHF. Dogs in this group were adults (>4 years old) and determined to be free of cardiac disease on the basis of results of physical and echocardiographic examinations. Six breeds were represented (Greater Swiss Mountain Dog, Australian Shepherd, Labrador Retriever, Standard Poodle, Labrador Retriever mix, and Boxer mix). There were 3 spayed females and 3 neutered males.

Twelve client-owned dogs with CHF as a result of CDVD (7 dogs) or DCM (5 dogs) were also used in the study. Among the dogs with CDVD, there were 7 breeds (Cairn Terrier, Miniature Schnauzer, Rhodesian Ridgeback, Maltese, Chihuahua, Pekingese, and a medium-sized mixed-breed dog). Among the dogs with DCM, there were 4 breeds (Doberman Pinscher [n = 2], Wirehair Pointer [1], Great Dane [1], and a large mixed-breed dog). In the CHF group, there were 6 spayed females, 1 sexually intact female, 3 neutered males, and 2 sexually intact male dogs. Dogs were included in the CHF group if they had radiographic evidence of pulmonary edema (determined at a previous hospital visit) but were not currently in heart failure (n = 5; 3 dogs with CDVD and 2 dogs with DCM) or if they had active heart failure at the time of blood sample collection (7; 4 dogs with CDVD and 3 dogs with DCM). Dogs were excluded if radiographic evidence of pulmonary edema was not conclusive. At the time of blood sample collection, 2 dogs with CHF had not received any treatment, whereas 10 dogs with CHF had been treated with furosemide (10/10 dogs), enalapril (10/10 dogs), digoxin (2/10 dogs), and pimobendan (7/10 dogs). The Oregon State University Institutional Animal Care and Use Committee approved all procedures used in the study, and written consent was obtained from all owners of the study dogs.

Collection of blood samples—Twelve milliliters of blood was collected via direct venipuncture from each dog, and 3-mL aliquots of each sample were placed into 1 of 4 identical chilled tubes containing EDTA and a combination of protease inhibitors. The protease inhibitor concentrations per mL of blood containing EDTA were as follows: DL-thiorphan, 10 µg/mL; benzamidine, 700 µg/mL; aprotinin, 20 µg/mL; leupeptin hemisulfate, 100 µg/mL; and D-thiorphan, 50 µg/mL. The tubes were placed on ice immediately and centrifuged at 4°C (1,600 X g for 15 minutes) within 10 minutes after collection. Plasma samples were then transferred to polyethylene tubes and stored at −80°C until time of analysis.

Validation of EIA kit for use with canine plasma samples—Validation of the commercially available human ADH EIA kit was performed with plasma samples obtained from the 6 healthy dogs. Sensitivity of the kit provided by the manufacturer was 3.39 pg/mL. Plasma samples were collected and stored as described, and then one 3-mL aliquot/dog was thawed prior to validation assays. Once thawed, the plasma samples were combined into a pooled plasma sample. The pooled canine plasma sample and ADH standard supplied with the EIA kit were used to produce a standard curve. Concentrations of ADH in pooled canine plasma were 1,000, 400, 160, 64, 25.6, 10.24, 4.1, and 1.64 pg/mL; 1 kit tube contained pooled canine plasma that was not spiked with ADH. Antidiuretic hormone was then ether extracted by use of the protocol recommended by the kit manufacturer. Briefly, the contents of each tube were transferred to a polyallomer tube and cold acetone (2 times the sample volume) was added. Tubes were vortexed and then centrifuged at 12,000 X g for 20 minutes. Each supernatant was transferred to a new polyallomer tube; ice-cold petroleum ether (5 times the sample volume) was added. The tube was then vortexed. The tube was centrifuged at 10,000 X g for 10 minutes. The top layer of ether was discarded, and the remaining aqueous solution was transferred to a glass tube and dried under nitrogen gas. The sample was then reconstituted to the original sample volume with assay buffer supplied with the EIA kit.

Finally, ADH concentration in the spiked and unspiked plasma samples was measured following the directions specified by the EIA kit manufacturer. Intra-assay variability was determined by performing the assay in triplicate for each spiked or unspiked sample. Dilutional linearity was assessed by measuring ADH concentrations in the plasma sample spiked with 10.24 pg of ADH/mL before and after serial dilutions (1:2, 1:4, and 1:8). The measured ADH concentrations were compared to predicted concentrations. Accuracy was assessed by spike and recovery, comparing recovered ADH concentrations to expected values in samples.
spiked at low (4.1 pg/mL), medium (10.24 pg/mL), and high (64.0 pg/mL) concentrations of ADH.

Echocardiography—Transthoracic 2-D, M-mode, color flow, and spectral Doppler echocardiographic evaluations were performed with a commercial echocardiographic unit6 and 7-, 5-, or 3-MHz phased array probes. Each of the 18 dogs was placed in right and then left lateral recumbency to obtain standard right and left parasternal views. Left atrial-to-aortic root ratio, LVID d, LVID s, and fractional shortening were measured from M-mode right parasternal short axis images. Measurements of LVID d and LVID s were indexed to body weight (BW) by use of formulas described by Cornell et al8 as follows:

\[
\text{LVID}_d \text{ index} = \frac{\text{LVID}_d}{\text{BW}^{0.33}} \\
\text{LVID}_s \text{ index} = \frac{\text{LVID}_s}{\text{BW}^{0.33}}
\]

All echocardiographic measurements were made in triplicate and averaged.

In the dogs with CHF, CDVD was diagnosed when echocardiography revealed characteristic valvular lesions (thickened mitral valve leaflets) and enlargement of the left atrium and ventricle in association with a large mitral regurgitant jet on 2-D Doppler color flow Doppler images.9 For the other dogs with CHF, DCM was diagnosed when echocardiography revealed increased left ventricular systolic and diastolic dimensions (compared with expected values based on body weight) with a reduction in fractional shortening (%) and moderate to severe left atrial enlargement in the absence of other identifiable cardiac disorders.9

Radiography—For each dog with suspected CHF, 2-view orthogonal thoracic radiographs obtained either during a previous hospital visit or during the visit at which the blood sample was collected were reviewed. Radiographic views were evaluated by a board-certified cardiologist (KFS) and radiologist for evidence of pulmonary edema and assessment of heart size by use of the vertebral heart scale method.10 Cardiogenic pulmonary edema was determined to be present when the pulmonary veins were distended, the left atrium was enlarged, and an interstitial or alveolar pulmonary pattern was observed.11

Analysis of plasma ADH concentrations—Blood samples from the 12 dogs with CHF that met the inclusion and exclusion criteria were collected, and plasma was obtained and stored as described. The unused plasma aliquots obtained from the healthy dogs were also analyzed. At the time of analysis, plasma samples were thawed and all samples were assayed in duplicate following the protocol recommended by the EIA kit manufacturer.

Statistical analysis—Data were assessed for normality by the D’Agostino and Pearson omnibus normality test. Data that were not normally distributed were reported as median with SD or range. Median age, body weight, La: Ao ratio, LVID d index, LVID s index, fractional shortening, and plasma ADH concentration for healthy dogs and dogs with CHF were compared by use of nonparametric Mann-Whitney U tests. Dilutional linearity was evaluated by ordinary linear regression analysis in which the measured concentrations of ADH in plasma samples were compared with the expected concentration. Statistical significance was designated at a value of \( P < 0.05 \) (2-tailed test). Statistical analysis was performed with commercial software.1

Results

Animals—Age, body weight, and echocardiographic and radiographic variables for 6 healthy dogs and 12 dogs with CHF were compared (Table 1). Median body weight of healthy dogs and CHF dogs did not differ. Median age, body weight, and echocardiographic and radiographic variables for the healthy dogs and dogs with CHF were compared (Table 1). Median La:Ao ratio, LVID d index, LVID s index, fractional shortening, and plasma ADH concentration for healthy dogs and dogs with CHF were compared by use of nonparametric Mann-Whitney U tests. Dilutional linearity was evaluated by ordinary linear regression analysis in which the measured concentrations of ADH in plasma samples were compared with the expected concentration. Statistical significance was designated at a value of \( P < 0.05 \) (2-tailed test). Statistical analysis was performed with commercial software.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Healthy dogs</th>
<th>Dogs with CHF</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>3.5 (2–7)</td>
<td>9 (6–14)</td>
<td>0.005</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>32.4 (28.6–36.4)</td>
<td>20.2 (32.6–64.5)</td>
<td>0.122</td>
</tr>
<tr>
<td>La:Ao ratio</td>
<td>1.13 (1.09–1.29)</td>
<td>2.04 (1.05–2.76)</td>
<td>0.005</td>
</tr>
<tr>
<td>LVID d index*</td>
<td>1.31 (1.13–1.46)</td>
<td>2.08 (1.65–2.42)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LVID s index*</td>
<td>0.93 (0.79–1.13)</td>
<td>1.25 (0.82–1.89)</td>
<td>0.016</td>
</tr>
<tr>
<td>FS (%)</td>
<td>28.5 (22.6–40.8)</td>
<td>38.4 (9.0–62.2)</td>
<td>0.373</td>
</tr>
<tr>
<td>VHS</td>
<td>NA</td>
<td>12.0</td>
<td></td>
</tr>
</tbody>
</table>

*Left ventricular dimensions were indexed9 as follows: LVID d index = LVID d/body weight\(^{0.33}\) and LVID s index = LVID s/body weight\(^{0.33}\). FS = Fractional shortening. NA = Not applicable. VHS = Vertebral heart scale measurement.

Figure 1—Dilution linearity for ADH concentrations in a pooled plasma sample (obtained from 6 healthy dogs) spiked with 10.24 pg of ADH/mL before and after serial dilutions (1:2, 1:4, and 1:8) and measured in triplicate. Data points are plotted as mean observed concentration (with SE bars) versus expected concentration. Linear regression analysis yielded the regression equation: observed = 1.171(expected) + 0.8644.
differ significantly ($P = 0.122$). Dogs with CHF were significantly ($P = 0.006$) older than the healthy dogs. The La:Ao ratio, LVIDd index, and LVIDs index were significantly greater in dogs with CHF, compared with findings in healthy dogs ($P = 0.006$, $P < 0.001$, and $P = 0.017$, respectively). As anticipated, comparison of data for the dogs with CDVD with those for the dogs with DCM revealed significant differences in body weight ($P = 0.03$), LVID index ($P = 0.003$), and fractional shortening ($P = 0.003$) but not in age ($P = 0.581$). La:Ao ratio

---

Figure 2—Box-and-whisker plots of plasma ADH concentration in 6 healthy dogs and 12 dogs with CHF. For each box, the horizontal line represents the median value and the upper and lower boundaries represent the 75th and 25th percentiles, respectively. Whiskers represent the minimum and maximum values. The median plasma ADH concentration in dogs with CHF (6.15 pg/mL [SD, 3.2 pg/mL; range, 4.18 to 15.47 pg/mL]) was significantly greater in dogs with CHF, compared with findings for healthy dogs (3.67 pg/mL [SD, 0.93 pg/mL; range, 3.49 to 5.45 pg/mL]; Figure 2). Among dogs with CHF, the median plasma ADH concentration for the dogs with CDVD (6.71 pg/mL [SD, 3.8 pg/mL; range, 4.18 to 15.47 pg/mL]) was not significantly ($P = 0.43$) different from the value for dogs with DCM (5.85 pg/mL [SD, 1.9 pg/mL; range, 4.20 to 9.34 pg/mL]). However, compared with the value determined in healthy dogs, median plasma ADH concentration in dogs with CDVD was significantly ($P = 0.004$) higher, whereas median plasma ADH concentration in dogs with DCM did not differ ($P = 0.051$; Figure 3).

Discussion

In the veterinary medical literature, reports of circulating ADH concentrations in dogs in the context of cardiovascular disease are sparse. This is, at least in part, attributable to the difficulty in collecting samples and performing a radioimmunoassay, which must be carried out at regulated laboratories because of the requirement for radioactive material and the potential human health hazard. The development of a commercial EIA for ADH allows a more affordable and practical assessment of plasma ADH concentrations for most veterinary clinical laboratories. The limit of detection of the EIA kit used in the present study was 3.39 pg/mL, whereas for most radioimmunoassays, the detection limit is ≤ 1.0 pg/mL, indicating that the EIA kit is less sensitive for detection of ADH. In the present study, the accuracy of the kit was tested at 3 levels (low, medium, and high) of ADH concentration by spiking recovery. Accuracy was acceptable at the medium and high ADH concentrations, but ADH concentrations were slightly overestimated at the concentration closest to the reported sensitivity limit of the kit. Despite the potential inability of the EIA kit to detect very low concentrations of ADH in canine plasma samples, ADH concentrations in healthy dogs determined in the present study were comparable to those measured by radioimmunoassay in apparently normal dogs and humans. The limitation of this kit at lower concentrations of ADH might be overcome by altering the quantities of extracted plasma and reconstituting diluent to increase the measured ADH concentration and adjusting the final concentration result accordingly.

---

**Table 3—Spiking recovery of ADH in pooled samples of plasma obtained from 6 healthy dogs.**

<table>
<thead>
<tr>
<th>ADH spike concentration</th>
<th>Observed (pg/mL)</th>
<th>Recovery* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (4.1 pg/mL)</td>
<td>5.61</td>
<td>134</td>
</tr>
<tr>
<td>Medium (10.24 pg/mL)</td>
<td>11.45</td>
<td>111</td>
</tr>
<tr>
<td>High (64.0 pg/mL)</td>
<td>53.72</td>
<td>84</td>
</tr>
</tbody>
</table>

*Value calculated as (observed value/expected [spike] value) × 100.

---

**Figure 3—Box-and-whisker plots of plasma ADH concentration in dogs with CDVD [n = 7] or DCM [5].** Median plasma ADH concentration in dogs with CDVD (6.71 pg/mL [SD, 3.8 pg/mL]) was significantly higher than the value in healthy dogs (3.67 pg/mL [SD, 0.93 pg/mL]). Median plasma ADH concentration in dogs with DCM (5.85 pg/mL [SD, 1.9 pg/mL]) was not significantly different from values in the other 2 groups. See Figure 2 for key.
More than 30 years ago, it was reported that plasma ADH concentration is high in humans with CHF.\textsuperscript{16} Results of several subsequent studies in humans\textsuperscript{3,6,17} and in dogs\textsuperscript{12} as well as those of the study here have corroborated that finding. Elevated plasma ADH concentration has been found in humans with acute or chronic CHF, including individuals who were hyponatremic.\textsuperscript{3,18} The major physiologic actions of ADH include the regulation of plasma osmolality and blood pressure. The release of ADH is stimulated by several mechanisms including an increase in plasma osmolality, reduction in blood pressure or volume, and an increase in angiotensin II activity.\textsuperscript{19} An increase in plasma osmolality, reduction in blood pressure or volume, and ADH include the regulation of plasma osmolality and hyponatremia.\textsuperscript{5,18} The major physiologic actions of ADH concentration has been found in humans with CHF.\textsuperscript{21,22} Elevated plasma ADH concentrations between affected and healthy dogs have corroborated that finding. Elevated plasma ADH concentrations have been found in dogs with CHF.\textsuperscript{12} Comparison of plasma ADH concentration in dogs with CHF and in dogs\textsuperscript{12} as well as those of the study reported here have corroborated that finding. Elevated plasma ADH concentration has been found in humans with acute or chronic CHF, including individuals who were hyponatremic.\textsuperscript{3,18} The major physiologic actions of ADH include the regulation of plasma osmolality and blood pressure. The release of ADH is stimulated by several mechanisms including an increase in plasma osmolality, reduction in blood pressure or volume, and an increase in angiotensin II activity.\textsuperscript{19} An increase in plasma osmolality, reduction in blood pressure or volume, and ADH concentrations in dogs with CHF cannot be attributed to the smaller number of dogs with CHF.\textsuperscript{12} Indeed, plasma ADH concentration in dogs with CHF induced by DCM did not differ from those of the study reported here.

Certainly, 1 difficulty in assessing circulating ADH concentrations in dogs relates to the pulsatile nature of plasma osmolality, arterial pressure, or RAAS activation for circulating ADH concentrations in healthy dogs. The mean plasma ADH concentration for healthy dogs was substantially lower (0.2 pg/mL \textsuperscript{12} versus that of the EIA kit used in the present study (3.39 pg/mL). Alternatively, this observed difference might simply be due to the lower limit of detection of the radioimmunoassay used for ADH concentration measurement in the earlier study\textsuperscript{12 (1.1 pg/mL) versus that of the EIA kit used in the present study (3.39 pg/mL). Interestingly, the mean plasma concentrations of ADH in dogs with CHF (measured via radioimmunoassays with similar detection limits) range from 0.85 pg/mL (SD, 0.88 pg/mL)\textsuperscript{12} to 2.4 pg/mL (SE, 0.02 pg/mL)\textsuperscript{26} and 3.2 pg/mL (SD, 0.7 pg/mL).\textsuperscript{27} This indicates that the difference in test sensitivity may not be the only cause of the observed variation. The temporal pattern of ADH secretion in dogs should be examined more closely, and the possibility that this pattern is pulsatile should be taken into consideration when designing future studies to assess circulating ADH concentrations in dogs with CHF. Thus, the EIA kit appears to be a reasonable means of measuring ADH in clinically affected dogs and can be used as an alternative to the previously used radioimmunoassay with the described limitations.

In the study reported here, plasma ADH concentrations in dogs with CHF as a result of either CDVD or DCM were not significantly different. Interestingly, plasma ADH concentration in dogs with CHF induced by CDVD was significantly higher than the value in healthy dogs; plasma ADH concentration in dogs with CHF induced by DCM did not differ from the value in healthy dogs. This latter finding may be attributable to the smaller number of dogs with DCM, and analysis of samples from additional dogs may have led to the identification of a significant difference.
The present study had several limitations that should be considered when interpreting the results. The number of dogs with CHF was small, although a significant difference in plasma ADH concentrations between healthy dogs and dogs with CHF was detected. Inclusion of larger numbers of dogs with CDVD and DCM may have allowed more definitive discrimination of plasma ADH concentrations in relation to the different diseases and variable degrees of disease severity. Additionally, the diagnosis of CHF was based on the subjective identification of pulmonary edema in radiographic views and was not quantitatively assessed by degree of edema or measurement of pulmonary capillary wedge pressures. Lastly, plasma sodium concentration and plasma osmolality were not measured prospectively during the study. Concurrent measurement of these variables with assessment of plasma ADH concentration would provide interesting and valuable information regarding the stimuli for ADH release in dogs with CHF.

On the basis of the results of the present study, it is feasible to measure ADH concentrations in canine plasma samples with a commercially available human EIA kit. In addition, data indicated that plasma ADH concentration is significantly higher in dogs with clinical CHF compared with that in healthy dogs. The expanded accessibility and absence of required radioactive material when using the EIA kit present clear advantages over the more traditionally used radioimmunoassay for measurement of plasma ADH concentration in dogs. Further study is warranted to assess circulating ADH concentrations in dogs with various types and degrees of acquired heart disease while concurrently assessing plasma osmolality and sodium status to evaluate the relative contributions of these stimuli to high ADH concentrations. Furthermore, the potential for use of ADH antagonists in dogs with refractory or hyponatremic CHF should be investigated.

References