Various adverse systemic effects related to glucocorticoid use have been reported in dogs, including hypertension, hepatomegaly, and high serum hepatic enzyme activities. Although the exact mechanism behind cortisol-induced hypertension remains unknown, systemic hypertension is sometimes found in dogs with glucocorticoid excess, and systemic blood pressure may increase in dogs administered hydrocortisone.

Glucocorticoid administration has also been associated with changes to the liver parenchyma characterized by vacuolar hepatopathy attributable to accumulation of cytoplasmic fat, water, or glycogen. Owing to the accumulation of these cytoplasmic compounds, the liver becomes enlarged. For instance, when prednisolone was administered at a high dosage (4 mg/kg/d, PO) to dogs for 15 consecutive days, the ratio of liver weight to body weight was found to be 1.7 times the ratio in control dogs. Clinically, hepatomegaly can be easily diagnosed on a lateral radiographic view of the abdomen by assessing the orientation of the gastric axis or measuring the ratio reflecting the distance between the ventral border of the caudal vena cava and caudal margin of the liver versus the length of the 11th thoracic vertebral body. This ratio in healthy, dolichocephalic dogs has been found to be $5.4 \pm 0.74$. Likewise, glucocorticoid administration has been associated with changes in hepatic echogenicity that can be detected with ultrasonography. However, identification of the diffuse changes seen with glucocorticoid-induced vacuolar hepatopathy is usually more difficult than visualization of focal lesions. Comparing echogenicity of the liver with that of the kidney or spleen and visualization of the portal ves-

**BODY WEIGHT, BLOOD PRESSURE, AND SYSTEMIC CHANGES FOLLOWING LOW-DOSAGE PREDNISOLONE ADMINISTRATION IN DOGS**

**OBJECTIVE**
To investigate systemic changes following low-dosage prednisolone administration in dogs.

**ANIMALS**
4 healthy purpose-bred adult male Beagles.

**PROCEDURES**
Dogs were administered prednisolone PO at a dosage of 2 mg/kg/d for 2 weeks, 1 mg/kg/d for 4 weeks, and 0.5 mg/kg/d for 3 weeks. Body weight, blood pressure, hepatic size and echogenicity, percentage of vacuolated hepatocytes, serum hepatic enzyme activities and glucose concentration, adrenal gland size, and pancreatic echogenicity were evaluated weekly for 9 weeks.

**RESULTS**
The only significant change identified was an increase in hepatic echogenicity, assessed by measuring liver-kidney contrast on ultrasonographic images. Increases in hepatic size and percentage of vacuolated hepatocytes were identified, but values did not differ from baseline values. Similarly, serum hepatic enzyme activities increased, but changes were mild and not significantly different from baseline values. Body weight, pancreatic echogenicity, and serum glucose concentration did not show noticeable changes. Mild systemic hypertension was seen, but blood pressure was not significantly different from the baseline value. Similarly, adrenal gland size steadily decreased during the first 6 weeks and increased again after the prednisolone dosage was decreased to 0.5 mg/kg/d. However, mean adrenal gland size was not significantly different from the baseline value at any time.

**CONCLUSIONS AND CLINICAL RELEVANCE**
Results suggested that in dogs, administration of prednisolone at a low dosage was associated with minimal systemic effects. (Am J Vet Res 2017;78:1091–1097)
sels can be used to evaluate hepatic echogenicity, but these methods are subjective and operator dependent. Therefore, ultrasound histogram assessment to quantify echogenicity has been used to supplement gross visualization. In particular, histogram assessment of liver-kidney contrast and depth attenuation of the hepatic image have been used to identify changes in hepatic echogenicity in dogs.

Serum hepatic enzyme (ALP, ALT, AST, and GGT) activities are increased to variable degrees in dogs treated with prednisolone, depending on dosage and duration of administration. In a previous study, ALP activity was most notably increased (64-fold) when prednisolone was administered to dogs at a high dosage (4.4 mg/kg/d, IM, for 14 days).

Finally, although glucocorticoid use has been suggested as a possible cause of acute pancreatitis in humans, pancreatitis did not develop in healthy dogs receiving high dosages of prednisolone (4 mg/kg/d, IM or PO, for 2 weeks) in an experimental study. In another study in which prednisolone (2.2 mg/kg/d, PO) was administered to dogs for a prolonged period, serum pancreatic lipase immunoreactivity concentration was not significantly changed.

Many of the previous studies evaluating the adverse effects of prednisolone administration in dogs have involved high dosages, prolonged durations, or an IM route of administration. In contrast, oral administration of prednisolone at a low dosage is more commonly used in clinical situations such as management of inflammatory or allergic diseases or as an adjunct to chemotherapy. Furthermore, if long-term use is necessary, the dosage is typically tapered over a period of days to weeks. Because the adverse effects of prednisolone administration are associated with total dose received, duration of treatment, and route of administration, systemic changes in dogs receiving low-dosage prednisolone PO may differ from the findings of previous studies in which prednisolone was administered at a high dosage for a prolonged period. Thus, the purpose of the study reported here was to investigate systemic changes following low-dosage prednisolone administration in dogs. We focused on the time of occurrence of effects and on the reversibility of those effects as the dosage of prednisolone was tapered.

Materials and Methods

Animals

Four sexually intact male purpose-bred Beagles with a median age of 3 years (range, 2 to 4 years) and median weight of 11.3 kg (range, 10 to 13 kg) were used in the present study. None of the dogs had received medications, including glucocorticoids and NSAIDs, within the previous 6 months. All of the dogs were determined to be healthy on the basis of physical examination findings and results of a CBC, serum biochemical analyses, thoracic and abdominal radiography, and abdominal ultrasonography.

Experimental protocol

Prednisolone was administered PO to all dogs at a dosage of 2 mg/kg every 24 hours for the first 2 weeks, at a dosage of 1 mg/kg every 24 hours for the next 4 weeks, and at a dosage of 0.5 mg/kg every 24 hours for the final 3 weeks of the 9-week study period. A physical examination, abdominal radiography, abdominal ultrasonography, serum biochemical analyses, and cytologic examination of a hepatic specimen obtained by means of ultrasound-guided fine-needle aspiration were performed before and at 1-week intervals after initiation of drug administration.

Physical examination and clinicopathologic testing

Body weight, systolic arterial blood pressure, and clinical signs were assessed at each evaluation time. Blood pressure was measured 5 times with the non-invasive Doppler ultrasonic flow detector technique. The maximum and minimum values were discarded, and the mean value of the remaining 3 blood pressure measurements was used for data analysis. Clinical signs associated with prednisolone administration such as polyuria, polydipsia, and hair loss were evaluated subjectively. Serum ALP, ALT, AST, and GGT activities and glucose concentration were measured with an automated analyzer.

Abdominal radiography

For evaluation of hepatic size, the ratio of the distance between the ventral border of the caudal vena cava and caudal margin of the liver versus the length of the 11th thoracic vertebral body was measured 3 times on a lateral radiographic view of the

Figure 1—Lateral radiographic view of the abdomen of a dog illustrating measurements used to assess hepatic size. Hepatic size was calculated as the ratio of the distance between the ventral border of the caudal vena cava and caudal margin of the liver (a) versus the length of the 11th thoracic vertebral body (b).
Abdominal ultrasonography

Ultrasonography was performed with a 10-MHz linear transducer after food had been withheld for at least 12 hours. A constant power output (89%) and gain setting (64 dB) were used throughout the entire study period. Images of the liver (in particular, the left lateral and quadrate lobes), kidneys, adrenal glands, and pancreatic body were obtained from the subcostal approach with the dog positioned in dorsal recumbency. Images of the left lateral and quadrate lobes adjacent to the gastric fundus and gallbladder, respectively, were obtained in the transverse plane. Images of the kidneys, adrenal glands, and pancreas were obtained in the longitudinal plane.

Hepatic echogenicity and texture were assessed and histogram analysis was performed by 2 examiners (SKL and BC). For histogram assessment of liver-kidney contrast, square ROIs (1.0 X 1.0 cm) were manually defined over the left lateral lobe of the liver and the cranial poles of both renal cortices at a fixed depth of 2 cm (Figure 2). Liver-kidney contrast was determined by subtracting mean echogenicity of the kidneys from that of the liver. For histogram analysis of depth attenuation of the hepatic image, 2 square ROIs (1.0 X 1.0 cm) were manually defined over the quadrate lobe of the liver at depths of 2 and 4 cm. The difference in echogenicity between the 2 ROIs was defined as the depth attenuation (Figure 3). Liver-kidney contrast and depth attenuation were measured 3 times by each of the 2 examiners, and mean values were used for analysis.

Pancreatic echogenicity was subjectively assessed by comparison with echogenicity of the adjacent fat and then quantitatively evaluated by means of histogram assessment after manually defining a square ROI (1.0 X 1.0 cm) in the longitudinal plane of the pancreatic body (Figure 4). The portal vein was used as a landmark to identify the pancreatic body.

Cytologic examination of hepatic aspirates

During each evaluation, fine-needle aspiration of the liver was performed 4 times in each dog with 23-gauge needles fitted to 5-mL disposable syringes. All slides (4/dog) were stained with Romanowsky stain, and severity of vacuolization was determined semiquantitatively by counting the number of hepatocytes with intracellular vacuoles/100 hepatocytes on each slide.

Statistical analysis

Data are reported as mean ± SD. The Wilcoxon signed rank test was used to compare pretreatment values with values obtained at each evaluation time following initiation of prednisolone administration. Reproducibility of histogram assessments between the 2 examiners was analyzed by calculating the ICC. Spearman correlation analysis was performed to investigate relationships among variables. All statistical analyses were performed with standard software.

Values of \( P < 0.05 \) were considered significant.

Results

All dogs were clinically normal throughout the study period, and clinical signs of polyuria, polydipsia, and hair loss were not noted. Mean body weight did not differ significantly from the baseline value at any time during prednisolone administration (Table 1). Mean blood pressure steadily increased through day 35 of prednisolone administration, at which time mean blood pressure (mean ± SD, 166.0 ± 4.5 mm Hg) was in the mild systemic hypertension range. Mean blood pressure then slowly decreased as the prednisolone dosage was tapered to 0.5 mg/kg/d. However,
mean blood pressure was not significantly different from the baseline value at any evaluation time.

On subjective evaluation of the abdominal radiographs, hepatomegaly was evident in all dogs 7 days after administration of prednisolone was initiated. However, the degree of hepatomegaly was mild, and the ratio of the distance between the ventral border of the caudal vena cava and caudal margin of the liver versus the length of the 11th thoracic vertebral body was not significantly different from the baseline value at any evaluation time.

On subjective evaluation of ultrasonographic images, hepatic echogenicity was increased 7 days after administration of prednisolone was initiated, and a hyperchoic hepatic texture was observed at all examination times. On histogram analysis, liver-kidney contrast showed a moderate degree of correlation (ICC for liver-right kidney contrast, 0.613; ICC for liver-left kidney contrast, 0.641) and depth attenuation of the hepatic image showed a poor degree of correlation (ICC for depth-attenuation, 0.56) between the 2 examiners. Because values for liver-left kidney contrast and liver-right kidney contrast were similar, the mean value was used for analyses. Mean liver-kidney contrast was significantly increased 7 days after administration of prednisolone was initiated and did not decrease with tapering of the prednisolone dosage. Depth attenuation of the hepatic image was increased, but not significantly so, 7 days after administration of prednisolone was initiated, and depth attenuation did not differ significantly from the baseline value at any evaluation time.

Table 1—Changes in body weight (BW), systolic arterial blood pressure (BP), size and echogenicity of the liver, serum hepatic enzyme activities and glucose concentration, percentage of vacuolated hepatocytes, adrenal gland size, and pancreatic echogenicity before (day 0) and during administration of prednisolone at a low dosage in 4 dogs.

<table>
<thead>
<tr>
<th>Variable</th>
<th>0</th>
<th>7</th>
<th>14</th>
<th>21</th>
<th>28</th>
<th>35</th>
<th>42</th>
<th>49</th>
<th>56</th>
<th>63</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW (kg)</td>
<td>11.3±1.2</td>
<td>11.4±1.6</td>
<td>11.1±1.2</td>
<td>11.3±1.5</td>
<td>11.0±1.4</td>
<td>10.5±1.1</td>
<td>10.9±1.3</td>
<td>11.0±1.3</td>
<td>10.9±1.3</td>
<td>10.9±1.2</td>
</tr>
<tr>
<td>BP (mm Hg)</td>
<td>149.8±9.3</td>
<td>158.0±12.2</td>
<td>156.8±13.6</td>
<td>166.8±7.9</td>
<td>165.5±11.1</td>
<td>160.0±4.5</td>
<td>160.0±7.7</td>
<td>154.8±10.5</td>
<td>150.8±15.0</td>
<td>152.0±12.0</td>
</tr>
<tr>
<td>Hepatic size</td>
<td>5.6±0.3</td>
<td>6.4±0.4</td>
<td>6.5±0.4</td>
<td>6.6±0.5</td>
<td>6.2±0.3</td>
<td>6.2±0.3</td>
<td>6.3±0.2</td>
<td>6.2±0.3</td>
<td>5.9±0.4</td>
<td>6.0±0.4</td>
</tr>
<tr>
<td>Liver-kidney contrast</td>
<td>0</td>
<td>1.7±2.2*</td>
<td>1.6±2.4</td>
<td>1.6±2.0</td>
<td>2.2±3.4</td>
<td>1.8±2.5</td>
<td>2.2±1.3*</td>
<td>1.7±1.6*</td>
<td>2.0±1.7*</td>
<td>1.9±2.5</td>
</tr>
<tr>
<td>Depth attenuation</td>
<td>3.4±0.9</td>
<td>5.4±0.8</td>
<td>4.1±0.9</td>
<td>4.0±0.7</td>
<td>4.2±1.2</td>
<td>2.2±1.0</td>
<td>1.3±0.9</td>
<td>2.1±0.5</td>
<td>2.4±0.3</td>
<td>3.0±0.4</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>32.0±5.4</td>
<td>92.5±26.6</td>
<td>99.8±21.0</td>
<td>80.3±5.8</td>
<td>122.3±19.0</td>
<td>164.8±33.0</td>
<td>145.5±32.1</td>
<td>126.0±42.6</td>
<td>83.3±26.6</td>
<td>76.5±30.4</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>66.8±13.0</td>
<td>70.3±31.5</td>
<td>84.3±35.1</td>
<td>97.0±45.1</td>
<td>83.5±54.7</td>
<td>71.3±21.1</td>
<td>95.8±25.4</td>
<td>111.8±40.7</td>
<td>101.0±25.5</td>
<td>98.5±21.1</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>27.5±3.3</td>
<td>25.0±8.7</td>
<td>28.3±4.1</td>
<td>28.5±5.2</td>
<td>37.3±20.5</td>
<td>64.5±53.4</td>
<td>31.8±6.8</td>
<td>33.0±13.1</td>
<td>25.5±6.1</td>
<td>32.0±8.5</td>
</tr>
<tr>
<td>GGT (U/L)</td>
<td>0.3±0.5</td>
<td>3.5±2.1</td>
<td>4.3±1.3</td>
<td>2.8±1.0</td>
<td>1.8±2.4</td>
<td>3.5±2.9</td>
<td>4.5±1.0</td>
<td>3.0±1.4</td>
<td>2.8±1.3</td>
<td>3.1±1.8</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>98.3±10.3</td>
<td>114.3±43.3</td>
<td>108.8±9.7</td>
<td>118.0±7.7</td>
<td>117.5±13.2</td>
<td>66.0±40.0</td>
<td>84.3±6.7</td>
<td>115.5±8.9</td>
<td>112.8±4.5</td>
<td>111.5±3.2</td>
</tr>
<tr>
<td>Hepatocellular vacuolization (%)</td>
<td>8.3±6.5</td>
<td>36.5±16.5</td>
<td>43.0±5.1</td>
<td>43.3±12.7</td>
<td>43.0±9.5</td>
<td>38.5±6.0</td>
<td>30.3±12.2</td>
<td>28.0±8.7</td>
<td>30.0±9.9</td>
<td>33.0±14.5</td>
</tr>
<tr>
<td>Left adrenal gland size (mm)</td>
<td>4.9±0.5</td>
<td>4.6±0.2</td>
<td>4.0±0.1</td>
<td>4.0±0.4</td>
<td>3.5±0.2</td>
<td>3.2±0.3</td>
<td>3.1±0.5</td>
<td>3.2±0.1</td>
<td>3.5±0.1</td>
<td>3.5±0.2</td>
</tr>
<tr>
<td>Right adrenal gland size (mm)</td>
<td>4.8±0.1</td>
<td>4.6±0.4</td>
<td>4.0±0.1</td>
<td>4.1±0.4</td>
<td>3.6±0.2</td>
<td>3.1±0.5</td>
<td>3.1±0.3</td>
<td>3.3±0.3</td>
<td>3.4±0.1</td>
<td>3.7±0.3</td>
</tr>
<tr>
<td>Pancreatic echogenicity</td>
<td>23.1±2.0</td>
<td>23.9±2.6</td>
<td>25.5±1.8</td>
<td>24.5±1.9</td>
<td>26.7±1.0</td>
<td>23.9±1.4</td>
<td>26.2±1.7</td>
<td>26.8±0.9</td>
<td>27.0±1.2</td>
<td>27.5±1.2</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD. Prednisolone was administered PO to all dogs at a dosage of 2 mg/kg every 24 hours for the first 2 weeks, 1 mg/kg every 24 hours for the next 4 weeks. and 0.5 mg/kg every 24 hours for the final 3 weeks of the 9-week study period. Hepatic size was calculated as the ratio of the distance between the ventral border of the caudal vena cava and caudal margin of the liver versus the length of the 11th thoracic vertebral body. Hepatocellular vacuolization was determined semiquantitatively by counting the number of hepatocytes with intracellular vacuoles/100 hepatocytes on slides of fine-needle hepatic aspirates. The width (dorsosventral dimension) of each adrenal gland was measured perpendicular to the long axis on longitudinal images of the adrenal glands. Pancreatic echogenicity was evaluated by means of histogram assessment.

*Value is significantly (P < 0.05) different from pretreatment value.
In addition, none of the dogs had ultrasonographic evidence of pancreatitis, such as pancreatic edema or hypoechoic changes, on subjective evaluation of ultrasound images.

**Discussion**

Results of the present study suggested that in dogs, administration of prednisolone at a low dosage (2 mg/kg/d) was associated with minimal systemic effects. The only significant change identified was an increase in hepatic echogenicity, assessed by measuring liver-kidney contrast on ultrasonographic images. Increases in hepatic size and percentage of vacuolated hepatocytes were identified, but values did not differ from baseline values. Similarly, serum hepatic enzyme activities increased, but changes were mild and not significant, compared with baseline values. Body weight, pancreatic echogenicity, and serum glucose concentration did not show noticeable changes. Mild systemic hypertension was seen, but again, blood pressure was not significantly different from the baseline value. Adrenal gland size steadily decreased during the 6 weeks that prednisolone was administered at a dosage of 2 or 1 mg/kg/d and increased again after the prednisolone dosage was decreased to 0.5 mg/kg/d. However, mean adrenal gland size was not significantly different from the baseline value at any evaluation time.

Severe hypertension can occur in dogs with spontaneous hyperadrenocorticism, with approximately 80% of dogs with pituitary-dependent hyperadrenocorticism developing systemic hypertension. However, administration of prednisolone at a low dosage in the present study did not significantly increase blood pressure, and only mild systemic hypertension was observed. Similarly, administration of hydrocortisone at a dosage of 8 mg/kg/d, PO, for 12 weeks was found to induce only mild hypertension. The discrepancy between development of systemic hypertension in dogs with spontaneous hyperadrenocorticism versus the lack of substantial blood pressure changes in dogs receiving exogenous glucocorticoids may be related to many factors. Spontaneous hyperadrenocorticism usually develops in older dogs that tend to be overweight, both of which are factors that can affect the blood pressure. In addition, not only cortisol but also cortisol precursors may increase blood pressure in dogs with spontaneous hyperadrenocorticism. In the present study, we used young adult dogs with a healthy body condition, and only exogenous cortisol was administered.

Hepatic echogenicity was significantly increased and hepatic size and percentage of vacuolated hepatocytes were higher (although not significantly so), compared with baseline values, 7 days after administration of prednisolone was initiated in the present study. Only mild hepatomegaly was noted, and the size of the liver decreased slightly after the prednisolone dosage was decreased to 1 mg/kg/d. This result was not consistent with findings of a previous study in which hepatic weight increased almost 3-fold after...
IM administration of prednisolone at a dosage of 4 mg/kg/d for 15 days. The route of administration and dosage of prednisolone may be factors that influence the degree of liver change.

On ultrasonographic images, changes in hepatic echogenicity and texture were obvious enough that they could be detected subjectively 7 days after prednisolone administration was initiated. However, it was difficult to assess further changes in echogenicity after this time. In the study, liver-kidney contrast and depth attenuation of the hepatic image were determined by means of histogram assessment to compensate for the variability in subjective assessment. Unfortunately, reproducibility of the results of histogram assessment was not particularly high. Various factors such as angle and contact of the probe with the dog, pressure applied by the operator, and intra-abdominal pressure of the dog may have been responsible. However, power output, gain setting, frequency, and time-gain compensation were fixed in an effort to minimize the effect of these factors on histogram assessment. Values for liver-kidney contrast and depth attenuation did not correlate with hepatic size, hepatic enzyme activities, or percentage of vacuolated hepatocytes. Liver-kidney contrast was significantly increased on day 7 and remained high until the end of the study, whereas hepatic size and percentage of vacuolated hepatocytes slightly decreased as the prednisolone dosage was tapered. Our findings were not consistent with results of a previous study in which liver-kidney contrast correlated well with histologic findings in dogs given prednisolone at a high dosage (4.4 mg/kg/d) for 30 days. Depth attenuation has been reported to be the earliest detectable change after administration of prednisolone at a high dosage. In the present study, however, depth attenuation did not show consistent changes over time.

The percentage of vacuolated hepatocytes in the present study was lower than values reported in a previous study in which dogs were given prednisolone at a low dosage for 2 weeks and > 70% of hepatocytes were vacuolated. In a separate study, when prednisolone was administered IM at a dosage of 4.4 mg/kg/d for 18 days, nearly 100% of hepatocytes were reportedly vacuolated. Percentage of vacuolated hepatocytes has been found to be related to both the dosage of prednisolone and the route of administration, with IM administration shown to induce more severe vacuolization of the liver than oral administration.

Changes in hepatic enzyme activities in the present study were not significant and were slow to develop. The most dramatic change was observed in mean ALP activity, which, at its peak, was approximately 5 times the baseline value. However, the mean value was still within the reference range. This result was consistent with findings of a previous study in which serum ALP activity was not markedly increased when prednisolone was administered at a low dosage (1 mg/kg/d, PO) for 3 weeks. By contrast, serum ALP activity increased approximately 64-fold after IM administration of prednisolone at a dosage of 4.4 mg/kg/d for 2 days. It has been suggested that the increase in hepatic enzyme activities depends on the dosage of prednisolone given and that damage to the liver caused by prednisolone can be minimized with administration of a low dosage that is gradually tapered. However, serum hepatic enzyme activities have not been found to necessarily correspond with degree of damage to the liver.

Adrenocortical suppression caused by prednisolone depends on the dosage of drug used. Change in adrenal gland size was the most obvious finding following administration of prednisolone; this occurred later than the hyperechoic changes to the liver. Adrenal gland size increased again after the dosage of prednisolone was decreased to 0.5 mg/kg/d, but values were not significantly different from the baseline value at any evaluation time. A previous study found that approximately 2 weeks were needed to recover adrenal function after administration of prednisolone at a low dosage (0.55 mg/kg, PO, q 12 h for 5 weeks) was discontinued.

In the present study, there was no evidence of acute pancreatitis, such as decreased pancreatic echogenicity, increased pancreatic size, or peripancreatic fat saponification, during prednisolone administration. However, clinicopathologic testing to confirm pancreatitis, such as measurement of pancreatic lipase immunoreactivity concentration, was not performed. Pancreatic echogenicity was slightly increased; however, this was not a significant change. Further investigation is needed to determine whether prednisolone administration results in pancreatic changes.

The present study had several limitations. First, a small number of dogs was used in the study. Thus, there was a low power to identify significant changes even if they existed. Second, vacuolar changes in the liver were evaluated by means of cytologic examination of fine-needle aspirates, rather than histologic evaluation of biopsy specimens. However, results of cytologic examination of ultrasound-guided fine-needle aspirates have been shown to have good agreement with histopathologic diagnoses in dogs with vacuolar hepatopathy. Third, serum pancreatic lipase immunoreactivity concentration was not measured. However, clinical and ultrasonographic evidence of pancreatitis was not observed. Finally, dogs were not followed up after prednisolone administration ended. Thus, recovery time for hepatic size and echogenicity, hepatocyte vacuolization, or adrenal gland atrophy could not be determined.

Given the results of the present study, radiography and ultrasonography for monitoring hepatic size and echogenicity should be used in addition to measurement of hepatic enzyme activities to evaluate the effects of low-dosage prednisolone administration. If markedly increased hepatic enzyme activities are observed in dogs receiving prednisolone at a low dosage, it is probable that another factor is the underlying-
ing cause. Because the changes seen in the present study appeared to be reversible once the prednisolone dosage was decreased, monitoring of the liver and adrenal glands after tapering of the prednisolone dosage is recommended to help distinguish the effects of prednisolone from other pathological conditions.

**Acknowledgments**

Supported by the Basic Science Research Program through the National Research Foundation of Korea, funded by the Ministry of Science, ICT and Future Planning (2015R1A2A2A01003313).

**Footnotes**

b. Catalyst Dx Chemistry Analyzer, Idexx, Westbrook, Me.
c. Prosound α7, Hitachi Aloka Medical, Tokyo, Japan.
d. SPSS Statistics 20, IBM Corp, New York, NY.

**References**