α-Lipoic acid is a coenzyme for several intramitochondrial α-keto-dehydrogenases (eg, pyruvate dehydrogenase) and is used as an antioxidant or mitochondrial nutrient in many animal species.1,2 Activity of pyruvate dehydrogenase is decreased in older animals; however, this may be mitigated by providing increased concentrations of α-lipoic acid in the diet.3 Furthermore, it has been suggested 4 that α-lipoic acid should be considered as a conditionally essential mitochondrial nutrient.

α-Lipoic acid may be obtained by the ingestion of foods that contain lipoyllysine or by de novo biosynthesis within mammalian cells.3 α-Lipoic acid occurs in nature as an amino acid–bound R-α enantiomer, lipoyllysine, which is believed to undergo minimal cleavage before gastrointestinal absorption.5 Cysteine is the source of sulfur and octanoate is the intermediate precursor for the 8-carbon fatty acid used during de novo biosynthesis of α-lipoic acid. A protein-bound complex is usually the product of de novo α-lipoic acid biosynthesis.1,2,6 Only minor amounts of unbound α-lipoic acid derived from ingested food or de novo biosynthesis are found in the noncellular mammalian blood matrix.7–9 Most of the free form of α-lipoic acid is partitioned into intracellular compartments, with the highest concentrations detected in liver, heart, and kidney.7–9

When radiolabeled DL-α-lipoic acid is administered orally to dogs, > 60% of the radiolabel undergoes urinary excretion within 24 hours after administration, and overall, 80% is renally excreted within 72 hours.10 However, most of the radiolabeled compounds recover.
Bioavailability of D,L-α-lipoic acid when administered orally in humans at dosages between 50 and 600 mg is between 0.5 and 1 hour and displays a dose-proportional relationship. The bioavailability of enantiomers of α-lipoic acid when administered orally in humans is decreased in solid formulations, compared with the bioavailability of α-lipoic acid in aqueous formulations. Additionally, concurrent food intake (fed status) significantly reduced bioavailability of α-lipoic acid when administered orally in humans. Investigators have reported differences in bioavailability between the 2 enantiomers of α-lipoic acid in humans.

Bioavailability of D,L-α-lipoic acid when comanufactured as an ingredient in a nutritionally complete dog food has not been directly assessed. However, dogs fed extruded foods that included D,L-α-lipoic acid as an ingredient resulted in an increase of the reduced glutathione-to-oxidized glutathione ratio in WBCs, which is consistent with improved antioxidant status. During the processing of nutrients in commercial pet foods, adducts of compounds may occur and impact bioavailability as seen with Maillard products and lysine. The purpose of the study reported here was to evaluate the effect of method of delivery and dosage on pharmacokinetic parameters of D,L-α-lipoic acid in dogs when administered in a capsule form and provided without a meal, in a capsule form and provided with a meal, or included as an ingredient in a nutritionally complete extruded dog food.

Materials and Methods

Animals—Twenty-seven clinically normal adult Beagles with ages ranging from 3.7 to 13.5 years (mean ± SD, 7.8 ± 2.8 years) were used for this study. The dogs included 13 neutered males, 1 sexually intact male, 12 spayed females, and 1 sexually intact female. A physical examination was performed on each dog, and all dogs were vaccinated against canine distemper virus, adenovirus, parvovirus, bordetellosis, and rabies. Because factors such as disease and inflammation could have confounded the results of the study, a CBC and serum biochemical analysis were performed to verify the health status of each dog.

Dogs were selected for their ability to consume an entire daily ration in ≤ 30 minutes after the ration was offered. Dogs were housed in pairs and fed once daily. Dogs received behavioral enrichment through dog interactions, daily interactions and play time with caretakers, and access to toys. The study protocol was reviewed and approved by the Hill’s Pet Nutrition Institutional Animal Care and Use Committee.

Food formulation—A nutritionally complete extruded canine maintenance food was fed to all dogs on all of the nontreatment days in an amount sufficient to achieve the daily caloric intake requirement of each animal based on historical records for each animal. Three variations of the base extruded food were specially formulated with D,L-α-lipoic acid to provide a target dosage of 2.5, 12.5, or 25 mg of D,L-α-lipoic acid/kg when administered orally on treatment days. Proximate analysis of the extruded dog foods included measurements for moisture content, protein, fat, ash, calcium, and phosphorus at a commercial laboratory.

Capsules containing D,L-α-lipoic acid—Quantities of a powder containing D,L-α-lipoic acid were weighed specifically for each dog to provide target dosage of 2.5, 12.5, or 25 mg of D,L-α-lipoic acid/kg dosages that were in a capsule form and provided without a meal; 2.5, 12.5, and 25 mg of D,L-α-lipoic acid/kg dosages that were in a capsule form and provided with a meal; and 2.5, 12.5, and 25 mg of D,L-α-lipoic acid/kg dosages that were included as an ingredient in a nutritionally complete extruded dog food. All treatments were separated by a minimum washout period of 7 days. Food was withheld from all treatment groups for 12 hours before the start of each phase of the study. Water was supplied ad libitum.

Sample collection—A vacutainer system was used for the collection of 2 mL of blood from a jugular vein immediately before (0 minutes) and 15, 30, 45, 60, and 120 minutes after treatment administration into evacuated tubes with K2EDTA. Tubes were centrifuged at 1,462 × g for 10 minutes at 4°C to separate plasma from the cellular fraction. One-milliliter aliquots of plasma were then transferred to microcentrifuge tubes and stored at −70°C until quantitation of D,L-α-lipoic acid was performed.

Quantitation of D,L-α-lipoic acid concentration in food and plasma by use of HPLC—Quantitation of D,L-α-lipoic acid concentration in extruded maintenance and specially formulated extruded dog foods was performed by use of a previously described analytic method. Quantitation of D,L-α-lipoic acid concentration in canine plasma was performed by use of a previously described HPLC method with some modifications. Samples were thawed and allowed to equilibrate to 25°C and then mixed. One hundred microliters of each plasma sample was
removed and transferred to a separate 2-mL microcentrifuge tube. Ten microliters of a 100 mg/mL solution of TCEP (tris[2-carboxyethyl]phosphine hydrochloride in water) was added to each sample, and samples then were mixed. Samples were then incubated at 4°C for ≥ 30 minutes. One hundred microliters of a sulfosalicylic acid solution (6% sulfosalicylic acid and 1mM EDTA in water) was added to each sample, and samples then were mixed. Samples were incubated for 10 minutes at 25°C. Samples were then centrifuged at 18,700 × g for 11 minutes at 5°C. A 100-µL aliquot of the supernatant solution from each sample was removed and transferred into a new 2-mL microcentrifuge tube. Two hundred microliters of a borate buffer (2.5M borate, 4m EDTA [pH, 10.5]) and 100 µL of an SBD-F solution (1 mg of an ammonium salt of 7-fluorobenzofurazan-4-sulfonic acid/mL added to the borate buffer [pH, 9.5]) were added to each sample. Samples were mixed and then centrifuged at 3,700 × g for 5 minutes at 5°C. Then, samples were incubated in a water bath at 60°C for 1 hour. Samples were removed from the water bath and cooled at 4°C for 20 minutes before being transferred to HPLC autosampler vials.

Chromatography was performed by use of an HPLC system equipped with a solvent degasser, quaternary pump, autosampler, column-heater compartment, and fluorescence detector. The α-lipoic acid derivative was analyzed via reversed-phase HPLC at 25°C by use of an HPLC analytic column (length, 150 x 4.6 mm; diameter, 5 µm) and a guard cartridge. Separation of analytes was performed by use of a gradient elution with a flow rate of 1 mL/min. Mobile phase A comprised methanol (proportion, 2%) and 0.1M phosphate buffer (pH 6; proportion, 98%). Mobile phase B comprised methanol (proportion, 50%) and water (proportion, 50%). A mobile phase gradient was used as follows: 0 minutes, 50% of A and 50% of B; 10 minutes, 100% of B; 15 minutes, 100% of B; 16 minutes, 50% of A and 50% of B; and 21 minutes, 50% of A and 50% of B. A 50-µL injection of each sample was used in the analysis. The α-lipoic acid derivative was quantified by use of fluorescences at 385 nm (excitation) and 515 nm (emission) and a photomultiplier tube gain of 15. A designation was not made between the concentration of the α and β enantiomers of α-lipoic acid during HPLC analysis. A commercial software program was used to control the HPLC analytic column (length, 150 x 4.6 mm; diameter, 5 µm) and a guard cartridge. A 50-µL injection of each sample was used in the analysis. The α-lipoic acid derivative was quantified by use of fluorescences at 385 nm (excitation) and 515 nm (emission) and a photomultiplier tube gain of 15. A designation was not made between the concentration of the α and β enantiomers of α-lipoic acid during HPLC analysis. A commercial software program was used to control the HPLC analytic column (length, 150 x 4.6 mm; diameter, 5 µm) and a guard cartridge. A 50-µL injection of each sample was used in the analysis. The α-lipoic acid derivative was quantified by use of fluorescences at 385 nm (excitation) and 515 nm (emission) and a photomultiplier tube gain of 15. A designation was not made between the concentration of the α and β enantiomers of α-lipoic acid during HPLC analysis.

Results

Physical examinations and analysis of the results of CBCs and serum biochemical analyses did not reveal chronic systemic disease in any of the dogs included in this study. Results of the analysis and concentrations of α-lipoic acid (as fed) in the extruded maintenance dog food and the 3 specially formulated variations of the extruded maintenance dog food were summarized (Table 1). Five dogs (1 dog orally administered the 2.5 mg of α-lipoic acid/kg dosage that was included in an extruded food, 2 dogs orally administered the 12.5 mg of α-lipoic acid/kg dosage that was included in an extruded food, 1 dog orally administered the 25 mg of α-lipoic acid/kg dosage that was included in an extruded food) did not receive ≥ 80% of the target dose. Therefore, results for these 5 dogs were excluded from all subsequent analyses. Included in the analyses were results for the 3 dogs that had consumed α-lipoic acid dosages in excess of the targeted dosages, which was attributable to overeating. Instead of being provided a 2.5 mg of α-lipoic acid/kg dosage that was included in an extruded food, 1 dog orally administered the 25 mg of α-lipoic acid/kg dosage that was included in an extruded food, 2 dogs orally administered the 12.5 mg of α-lipoic acid/kg dosage that was included in an extruded food, and 1 dog orally administered the 2.5 mg of α-lipoic acid/kg dosage that was included in an extruded food. In all 3 instances, the actual dosage of α-lipoic acid consumed was used as the dosage in the noncompartmental pharmacokinetic analyses.

HPLC analysis—In 3 dogs at 1 time point each, plasma concentrations of α-lipoic acid were 3 to 8 times as high as concentrations of other dogs in the study. These increased plasma concentrations were detected 30 minutes after treatment in 2 dogs; this occurred in 1 dog administered dosages of 2.5 and 12.5 mg of α-lipoic acid/kg in a capsule form and provided without a meal and at 15 minutes for the other
Table 1—Results of proximate analysis and concentrations of α-lipoic acid (as fed) in a nutritionally complete extruded dog food and 3 variations of the extruded dog food formulated to provide target dosages of 2.5, 12.5, or 25 mg of α-lipoic acid/kg.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Maintenance</th>
<th>2.5 mg of α-lipoic acid/kg</th>
<th>12.5 mg of α-lipoic acid/kg</th>
<th>25 mg of α-lipoic acid/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moisture content (%)</td>
<td>8.2</td>
<td>8.1</td>
<td>8.3</td>
<td>8.5</td>
</tr>
<tr>
<td>Protein (%)</td>
<td>23.5</td>
<td>23.9</td>
<td>23.3</td>
<td>23.9</td>
</tr>
<tr>
<td>Fat (%)</td>
<td>14.9</td>
<td>14.6</td>
<td>15.4</td>
<td></td>
</tr>
<tr>
<td>Ash (%)</td>
<td>4.9</td>
<td>5.0</td>
<td>4.8</td>
<td>5.1</td>
</tr>
<tr>
<td>Calcium (%)</td>
<td>0.74</td>
<td>0.81</td>
<td>0.74</td>
<td>0.81</td>
</tr>
<tr>
<td>Phosphorus (%)</td>
<td>0.54</td>
<td>0.58</td>
<td>0.56</td>
<td>0.59</td>
</tr>
<tr>
<td>α-lipoic acid (μg/mL)*</td>
<td>15</td>
<td>191</td>
<td>602</td>
<td>1,145</td>
</tr>
</tbody>
</table>

One sample was analyzed for each extruded dog food.

*A designation was not made between the concentrations of the α and l enantiomers of α-lipoic acid during the analysis.

Table 2—Range, mean ± SD, and median values for pharmacokinetic parameters determined via noncompartmental analysis for dl-α-lipoic acid in plasma samples obtained from Beagles orally administered α-α-lipoic acid in a capsule form and provided with or without a meal and included as an ingredient in an extruded dog food.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Capsule without meal</th>
<th>Capsule with meal</th>
<th>Extruded dog food</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (ng/mL)</td>
<td>Range</td>
<td>Mean ± SD</td>
<td>Median</td>
</tr>
<tr>
<td>α-lipoic acid</td>
<td>96–2,089</td>
<td>962–3,210</td>
<td>1,602</td>
</tr>
<tr>
<td>β-lipoic acid</td>
<td>97–2,129</td>
<td>1,408–9,928</td>
<td>3,649</td>
</tr>
<tr>
<td>γ-lipoic acid</td>
<td>12.5</td>
<td>12.5</td>
<td>12.5</td>
</tr>
<tr>
<td>Absolute bioavailability</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
| *A designation was not made between the concentrations of the α and l enantiomers of α-lipoic acid during the analysis.

Values in parentheses are the number of dogs.

†Within a row within a dosage, values differ significantly (P < 0.05). †Within a dosage, values were not significantly different.

Noncompartmental analysis—Range, mean ± SD, and median values for pharmacokinetic parameters of α-lipoic acid determined via noncompartmental analysis were summarized (Table 2). It is noteworthy that the terminal slope on the semilogarithmic plots for all plasma concentrations of dl-α-lipoic acid in dogs fed the extruded foods at all dosages were almost 0 or > 0. Thus, few subjects were qualified for estimation of λz; therefore, all variables that were calculated by use of λz, including T1/2 and AUC0–last, may not have accurately defined the true pharmacokinetic profile for dl-α-lipoic acid when included in an extruded dog food.

Cmax—Dosage had a significant effect on Cmax regardless of the method of delivery. A significant difference was detected for method of delivery within each dosage group. Dogs orally administered dl-α-lipoic acid at dosages of either 2.5 or 12.5 mg/kg displayed the highest Cmax when dl-α-lipoic acid was administered in a capsule form and provided without a meal. The second highest Cmax from these same 2 dosage groups was detected in dogs administered a capsule form and pro-

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vided with a meal. Conversely the highest mean plasma concentration in the group of D,L-α-lipoic acid at the dosage of 25 mg/kg was observed when administered the oral capsule form provided with a meal. The second highest mean plasma concentration in this same group was observed in dogs administered a capsule form provided without a meal. A significantly lower mean C\text{max} was detected at all dosage levels when D,L-α-lipoic acid was included as an ingredient in an extruded dog food, compared with the mean C\text{max} when D,L-α-lipoic acid was orally administered in a capsule form and provided with or without a meal.

C\text{\text{max}⁠}—A significant effect of route of delivery was only detected for the 2.5 mg of α-lipoic acid/kg dosage; this may have been attributable to the higher C\text{max} of D,L-α-lipoic acid achieved when administered in a capsule form after a 12-hour food withdrawal. The C\text{max} was not significantly different between methods of delivery when D,L-α-lipoic acid was administered at the 2.5 mg/kg dosage in a capsule form and provided with a meal or administered as an ingredient in an extruded dog food. There was no effect of delivery method on C\text{\text{max}} for the 12.5 or 25 mg/kg dosages.

AUC\text{0–\text{\text{last}}} —Method of delivery had a significant effect on AUC\text{0–\text{\text{last}}} for dogs orally administered the 12.5 and 25 mg/kg dosages of D,L-α-lipoic acid. A comparison between plasma concentrations when D,L-α-lipoic acid was administered orally in a capsule and provided with or without a meal did not reveal a significant difference in plasma concentrations at any dosage and suggested that the significant differences observed when a comparison was made between methods of delivery were attributable to a decrease in AUC\text{0–\text{\text{last}}} when D,L-α-lipoic acid was included as an ingredient in an extruded food. A similar pattern was observed for the 2.5 mg/kg dosage as in the 12.5 and 25 mg/kg dosages; the largest AUC\text{0–\text{\text{last}}} was calculated from data from dogs orally administered D,L-α-lipoic acid in a capsule form without a meal followed respectively by the capsule form provided with a meal and finally when included as an ingredient in an extruded dog food. The oral administration of D,L-α-lipoic acid in a capsule form and provided with a meal resulted in a 51% decrease in the AUC\text{0–\text{\text{last}}} at the 2.5 mg/kg dosage. However, calculations for AUC\text{0–\text{\text{last}}} at the 2.5 mg/kg dosages were based on many results of D,L-α-lipoic acid in plasma concentrations that were below the level of quantitation, especially when D,L-α-lipoic acid was included as an ingredient in an extruded food; therefore, this may have resulted in an artificially decreased AUC\text{0–\text{\text{last}}} for this dosage group.

T\text{\text{\text{max}⁠}—There was a significant effect of method of administration on T\text{\text{\text{max}} only at the 2.5 mg/kg dosage where the greatest time value was observed for the α-lipoic acid when it was included as an ingredient in an extruded dog food, compared with the oral administration of α-lipoic acid in a capsule form and provided with or without a meal. There was no significant difference detected at the 12.5 or 25 mg/kg dosages.

Discussion

Analysis of the results of the study reported here revealed that the pharmacokinetic parameters of D,L-α-lipoic acid were affected by both dosage and method of administration. Absorption is decreased when D,L-α-lipoic acid is included as an ingredient in an extruded food, compared with absorption of a comparable dosage of D,L-α-lipoic acid when administered orally in a capsule form and provided with or without a meal. Minimal and mostly nonsignificant differences were detected between reported pharmacokinetic parameters when D,L-α-lipoic acid was administered orally in a capsule form and provided with or without a meal. Most of the significantly different results detected were because of the comparatively reduced absorption of D,L-α-lipoic acid from all 3 of the specially formulated extruded dog foods. The present study also revealed that plasma concentrations of α-lipoic acid increased in proportion with the dosage administered, regardless of the method of administration.

The C\text{max} for enantiomerically pure R-α-lipoic acid in humans varies from 400 to 1,150 ng/mL when 1,000 mg of R-α-lipoic acid is administered orally. A C\text{max} of 5,000 to 10,000 ng/mL has been reported for 300 and 600 mg of R-α-lipoic acid when administered as the tromethamine salt, respectively. A C\text{max} of 16 µg/mL was observed when 600 mg of R-α-lipoic acid was administered orally to humans. When 600 mg was administered orally to the same individual, the C\text{max} of the sodium salt form of R-α-lipoic acid was 25.86 times as high as the C\text{max} observed for the aqueous form of R-α-lipoic acid. The oral administration of a 2.6 mg of a racemic mixture of RS-α-lipoic acid/kg dosage in a capsule to humans resulted in a C\text{max} of 1.95 and 1.17 µg/mL for the R and S forms, respectively. Body weights of the humans in these studies were not reported; however, if a 70-kg body weight is used, an approximate oral dosage of 8.6 to 14.3 mg of α-lipoic acid/kg would result from the intake of 600 to 1,000 mg of α-lipoic acid. These dosages of α-lipoic acid are within the range of dosages for oral administration to dogs in the present study and resulted in comparable values for C\text{max} (C\text{max range, 47 ng/mL [2.5 mg of D,L-α-lipoic acid/kg dosage that was included in an extruded dog food] to 5,441 ng/mL [25 mg of α-lipoic acid/kg dosage in a capsule form and provided with a meal]). The variance in the values for C\text{max} in humans may be attributable to the forms of α-lipoic acid administered, methods of quantitation, and differences in fasting or withholding food before the administration of α-lipoic acid. The oral administration of α-lipoic acid followed by ingestion of fat 100 minutes later results in a second peak in the plasma concentration of α-lipoic acid and indicates that ingestion of fat enhances absorption of α-lipoic acid after an initial administration. Thus, food, nutrient profile of a food, and time of food ingestion may influence the plasma concentration of α-lipoic acid detected.

The C\text{\text{max}⁠ of α-lipoic acid for the dogs in the study reported here was within the range of values reported for other species. Analysis of results of the present study revealed that concentrations of D,L-α-lipoic
acids in plasma increased with increasing dosages of \( DL-\alpha \)-lipoic acid for each method of delivery. When \( DL-\alpha \)-lipoic acid was administered as a capsule, the concomitant administration of food generally reduced concentrations in plasma. An exception to this was increased concentrations for dogs administered a 25 mg of \( \alpha \)-lipoic acid/kg dosage in a capsule form that was concomitantly administered with a meal. The reasons for this phenomenon remain unknown, but they could have been related to incomplete dosage administration, errors during analysis, or some other technical abnormality. However, because the differences between the mean values for the \( C_{\text{max}} \) of orally administered \( DL-\alpha \)-lipoic acid when in a capsule form and provided with or without a meal were not significant, the technical issues of the events that led to this may not be important. The real difference also may have been related to the variability of \( C_{\text{max}} \) among dogs.

The \( T_{\text{max}} \) of orally administered \( DL-\alpha \)-lipoic acid ranged between 21.7 minutes (2.5 mg/kg dosage that was included as an ingredient in an extruded food) and 105 minutes (2.5 mg/kg dosage that was included as an ingredient in an extruded food). This range of \( T_{\text{max}} \) values approximates that reported\(^{1,17} \) in other animal species. In plasma, \( \alpha \)-lipoic acid is rapidly absorbed into cells and converted to dihydro-\( \alpha \)-lipoic acid. \( \alpha \)-Lipoic acid is partitioned in plasma between the protein-bound and unbound forms. Most analytic methods detect total \( \alpha \)-lipoic acid in plasma and do not distinguish between protein-bound and unbound forms. Movement of \( \alpha \)-lipoic acid from plasma is likely the result of cellular absorption, metabolism into other metabolites, or elimination from the vascular space by renal or hepatic mechanisms.\(^{2} \)

The \( T_{\text{max}} \) of \( \alpha \)-lipoic acid from plasma was similar among the dosages administered orally in a capsule form and provided with or without a meal but less than when \( \alpha \)-lipoic acid was included in an extruded dog food. The \( T_{\text{max}} \) of \( DL-\alpha \)-lipoic acid when administered orally in a capsule form and provided with or without a meal was similar to that of other species.\(^{1,2,7,17,18} \) Despite the longer \( T_{\text{max}} \), the \( C_{\text{max}} \) of \( DL-\alpha \)-lipoic acid was attributed to a lower \( C_{\text{max}} \). The longer \( T_{\text{max}} \) observed in dogs fed the extruded foods may have been attributable to slower absorption from the gastrointestinal tract because of the complex matrix used to formulate the extruded foods.

Pharmacokinetic parameters of \( DL-\alpha \)-lipoic acid when administered orally to the dogs of the present study were significantly affected by whether a capsule or extruded dog food was used to provide \( DL-\alpha \)-lipoic acid and, to a lesser extent, whether \( DL-\alpha \)-lipoic acid was administered in a capsule form and provided with a meal. The inclusion of \( DL-\alpha \)-lipoic acid as an ingredient in an extruded dog food significantly decreased \( C_{\text{max}} \) and delayed \( T_{\text{max}} \), compared with \( C_{\text{max}} \) and \( T_{\text{max}} \) when \( DL-\alpha \)-lipoic acid was administered orally to dogs in a capsule form and provided with or without a meal following withholding of food for 12 hours. The pharmacokinetic parameters of \( DL-\alpha \)-lipoic acid when administered orally in capsules were minimally affected by the fed status; furthermore, these parameters were similar when compared with the results of other species. In addition, the plasma concentration of \( \alpha \)-lipoic acid was proportional to the dosage administered, regardless of whether it was administered orally in a capsule form or included as an ingredient in an extruded dog food.

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Correction: Evaluation of peptide- and recombinant protein–based assays for detection of anti–Ehrlichia ewingii antibodies in experimentally and naturally infected dogs

In this report, published October 2010 (Am J Vet Res 2010;71:1195–1200), the title was printed in error and should appear as follows: Evaluation of peptide- and recombinant protein–based assays for detection of anti–Ehrlichia ewingii antibodies in experimentally and naturally infected dogs.