TACKLING EXOCRINE PANCREATIC INSUFFICIENCY (EPI)

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Images from Nutramax

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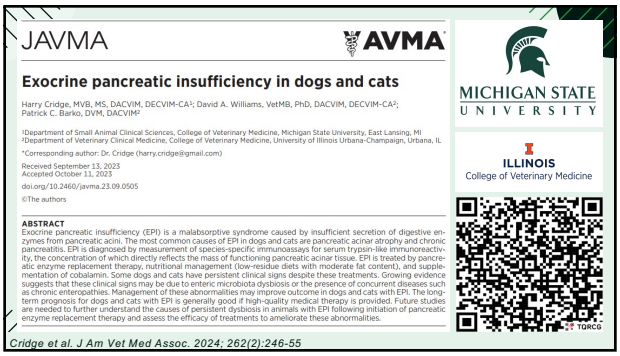

JAVMA AVMA

Exocrine pancreatic insufficiency in dogs and cats

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ABSTRACT

Exocrine pancreatic insufficiency (EPI) is a malabsorptive syndrome caused by insufficient secretion of digestive enzymes from pancreatic acini. The most common causes of EPI in dogs and cats are pancreatic acinar atrophy and chronic pancreatitis. EPI is diagnosed by measurement of species-specific immunoassays for serum trypsin-like immunoreactivity, the concentration of which directly reflects the mass of functioning pancreatic acinar tissue. EPI is treated by pancreatic enzyme replacement therapy, nutritional management (low-residue diets with moderate fat content), and supplementation of cobalamin. Some dogs and cats have persistent clinical signs despite these treatments. Growing evidence suggests that these clinical signs may be due to enteric microbiota dysbiosis or the presence of concurrent diseases such as chronic enteropathies. Management of these abnormalities may improve outcome in dogs and cats with EPI. The long-term prognosis for dogs and cats with EPI is generally good if high-quality medical therapy is provided. Future studies are needed to further understand the causes of persistent dysbiosis in animals with EPI following initiation of pancreatic enzyme replacement therapy and assess the efficacy of treatments to ameliorate these abnormalities.

MICHIGAN STATE UNIVERSITY
ILLINOIS College of Veterinary Medicine

Cridge et al. J Am Vet Med Assoc. 2024; 262(2):246-55

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Exocrine Pancreatic Insufficiency (EPI)

- Relatively uncommon disorder
- Cats & dogs have **different clinical presentations**
- **Important DDX** for GI signs → requires specific testing – need to actively consider EPI as a DDx
- **Good prognosis** with enzyme replacement, B12 supplementation, & nutrition

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AI-generated illustration created with OpenAI's ChatGPT, 2025

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Signalment & Genetics

No. 1 breed = GSD

Any breed can be affected

Other predisposed breeds:
- CKCS
- Rough Collie
- WHWT

Due to PAA or Secondary Pancreatic Damage (e.g., chronic pancreatitis)

Photo provided by EPI4Dogs Foundation

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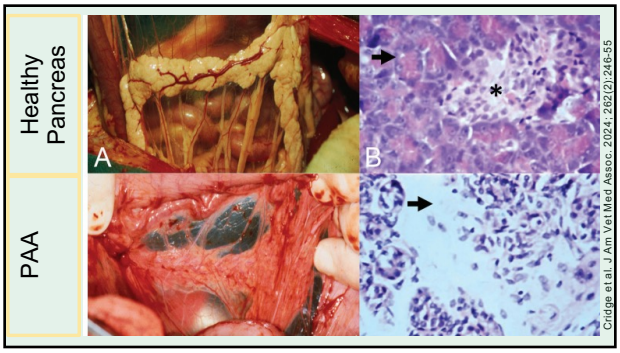

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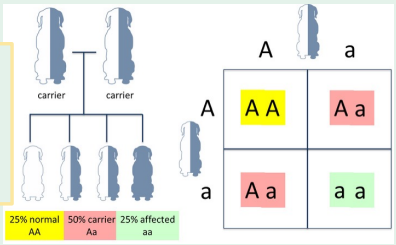
Genetics – German Shepherd Dogs

Initially proposed autosomal recessive inheritance



Paw Print Genetics

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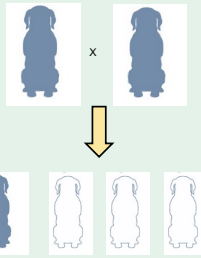
Test mating of affected dogs ruled out simple autosomal recessive inheritance



Likely multiple genetic factors involved → complex inheritance (harder to test for)

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Clinical Signs of EPI - Dogs

Can be asymptomatic / subclinical

Require substantial loss of pancreatic acinar cells to result in functional deficiency of pancreatic enzymes.

Diagnosing animals at this stage means they don't have poor BCS which can be hard to correct if diagnosed late in course of dz

Consider repeat testing if low TLI but clinical picture doesn't fit

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Often diagnosed LATE in course of dz

Wt loss despite a good appetite

↑ stool volume

Steatorrhea

Poor haircoat

Photo provided by EPI4Dogs Foundation

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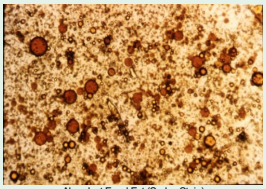
Diagnosis of EPI - Dogs

Minimum database → relatively unremarkable



Abundant Fecal Fat (Sudan Stain)

NOT specific to EPI

Fecal fat stain image from Vetlexicon

Gold Std = TLI

8-12 hour fasting (?)*

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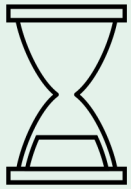
Effect of withholding food on serum concentrations of cobalamin, folate, trypsin-like immunoreactivity, and pancreatic lipase immunoreactivity in healthy dogs

RESULTS

The median serum cobalamin concentration was lower at 4 hours (428 ng/L) and 8 hours (429 ng/L) postprandially, compared with baseline (479 ng/L), but this difference was not clinically meaningful. Although there were no substantial differences in serum concentrations of folate, cPLI, or cTLI, postprandial changes in serum concentrations of cTLI or folate could potentially affect diagnoses in some dogs.

CONCLUSIONS AND CLINICAL RELEVANCE

Although results indicated that feedings rarely resulted in clinically important differences in the median serum concentrations of cobalamin, folate, cPLI, or cTLI in healthy dogs, given the further processing required for lipemic samples, withholding food for at least 8 hours is an appropriate recommendation when measuring these analytes. Similar research is needed in dogs with gastrointestinal disease to determine whether the withholding of food is necessary when measuring these analytes in affected dogs. (*Am J Vet Res* 2021;82:367–373)



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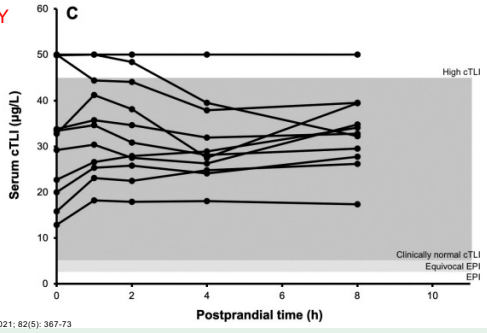
HEALTHY DOGS



Saver et al. AJVR. 2021; 82(5): 367-73

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DOGS WITH GI SIGNS

DOI: 10.1111/jvim.17064
STANDARD ARTICLE
Journal of Veterinary Internal Medicine ACVIM

The effect of feeding on serum concentrations of cobalamin, folate, trypsin-like immunoreactivity, and pancreatic lipase immunoreactivity in dogs with signs of chronic gastrointestinal disease

Ashley Melco[1] | Jessica C. Pritchard[1] | Scott J. Hetzel[2] | Alexander Saver[1] | Joao Pedro Cavasin[3] | Jörg M. Steiner[3]

cTLI (µg/L)	Baseline (0)	31.1 (15.0)	...	...	...
	Hour 2	31.3 (14.0)	0.2 (−2.3 to 2.6)	5	<.001[a]
	Hour 4	29.6 (13.1)	−1.5 (−4.6 to 1.7)	5	.03[a]
	Hour 8	28.7 (13.2)	−2.3 (−5.6 to 0.9)	5	.12

Melco et al. JVIM. 2024; 38:1465-74

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Variable	Time (h)	Mean (SD)	Difference (95% CI)	MoE	Equivalence *P*
Cobalamin (ng/L)	Baseline (0)	517.3 (211.5)	...	...	...
	Hour 2	498.1 (213.1)	−19.8 (−46.3 to 6.7)	50	.02[a]
	Hour 4	501.9 (207.4)	−15.4 (−41.5 to 10.6)	50	.01[a]
	Hour 8	482.6 (201.6)	−34.7 (−62.5 to −6.9)	50	.36
Folate (µg/L)	Baseline (0)	13.7 (8.3)	...	...	...
	Hour 2	15.0 (7.7)	1.2 (−0.5 to 3.0)	5	<.001[a]
	Hour 4	17.3 (9.6)	3.6 (1.8 to 5.4)	5	.13
	Hour 8	16.4 (9.5)	2.7 (0.1 to 5.3)	5	.09

"Feeding altered the clinical interpretation in 27% (cobalamin), 35% (folate), 20% (cTLI), and 12% (cPLI) of dogs".

Changes appear to be of small magnitude when considered in the context of clinical decision making.

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Interpretive Criteria:

Feeding pancreatic enzymes does NOT affect results of TLI assay

0 to 5.5 µg/L	Diagnostic for EPI
5.6 to 7.5 µg/L	Subnormal cTLI concentration, EPI cannot be excluded. If signs are consistent with EPI, consider assessing response to pancreatic enzyme replacement therapy and/or remeasuring serum cTLI concentration in 1 to 2 months using a fasted sample (enzyme therapy will not interfere with testing). **CONSIDER ENZYME TRIAL**
7.6 to 10.8 µg/L	Subnormal cTLI concentration, but EPI is unlikely. Consider other differential diagnoses depending on the clinical signs observed. **LOOK FOR SMALL INTESTINAL DISEASE**
10.9 to 50.0 µg/L	Result is within the reference interval.
> 50.0 µg/L	In dogs without clinical signs of pancreatitis or with normal cPLI concentrations, a cTLI > 50 µg/L is unlikely to be clinically important.

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Treatment of EPI - Dogs

1. Pancreatic enzyme replacement
2. Dietary modification
3. +/- Cobalamin supplementation

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Pancreatic Enzyme Replacement Therapy (PERT)

No formulation type (coated vs non) has been shown to be superior

Fresh-raw pancreas can be fed → biohazard concerns

Starting doses for enzymes can be guided by manufacturer but a dose per cup of food method is used by some

PERT Considerations

- Cost
- Reputable company
- Enzyme concentrations
- Protein source (if concurrent CE)
- Additional B12?
- Additional fiber?

Enzyme Analysis

Each 2.8g (1 teaspoon) of Panzquin® contains a minimum of:
Lipase..... 71,400 USP units
Protease.....388,000 USP units
Amylase..... 460,000 USP units

Plus
Inulin - prebiotic fiber
Cyanocobalamin – vitamin B12.....500 µg
active ingredient in COBALEQUIN

Average administration amount per meal (¼ teaspoon scoop included):

For Cats
Cats: ¼–¾ teaspoon (1-3 scoopfuls)

For Dogs
Dogs: ¾–1 teaspoon (3-4 scoopfuls)

Protein source: pig pancreas

Images from Nutramax

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Dietary Modification +/- B12 Supplementation

Hx → low fat diets. BUT they can exacerbate malnutrition due to being calorie poor.

Now → GI diets (easily digestible) are recommended

B12 is frequently low → supplement

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J Vet Intern Med 2007;21:54–60

Prognostic Factors in Canine Exocrine Pancreatic Insufficiency: Prolonged Survival is Likely if Clinical Remission is Achieved

Daniel J. Batchelor, Peter-John M. Noble, Rebecca H. Taylor, Peter J. Cripps, and Alexander J. German

- **Pancreas is a major source of intrinsic factor** which is needed to absorb cobalamin → not expected to resolve with enzyme supplementation alone

- **82%** of dogs with EPI are cobalamin deficient!

- Need to be **proactive** and screen for &/or supplement B12 in these cases

- **Hypocobalaminemia** (<100 ng/L) is associated with **shorter survival**

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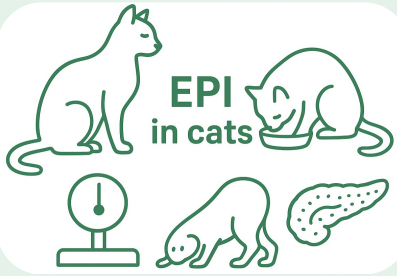

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Journal of Veterinary Internal Medicine — ACVIM — Open Access

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

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.

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Signalment / Etiology

- Median age at time of diagnosis ~ 7.7 years
  - Any age affected
  - Wide age range (3m -19yr)
- DSH
- Males > females
- Chronic pancreatitis

Clinical Signs

"EPI should be suspected in cats with unexplained weight loss or anorexia even when clinical signs that are considered classical for EPI in dogs are not present"

Xenoulis et al. J Vet Intern Med. 2016; 30(6): 1790-1797

- Most common: Weight loss (90%)
- Diarrhea - only 62% (unlike dogs)
- Clinical signs of concurrent dz

CLINICAL SIGNS OFTEN MISSED

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Diagnosis of EPI - Cats

Feline TLI

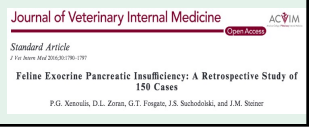
- Gold standard
- > 12 ug/L → exclude EPI
- 8 - 12 ug /L → equivocal
- < 8 ug/L → EPI

Cobalamin

- 77% of EPI cases: ↓ cobalamin
- **Cobalamin supplementation favorably affects outcome** even if cobalamin levels are normal

Histopathology

- Not required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Treatment of EPI - Cats

1. Pancreatic enzyme replacement therapy (PERT)
2. Diet → high-quality 'easily digestible' diet
3. B12 supplementation
4. Supportive care

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Cobalamin (Vit. B12) Deficiency

- Cobalamin (vitamin B12) deficiency is likely under-recognized in dogs and cats

- Needs specific testing – serum B12 concentrations

- C/S of deficiency may include GI signs (cause vs effect), failure to thrive, neurologic signs, and potentially non-regenerative anemia.

- **Treatment is indicated even at "low-normal" B12 concentrations (< 400 ng/L)**

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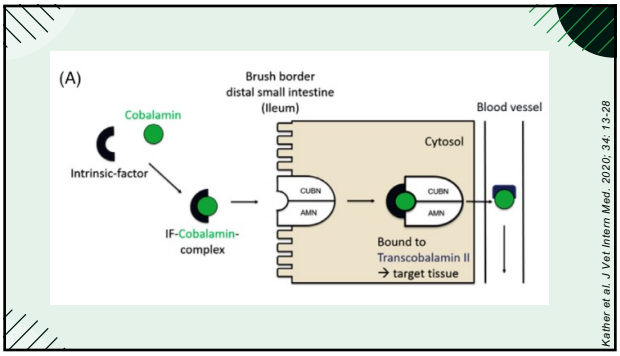

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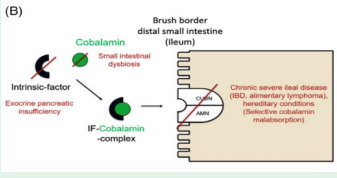

Kather et al. J Vet Intern Med. 2020; 34: 13-28

Vit. B12 Deficiency

- Intestinal disease (esp. ileal involvement) – **neg prognosis**
- EPI – **neg prognosis**
- Short-bowel syndrome
- Dysbiosis
- Vegan diets
- Hereditary B12 deficiency

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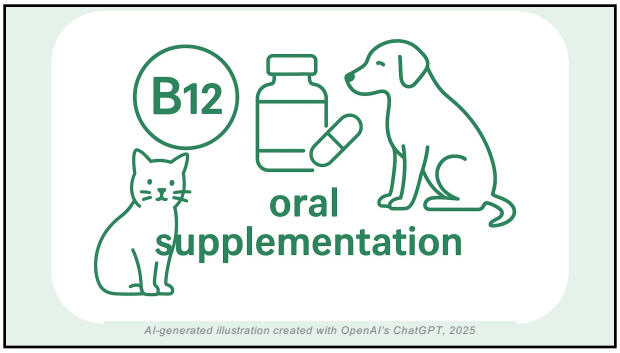

AI-generated illustration created with OpenAI's ChatGPT, 2025

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DOI: 10.1111/jvim.16528

STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM Open Access

American College of Veterinary Internal Medicine

Effect of oral or injectable supplementation with cobalamin in dogs with hypocobalaminemia caused by chronic enteropathy or exocrine pancreatic insufficiency

Chee-Hoon Chang | Jonathan A. Lidbury | Jan S. Suchodolski | Joerg M. Steiner

Conclusions and Clinical Importance: Oral supplementation is an alternative for cobalamin supplementation in dogs with hypocobalaminemia caused by CE or EPI.

J Vet Intern Med. 2022;36:1607–1621.

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Oral may be easier for some owners vs driving weekly to clinic

DOI: 10.1111/jvim.17195

STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM Open Access

American College of Veterinary Internal Medicine

Effect of oral or subcutaneous administration of cyanocobalamin in hypocobalaminemic cats with chronic gastrointestinal disease or exocrine pancreatic insufficiency

Chee-Hoon Chang | Jonathan Lidbury | Jan S. Suchodolski | Joerg M. Steiner

Conclusions and Clinical Importance: In hypocobalaminemic cats with CGID or EPI, in conjunction with other medical and dietary interventions, both oral and SC supplementation are effective at normalizing serum cobalamin and MMA concentrations.

J Vet Intern Med. 2024;38:2464–2479.

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Cobalequin® is now available in two variations:

Unflavored sprinkle capsule → easy to give

	Cobalequin®	Cobalequin® Advanced
Form	Tasty chewable tablets *(tablets may be easily crushed)*	Easy-to-administer sprinkle capsule *(contents may be easily dissolved)*
Flavor	Hydrolyzed chicken flavor	No added flavor
5-MTHF	✓	✓
Prebiotic fiber	✗	✓
Same MSRP	✓	✓

If using an oral B12 supplement be cognizant of any flavorings (potential protein sources)

→ Cobalequin is hydrolyzed and Cobalequin Advanced has no added flavor

Cobalequin also contains 5-MFT which is the metabolically active form of folate

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CASE: ~ 2 y/o MN GSD

Photo provided by EPI4Dogs Foundation

- rDVM → weight loss, poor BCS
  - Supportive/symptomatic care
  - Increased caloric intake
  - No response
- Submitted a GI panel
  - TLI 1.2 ug/L→ EPI
  - B12 < 150 ng/L

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Royal Canin

Raw K9

Nutramax

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At time of referral …

Photo provided by EPI4Dogs Foundation

Diagnosis of EPI was solid

Stool quality had improved (original on left)

Owners biggest concern → progressive weight loss

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Activities

When poll is active respond at **PollEv.com /harrycridge400**

Send **harrycridge400** and your message to **37607**

Loading...

What could be going on in this dog?

Nobody has responded yet.

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TROUBLESHOOTING THE CASE

1. Diet
2. Enzyme dose, formulation, or timeline to response
3. Concurrent chronic enteropathy
4. Persistent dysbiosis (changes in bacterial populations in gut)

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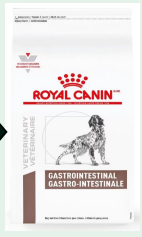
1 Diet

Royal Canin



Royal Canin

Hx → low fat diets. BUT they can exacerbate malnutrition due to being calorie poor.

Low fat diets may also worsen fat soluble vitamin deficiencies

Now → GI diets (easily digestible) are recommended

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2 Enzyme dose, formulation, or timeline to response

On a high-quality enzyme product + stool quality improved → unlikely to be an issue in this case

3 Concurrent Chronic Enteropathy

Doing an abdominal ultrasound to evaluate intestinal wall is reasonable ($$$)

4 Persistent dysbiosis (changes in bacterial populations in gut)

Persistent dysbiosis is noted in cases of EPI. May need targeted treatment e.g., probiotics

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Back to the plan …

- Switched to a 'digestible' non-low-fat diet → higher calories
- Offered AUS to evaluate for SI changes – will pursue if no response to diet change
- If no response to diet and no overt SI dz → consider probiotic

Cridge et al. J Am Vet Med Assoc. 2024; 262(2):246-55

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SUMMARY

1 – CLINICAL SIGNS

Dogs → weight loss despite a good appetite, steatorrhea
Cats → non-specific clinical signs, may have just weight loss

2 – DIAGNOSIS

TLI assay is test of choice – change in RI recently – may need to re-eval some cases
Pancreatic enzyme trial or re-test may be needed in 'equivocal' TLI result cases

3 – DIET

Highly digestible diet is preferred
Only use low fat if refractory steatorrhea occurs (dogs)

4 – B12 SUPPLEMENTATION

Cats with EPI benefit from B12 supplementation
Most dogs with EPI are B12 deficient and this should be supplemented if low or low-normal

5 – ENZYMES

High quality PERT is critical to the management of EPI
If poor response consider enzyme formulation, timeline to response, diet, persistent dysbiosis, and concurrent small intestinal dz

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