

Peer Reviewed

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Exocrine Pancreatic Insufficiency in Dogs



PROFILE

Definition

- Exocrine pancreatic insufficiency (EPI) is a syndrome characterized by the inadequate synthesis and secretion of pancreatic digestive enzymes due to severe damage to or lack of pancreatic acinar cells.
- Patients with an obstructed pancreatic duct or a deficiency in enteropeptidase in the small intestine have the same clinical signs and are thus also classified as having EPI, though they do not lack pancreatic enzymes.
- In general, EPI is due to a lack of functional pancreatic acinar cells, which in turn can be due to acinar atrophy or damage through chronic pancreatic inflammation (ie, chronic pancreatitis).
- Clinical signs are attributable to maldigestion and malabsorption of nutrients and develop after approximately 90% of the secretory capacity of the exocrine pancreas has been lost.¹
- **System**
 - ▮ EPI primarily affects the gastrointestinal (GI) system.
- **Genetic implications**
 - ▮ EPI is due to pancreatic acinar atrophy (PAA) in approximately 50% of cases (based on epidemiological data from the GI Laboratory at Texas A&M University; unpublished data, 2009).

- ▮ To date, PAA has only been described in German shepherds, rough-coated collies, and Eurasians.
- ▮ Although several studies have suggested an autosomal-recessive trait for PAA in German shepherds, a recent study has definitively shown that this condition is not caused by a simple autosomal-recessive trait.²

Incidence/prevalence

- ▮ The true incidence and prevalence remain unknown.
- ▮ Approximately 42% of all affected dogs are German shepherds (based on epidemiologic data from the GI Laboratory at Texas A&M University; unpublished data, 2009).

Signalment

● Breed predilection

- ▮ EPI can be seen in any canine breed, but German shepherds, rough-coated collies, and Eurasians have a familial predisposition.

● Age

- ▮ Dogs with EPI attributable to PAA are typically young adults (1–2 years of age). Dogs with EPI due to chronic pancreatitis are often middle-aged to older but can be of any age.
- ▮ German shepherds are younger at the time of diagnosis than dogs of other breeds.

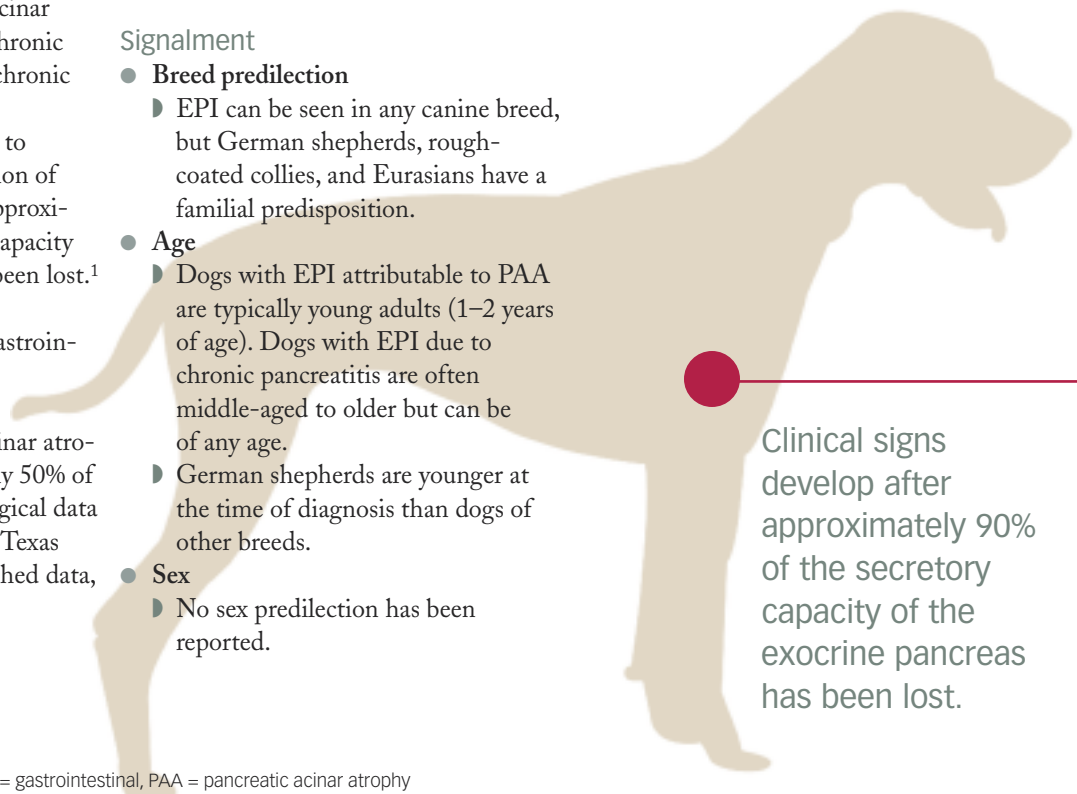
● Sex

- ▮ No sex predilection has been reported.

Causes

- Idiopathic PAA is the most common cause in German shepherds, rough-coated collies, and Eurasians. Lymphocytic infiltration before the onset of PAA suggests an immune-mediated pathogenesis.
- Chronic pancreatitis (**Figure 1**) can result in destruction of acinar cells (all breeds are affected, but cavalier King Charles spaniels and Jack Russell terriers may be predisposed).
- Other rare causes might include EPI due to pancreatic duct obstruction (eg, due to tumors or surgery), congenital aplasia, or pancreatic hypoplasia.

CONTINUES



Clinical signs develop after approximately 90% of the secretory capacity of the exocrine pancreas has been lost.

EPI = exocrine pancreatic insufficiency, GI = gastrointestinal, PAA = pancreatic acinar atrophy

The true incidence and prevalence of exocrine pancreatic insufficiency remain unknown.

Risk Factors

- Breed predilection (see above)
- Factors predisposing to chronic pancreatitis

Pathophysiology

- Loss of pancreatic acinar cells leads to lack of digestive enzymes in the small intestinal lumen, leading to impaired nutrient absorption and transport and resulting in loose voluminous stools and weight loss.
- Undigested luminal food stuff may alter the intestinal microbiota, which may lead to dysbiosis.
- GI mucosal trophic factors, regulatory peptides, and intrinsic factor are also deficient in pancreatic secretions, leading to changes in small intestinal mucosal function and microanatomy.
- Generalized malnutrition might further affect the GI mucosa.
- Diabetes mellitus due to loss of islet cells has been reported in patients with EPI secondary to chronic pancreatitis but does not occur in patients with PAA.

Signs

- **History**
 - Weight loss despite a normal or increased appetite
 - Foul-smelling loose stools
 - Increased fecal volume with cow patty-like consistency (**Figure 2**)
 - Increased number of defecations (usually >3/day)
 - Coprophagia or even pica, flatulence, or borborygmus
 - Vomiting (rare)
 - Polydipsia or polyuria in patients with concurrent diabetes mellitus

- Nervousness and aggression (rare)³

Physical examination

- Poor body condition and muscle wasting (**Figure 2**)
- Poor-quality hair coat



DIAGNOSIS

In General

- History and clinical signs can help raise suspicion that EPI may be present.

Definitive Diagnosis

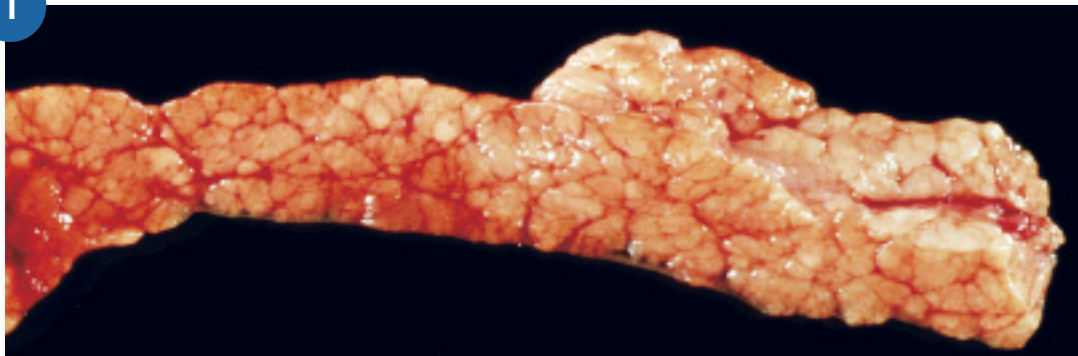
- **Canine trypsin-like immunoreactivity (cTLI)**
 - This species-specific test is used to quantify trypsinogen and trypsin in serum.
 - A cTLI concentration < 2.5 mcg/L after withholding food for > 8 hours is considered confirmatory.⁴
 - A serum cTLI concentration between 2.5 and 5.7 mcg/L may be associated with occult EPI. Serum cTLI should be retested in 1 to 2 months.
 - Decreased cTLI concentration is highly sensitive and specific for EPI and is not affected by enzyme supplementation.
- **Fecal elastase**
 - This enzyme-linked immunosorbent assay has high sensitivity but low specificity.
 - A value > 20 mcg/g helps to eliminate EPI.
 - Values < 10 mcg/g will require confirmation with cTLI.

Differential Diagnosis

- Primary or secondary causes of chronic small-bowel diarrhea
- Disorders associated with weight loss (eg,

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Pancreatic atrophy and fibrosis. This section of pancreas is from a 10-year-old poodle. The pancreas is small and shows signs of remodeling, suggestive of chronic pancreatitis that has led to severe pancreatic atrophy and fibrosis. (Courtesy of Dr. John Edwards, Texas A&M University)





Dog with EPI: Note that the dog is severely emaciated, suggesting either a systemic catabolic disease or a disease associated with maldigestion, malabsorption, or both (A). A fecal sample obtained from this dog is typical for an animal with severe maldigestion or malabsorption. The dog also had a serum cTLI concentration of 0.4 mcg/L, which is considered diagnostic for EPI. Note that the stools are voluminous and soft (B). Stools from these dogs can also be light in color and sometimes contain undigested food particles. (Courtesy of Dr. Erin Allgood, Case Veterinary Hospital, Savannah, Georgia)

systemic conditions, diabetes mellitus, hepatic failure, malignancies, and many others)

Laboratory Findings

- Complete blood count is usually unremarkable.
- Serum alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase activities can be increased in some patients.
- Hyperglycemia may occur in patients with concurrent diabetes mellitus.
- Serum folate concentration may be increased. Serum cobalamin concentration is decreased in more than 80% of patients.⁵



TREATMENT

Inpatient or Outpatient

- Outpatient medical management should be directed toward replacement of pancreatic digestive enzymes and cobalamin supplementation when necessary.
- Inpatient treatment may be necessary in dogs with concurrent diabetes mellitus that require insulin therapy.

Medical (also see Medications)

- **Digestive enzyme replacement**
 - ▮ Treatment of choice includes providing digestive enzymes with each meal.⁶
 - ▮ Powdered pancreatic enzyme supplements of porcine or bovine origin are mixed with the diet (initially 1 tsp/10 kg body weight with each meal mixed into the food immediately before feeding). After a complete response, this dose can usually be significantly decreased.
 - ▮ Tablets, capsules, and enteric-coated preparations are less effective in dogs.
 - ▮ Preincubation of the diet with the enzyme supplement or addition of antacids or bile acids is not necessary.
 - ▮ Enzyme activity may vary with the product used and also within containers.
 - ▮ A strong body odor has been anecdotally reported in some dogs treated with replacement enzymes.
 - ▮ Some dogs may develop oral bleeding, which often resolves after the dose of enzymes is lowered.⁷
- **Cobalamin** should be supplemented if the patient is cobalamin deficient.
 - ▮ Cobalamin must be administered parenterally (usually given by subcutaneous injection).

Treatment of choice includes providing digestive enzymes with each meal.

CONTINUES

cTLI = canine trypsin-like immunoreactivity, EPI = exocrine pancreatic insufficiency, GI = gastrointestinal, PAA = pancreatic acinar atrophy

CLIENT EDUCATION

- Lifelong treatment is required in most cases (depending on the size of the dog, this can be expensive).
- Familial predisposition and hereditary nature of the disease (German shepherds, Eurasians).
- Development of diabetes mellitus in breeds other than the German shepherd is possible.



About 20% of dogs do not respond to initial enzyme replacement therapy.

- ▶ Pure cyanocobalamin should be used.
 - Dose is 250 to 1200 mcg per injection, depending on the size of the dog.
 - Initially given once a week for 6 weeks, then 1 more dose 30 days later; serum cobalamin concentration is rechecked 30 days after that.
 - Some dogs need only short-term cobalamin supplementation; others require lifelong supplementation.

Surgical

- German shepherds in Finland have a high prevalence of mesenteric torsion, but this has not been confirmed in the U.S.⁸

Nutritional

- Maintenance diets or light maintenance diets fed twice daily usually work well.
- High- or low-fat and high-fiber diets should be avoided.
- **Alternative therapy**
 - ▶ Chopped raw cow, mutton, pig, or game pancreas
 - Can be kept frozen for months without losing enzyme activity.
 - Should be supplemented at approximately 30 g per 10 kg body weight.

- May overcome food aversion and food allergies due to enzyme supplementation.
- Risk for transmission of *Echinococcus multilocularis* from game pancreas. There is a theoretical risk for transmission of bovine spongiform encephalopathy or Aujeszky's disease. However, this risk is not any higher than with use of powdered products.



MEDICATIONS

- **Antimicrobials**
 - ▶ Consider for patients that do not respond to enzyme replacement therapy and cobalamin supplementation alone.
 - ▶ Can be used to treat small intestinal dysbiosis (however, this condition usually resolves without antimicrobial therapy).
 - ▶ Tylosin (25 mg/kg PO Q 12 H) for 6 weeks is preferred.
- **Antacids**
 - ▶ Treatment reduces gastric pH.
 - ▶ Failure to respond to enzyme supplementation may be the result of destruction of the pancreatic lipase in the enzyme supplement by the low gastric pH.
 - ▶ Omeprazole (0.6 mg/kg PO Q 12 H) is recommended.
- **Other** depends on concurrent conditions diagnosed in patients that do not respond to initial therapy.
- **Contraindications**
 - ▶ Coatings of enteric-coated preparations can lead to unpredictable dissolution and may lead to treatment failure.
 - ▶ Some pancreatic enzyme supplements do not contain sufficient amounts of lipase. For comparison, products should contain approximately 70,000 U.S. Pharmacopeia units of lipase activity per teaspoon of product.



FOLLOW-UP

Patient Monitoring

- Rapid weight gain is expected, but body weight may fail to normalize despite remission of clinical signs.
- Diarrhea resolves in 2 to 7 days in uncomplicated cases.

Complications

- Food aversion may result from enzyme addition (rare in dogs).
- Approximately 20% of dogs do not respond to initial enzyme replacement.
- Concurrent cobalamin deficiency, small intestinal dysbiosis, inflammatory bowel disease, diabetes mellitus, or other conditions may need to be addressed.



IN GENERAL

Relative Cost

- Initial diagnostic evaluation (physical examination; complete blood count; serum biochemistry profile; serum cTLI, folate, and cobalamin concentrations): \$\$

- Medical treatment and follow-up: \$\$\$\$

Cost Key

\$ = < \$100	\$\$\$\$ = \$500-\$1000
\$\$ = \$100-\$250	\$\$\$\$\$ = > \$1000
\$\$\$ = \$250-\$500	

Prognosis

- This is a lifelong condition in almost all patients.
- Anecdotal recovery from EPI has been reported.
- Prognosis is favorable, and response to long-term enzyme therapy is good after stabilization.
- Occasional short relapses can occur.
- Dogs can lead a normal life and can

have a normal life expectancy.

- Some dogs do not adequately respond to therapy.
- Concurrent cobalamin deficiency has been associated with a poor outcome and must be treated.⁵

Prevention

- A patient with EPI due to PAA should not be bred.

Future Considerations

- Little is known about the pathogenesis and progression of subclinical to clinical EPI. Studies directed at this might help prevent progression of the disease during the subclinical phase.

See Aids & Resources, back page, for references & suggested reading.

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