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NEW DEVELOPMENTS IN THE DIETARY MANAGEMENT OF EXOCRINE PANCREATIC INSUFFICIENCY

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INTRODUCTION
Exocrine pancreatic insufficiency (EPI) is a clinical syndrome that arises secondary to a deficiency of pancreatic enzymes. The predominant cause of EPI is an immune mediated, lymphocytic pancreatic acinar atrophy. Less common causes include pancreatitis and neoplasia. In these situations, concurrent diabetes mellitus may also be observed.

EPI typically affects young dogs, 1-5 years of age, with reported breed dispositions including the German Shepherd, Rough Collie, English and Irish Setters. Clinical signs are the result of nutrient malabsorption secondary to failure of intraluminal digestion. Although the digestion of protein and carbohydrate will be affected, the digestion of fat is most severely impaired since lipases are absent from the normal array of intestinal brush border enzymes.

Studies have suggested that 70% of dogs with EPI have concurrent small intestinal bacterial overgrowth (SIBO) and secondary damage to the small intestine. Bacteria in the intestinal tract can metabolize undigested fat to hydroxy-fatty acids which can lead to secretory diarrhea in the large intestine. Bacteria also deconjugate bile acids further impairing fat digestion and absorption. Some dogs will also exhibit reduced duodenal enzyme activity. This can arise because of SIBO, or as a result of generalized cachexia.

The clinical signs of EPI include severe weight loss (cachexia), large, voluminous pale feces, ravenous appetite, coprophagia, borborygmus, abdominal discomfort, poor skin and haircoat. Diagnosis is confirmed by a serum TLI concentration less than 2.5 µg/L in the dog, and < 9 µg/L in the cat. Recently, it has been shown that measurement of serum TLI can be utilized to diagnose subclinical EPI, before the onset of clinical signs of severe pancreatic loss. Subclinical EPI is suspected in dogs with repeatedly low serum c TLI concentrations (< 5.0 µg/L) but no clinical signs of EPI.

Measurement of vitamin B12 (cobalamin) and folate is also useful in patients with EPI. A diagnosis of concurrent small intestinal bacterial overgrowth is supported by an elevated folate and low vitamin B12 concentrations.

MANAGEMENT
Client understanding and compliance are key to successful therapeutic management. The client should be informed that several weeks to months may be required for the therapeutic response to occur, and therapy is life-long. Dietary management in conjunction with pancreatic enzyme supplementation is the cornerstone of management. The amount of food to feed the EPI patient should be calculated on the current body weight. Once the maldigestion and malabsorption are controlled with concurrent enzyme therapy, the amount fed can be gradually increased to facilitate weight gain. The food should be offered in at least two meals per day.

Since fat is the most difficult nutrient to digest, requiring the interplay between the intestine, liver and pancreas, fat digestion is most severely affected by pancreatic enzyme deficiency. Therefore, it is intuitive that a highly digestible, low fat diet is appropriate for the management of exocrine pancreatic insufficiency. However, what constitutes a restricted fat diet varies considerably among manufacturers. Nutritionists consider a restricted fat diet to be one that contains less than 18% of the energy from fat. Using this recommendation, it is clear that many diets formulated for the management of gastrointestinal disease are not actually low fat diets.

Simpson et al evaluated the effect of a low fat diet in conjunction with enzyme supplementation in the management of 20 dogs with exocrine pancreatic insufficiency. Clinical signs resolved in all 20 dogs within 4 months of instituting therapy. The body weight of the dogs increased on average by 24%. Long term contact was available for 17 of 20 dogs. Eleven of these dogs were progressing well, 3 were euthanized for poor progress, and 3 were euthanized for unrelated reasons. Once the dogs were stabilized, they required 6-58% less enzyme supplementation compared to the initial dose needed for stabilization.

A study by Westermarck et al failed to demonstrate a benefit of severe dietary fat restriction in 21 dogs with naturally occurring EPI. However, there was considerable variation between dogs in this study. Suzuki et al reported that dogs with experimental EPI tolerated a diet consisting of 43% fat (ME basis). The dogs in this study absorbed protein, fat and carbohydrate more effectively compared to when they were fed diets with 18 and 27% of the calories from fat. The improved digestibility was attributed to preservation of the exogenous pancreatic enzymes, particularly lipase, in the higher fat diets.

Medium chain triglycerides, which contain 8-12 carbons, have been recommended by some authors. It has been suggested that MCT’s are less dependent on micelle formation and the lymphatic vasculature for digestion and absorption. It has been suggested that MCT’s reduce the palatability of the diet. In addition, MCT’s have been associated with the development of hepatic lipidosis in cats.

Dietary fiber can interfere with the effect of pancreatic enzymes. Dutta et al evaluated the effect of high dietary fiber in twelve human patients with EPI. The high fiber diet (28.75 g TDF/1000 kcal) was associated with an increase in fecal weight, fecal fat excretion and flatulence. In vitro studies using different concentrations of cellulose, pectin, and wheat bran incubated with amylase, lipase, and trypsin demonstrated that increasing the dietary fiber concentration reduced pancreatic enzyme activity.

Maldigestion of fat may result in malabsorption of the fat soluble vitamins. Indeed, very low concentrations of tocopherols and vitamin K coagulopathies have been reported in patients with EPI. Therefore the diet should contain adequate fat soluble vitamins. Additional subcutaneous supplementation with vitamin K may be necessary in some patients. Malabsorption of cobalamin can occur from a combination of decreased availability of pancreatic intrinsic factor and pancreatic proteases necessary to release cobalamin from R proteins, coupled with overgrowth of cobalamin binding intestinal bacteria. Therefore, cobalamin concentrations should be measured every 3 to 6 months and subcutaneous therapy instituted where necessary. Some studies have suggested that patients with EPI may be zinc and/or copper deficient from depressed absorption. Therefore, the diet that is chosen should have adequate zinc and copper concentrations.
Recently, protein hydrolysate diets have become available for the management of adverse food reactions. These diets are highly digestible with "pre-digested" protein, and are of interest in the management of dogs with EPI. Biourge et al recently reported the use of a commercially available hydrolyzed soy isolate protein diet (consisting of 40% of calories from fat) in four male German Shepherd Dogs with EPI and severe skin disease. The age of the dogs ranged from 2.5 years to 9.0 years. All four dogs had a previous diagnosis of EPI on the basis of history, clinical signs, indirect pancreatic function test (one dog) and serum canine TLI (three dogs). All dogs were lean (BSC 2/5), and, at the time of presentation, managed with high digestible diets, pancreatic enzyme supplementation and occasional antibiotic therapy. Within 7 days of feeding the hydrolyzed soy protein isolate diet, all dogs had well formed feces, and no episode of diarrhea was observed over the 3 month follow-up. In addition, all 4 dogs gained weight (2-10kg), and were in optimal body condition after two months of dietary therapy. The results of this case series suggested that a high fat, highly digestible, soy-protein isolate diet is effective for the management of EPI in dogs.

EPI requires life-time enzyme replacement therapy. Commercial enzyme replacers are available in powder, capsule and tablet format. Generally, enteric coated capsules and tablets appear to be less effective than enzyme powder. The enzyme should be mixed with the food prior to feeding. There have also been reports that suggest utilizing beef or pig pancreas. The only concern with this approach is the health risks associated with handling and feeding raw meats. Up to 83% of the lipase activity and 65% of the trypsin activity are lost in the acid pH of the stomach. Therefore the actual dose needed to control the clinical signs will need to be tailored to each patient. Some authors have suggested that controlling the acidity of the stomach using histamine-blocking agents may increase the effectiveness of the pancreatic enzyme supplementation. This theory remains to be proven.

With diet and enzyme replacer therapy, the diarrhea typically resolves in 3-7 days. The time to respond will also depend on concurrent small intestine bacterial overgrowth and mucosal dysfunction. Small intestinal overgrowth can be managed with antibiotic therapy such as metronidazole.

Wiberg et al studied the effect of long term enzyme replacement treatment in 76 German Shepherd Dogs or Rough Coated Collies with EPI. The gastrointestinal signs of EPI were controlled in approximately half of the dogs, and their general health was considered to be similar to normal dogs. Twenty percent of the dogs had a poor response to treatment, characterized by persistent high fecal volume, yellow feces and flatulence. Nonenteric-coated enzyme supplement, powdered enzyme, and raw chopped pancreas appeared to be equally effective in controlling clinical signs.

REFERENCES