

Standard Article

J Vet Intern Med 2016;30:1790–1797**Feline Exocrine Pancreatic Insufficiency: A Retrospective Study of 150 Cases**

P.G. Xenoulis, D.L. Zoran, G.T. Fosgate, J.S. Suchodolski, and J.M. Steiner

Background: Little information is available about the clinical presentation and response to treatment of cats with exocrine pancreatic insufficiency (EPI).

Objectives: To describe the signalment, clinical signs, concurrent diseases, and response to treatment of cats with EPI.

Animals: One hundred and fifty cats with EPI.

Methods: Retrospective case series.

Results: Questionnaires were sent to 261 veterinarians, and 150 (57%) were returned with data suitable for statistical analysis. The median age of the cats with EPI was 7.7 years. The median body condition score was 3 of 9. Ninety-two of 119 cats (77%) had hypcobalaminemia, and 56 of 119 cats (47%) had increased and 6 of 119 cats (5%) had decreased serum folate concentrations. Clinical signs included weight loss (91%), unformed feces (62%), poor hair coat (50%), anorexia (45%), increased appetite (42%), lethargy (40%), watery diarrhea (28%), and vomiting (19%). Eighty-seven cats (58%) had concurrent diseases. Treatment response was reported to be good in 60%, partial in 27%, and poor in 13% of 121 cats. Trypsin-like immunoreactivity <4 µg/L was associated with a positive response to treatment (OR, 3.2; 95% CI, 1.5–7.0; *P* = .004). Also, cobalamin supplementation improved the response to treatment (OR, 3.0; 95% CI, 1.4–6.6; *P* = .006).

Conclusions and Clinical Importance: Exocrine pancreatic insufficiency in cats often has a different clinical presentation than in dogs. The age range for EPI in cats is wide, and many cats can be ≤5 years of age. Most cats respond well to appropriate treatment for EPI, and cobalamin supplementation appears to be necessary for a good response.

Key words: Cat; Cobalamin; Exocrine pancreatic insufficiency; Treatment.

Exocrine pancreatic insufficiency (EPI) is characterized by inadequate production of pancreatic enzymes from pancreatic acinar cells and has been previously considered rare in the cat.¹ The related literature consists mainly of case reports of confirmed or suspected EPI cases in cats, with only 10 reports published between 1975 and 2009.^{2–11} In addition, there have been only 2 small case series of EPI in cats that have been reported in the English peer-reviewed literature. The first of those studies evaluated the clinical utility of serum feline trypsin-like immunoreactivity (fTLI)

Abbreviation:

EPI	exocrine pancreatic insufficiency
BCS	body condition score
ERT	enzyme replacement treatment
fTLI	feline trypsin-like immunoreactivity
IQR	interquartile range
SIBO	small intestinal bacterial overgrowth

concentration in 20 cats with a diagnosis of EPI.¹² The results of that study established serum fTLI concentration as the most useful test for the diagnosis of EPI in cats. In the second, more recent study, the aim was to describe the clinical and clinicopathologic findings in 16 cats with EPI.¹¹

Since the introduction and validation of the fTLI test,¹³ EPI in cats has been diagnosed more frequently.¹ However, many cases still may remain undiagnosed.¹ This suggestion is not surprising if one takes into consideration the fact that the clinical presentation, clinicopathologic findings, treatment options, and response to treatment of cats with EPI have not been well described. Therefore, the aim of our study was to describe the signalment, clinical signs, clinicopathologic abnormalities, concurrent diseases, and response to treatment in cats with EPI. In addition, data were analyzed to identify factors that may be associated with response to treatment.

Materials and Methods**Study Population and Data Collection**

The database of the Gastrointestinal Laboratory, College of Veterinary Medicine and Biomedical Sciences at Texas A&M University, was searched for a period of 23 months (from

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This work was performed at the Gastrointestinal Laboratory, Department of Small Animal Clinical Sciences, Texas A&M University, College Station, TX.

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March 2008 to January 2010) for cats with a serum trypsin-like immunoreactivity (fTLI) concentration diagnostic for EPI. The diagnostic criterion for EPI was a serum fTLI concentration ≤ 8 $\mu\text{g/L}$, which is the currently recommended cutoff value for the diagnosis of EPI in cats.^{1,12} A random subset ($n = 261$) of submitting veterinarians were contacted by phone (up to 3 times each) and asked to participate in this study by filling out a standardized questionnaire for each affected cat. Questions included age at diagnosis, breed, sex and neuter status, body weight and body condition score (BCS), medical history, clinical signs, concurrent medical problems, and treatment (including type of pancreatic enzyme replacement, dietary modifications, and adjunctive treatment). For each cat, the response to treatment was subjectively graded by the submitting veterinarian as good, partial, or poor. In general, a cat was considered to have a good response to treatment when no or only minimal clinical signs were present (eg, occasional soft feces), partial response when improvement was observed but clinical signs still were present (eg, less than ideal weight gain, diarrhea less severe than before), and poor when there was no or only minimal improvement. Where available, serum cobalamin and folate concentrations at the time of diagnosis were retrieved from the medical records. Cats for which it was reported by the veterinarians that the owners did not closely follow the recommended treatment were excluded from the study.

Assays

Serum fTLI concentrations were measured by a validated radioimmunoassay.^{12,13} The reference interval of the assay is 12–82 $\mu\text{g/L}$, and serum concentrations ≤ 8 $\mu\text{g/L}$ are considered diagnostic for EPI.^{12,13} Serum cobalamin^a and folate^b concentrations were measured using commercially available chemiluminescent assays validated for use in cats. The reference intervals in cats are 290–1,500 ng/L for cobalamin and 9.7–21.6 $\mu\text{g/L}$ for folate.

Statistical Analyses

The normality assumption was assessed for quantitative variables by plotting histograms, calculating descriptive statistics, and performing the Anderson–Darling test^c or the Kolmogorov–Smirnov test.^d Categorical data were described using frequencies, proportions, and mid- P exact 95% confidence intervals.^e Quantitative data with a Gaussian distribution were reported as mean \pm standard deviation (SD) and non-normal data using median and interquartile range (IQR). Data were compared among groups using Kruskal–Wallis and Mann–Whitney U -tests for 3 and 2 group comparisons, respectively. Associations between exposure variables and clinical response to enzyme replacement treatment (ERT) were estimated using binary logistic regression. Quantitative data were categorized before statistical analysis using reference intervals or medians of the distributions. Univariate screening models were fit, and all variables with $P < .20$ were selected for inclusion in a multivariable logistic regression model. The multivariable model was fit using a backward stepwise approach starting with all main effects identified in the screening models. Variables were removed one by one based on the largest Wald P values and continued until all remaining variables were $P < .05$. Interaction terms were not evaluated, and the fit of the final multivariable model was assessed using the Hosmer–Lemeshow test. Statistical comparisons and modeling were performed with a commercially available software package^f and results interpreted at the 5% level of significance.

Results

Study Population

Serum from 46,529 cats was submitted for measurement of fTLI concentration during the study period. Of these, 1,095 (2.4%) cats had a fTLI concentration ≤ 8 $\mu\text{g/L}$. Questionnaires were sent to a random sample ($n = 261$) of the submitting veterinarians of these 1,095 cats. A total of 150 questionnaires (57%) were returned and contained sufficient information for inclusion in the study. Breeds included domestic short-haired (94 cats), domestic long-haired (15), domestic medium-haired (11), Maine Coon (7), British Shorthair (6), Siamese (6), Ragdoll (3), Abyssinian (1), Balinese (1), Himalayan (1), and Savannah (1), whereas 4 cats were of mixed breed. Sixty-one cats (41%) were female (all neutered), and 89 (59%) were male (86 neutered). The median (IQR) age of the cats was 7.7 (5.5, 11.4) years with an absolute range of 3 months to 18.8 years.

Clinical Signs

The most common clinical sign was weight loss, which was reported in 137 (91%) cats. In 8 cats (5.3%), weight loss was the only clinical sign reported. The median weight loss was 1.41 kg (range, 40 g to 6.8 kg). The median body condition score was 3 of 9 (range, 1 of 9 to 7 of 9). The median duration of weight loss was 6 months (range, 0.5 months to 4 years). Other clinical signs reported included unformed feces in 93 of 149 cats (62%; of these, 66% also had occasional watery diarrhea), poor hair coat in 73 of 145 cats (50%), increased appetite in 63 of 150 cats (42%), anorexia in 68 of 150 cats (42%), lethargy in 60 of 149 cats (40%), and vomiting in 29 of 150 cats (19%). Only 48 of 149 cats (32%) were presented with a combination of weight loss, unformed feces, and increased appetite, whereas 83 of 149 cats (56%) were presented with a combination of weight loss and unformed feces.

Serum Cobalamin and Folate Concentrations

Serum cobalamin and folate concentrations were measured in 119 cats. Of these 119 cats, 92 (77%) had serum cobalamin concentrations below the lower limit of the reference interval (median, 149 ng/L; range, 149–1,001 ng/L; Fig 1). Eighty-three cats (70%) had serum cobalamin concentrations below the detection limit of the assay (<150 ng/L). Serum fTLI concentrations in cats with hypcobalaminemia (median, 3.2 $\mu\text{g/L}$) were significantly lower than in cats with normal serum cobalamin concentrations (median, 5.5 $\mu\text{g/L}$; $P = .0013$; Fig 2). Fifty-six of 119 cats (47%) had increased and 6 cats (5%) had decreased serum folate concentrations (median, 21.1 $\mu\text{g/L}$; range, 3.9–121 $\mu\text{g/L}$; Fig 3). Forty-five cats (38%) had low serum cobalamin and high serum folate concentrations.

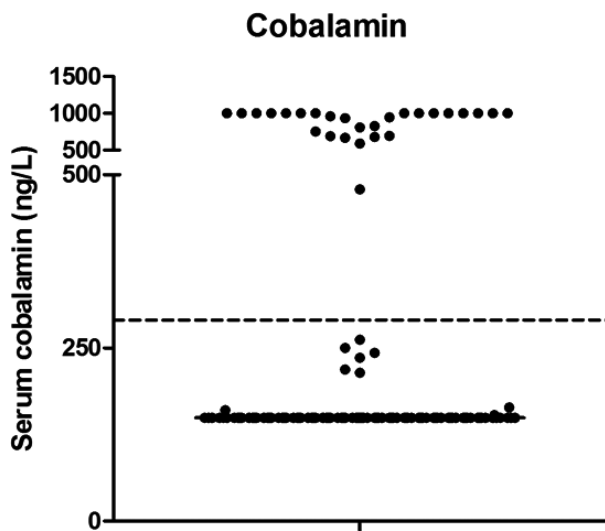


Fig 1. Serum cobalamin concentrations in cats with exocrine pancreatic insufficiency. The dashed line represents the lower limit of the reference interval. The solid line represents the median. Note that the y-axis is split.

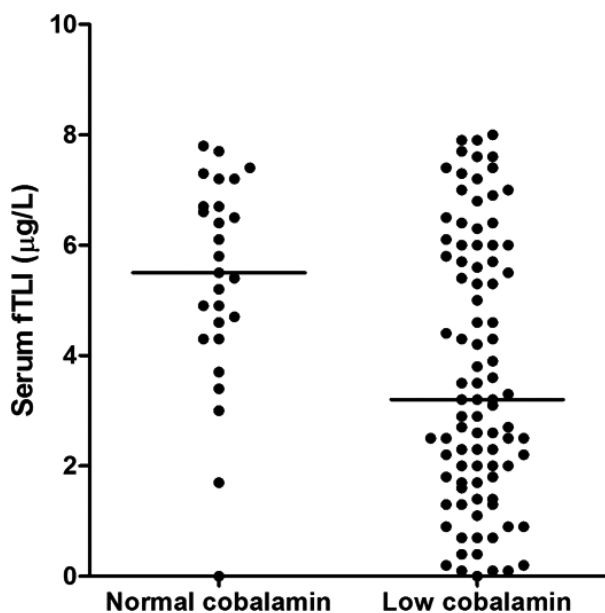


Fig 2. Serum feline trypsin-like immunoreactivity concentrations in cats with normal serum cobalamin concentrations and cats with low serum cobalamin concentrations. The horizontal lines represent the median for each group. There was a statistically significant difference between the two groups ($P = .0013$).

Concurrent Medical Problems

Eighty-seven cats (58%) were reported to have concurrent medical problems. The most common were gastrointestinal problems (30 of 150 cats; 20%), endocrine disorders (21 of 150 cats, 14%; including 13 cats [9%] with diabetes mellitus), pancreatitis (11%), and hepatic lipidosis (6%).

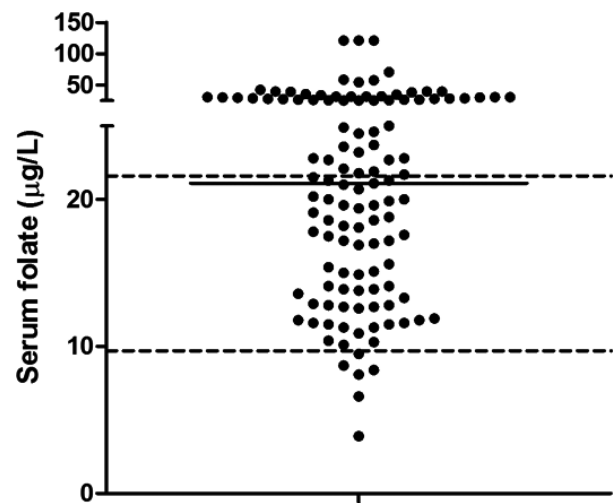


Fig 3. Serum folate concentrations in cats with exocrine pancreatic insufficiency. The dashed lines represent the reference interval. The solid line represents the median. Note that the y-axis is split.

Treatments

Accurate information regarding ERT was available for 121 cats. Products used included both enzyme powder and tablets, although the questions relating to enzyme treatment on the questionnaire did not require veterinarians to specify the exact type of product used in each case (ie, whether it was in powder or tablet form, whether it was enteric-coated or not). None of the cats received any form of raw pancreas as part of the ERT. Cats receiving ERT had lower BCS, more weight loss of longer duration, lower fTLI concentrations, and lower cobalamin concentrations (Table 1).

Antibiotics were used in 65 of 146 (45%) cats. The most commonly used antibiotic was metronidazole, which was used as the sole antibacterial in 39 cats (60% of cases treated with antibiotics or 27% of 146 cases). Other antibiotics, including enrofloxacin, amoxicillin, amoxicillin/clavulanic acid, tylosin, and clindamycin, were used in small numbers of cats (<5 each), whereas several cats were treated using different combinations of 2 or 3 antibiotics.

Cobalamin was given as part of EPI treatment in 72 of 147 cases (49%). None of the cats had received cobalamin before the diagnosis of EPI. Of the 72 cats that were supplemented with cobalamin, 18 (25%) had normal (10) or unknown (8) serum cobalamin concentrations.

Glucocorticoids were used in 34 of 146 cats (23%). Other treatments that were used in a small number of cases included probiotics ($n = 11$), H_2 -receptor antagonists ($n = 7$), antiparasitic drugs ($n = 4$), as well as medications to treat concurrent diseases.

The diet was changed in 64 of 124 cats (52%). Diets included elimination diets, hypoallergenic diets, gastrointestinal diets, and high fiber diets, whereas other cats were switched to homemade diets or regular commercial diets. Similarly, cats that were not switched to a

Table 1. Descriptive statistics and comparison of quantitative factors related to whether or not cats received ERT.

Variable	ERT Treated		ERT not Treated		P Value ^a
	n	Median (IQR)	n	Median (IQR)	
Age	125	7.9 (5.5, 11.5)	23	7.0 (5.7, 11.9)	.613
BCS	123	3.0 (3.0, 4.0)	22	4.0 (3.0, 5.3)	.010
Weight loss (kg)	115	1.36 (0.78, 2.20)	22	0.53 (0, 1.37)	.006
Weight loss duration (months)	109	5.0 (2.0, 10.5)	22	2.5 (0, 8.3)	.038
Clinical signs duration (months)	120	3.8 (2.0, 9.0)	20	2.5 (0.8, 7.8)	.112
fTLI ($\mu\text{g/L}$)	125	3.6 (2.0, 5.8)	23	6.0 (2.7, 6.7)	.012
Cobalamin (ng/L)	98	149 (149, 174)	20	157 (149, 988)	.029
Folate ($\mu\text{g/L}$)	98	21.2 (15.0, 28.7)	20	20.4 (11.6, 26.4)	.274

IQR, interquartile range; BCS, body condition score; ERT, enzyme replacement treatment; fTLI, feline trypsin-like immunoreactivity.

^aBased on Mann-Whitney *U*-tests.

specific diet also were on a variety of diets that included both prescription and commercial diets.

Response to Treatment

Fifty-seven percent (78 of 137) of cats were free of clinical signs at the time the questionnaire was completed. Of the 121 cats for which information was available, the response to treatment was reported to be good in 72 (60%), partial in 33 (27%), and poor in 16 (13%) cats.

Only serum fTLI concentration and cobalamin treatment were predictive of good clinical outcome (Table 2). Multivariable logistic regression suggested that the effects of these variables were independent because they were both significant in the final model (Table 3). Cats with a serum fTLI concentration $<4 \mu\text{g/L}$ were 3.2 times more likely to have a good response to ERT (OR, 3.2; 95% CI, 1.5–7.0). Also, cats receiving cobalamin treatment were 3.0 times more likely to have a positive clinical response when adjusting for the initial fTLI concentration (OR, 3.0; 95% CI, 1.4–6.6). Interestingly, the presence of hypcobalaminemia before treatment did not affect the response to treatment.

Discussion

Ours is the largest case series of cats with EPI reported to date. One hundred and fifty cases of feline EPI were enrolled to describe the signalment, clinical signs, clinicopathologic abnormalities, concurrent diseases, response to treatment, and factors that may affect the response to treatment. This information can be used in clinical practice to more effectively identify cats that may have EPI and determine the best therapeutic plan and prognosis. To this end, a retrospective study design was employed and clinical information was gathered using a questionnaire. Diagnosis was based on the measurement of serum fTLI concentration, which is considered the current gold standard for the diagnosis of EPI in cats.^{1,12}

Domestic short-haired cats were most commonly affected by EPI in our study, which likely reflects the common occurrence of this breed in the general cat

population. Males were slightly overrepresented. The median age of cats with EPI in the present study was 7.7 years, which is in agreement with previous studies.^{11,12} However, the age range was considerably wide, ranging from 3 months to almost 19 years. This finding is important because EPI has been traditionally considered a disease of middle-aged to older cats, although a previous study had reported similar findings with several cats with EPI being <1 year of age.^{11,12} The results of our study suggest that EPI should be considered in cats of any age. In addition, it has been suggested previously that EPI is a sequela of chronic pancreatitis in the cat in most cases.¹⁴ The fact that several cats in our study were of young age might suggest that a different etiology exists in those cases. Alternatively, chronic pancreatitis may be able to destroy enough pancreatic tissue to produce EPI in a shorter period of time than previously assumed. Potential etiologies for EPI in younger cats could include pancreatic acinar atrophy, pancreatic hypoplasia or aplasia, and *Eurytrema procyonis* infestation.¹ Pancreatic acinar atrophy, the most common cause of EPI in dogs, has been reported in a very small number of cats with EPI in literature, but may be underdiagnosed in young cats.^{1,11} Additional studies are needed to investigate the spectrum and frequency of conditions that can lead to EPI in cats.

By far, the most common clinical sign in our cats with EPI was weight loss, which was present in $>90\%$ of cats and was the only clinical sign in 5% of them. This finding is similar to what has been reported in dogs with EPI.¹⁵ Diarrhea (unformed feces) was present in only 62% of cats, which is much lower than what has been reported in dogs with EPI (95% in 1 study).¹⁵ Interestingly, almost 33% of cats had watery diarrhea, at least occasionally, a characteristic that has been considered uncommon in dogs with EPI. However, this finding, along with other reported clinical signs (eg, anorexia, lethargy, vomiting), is more likely to be associated with concurrent diseases rather than EPI itself. Overall, the clinical presentation of many cats with EPI in our study did not closely resemble the typical presentation seen in dogs (ie, diarrhea, weight loss, polyphagia), and therefore, many cases might escape diagnosis. Therefore, EPI should be suspected in cats with

Table 2. Univariate analysis to determine factors related to whether or not cats were reported as having a good response to ERT.

Variable	Level	Good Response n (%)	Total n	Odds Ratio (95% CI)	P Value
Sex	Male	42 (56)	75	0.68 (0.32, 1.45)	.317
	Female	30 (65)	46	Referent	
Age	<8 years	40 (65)	62	1.53 (0.74, 3.18)	.251
	≥8 years	32 (54)	59	Referent	
Breed	Domestic ^a	59 (61)	96	1.47 (0.61, 3.57)	.392
	Other	13 (52)	25	Referent	
BCS	≤3	46 (67)	69	2.08 (0.99, 4.37)	.053
	>3	25 (49)	51	Referent	
Weight loss	Yes	68 (59)	115	0.72 (0.13, 4.11)	.715
	No	4 (67)	6	Referent	
Weight loss duration	<1 mn ^b	2 (100)	2		
	1–6 mns	28 (55)	51	0.50 (0.16, 1.61)	.246
	6–12 mns	13 (52)	25	0.42 (0.11, 1.52)	.185
	>12 mns	13 (72)	18	Referent	
Clinical signs duration	<1 mn	6 (60)	10	0.47 (0.09, 2.36)	.469
	1–6 mns	35 (60)	58	0.48 (0.15, 1.48)	.476
	6–12 mns	14 (50)	28	0.31 (0.09, 1.09)	.068
	>12 mns	16 (76)	21	Referent	
Diarrhea	Yes	22 (55)	40	0.73 (0.34, 1.58)	.430
	No	50 (63)	80	Referent	
Anorexia	Yes	29 (52)	56	0.53 (0.25, 1.10)	.087
	No	43 (67)	64	Referent	
Poor hair coat	Yes	41 (64)	64	1.27 (0.60, 2.67)	.538
	No	31 (58)	53	Referent	
Lethargy	Yes	31 (62)	50	1.11 (0.53, 2.35)	.776
	No	41 (59)	69	Referent	
Vomiting	Yes	14 (67)	21	1.45 (0.54, 3.90)	.464
	No	58 (58)	100	Referent	
fTLI (μg/L)	<4	46 (72)	64	3.05 (1.43, 6.48)	.004
	≥4	26 (46)	57	Referent	
Cobalamin (ng/L)	<290	43 (57)	75	0.78 (0.28, 2.21)	.646
	≥290	12 (63)	19	Referent	
Folate (μg/L)	<9.7 ^b	3 (60)	5		
	9.7–21.6	27 (59)	46	1.03 (0.45, 2.34)	.947
	>21.6	25 (58)	43	Referent	
ERT	Pancrezyme	28 (65)	43	1.28 (0.50, 3.28)	.611
	Viokase	25 (54)	46	0.82 (0.33, 2.03)	.606
	Other	19 (59)	32	Referent	
Antibiotics	Metronidazole	23 (56)	41	0.96 (0.43, 2.12)	.916
	Other	12 (75)	16	2.25 (0.65, 7.75)	.199
	None	36 (57)	63	Referent	
Corticosteroids	Yes	14 (50)	28	0.59 (0.25, 1.38)	.220
	No	58 (63)	92	Referent	
Cobamamin treatment	Yes	45 (73)	62	3.04 (1.42, 6.50)	.004
	No	27 (47)	58	Referent	
Diet change	Yes	28 (52)	54	0.60 (0.28, 1.31)	.199
	No	34 (64)	53	Referent	

CI, confidence interval; BCS, body condition score; ERT, enzyme replacement treatment; fTLI, feline trypsin-like immunoreactivity.

^aDomestic includes domestic short, medium, and long hair.

^bCombined with adjacent group for statistical analysis.

unexplained weight loss or anorexia even when clinical signs that are considered classical for EPI in dogs (eg, diarrhea and polyphagia) are not present.

Serum cobalamin concentrations were decreased in most cats with EPI in our study (77%). This finding was not unexpected because the pancreas is the main source of intrinsic factor in cats, and in previous reports, almost all cats with EPI in which cobalamin

had been measured were reported to have low serum cobalamin concentrations.^{1,11,16} Cats with hypocobalaminemia were found to have significantly lower serum fTLI concentrations compared to cats with normal serum cobalamin concentrations. Because serum fTLI concentrations reflect the functional capacity of the exocrine pancreas, this observation suggests that normocobalaminemic cats with EPI have milder or early stage

Table 3. Multivariable logistic regression analysis to determine factors related to whether or not cats were reported as having a good response to ERT.

Variable/ Concentration	Parameter Estimate ($\hat{\beta}$)	Odds Ratio (95% CI)	P Value (Wald)
fTLI ($\mu\text{g/L}$)			
<4	1.162	3.20 (1.45, 7.04)	.004
≥ 4	Referent		
Cobalamin treatment			
Yes	1.102	3.01 (1.37, 6.63)	.006
No	Referent		

CI, confidence interval; ERT, enzyme replacement treatment; fTLI, feline trypsin-like immunoreactivity.

Hosmer and Lemeshow $\chi^2 = 2.332$, $df = 2$, $P = 0.312$.

disease and thus might not have had enough time to develop hypocobalaminemia. Tissue cobalamin, however, is depleted before hypocobalaminemia develops, and therefore, normocobalaminemic cats in our study still could have had cobalamin deficiency at the cellular level.^{17–19}

Despite the fact that hypocobalaminemia was diagnosed in 77% of cats with EPI in our study, cobalamin supplementation was instituted in only 49% of cats. Twenty-five percent of cats that received cobalamin supplementation had normal or unknown serum cobalamin concentrations. Cobalamin supplementation favorably affected response to treatment. This observation is not surprising because most cats were hypocobalaminemic, and cobalamin supplementation has been shown to be beneficial in hypocobalaminemic cats with gastrointestinal disease.¹⁸ In dogs, hypocobalaminemia associated with certain gastrointestinal diseases has been shown to be a negative prognostic factor.²⁰ Also, severe hypocobalaminemia in dogs with EPI was found to be associated with shorter survival.¹⁵ In our study, however, hypocobalaminemia before treatment was not associated with response to treatment. This finding in conjunction with the fact that cobalamin supplementation was also instituted in normocobalaminemic cats and was found to favorably affect outcome suggests that not only hypocobalaminemic but also normocobalaminemic cats with EPI could benefit from cobalamin supplementation. It is not clear why cobalamin supplementation may have a positive effect on hypocobalaminemic cats with EPI, but these cats may have depleted tissue cobalamin concentrations before hypocobalaminemia develops.^{19,21} Therefore, it may be helpful to supplement cats with EPI with cobalamin regardless of their serum cobalamin concentration. However, the benefit of cobalamin supplementation in normocobalaminemic cats with EPI warrants further investigation.

Serum folate concentrations were abnormal less commonly than serum cobalamin concentrations and more commonly were increased. A combination of increased serum folate and decreased serum cobalamin concentrations was identified in 38% of cases. Although this combination of findings has been used in dogs to diagnose small intestinal dysbiosis (previously called small

intestinal bacterial overgrowth [SIBO]), controversy exists with regard to the usefulness of this diagnostic criterion.^{22,23} In cats, the value of identifying increased serum folate and decreased serum cobalamin concentrations is unknown. Multivariable analysis did not show that altered serum concentrations of cobalamin or folate affected response to treatment, although cobalamin supplementation was beneficial.

Another finding of our study was that cats with lower serum fTLI concentrations responded better to treatment. Although this might initially seem counterintuitive, it could mean that cats with more severe EPI (reflected in lower serum fTLI concentrations) would benefit more from treatment and therefore show a better response to treatment compared to cats with mild disease. However, it also could indicate that the specificity of the assay at $<8 \mu\text{g/L}$ is $<100\%$ and that some of these cats may have been misclassified as having EPI.

Overall, response to treatment was considered good in 60% of affected cats, which is similar to what has been reported for dogs.¹⁵ Only 13% of cats were reported to have a poor response to treatment, which is less than that reported for dogs.¹⁵ The reason that some cats do not respond well to treatment for EPI is not clear. In the present study, cobalamin supplementation was found to affect response to treatment, and therefore, it can be assumed that partial or poor response to treatment could be associated, at least in part, with lack of cobalamin administration. Another factor that should be taken into consideration is that many of the cats enrolled in our study had concurrent diseases, and therefore, partial or poor response to EPI treatment could have been affected by these other conditions. Prospective clinical studies are needed to accurately determine the response to treatment of cats with EPI and identify factors associated with good response.

Antibiotics were used in approximately 50% cases in our study but their use was not found to affect outcome. In dogs, antibiotics often are used in the treatment of EPI to control concurrent intestinal dysbiosis, although no clear benefit has been shown in some studies.^{15,24} However, disturbances of the microbiota in cats with EPI have not been fully described or confirmed, and therefore, antibiotic use is of unknown benefit in these cases. Given the difficulty in identifying small intestinal dysbiosis in cats and dogs, a trial with antibiotics often is used in EPI patients that do not respond to enzyme and cobalamin supplementation. Additionally, cats with pancreatic disease commonly have concurrent intestinal and or hepatic inflammation, and antibiotic treatment often is used as part of the management of intestinal and hepatic disease.²⁵ Similarly, other treatments used in this group of cats, such as glucocorticoids, were likely used to treat concurrent inflammatory disease of the intestine, liver, or both.²⁵

As with all retrospective and questionnaire-based studies, our study has limitations that should be taken into consideration. One of the limitations is related to the fact that the information was extracted

retrospectively from medical records and based on referring veterinarians. However, all contacted veterinarians were asked to retrieve the information directly from the medical record of each cat and not answer questions based on memory alone. They also were asked to be as accurate and careful as possible in answering questions and to not answer questions if they were unsure about the answer. Unfortunately, it is not possible to determine how closely veterinarians followed these instructions. Another limitation is related to the assessment of response to treatment, which was subjectively scored as good, partial, or poor by the participating veterinarians. No validated scoring systems for response to treatment of cats or dogs with EPI have been reported, and the approach used in the present study also has been used in previous studies in dogs. In addition, an effort was made both during questionnaire design and data analysis to control for inaccuracies. For example, although there was a specific question on response to treatment, which was scored as good, partial, or poor, there was an additional question on whether the cat was free of clinical signs at the time of questionnaire completion. There was very good agreement between the answers to these 2 questions: 60% of cats were reported to have a good response to treatment and 57% of cats were reported to be free of clinical signs.

In conclusion, EPI in cats often has a different clinical presentation than that expected based on the typical presentation in dogs, and a portion of cases likely escapes diagnosis. Therefore, cats with unexplained weight loss, with or without diarrhea and regardless of the presence or absence of other clinical signs, should have EPI as a differential diagnosis. In addition, although most commonly seen in middle-aged to older cats, the age range for EPI in cats is very wide and many cats can be ≤ 5 years of age. Cobalamin supplementation had a positive impact on treatment response, potentially even in cases that had serum cobalamin concentrations within the reference interval. Antibiotic use was not found to affect response to treatment. Overall, most cats responded well to appropriate treatment for EPI.

Footnotes

^a Immulite 2000 Vitamin B12 solid-phase, competitive chemiluminescent enzyme immunoassay. Siemens Healthcare Diagnostics, Deerfield, IL

^b Immulite 2000 Folic Acid competitive immunoassay. Siemens Healthcare Diagnostics, Deerfield, IL

^c MINITAB Statistical Software, Release 13.32, Minitab Inc, State College, PA

^d Prism 5, GraphPad, San Diego, CA

^e Epi Info, version 6.04, CDC, Atlanta, GA

^f IBM SPSS Statistics Version 22, International Business Machines Corp., Armonk, NY

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Conflict of Interest Declaration: Drs. Suchodolski and Steiner direct the Gastrointestinal Laboratory at Texas A&M University, which offers measurement of fTLI on a fee-for-service basis.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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